PAIN MEASUREMENT AND ACUPUNCTURE ANALGESIA

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I declare the composition of this thesis, and the design and completion of the experimental work reported therein to be entirely my own work.

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1979.
At the outset of this work there was much lay credulity, and premature professional neurophysiological speculation, concerning reports of 'Acupuncture analgesia' from China. However, critical evaluation implicated well known suggestion or placebo effects as the most parsimonious explanation. When adequately controlled for such responses, clinical studies reviewed indicated little residual analgesic effect, whilst experimental work provided conflicting results and evident need for methodological improvement.

An initial study (12 subjects) compared the increases in 'Detection Thresholds' and 'Tolerances' for thermally induced pain at six cutaneous locations, during a control session (without needles), a session in which electrically-stimulated needles were inserted in accord with Chinese practice ('Genuine Acupuncture'), and another in which needles were inserted to avoid all recognised Acupuncture 'points' ('Pseudo Acupuncture').

'Genuine Acupuncture' was significantly more effective than suggestion ('Pseudo-Acupuncture') in raising overall body 'Pain Detection Thresholds' and 'Pain Tolerances'. A significantly disproportionate analgesic effect on the epigastrium, predicted by the choice of Acupuncture 'points' was also observed for both measures. All analgesic effects displayed progressive increase during Acupuncture stimulation (35 min.) with substantial residual effects still remaining thirty minutes after termination. The localised epigastic effects peaked 10 minutes after removal of needles.

Likely neurophysiological substrates for these results are discussed, and the specific involvement of endogenous opiates (e.g. morphine) suggested by recent literature was investigated in a second study.

Following extensive pilot work and literature review, an optimal design was developed to permit concurrent application of the methods of Signal Detection Theory (S.D.T.) analysis, novel to pain experimentation, together with conventional pain measures.

Shifts in sensory rating scale responses (descriptive categories 'Nothing' - 'Withdraw') to sequences of radiant heat intensities applied to the abdomen were compared for four experimental treatments (the three conditions employed in the first study, and an additional 'Genuine Acupuncture plus Naloxone' treatment). The 2 x 2 hour sessions were administered in balanced order to 16 subjects.

Conventional analysis again demonstrated significant analgesic shifts following Acupuncture compared with 'Pseudo-Acupuncture' or no treatment; and the S.D.T. d measure confirmed the presence of true sensory sensitivity attenuation, confined to noxious stimulus levels only.
Although 'Acupuncture analgesia' was significantly antagonised by Naloxone in both analyses, and there was other support for opiate-like endogenous mechanisms from significant temperature changes observed, and also from arousal and mood shifts, radioimmunoassay failed to detect significant alteration in plasma \( \beta \)-Endorphin levels. There was significant indication of possible hyperalgesic effects associated with Naloxone.

None of the observed effects were related to sex, extraversion or neuroticism.

Pain attenuation associated with Acupuncture, although statistically significant, represented mild hypalgesia rather than analgesia in both studies.

Extensive appendices outlining methodological logic, and equipment construction and calibration, are included to aid replication and promote standardisation.
With the appearance of any new potential pain relieving agent, any attempt at scientific evaluation of its effectiveness is faced with perhaps the oldest problems in medicine, namely the measurement of pain and its relief on a more objective basis than is possible by simply asking the patient.

It is no new observation that putative analgesics work if patients believe sufficiently that they will; but there is little point in the continued administration of agents, often associated with undesirable side effects, which may have no more effect than inert placebos. Equally obviously, it is impossible to directly measure 'pain'. Indirect indications from various physiological indices in human patients are often impracticable to obtain, or unreliably related to pain, and clinical trials with placebo control conditions can be ethically problematic in an area of such emotional significance.

Application of the less constrained laboratory based approach with experimentally induced pain at least offers the advantage of precise stimulus quantification, and the possibility of more controlled response conditions when evaluating 'analgesics'. A major endeavour of the work reported here was thus the development, and validation, of more precise optimal experimental methodologies for eliciting noxious sensation, and for distinguishing direct sensory attenuation effects from attitudinal shifts resulting from the suggestive or placebo qualities of putative pain relieving treatments.
The intriguing phenomenon of 'Acupuncture analgesia' reported from China offered an exciting focus for the application of these experimental techniques, in addition to representing an important topic for research in its own right as a possible alternative, or supplement, to conventional western analgesics. It may also have served to elucidate novel antinociceptive mechanisms within the body, and generally illuminate our understanding of the complex and often paradoxical phenomena of pain.

In the completion of this work I am grateful to acknowledge the statistical advice and computer programming assistance of Dr B. Millar, Dr P. McMillar, and Dr V. Brezinova, the medical assistant of Dr J. Thomson, Dr S. Babiker, Dr J. Chick, Dr C. Freeman, the technical assistance of Mr G. Burt and Mr P. Goodenough, the photographic assistance of Mr J. Fraser, the helpful discussion of ideas by Dr J. Ingham, Dr J. Beloff, Dr K. Adam and Mr D. Peck, the secretarial and clerical services of Mrs D. Redpath, Mrs C. Urquhart and Miss V. Wimbush, all the volunteer subjects who participated in the experiments, and the staff of the University of Edinburgh, Department of Psychiatry, who have otherwise assisted over the years.

Finally my special thanks are extended for the help, advice and general supervision of Professor Ian Oswald, without whom completion of this work could not have been achieved.

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PART I
CHAPTER 1.

THE PROBLEM OF 'ACUPUNCTURE ANALGESIA'

Introduction:

'Chung Guo I hseh', or middle kingdom therapy, has been practised as an important routine medical treatment not only in China, but in other countries such as Japan and Korea, for perhaps several thousand years. The system was already fully developed and codified in its earliest documented presentation, the 'Nei Ching' or 'Yellow Emperor's Classic of Internal Medicine', dated around 2,600 BC, and its unknown origins probably extend considerably further back.

Couched in pre-scientific terms the treatment was conceptualised as restoring equilibrium to the flow of vital energy, or 'Chi', through a system of channels known as meridians linked to the various internal organs of the body. Excesses or deficits of the positive and negative aspects (Yang and Yin) of 'Chi' were corrected by application of treatment to appropriate 'points' on the affected meridian system.

Not only needles (hence the Western name 'Acupuncture' from 'Acus' - needle, 'pungere' - to puncture) but massage, vibration, heat (moxibustion), cold etc., might be applied to these points. In addition, herbal medicines, dietary control, manipulation of the spine and joints (rather like chiropractice), and extensive psychotherapy could be included in this very holistic approach to medicine.

Although Acupuncture has been known in Western countries since at least the 17th century, it has been its introduction, and accelerated use, since 1959 for surgical analgesia in China which has attracted most interest and debate. This situation appears to have turned to decline since about 1972.
Numerous anecdotal and observational journal reports \(^{(15,57,113,215)}\) of earlier years, in addition to extensive media coverage, produced widespread popular acceptance of the analgesic properties of Acupuncture, and premature speculation as to its possible neuro-physiological mechanisms \(^{(83,261,430,438,461)}\).

Clearly, if as claimed the simple procedure of insertion, followed by mild manual or electrical stimulation, of a number of fine stainless steel needles, in generally innocuous locations such as the limbs or pinnae, can produce adequate analgesia for surgical procedures, a number of benefits may accrue. The patient can remain conscious and thus assist as necessary during the operation. Hemodynamics and respiratory, metabolic, digestive, and neuromotor functions are said to remain largely unimpaired, with minimal post-operative \(^{(47,220)}\) side effects. In addition the techniques are safe and could be economical and easy to learn and administer.

All these benefits, however, also accrue to other, more parsimonious, conventional\(^{*}\) explanations of the 'Acupuncture analgesia' phenomenon which offer established, if limited, effectiveness without recourse to oriental mythology and invasive mechanics. The contention that 'Acupuncture analgesia' may be quite adequately accounted for by suggestion and distraction mechanisms receives considerable support from the evidence\(^{**}\) discussed below.

\* In the sense of familiar although not necessarily properly understood or less mysterious.

\** The author is indebted to a review paper by Chaves & Barber (1974) \(^{(82)}\) for many of the ideas and supportive details discussed in this section.
(1) Alternative Explanations of 'Acupuncture Analgesia'*

A number of misconceptions about the use of acupuncture for surgical analgesia in China which have perhaps contributed to Western credulity will be discussed below.

(a) Extent of Application of 'Acupuncture analgesia' in China:

It is often assumed from exaggerated press reports that the technique is widely used with surgical patients. In fact available evidence \((47, 113, 220, 379)\) suggests that it has certainly not become the method of choice since, where trained anaesthetists are available, conventional Western local, regional, or general anaesthesia accounts for probably 80-90% of operations. In addition there is little evidence even to suggest the use of Acupuncture for surgical analgesia under the more primitive conditions of the Chinese interior. This is explained by the Chinese description of the techniques as experimental or "not yet fully developed" \((15, 47)\).

(b) Patient Preparation and Selection Criteria:

Another unfortunate assumption concerns the selection of patients for the use of Acupuncture. Evidence from films and other reports has tended to imply indiscriminate application of the technique, but again it appears that it is reserved for elective surgery only, rarely used with children, and not employed with old or high risk patients unless conventional anaesthesia itself is considered too stressful for debilitated cases \((220)\).

Perhaps most informative of all is the exclusion of anxious, apprehensive, or otherwise inadequately 'prepared' patients since, as

* The term 'analgesia' will be used, unless otherwise stated, to include various lesser states of 'hypoalgesia'. Although in some cases this is strictly incorrect, it is in line with convenient usage in other publications and affords economies of repetition.
the Chinese quite happily state, 'Acupuncture analgesia' usually fails with such cases (15, 379, 456). In a Western country this would probably exclude virtually the entire population. However, the historical background and present political climate of China may uniquely prepare the people for these circumstances whilst, unfortunately, simultaneously providing an environment loaded with arte-factual support for the apparent efficacy of 'Acupuncture analgesia'.

For example, until very recently, probably at most 2% of Chinese operations were carried out under general anaesthesia, with regional anaesthesia, mainly epidural blockade, extended to perhaps only another 18% of cases (15). Consequently consciousness during operations may elicit less anxiety in Chinese patients, and they may be more prepared than Western patients to expect little or no discomfort from surgery.

Added to this are the familiarity from birth with the general use of Acupuncture therapy, and the traditional belief in its validity throughout the culture. It is, after all, hardly surprising that a new variant of a treatment which has survived for perhaps 5,000 years should receive ready acceptance.

The process has been further highlighted by the espousal of the technique by Maoist thought, and the considerable political propaganda associated with its practice. Indeed it appears that a major requirement for patient selection may even be a stated belief in Acupuncture since all patients are volunteers and surgeons typically "decide whether the type of operation would be suitable, whether the patient would be too hysterical, whether the patient believes firmly in Mao's teaching, or would Mao's teaching carry him through" (462).

* This is, of course, not unique to the Chinese, as there is ample evidence of the reduced effectiveness of most limited analgesic agents with such patients (456).

** There is even evidence that the Chinese may dislike or fear unconsciousness for spiritual reasons (106).
It will be noted that in addition to appropriate ideological zeal and beliefs, patients are carefully selected for their emotional stability. Furthermore, considerable effort is directed towards explaining all Acupuncture procedures and their likely effects, and to giving details of the surgical procedures and associated sensations to be expected. There is also opportunity to talk to other patients who have experienced the same surgical conditions.

It is likely that these preoperative instruction and indoctrination practices could exert significant effects upon reactions to surgical pain. For Western patients, even limited intervention such as a 5-10 minute pre-operative visit by an anaesthetist can be more calming than 2mg/Kg of Pentobarbital Sodium, whilst information concerning likely post-operative pain can reduce narcotic requirements and accelerate discharge times.

(c) Use of Analgesic and Sedative Drugs as Adjuncts to Acupuncture:

A further general assumption concerning 'Acupuncture analgesia' is that it is the sole treatment administered. From most Western eye-witness accounts this is manifestly untrue, since narcotic analgesics, local anaesthetics, and sedatives are reported in use almost routinely with the Acupuncture stimulation. Various authors report the use of 50 to 60mg. of Meperidine Hydrochloride (Demerol) i.v. (113,286), 10mg. of Morphine s.c. (113), and Phenobarbital Sodium with Scopolamine (0.3mg)s.c. prior to surgery, with local Procaine Hydrochloride during surgery for incision through, and manipulation of, fascia, pleura, and peritoneum, the viscera, and occasionally, the skin. Occasionally local anaesthesia may even be induced by direct tetanic fatigue of peripheral nerves (57,66,113,428). One author (66),
noting that typically barbiturates were given preoperatively, with Neperidine Hydrochloride and Promethazine Hydrochloride given intravenously during the operation, in addition to the use of local anaesthetics, reasonably commented that

"the real question to be answered, therefore, is which therapy, the Acupuncture needle or the concomitant Western medication, is the adjunct?"

Surgery has recently been performed with Acupuncture in the United States (198,223,273) and Europe (332,367), but again narcotic analgesics and sedatives were employed. For example one successful tonsillectomy is reported in which Acupuncture was augmented by a preoperative medication (2ml Innovar which included a narcotic analgesic (Fentanyl Citrate) and a Phenothiazine-like psychosedative (Droperidol) (273), which is known to produce a "general quiescence and a state of psychic indifference to environmental stimuli" (35). Chinese children, of course, appear used to the practice of tonsillectomies which are successfully completed within 60 seconds and aided only by a quick anaesthetic spray of the throat (57).

(d) Analgesic Effectiveness of Acupuncture:

Despite the extensive drug support and careful selection and psychological preparation of patients, it appears that 'Acupuncture analgesia' is usually incomplete, often with both physiological and behavioural evidence of discomfort. In approximately 10% of cases this is severe enough to require completion of the operation under general anaesthesia (15, 47, 113).

Even in the cases classified as successful the results could hardly be described as acceptable in Western terms. Table 1(a) Page 7 shows the criteria used by the Shanghai group in evaluating the results
TABLE 1: SHANGHAI ACUPUNCTURE ANESTHESIA COORDINATING GROUP (1973)

(a) Criteria for Evaluation of Results of Acupuncture Anesthesia

<table>
<thead>
<tr>
<th>Grade</th>
<th>Excellent</th>
<th>Good</th>
<th>Moderate</th>
<th>Poor (Failure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Brief periods, mild, patient calm</td>
<td>Periods of moderate pain</td>
<td>Obvious pain, but operation could still be accomplished</td>
<td>Severe pain</td>
</tr>
<tr>
<td>Changes in blood pressure, heart rate, and respiration</td>
<td>Little or none</td>
<td>Mild</td>
<td>Moderate</td>
<td>Marked</td>
</tr>
<tr>
<td>Supplementation</td>
<td>Meperidine hydrochloride, mg/kg/2 hr</td>
<td>None</td>
<td>Small dose</td>
<td>Moderate dose</td>
</tr>
<tr>
<td>Local anesthetics</td>
<td>None</td>
<td>Small dose</td>
<td>Moderate dose</td>
<td>Necessary to change to drug anesthesia</td>
</tr>
<tr>
<td>Operating conditions</td>
<td>Good</td>
<td>Satisfactory</td>
<td>Fair</td>
<td>Necessary to change to drug anesthesia</td>
</tr>
</tbody>
</table>

(b) Results of Acupuncture Anesthesia

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of Cases</th>
<th>Grade (in % of cases)</th>
<th>Effective Rate, % (1, 2, 3 combined)</th>
<th>Grade 4 Failure (in % of cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craniotomy</td>
<td>606</td>
<td>34 35 26</td>
<td>96</td>
<td>4</td>
</tr>
<tr>
<td>Thyroid operations</td>
<td>670</td>
<td>54 31 10</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary resection</td>
<td>656</td>
<td>17 26 52</td>
<td>96</td>
<td>4</td>
</tr>
<tr>
<td>Heart operations</td>
<td>172</td>
<td>24 51 16</td>
<td>92</td>
<td>8</td>
</tr>
<tr>
<td>Subtotal gastrectomy</td>
<td>763</td>
<td>16 45 34</td>
<td>96</td>
<td>4</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>590</td>
<td>34 40 11</td>
<td>87</td>
<td>13</td>
</tr>
<tr>
<td>Mean % of total</td>
<td>-</td>
<td>30 37 27</td>
<td>94</td>
<td>6</td>
</tr>
</tbody>
</table>
of some 80,000 operations carried out with 'Acupuncture analgesia', whilst Table 1(b) Page 7 presents the percentages of six representative operations falling into the four outcome categories. It will be noted that even though the grade 1 classification (described as excellent) allows for brief periods of pain, and includes intravenous narcotic analgesics given at two hour intervals, it still accounts for less than one third of the total sample. Grade 2 which permits "occasional light groans for pain" as well as blood pressure, pulse and respiratory rate changes, together with grade III ("obvious pain sensation") account for almost two thirds of the sample and really cannot be accepted as providing adequate pain relief.

From the available statistics it is impossible to determine the proportion of patients, if any, exhibiting complete analgesia, but a compelling case emerges for the most accurate description of Acupuncture as, at best, a hypalgesic rather than analgesic agent. It certainly does not appear to possess anaesthetic qualities.

(e) Baseline Levels of Surgical Pain without Anaesthetics:

Even the modest apparent pain relief described above must be viewed in the light of evidence from our own pre-anaesthetic era which suggests that surgical procedures, although eliciting considerable fear and anxiety, may give rise to less pain than is commonly believed. Although probably rare, there are examples of patients undergoing major surgery completely without complaint or drugs, whilst other case reports from the early 1900s indicate the accomplishment of major operations including amputations, thyroidectomies, mastectomies, suprapubic cystostomies, laparotomies, herniorrhaphies, cholecystostomies, 

* One reporter failed to find a single case of complete insensitivity during a three week visit.
and appendectomies, with only the use of local anaesthetics to dull cutaneous sensation (318).

It would appear that, although the skin is very sensitive, the muscles, bone, and the majority of the internal organs are generally insensitive to incision (although other forms of stimulation such as traction or distention may cause discomfort) (257). Overall this evidence suggests that pain is in no way directly proportional to the extent of the surgical intervention. If the patient is relaxed and not anxious (a process assisted by the narcotic analgesics and sedatives usually administered in conjunction with Acupuncture), usually the only severe pain to be expected from the knife would arise from the skin. If either the patient can tolerate this initial incision procedure unaided, or else a local anaesthetic is employed, further pain from this source may be slight.

Greater difficulty may be experienced, however, with traction or distention of tissues such as the pleura and peritoneum which are extremely sensitive to such stimulation. Although only the more experienced and skilful surgeons are employed for operations using Acupuncture, and great care and gentleness is evident for procedures such as rib-spreading during thoracotomies, and traction upon viscera etc., observers unanimously report the expected behavioural and physiological (vasopressor and sweating responses) signs of extreme discomfort from patients at such times. This occurs despite additional efforts to distract patients by breathing exercises or doctrinal conversation (15, 47, 57, 67). Furthermore it would appear that the application of Acupuncture is usually limited to certain less sensitive operations such as craniotomy, thyroidectomies, Caesarian section,

* Procaine Hydrochloride may also be locally injected in, for example, the parietal pleura or parietal peritoneum (47).
dental extractions, and some eye, nose, and throat surgery, whilst it is considered less suitable where reflex muscular relaxation is required such as in abdominal operations (15, 47, 113, 215, 220).

(f) Suggestion or Placebo Effects:

There is, of course, nothing new in the idea that simple suggestion of analgesia, or administration of an inactive drug, may have marked effects upon the experience of, and reaction to, pain. Indeed, since about 35% of patients with severe post-surgical or chronic pain may obtain adequate relief after a placebo (18, 114, 206, 225, 245), whilst even large doses of Morphine will relieve only about 75% of these patients, it has been suggested that nearly half of the drug's effectiveness is really a placebo effect (25). This is not surprising in view of evidence that a large proportion of the effect of Morphine may be upon anxiety related 'pain reaction' components (Pain Tolerance) rather than upon more directly sensory aspects (Pain Thresholds) (48, 41). Furthermore, a vast body of literature attests to the fact that the relative success of suggestion and placebos is often largely a matter of how effectively the intervening variable of anxiety is reduced (25, 408). It is significant here that two American studies applying Acupuncture to chronic pain reported success rates which could be entirely attributable to placebo effects, and one also clearly demonstrated reduced effectiveness in depressed or anxious patients (205, 232). Two American studies also observed a strong relationship between the success of Acupuncture and the suggestibility scores of patients (224, 232).

Evidence has already been presented by the Chinese themselves, as well as Western observers, that the chronically anxious or

* Caution must be exercised in assuming the two effects are synonymous in view of poor correlations reported (124).
emotionally unstable* patients have to be excluded from Acupuncture surgery (220), whilst much of the normal situational anxiety is controlled by careful preparation, both in terms of indoctrination and information. It has been demonstrated elsewhere that such reduction of uncertainty alone can produce significant increases in the toleration of pain (219).

In addition to rather more indirect effects from the reduction of anxiety, there is much evidence, from historical and more recent wartime reports of surgery under primitive conditions, to indicate that the mere suggestion of anaesthesia can be highly effective (372,414). It also appears that suggestion may still be perfectly effective under normal circumstances (21,235, 239,271,480).

There can be little doubt that the Acupuncture patient in China is loaded with both direct as well as indirect suggestion towards an analgesic outcome (47, 362). Indeed one Western observer was assured in China that "Acupuncture analgesia does not work unless the patient believes it will" (456). In Western patients, where no attempt is made to induce belief, it appears to be extraordinarily difficult to produce any analgesia at all in perhaps 90% of cases (291). It is interesting to remember that 10% is the proportion of the population commonly reported as displaying maximal suggestibility (19). This element has, perhaps, been underestimated by some observers because there was no evidence of any state resembling a hypnotic trance or associated elaborate induction procedure. The necessity for any narrowed span of attention, loss of conscious, or sleep-like trance state, for the manifestation of virtually any hypnotic phenomenon (including surgical anaesthesia) has, however, been virtually discounted by recent

* Patients with psychiatric histories are specifically excluded.
systematic review and investigation (19). In addition the "ceremonial or ritualistic" approach to the production of 'Acupuncture analgesia' is considered by some to constitute a hypnotic procedure per se. (239).

Certainly many of the standard elements of hypnotic induction procedures are present including limited bodily activity, monotonous rhythmic stimulation (ie. manual and electrical stimulation of needles), motivational instructions, etc. (142). The effects of the last element, motivational instructions, have, of course, been shown to reduce the experience of pain unaided (140, 484).

There is also evidence to indicate that the attenuation of clinical pain may be as much related to the interpersonal setting between the patient and physician, as to suggestion directly. It appears that a wide variety of patients with acute and chronic pain may derive as much pain relief by virtue of close personal attention from the physician alone as from any suggestive or elaborate hypnotic procedure (65, 24, 477).

Again with Acupuncture patients, there is ample evidence of close attention and preparation by the physicians, often for days in advance of surgery, and the patient is both involved in preoperative discussions and active cooperation during the operation. A rapport and feeling of brotherhood "in a Chinese sense", with all the associated secondary gains for the patient, are considered essential to the successful induction of analgesia (47, 220, 456).

A perhaps more cynical extension of these lines of thought concerns the social and political pressure upon patients. An example of the propagandist approach to the treatment is evident in an extract from a widely distributed pamphlet for laymen (13):

"The creation of acupuncture anaesthesia is an example of the good results that come from carrying out Chairman Mao's instructions on combining
Chinese and Western medicine, and taking China's own road in the development of medicine. It is a great victory for Chairman Mao's proletarian line in health work and scientific research."

Social pressure resulting from this stance may generate a climate in which it is difficult for the patient to maintain a correct political position and to admit the presence of pain during surgery with Acupuncture. This may partly explain the refusal of many patients to admit pain, and their "admirable fortitude which would be rare in a Western patient", despite involuntary behavioural and physiological signs of nociception, as reported by Western observers (15, 456).

An interesting possible application of cognitive dissonance concepts is suggested by one study where subjects continuing to commit themselves to a known painful stimulus, despite low justification, subsequently lowered their pain intensity ratings. Low dissonance subjects did not do this. Evidence has already been presented that Acupuncture patients are generally highly motivated volunteers for whom, as a Chinese surgeon put it,

"some pain does not mean much ... because he knows, that by being operated on under Acupuncture, an old traditional Chinese method, he is helping the people's faith in China" (220).

For the others, if any, volunteering for the known pain of surgery, without adequate belief in Acupuncture as a justification, might well induce dissonance requiring some self-denial of the pain experienced.

As an adjunct to this, some authors have pointed to the steadfast denial of pain which can accompany many tissue destructive initiatory or culture rites (428). It would, however, seem rather excessive to compare the ritualistic elements and social status consequences of
'Acupuncture analgesia' in China with such phenomena.

It is also well known that different cultural and ethnic groups differ in their readiness to express and tolerate pain\(^{(179,493)}\), although there is little to indicate any differential sensory sensitivity substrate \(^{(179,409,467)}\). As an extension of this some authors have evoked the stereotype of the stoic oriental as an additional factor in 'Acupuncture analgesia'. It must, however, be said that the anecdotal evidence \(^{(220,224,239)}\) presented is slender indeed, and at least one experimental study has, in fact, reported orientals as less tolerant of pain than either blacks or whites \(^{(490)}\). Generally the contradictory nature of available evidence would render any explanation or investigation based on a racial hypothesis most unsound \(^{(25)}\).

\((g)\) Attentional and Counter-irritation Effects:

A number of cognitive variables which may have parallels in the Acupuncture situation have been shown to affect reactions to pain. For example some investigators have demonstrated substantial increases in 'Pain Threshold' when subjects are distracted by concentrating on performing other physical \(^{(336)}\) or mental \(^{(222)}\) tasks, or attending to interesting presented material \(^{(20, 21)}\). Cognitive strategies of imagining pleasant events appear highly effective, particularly when employing emotive imagery which induces feelings of self-assertion and pride \(^{(39, 202)}\). It has already been reported that Acupuncture patients receive constant distractive interaction by conversation with the medical staff following often stirring doctrinal themes of pride in the achievements of Chairman Mao and the people in the success of 'Acupuncture analgesia'. Patients also actively cooperate in the progress of the operation whenever necessary, and are deluged in

* This is supported by another study which also failed to observe any greater response of indigenous orientals to 'Acupuncture analgesia' \(^{(236)}\).
conversational attention at any sign of nociception. In addition, sometimes patients are often requested to perform relaxation and breathing exercises which in addition to assisting control of any surgical pneumothorax disturbances etc. may provide valuable distraction (47, 57, 462).

There is also evidence to suggest that patients can provide their own distractions (often motor responses) given warning of likely impending painful stimulation, and these may increase Pain Tolerance (219). Some reports have indicated that surgeons often warn Acupuncture patients immediately prior to a manipulation likely to cause pain (2, 3). This, together with distraction during the actual experience of pain, may contribute strongly to diminished discomfort.

Clearly an additional source of distraction may be provided by the stimulation associated with Acupuncture needles themselves. This may be subsumed under the general class of counter-irritant stimuli which have been shown to affect the perception of pain. For example, cold, vibration, electric stimulation, and static electricity, have all been demonstrated as effective in reducing both clinical and experimentally induced pain (137). The best counter-irritant stimuli are probably those which produce some pain themselves and, although best results are obtained by application close to the painful lesion or primary pain stimulus site, effects may generalise to the whole body (89, 174, 329, 436, 455). Indeed, in some cases, counter-irritation is most effective at specific sites other than the locus of pain (440), and, of course, remote puncture sites are commonly prescribed in Acupuncture formulae (427). Most patients report local "soreness" or even marked pain in association with Acupuncture needle stimulation (84, 286, 361). In addition the rapid manual manipulation of needles
or electrically induced clonus, although of rather low frequency, may possibly contribute pain inhibitory effects similar to those reported with vibratory and pressure stimulation \(^{(312,420,459)}\). It is at least well known that repetitive, monotonous stimulation can lower arousal, and habituate orienting reactions \(^{(43)}\).

Considerable debate currently surrounds possible neurological substrates for these phenomena. This will remain outside the scope of discussion at this point, but it is of relevance to note that the use of 'white noise' as an analgesic in dentistry illustrates the fact that a successful counter-irritant need not make use of cutaneous pathways \(^{(138)}\).

(h) 'Animal Hypnosis' or the 'Still Reaction':

Successful use of 'Acupuncture analgesia' in veterinary hospitals has been widely reported in China and Western countries \(^{(368)}\) and has been taken as indicative of the validity of this technique. However, a reversible and involuntary 'tonic immobility' or 'still reaction' occurs in many species as a defensive reaction to sudden pain or fright \(^{(136)}\). The reaction is characterised not only by immobility but also reduced responsiveness to external stimulation including skin incision and electric shock \(^{(357)}\), and often by sleep or drowsiness \(^{(64)}\). Minor surgery may even be performed without apparent pain response, and it is particularly interesting to note that included amongst methods for inducing the 'still reaction' are repetitive monotonous stimulation (such as rhythmic Acupuncture stimulation perhaps), pressure on body parts, and restraint.

Although the possibility of a relationship between 'hypnosis' in man and the 'still reaction' in animals is uncertain, it is, at least,
worth noting that heightened suggestibility in man can also sometimes
be induced by fright and confusion, whilst monotonous stimulation is
common to both (450). It is thus at least conceivable that the 'still
reaction' may play some part in the apparent induction of analgesia
by acupuncture in humans.

Summary and Conclusions:

Evidence has been presented to the effect that 'Acupuncture
analgesia' is used for surgical procedures in China on a considerably
more limited and experimental basis than the West has been led to
believe. Only the most appropriate patients and types of operation
are selected, and Acupuncture is used in conjunction with often
extensive drug and suggestive support. Despite these adjuncts, and
additional evidence that surgery without anaesthetics may generate
less pain than is commonly assumed, pain relief from Acupuncture
appears incomplete, and is often inadequate even with strongly moti-
vated and non-anxious selected patients.

These factors, taken together with the known pain-relieving
efficacy of other procedures involving suggestion, distraction and
counter-irritation, strongly imply that there may be no residual or
unexplained analgesic effects of Acupuncture to require the invocation
of hypothetical novel mechanisms.

Clearly until 'Acupuncture analgesia' has received extensive
investigation under conditions adequately controlled for the alterna-
tive mechanisms hypothesised in this chapter, its clinical application
and neurophysiological investigation would appear premature.
CHAPTER 2.

CONTROLLED INVESTIGATION OF "ACUPUNCTURE ANALGESIA"

Before outlining the experimental approach adopted in this laboratory to investigate the problems of "Acupuncture analgesia" raised in the previous chapter, relevant studies undertaken by other authors will be reviewed.

(1) Clinical Studies:

A blossoming plethora of inadequately, or completely uncontrolled clinical studies, mainly with positive findings, have been reported over the past few years. Only information from the very few relatively well controlled investigations available will be reviewed here.

An informative study by Moore and Berk (1976)\(^{(320)}\) of 42 shoulder pain patients failed to observe significant differences in the degree of freedom of motion, or in pain relief, resulting from Acupuncture compared to placebo-Acupuncture. This occurred despite the earlier apparent success of Acupuncture for shoulder pain during uncontrolled treatments, and the fact that 'placebo-Acupuncture' merely involved pin-prick and rhythmic pressure, without skin penetration, and thus may have provided less intense subjective stimulation. The study, in line with findings elsewhere\(^{(224,232)}\), also indicated a positive correlation between hypnotic susceptibility (Speigel test\(^{(405)}\)) and pain relief.

* It should be noted that only studies published prior to the early part of 1975 were available before commencement of the first Acupuncture study in this laboratory.
Two large (n=200) studies (Lee et al (1975)(247) and Kepes et al (1976)(232)), using patients as their own controls for comparison of classical Acupuncture and insertion of needles at placebo "points", failed to observe any significant difference between the treatments for a wide variety of chronic painful complaints. Although these studies represented considerable methodological improvement, both, in common with almost all Acupuncture investigations, suffered from an almost unavoidable problem in that the Acupuncturist was aware of the genuine or placebo nature of the treatment administered. In these cases, however, this source of bias was counteracted, at least to some extent, by the employment of an uninformed interviewer to collect patients' pain relief ratings after the different treatments. It is, however, questionable whether these conditions may be described as "double-blind" in the strict sense. Of particular importance in this work was the observation that the insertion of needles at any site may have considerable suggestive potency, since a trend towards progressively increasing pain relief was evident for both treatments.

A smaller study (n=36) conducted by Man and Chen (1974)(289), under similar "double-blind" conditions reported positive findings of a 75% success rate for Acupuncture compared to 11% for 'placebo-Acupuncture'. This result cannot, however, really be accepted as valid since the placebo treatment did not include electrical stimulation of needles, and thus must have provided markedly less intense sensations than the "Genuine" Acupuncture
procedures. This is particularly important in view of the fact that patients served as their own controls and did not receive the two treatments in balanced order.

The situation with regard to the use of Acupuncture for relief of chronic pain appears pessimistic. Despite the many positive uncontrolled studies it would appear that there is little evidence to support the conclusion that, in carefully controlled clinical conditions, Acupuncture has any novel analgesic effects beyond those attributable to its suggestive, distractive, and allied elements.

For fairly obvious reasons studies of Acupuncture for surgical analgesia do not appear to have been conducted with controls for suggestion of the type discussed above. This is unfortunate since there are indications that different mechanisms may underlie chronic and acute pain, the former tending to give rise to immobilization and a state of rest, whilst the latter may generate reflex withdrawal and a general arousal \( (8,311) \). Fortunately, information provided in sections below is of some assistance.

(2) Conventional Experimental Studies:

Quite a number of studies over the past few years have examined the effects of Acupuncture upon experimentally-induced pain.

Again only the more rigorous and adequately controlled studies will be fully reviewed here, although other studies yielding serendipitous observations of interest may be briefly discussed.

* Studies not employing Signal Detection Theory methodology.
(a) Studies Employing Noxious Electrical Stimulation:

Goldberger and Tursky (1976)(146) applied electric shocks to both forearms of 10 subjects, and assessed the effects of surface electrode stimulation over Acupuncture "points" in one hand and arm upon four "Reactive Judgement" points (Sensation, Discomfort, Distinct Pain, Tolerance) and upon "Magnitude Estimations"(413) of pain experience. A similar 'placebo-Acupuncture' was applied at sites 1 cm. lateral to the putatively correct Acupuncture loci in a separate group (n=10). This otherwise excellent control condition was unfortunately confused by the inclusion of suggestions of analgesia in the placebo treatment, and suggestions of sensitization in the Acupuncture group.

Results indicate that both during, and ten minutes after, Acupuncture, significant elevations above baselines were evident only for "Definite Pain" and "Pain Tolerance" report points. No effects were present on the untreated control arm in the Acupuncture condition, or on either arm for the 'placebo-Acupuncture' treatment.

The authors interpret these results as indicating that, whilst sensitivity ("Magnitude Estimation") appeared unaltered by Acupuncture, the aversiveness of pain was significantly altered ("Reactive Judgements"). In view of the absence of similar changes accompanying 'placebo-Acupuncture' they reasonably posit a direct physiological effect upon the motivational-emotional dimension of pain. A similar situation is, of course, found in relation to
conventional accepted analgesics such as Aspirin, Morphine, and alcohol, which often fail to significantly alter "Pain Thresholds", whilst substantially altering the tolerance to pain(25,78).

The possibility of a purely psychological explanation remains although, as the authors point out, the effects of Acupuncture were obtained despite accompanying suggestions of hyperalgesia; whilst direct suggestion of analgesia produced no comparable changes in the placebo group. Although these observations may indeed support a physiological mechanism interpretation, it would seem an unnecessary, and perhaps unfortunate, initial decision to diminish the likely visibility of "Acupuncture analgesia" by inclusion of these suggestive elements. As will be seen later, adequate controls for these psychological factors can be implemented without disturbing the simplicity of the original 'placebo-Acupuncture' method.

The lack of effect of suggestion upon the placebo group also requires some consideration. The authors suggest several possibilities including an inadequate scale sensitivity to detect small placebo effects, and disbelief of the explicit suggestions by subjects. It is indeed surprising, from evidence elsewhere, that placebo group responses were not larger, and this may indicate insufficient measure sensitivity. However, there were at least small changes evident in the predicted direction. The authors do not report using the simple expedient of asking their subjects in order to resolve the second possibility.
A third possibility may be raised concerning "negative response bias" problems. This refers to an observation by Chapman (1975) whereby some small specialist groups of subjects (e.g., anesthesiology residents) may be so highly skeptical of "Acupuncture analgesia" as to display more large magnitude pain reports than under control conditions. Although the methodology employed by Goldberger and Tursky did not employ any direct measures for this type of effect, it appears unlikely, as placebo subjects increased "pain" and "tolerance" points during treatment, with reduction afterwards, whilst Acupuncture subjects actually recorded their highest values 10 minutes after termination of treatment.

The last finding to some extent diminishes the importance of one of the criticisms which may be levelled against the study design, namely the procedure of obtaining pain measure responses whilst continuing Acupuncture electrical stimulation. This in itself would probably elevate pain measures in view of evidence (Chapter 1) presented for counter-irritation and distraction effects. In addition, the authors themselves admit to necessary differences in the sensations associated with stimulation of their genuine and placebo "points".

It is also important to note that, since needles were not actually inserted, it is difficult to be certain that the results really relate to Chinese Acupuncture rather than reflecting some allied but distinct phenomenon.
On the basis of evidence elsewhere\(^{(13,270)}\) the authors claim that the sensations and analgesic effects produced are similar to those resulting from needle insertion. Experience in this author's laboratory, however, suggests that differences in sensation may be marked and differences in analgesic effect have already been reported elsewhere\(^{(12,77)}\).

Finally, the 15 minute duration of Acupuncture treatment employed by Goldberger and Tursky must be considered at best overly short, if not actually inadequate. Although it appears that dental analgesia may perhaps be induced by Acupuncture within such a time period\(^{(15)}\), almost all the available evidence concerning other body loci indicates that stimulation should be continued for at least 30 minutes, whilst longer periods, if possible, may be advantageous. Although some analgesia is often reported after 15 minutes, the gradient does not begin to plateau until 30–40 minutes after stimulation onset\(^{(15,348,359)}\). There are also suggestions in the literature that analgesia may be more difficult to induce in the extremities than in the head and trunk\(^{(73,220)}\).

Another study by Stacher et al (1975)\(^{(406)}\) applying noxious electrical stimuli to the thyroid area in 12 subjects again provided inadequate duration of stimulation (16 minutes), but did at least actually insert needles in both genuine and "placebo-Acupuncture" "points".

The design was also improved by the use of a balanced cross-over format, a most advisable procedure for pain
experimentation unless groups are relatively large, owing to the considerable individual differences in pain responses (92,483). Unfortunately, however, the placebo-Acupuncture control condition was only administered single-blind.

Analysis of results provides certain important methodological indications. First, baseline measures clearly reflected significant "Pain Tolerance" order effects for first and second treatment. This indicates the vital need for balanced order presentation. In addition, both pain measures displayed significant increases over time during the baseline period suggesting that adaptation or habituation to the noxious stimulus occurred. Although this appeared to stabilize by the end of the baseline period, it does further emphasize the need for controls to avoid interpretation of baseline drift as treatment-induced analgesia. Fortunately, baseline values prior to the two experimental treatment conditions did not differ significantly.

The "Genuine Acupuncture" treatment provided significantly more elevation of "Pain Thresholds" (with a similar non-significant trend for "Pain Tolerance" values) compared to the placebo treatment. This must, however, be viewed with some reserve in the light of a paradoxical significant superiority of "Pain Tolerance" values observed under the placebo condition during the 16 minute monitoring period after removal of the needles. Not surprisingly the authors are unable to offer any explanation for this outcome.
It is also important to note that, in general, subjects responding to "Genuine Acupuncture" also responded to the needling of "false" points and vice versa. As, in addition, two subjects did not respond at all to either treatment, it does appear that subjects may be classified as "responders" or "non-responders".

(b) Studies Employing Noxious Radiant Heat Stimulation:

Several conventional studies have employed variants of the well known Hardy-Wolff-Goodell (179) Dolorimeter as a radiant heat cutaneous pain stimulus source for testing the effects of Acupuncture. Only one of these, however, was sufficiently adequately controlled and reported to merit discussion here.

A small study (n=30) by Berlin et al (1975) (33) observed significantly greater elevations of forearm Pain Tolerance after 20 minutes of "Electro-Acupuncture" at traditional "points" compared to placebo loci although the latter were only 1-2 cm. distant. This is also surprising in view of the apparent association of the placebo locations with many of the subjective sensations said to be characteristically elicited by needling Acupuncture "points".

The placebo treatment group also displayed significant elevations above a "no treatment" control group.

Although the experiment was conducted single-blind, the experimenters usefully included the simple, but rarely reported, expedient of directly asking the subjects post-experimentally to ensure that no suspicions had been present. In addition the experimenter was screened from
the subject, although there is no mention of efforts to control conversational and tactile cues.

Although statistically significant, the authors emphasize that all elevations were slight (perhaps due to the rather short stimulation period), and clearly inadequate for surgical requirements as assessed by the subjects themselves. The results do, however, appear to contradict a purely placebo based explanation of "Acupuncture analgesia" and support other indications\(^{(162)}\) for a fairly precisely localized functional or structural entity corresponding to the Acupuncture "point".

(c) Studies Employing Noxious Cold-Pressor Stimulation:

Two well controlled studies have induced pain in subjects by cold stimulation in order to investigate "Acupuncture analgesia".

Anderson et al (1974)\(^{(9)}\) observed the effects of "Electro-Acupuncture" at "points" in one arm, or placebo locations one inch away, upon endurance of immersion of each hand in 1°c. ice-water. The authors followed a rather more careful approach to maintaining the approximation to "double-blind" conditions than is usual. Subjects were blindfolded and instructed before the Acupuncturist ascertained which treatment was to be applied. No further conversation ensued thereafter, although, of course, tactile cues may still have been available. After removal of the needles another experimenter, unaware of the subjects treatment group, administered the cold-pressor task and obtained additional pinprick pain ratings.
Results indicate significantly lower mean pain ratings, confined to the treated arm, for the Acupuncture group (n=10) compared to the "placebo-Acupuncture" and "no-treatment" control groups (n=10 each) which did not significantly differ from each other. Although these effects were not large or uniform, and did not apply to pinprick pain (which might be argued as a better approximation to the pain of tissue incision than is cold-pressor pain) this still represents an important, and relatively well controlled, indication of the validity of specific Acupuncture loci effects.

The persistent problem of possible suggestive differences in sensations at genuine and placebo needle locations remains despite the close proximity of the sites employed, particularly as no descriptions or intensity ratings were obtained from subjects. However, a surprising, and relevant, observation occurred in that the control group receiving no treatment other than application of an alcohol swab to various sites (whilst blindfolded) actually reduced their mean ratings of the effectiveness of Acupuncture significantly at the end of the session. If, as this finding suggests, some of this group really believed that Acupuncture had been administered, subjects may be less psychologically sensitive to, and have fewer expectations concerning, treatment stimulation than feared. It is also, however, relevant to note that, whilst both Acupuncture groups lowered their ratings of the effectiveness of Acupuncture after treatment, the decrease was larger (although not significantly) for the placebo group. It is
possible that this reflects differential psychological potency of stimulation sensations as subjects did not receive a baseline cold-pressor test to assist them in making comparative judgements of pain before and after treatment*. The inclusion of baseline testing, and use of pain measure shift as an index of analgesia, might also have been helpful in view of the relatively small number of subjects in each group (n=10), and the known variability of individual responses to pain\(^{(92,482)}\).

The second study (Lynn and Perl (1976)\(^{(280)}\)) to be reviewed in this section induced cold pain by applying a metal cylinder, cooled by circulating alcohol, to various cutaneous areas. Although "placebo-Acupuncture" as such was not included, an extremely important and simple control was employed whereby multiple body areas were tested, only one of which was expected to display disproportionate analgesic shifts by virtue of the particular Acupuncture "points" chosen on the basis of standard Chinese formulae**. Subjects (n=18) and pain testers were blind as to the expected target area, and the Acupuncturist took no part in carrying out sensory tests.

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* This would, at least, have to be specific to the treated arm, as no treatment differences were observed for the control arm.

** As will be seen in the next chapter, similar controls were adopted by the present author for the first study in this laboratory. This was completed prior to publication of the paper by Lynn and Perl in 1976.
Results indicated that, after correction for differential baseline pain sensitivity of the various cutaneous test locations, no significant differences were observed for "target" versus "non-target" zones despite highly significant reductions in ratings at all pain report levels for the body as a whole. Even the overall analgesic changes observed were relatively small and could have entirely resulted from fatigue, expectation, or other non-specific effects. In particular, however, the failure to detect specific target effects appears crucially damaging to the validity of the system of localized relationships claimed by Acupuncture practitioners. It is, however, possible that the rather crude three point pain rating system and analytical controls for test site baselines, may have obscured modest local differences. In addition, in the absence of the required information in the publication, it is possible that an inadequate duration, or intensity, of Acupuncture stimulation was applied.

(d) Studies Employing Other Noxious Stimulation Sources: Smith et al (1974) report two studies employing ischemic pain induced by the submaximum-effort tourniquet technique. This procedure has been claimed to more adequately mimic, or equate with the emotional anxiety and sensory qualities of clinical pain (particularly chronic pain) than most experimental pain stimuli. Certainly it has been found to dependably respond to Morphine, Aspirin, and other analgesics which have proven problematic to other methods.
In one experiment where balanced order treatments of "genuine Acupuncture", "placebo-Acupuncture" (3 cm. from "points"), 10 mg. i.v. Morphine, and Saline placebo were administered to 15 subjects, Acupuncture just failed to significantly exceed "placebo-Acupuncture" in analgesic effect. It is interesting to also note, however, that Morphine was only significantly superior to Acupuncture for the "unbearable pain" rating level, although it surpassed Saline injection significantly at all levels of discomfort.

The second study (n=10) provided only balanced order genuine and "placebo-Acupuncture" treatments, but with the important improvement towards "double-blind" conditions of the collection of pain reports by a different "blind" experimenter. Although also independently non-significant, the results of the study, when pooled with the data of the first experiment, yielded significant superiority of "genuine Acupuncture" for "moderately distressing", "very distressing", and nearly for "unbearable", pain rating levels. Despite reservations concerning the pooling procedure, due to methodological differences between the two studies, this result appears supportive of "Acupuncture analgesia".

Another study by Lynn and Perl (1974) (279) followed a similar methodology to their cold stimulus experiment (1976) reported in section (c) above. Again Acupuncture "points" were selected for specified cutaneous target areas, with additional pain testing at non-target control areas which were
sometimes closest and sometimes farthest from the needles. Skin sensitivity was assessed by the force required to elicit pain when squeezing a skin flap, and ability to identify sharp and blunt contacts. Conditions were "double-blind" in that neither subjects (n=18) nor the experimenters making the measurement were aware of the target zones.

Like the "cold pain" study, results indicated a significant fall in pain sensitivity during Acupuncture, but failed to demonstrate the crucial predicted target specificity. The only significant pattern was for the area closest to the Acupuncture needles to display the greatest reduction in sensitivity, an outcome readily explicable in terms of counter-irritation mechanisms. In conclusion, however, the result must be interpreted with caution as no mention is made of correction for the almost certain differential baseline sensitivity at the different cutaneous test areas. As will be seen in the next chapter, there is evidence to suggest that it is the proportional or percentage change, rather than the absolute change, in pain measure units which most comparably reflects sensitivity changes at different body locations.

Summary and Conclusions:

The evidence from the experimental studies reviewed appears more promising than the clinical investigations as a support for significant analgesic effects of Acupuncture, beyond those evident from various "placebo-Acupuncture" or other "control" treatments. Significant positive analgesic
results have been reported for a wide range of noxious experience, under relatively well controlled conditions. Other well controlled studies have, however, provided overall negative findings, and the system of localized relationships between needle "points" and locus of effect as claimed by Acupuncturists appears particularly in doubt.

It is also evident, on an individual study basis, that considerable scope remains for improvement in comparability of "control" conditions and methods of analysis employed. These considerations may be particularly important in so far as the demonstrated analgesic, or more correctly hypalgesic, effects of Acupuncture appear rather small. Indeed the use of surface electrodes, and even direct suggestion, may be more effective, whilst relatively well controlled and sensitive pain measures appear necessary to achieve significant results.

On the basis of the available evidence, the possibility still remains that application of more optimal methodology (as described in the next chapter) may entirely reduce "Acupuncture analgesia" to a placebo or suggestive phenomenon, rather than improve its visibility as a process of true sensory attenuation.

The interested reader who may wish to explore some of the more descriptive, and less rigorously controlled, conventional studies of "Acupuncture analgesia" available in the literature is referred to reference numbers 11,12,109,111,139,201,209,224,232,237,238,240,262,289,291,304,305,359,476,492 in the bibliography.
CHAPTER 3.

ACUPUNCTURE EXPERIMENT NO 1

A Pilot Study

Introduction:

In view of the evidence discussed in the two previous chapters, it is clear that a major thrust of research concerning 'Acupuncture analgesia' should be directed towards examination of the possible placebo, suggestive, and distractive elements of the procedures. Given the common problems of pain location and measurement, and the practical and ethical problems associated with 'control' conditions in clinical studies, the use of experimentally-induced pain in normal volunteers, under the controlled conditions possible in the laboratory, would appear to offer an optimal approach.

Accordingly, the experiment described in the following pages attempts to address and resolve many of the methodological problems encountered in previous discussion. Clearly the major problem is to achieve a 'control' condition which adequately equates in suggestive and distractive/irritational potency with Acupuncture under 'double-blind' conditions.

The majority of studies reviewed earlier applied a placebo-Acupuncture by inserting needles at various distances from the classic Acupuncture 'points' listed by Chinese sources. Whilst this must undoubtedly provide a useful 'control', it is associated with certain problems. Correct location of needles in 'points', for example, is achieved by virtue of reports from the subject of local sensations of numbness, distention, tingling etc. Although some studies (9, 33, 359)
have suggested that either there is less difference between sensations at 'points' and supposedly neutral sites, or else subjects are less sensitive to differences than may be supposed, general opinion appears to regard this area as problematic. A number of possible simple controls for the problem appear to have generally eluded experimenters. The expedients of obtaining intensity rating scale and qualitative descriptions of sensations associated with needle insertion, together with pre- and post-experience ratings of treatment effectiveness from subjects*, should provide valuable direct, and indirect, information on these sources of attitudinal bias. Once needles are inserted it should be perfectly possible to compensate for any needle placement differences by applying electrical stimulation to an equal subjective intensity. In addition, as qualitative differences may still remain, the subjects may be simply directly asked at the end of the experiment to comment upon any experienced treatment differences and their effects upon attitudes and beliefs**.

A far superior additional method of control is available, however, simply by selecting classic Acupuncture 'point' prescriptions for specific disproportionate effects at one local area of the body. If an Acupuncturist-physician unacquainted with Acupuncture theory, other than the physical techniques for inserting needles at the specific 'points' selected, is employed, and if multiple body areas on naive subjects in an isolated cubicle are tested in balanced order, with

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* Subjects should, of course, be entirely naive with regard to sensations to be expected in association with Acupuncture.

** This may extend to outright questions relating to possible realisation of the simulated nature of the placebo-Acupuncture treatment.
fully automated stimulus-response equipment systems, e.g., extremely powerful control for all but the most improbable and specific inadvertent cueing of subjects is obtained. Additional rating scales and direct questioning of subjects at the end of the experiment may also confirm the successful maintenance of this 'double-blind' control.

A number of other important methodological considerations raised in the previous chapter may also be taken into account. For example, it would appear advisable to obtain 'Pain Tolerance' measures in addition to the commonly employed 'Pain Threshold' assessment since, in common with many conventional analgesics (25, 78), there is evidence in the literature review of possible differential responses to Acupuncture. In view of the considerable inter and intra-subject pain measure variability often reported (92, 179, 482), it is also important to obtain pre-trial baseline measures and to apply appropriate statistical correction (as outlined in the results section of this chapter) for any differential sensitivity evident at the various cutaneous test locations. Correction for day to day baseline variation, and the use of subjects as their own controls under experimental conditions presented in balanced order, would also seem appropriate in this connection, although rarely included in studies of 'Acupuncture analgesia' to date.

With regard to the selection of optimal Acupuncture procedures, it would appear advisable, from evidence in chapter 2, to ensure that needles are electrically stimulated for at least 30 minutes at maximal comfortably tolerable levels, and that 'points' are selected for analgesic target areas on the torso rather than the limbs (73, 220).

The above procedural details and many other minor controls are implemented in the study design for a pilot investigation of 'Acupuncture analgesia' as reported below.
Hypotheses

On the basis of evidence in the literature reviewed earlier, several principal operational hypotheses were generated for testing:

(1) For the skin surface of the body as a whole, 'Genuine Acupuncture', as directed by Chinese sources, will significantly elevate mean 'Pain Detection Threshold' (P.D.T.) and/or mean 'Pain Tolerance' (P.T.) above levels prevailing during both a 'Pseudo-Acupuncture' or a no-treatment ('Control') condition.

(2) For the skin surface of the body as a whole, the suggestive and other effects of 'Pseudo-Acupuncture' will significantly elevate mean P.D.T. and/or P.T. above levels prevailing during a no-treatment ('Control') condition.

(3) For one specific skin test area (abdominal), P.D.T. and/or P.T. will be disproportionately elevated compared to other areas of the body during the 'Genuine Acupuncture' condition only. This will occur by virtue of needle insertion at anatomical loci designated for this local effect by Chinese sources.

Experiment-1 Design

(1) Subjects:

Twelve paid volunteers (6 male), aged 18-32 years, and mainly students (non-science), were selected.

A specially constructed medical questionnaire (Appendix 1 Page 18) was administered. This was designed to eliminate anyone with general health problems, and specifically those with any congenital or other abnormality of skin sensation; and those liable to experience undue anxiety and stress as a result of the experimental
procedures. The normal...motivation for participation in a pain assessment experiment was also investigated.

Ignorance, apart from the vaguest general public knowledge, of the details of Acupuncture procedures and likely effects, was a prerequisite for subject selection.

A complete practical demonstration of all stimuli (including Acupuncture needles), and response systems to be used in the experiment, was given to all subjects in an initial adaptation and training session. If all procedures were acceptable to the subject, and he appeared competent to participate, the 'Experimental Consent Form' (Appendix 2, Page 463) was completed. It should be noted that the wording did not obviate the subject's right of claim against the medical defence insurance of the physicians involved in the study.

As an additional ethical safeguard, details of all experimental procedures, and subject selection criteria, were submitted to, and approved by, the Royal Edinburgh Hospital Ethics Committee prior to the beginning of any experimental work.

Finally, subjects were instructed, on penalty of their continued participation in the study, not to discuss any aspect of the experiment with anyone, especially other volunteers, or attempt to acquire information about Acupuncture, until the investigation was fully complete.

(2) Experimental Equipment System:
ACUPUNCTURE EXPERIMENT NO 1

EXPERIMENTAL EQUIPMENT SYSTEM
(Description and calibration)

General System Description (see Fig. 38 Page 40)

A. Thermal Stimulus System

1. Generation and termination:

A channel selector unit with a pseudo-random hard-wired programme was used to sequentially supply stabilised 12v DC to six individual skin heating units, consisting of specially mounted miniature bulbs, attached to various sites on the subject's skin. Upon illumination, bulb temperature increased regularly over time and subjects indicated their pain detection threshold by depression of a button to initiate a punch tape print-out of time elapsed since stimulus onset. A similar button, which also switched off the bulb, was subsequently depressed to record their pain tolerance point. If subjects failed to depress this button an automatic safety cut-out cancelled the stimulus after 50 seconds.

2. Calibration:

Surface contact temperature of the bulb which was to be attached to the subject's epigastrium was assessed by a thermocouple connected to an electronic thermometer with output to a pen recorder. Temperature was determined as a function of duration of bulb illumination in seconds.

B. Miscellaneous Monitoring and Stimulation Systems (Fig. 38 Page 40)

1. Neurostimulator: A purpose-built device was connected to pairs of needle electrodes to provide low current, low repetition rate, biphasic electrical stimulation to the subject.
FIG. 38  ACUPUNCTURE EXPERIMENT NO. 1
EXPERIMENTAL EQUIPMENT FUNCTIONAL SCHEMATIC

PROGAMMED CHANNEL SELECTOR

1. Sequencer

Step-On Command

SUBJECT

"TOLERANCE" BUTTON

"THRESHOLD" BUTTON

print command

SUBJECT

PAPER TAPE PUNCH

6. Skin Heating Units (bulbs)

NEUROSTIMULATOR

ENVIRONMENTAL CONTROL/MONITOR UNIT (27°C)

TAPE RECORDER

12v.

= Electrical Contact

= Mechanical or other contact

Reset and Hold
2. Tape Recorder: A tape recorder was employed to play restful music to subjects during inactive periods between trials.

3. Environmental Control Unit: A thermostatically controlled air conditioning/heating system maintained the experimental cubicle at approximately 27°C.

Construction Design Specifications

A. Thermal Stimulus System

1. Skin Heating Units (Figs. 6, 39 Pages 58, 47):

Six individual skin heating units were constructed. Each consisted of one tubular 12v, 100mA miniature flange bulb with tungsten filament recessed into a machined stainless steel well mounting. Bulb diameter was 6mm and mounting diameter 15mm. The bulb was recessed into the mounting such that only the curved tip area of the U shaped bulb projected to make contact with the skin. The bulb mounting, connections, and power supply cable were securely harnessed by heat shrinking sleeving. Heating units were attached to the skin by means of Beckman double adhesive sided electrode mounting collars.

2. Power supply:

Skin heating units were powered by 12v DC, fully stabilized supply with current limiting and short-circuit shut-down protection, from the Channel Selector/Programmer Unit.

B. Channel Selector/Programmer (Fig. 38 Page 40)

This device, in slightly modified form, is fully discussed in Chapter 7. Description now will, therefore, be largely limited to functions differing or not covered there.

The unit served to sequentially select, and power, six output channels supplying skin heating units. The hard-wired pseudo-random
Fig. 39: Skin Heating Unit for Production of Noxious Thermal Stimulation (Acupuncture Experiment No. 1).
sequence of channel selection is presented in Fig. 40 below.

**FIG. 40 : PROGRAMMER - SEQUENTIAL CHANNEL SELECTION PROGRAMME**

<table>
<thead>
<tr>
<th>Programmer (Experimenter)</th>
<th>Start Command</th>
<th>Auto-Stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel Nos. --&gt;</td>
<td>1 → 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 → 4</td>
<td>5 → 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 → 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 → 3</td>
<td>1 → 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 → 6</td>
<td>2 → 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Control of all hardware associated with the presentation of each stimulus and associated functions was divided into two cyclical timed steps as outlined in Fig. 41 page 44.

In Step 1 an output channel and associated Skin Heating Unit (S.H.U.) were selected and powered and timing of the monitory thermal stimulus was initiated. The two response buttons for the subject to indicate his 'Pain Detection Threshold' (P.D.T.) and 'Pain Tolerance' (P.T.) points were armed at this point. Depression of the P.D.T. button initiated print-out of time elapsed since stimulus onset, and the P.T. button additionally disconnected power to the S.H.U. In the event of failure of the subject to depress the P.T. button, the programmer automatically terminated the stimulus after 50 sec. with print-out of this time, as it moved to Step 2. Immediately after print-out the timer was zeroed and held. Subject response buttons were disarmed throughout Step 2. Upon
FIG. 41: PROGRAMMER UNIT - SEQUENTIAL EQUIPMENT COORDINATION SEQUENCES

Step 1 (50 sec.)

Programmer:
New Channel Selected
Skin Heating Unit Powered
Subject Response Buttons Armed
Digital Timer Count Started Gate Open

'Pain Threshold' Button
Close Gate Print Time

Step 2 (15 sec.)

Programmer:
Safety Cut-out Activated
S.H.U. Cancelled
Subject Response Buttons Disarmed
Digital Timer Count stopped

'Pain Tolerance' Button
Stop Count Close Gate Print Time
Gate Closed Gate Open to initiate Print-out (50 sec.)

or

Skin Heating Unit Cancel

Return
completion of Step 2 the programmer returned to Step 1 and selected the next stimulus channel, and continued thus until presentation of all six stimuli, with their 15 sec. intervening periods, was completed. The programmer then automatically stopped until activated, at ten minute intervals, by the experimenter whereupon the next cycle of stimuli would be engaged and completed.

C. **Digital Timer/Logger (Fig. 38 Page 40)**

This unit is fully described in Chapter 7, Section 3C, Page 272.

D. **Subject Response Buttons (Figs. 38, 54 Pages 40, 273)**

These are fully described in Chapter 7, Section 3D, Page 274. It should, however, be noted that the 'Pain Detection Threshold Button' performed no function other than to initiate print-out of stimulus duration when depressed. The 'Pain Tolerance Button', when depressed, also cancelled the stimulus and terminated the timer count as well as providing print-out.

E. **Neurostimulator (Figs. 38, 55 Pages 40, 273)**

This is fully described in.

F. **Tape Recorder (Fig. 38 Page 40)**

This was employed to present restful music to subjects during each ten minute period of inactivity between pair trials.

G. **Environmental Control/Monitor Unit (Fig. 38 Page 40)**

This unit is fully described in Chapter 7, Section 3E, Page 280.
Calibration

A. Thermal Stimulus System

1. Energy Source:
   As described above (Construction Design Specification A.1 page

2. Calibration Sensor:
   Ni Cr/Ni AL point Thermocouple.

3. Calibration Procedure:
   A recess was machined into a disc of low thermal transmission
   P.T.F.E. such as to accommodate the protruding dome of the skin heating
   unit glass. Flush fitting was ensured so as to prevent airflow over
   the unit. The point thermocouple was sandwiched between the glass and
   P.T.F.E. in direct contact with the centre of the glass dome. Ambient
   room temperature was maintained at approximately 27°C by the environ-
   mental control unit.

   The thermocouple, together with an identical reference unit
   immersed in melting ice, was connected to the electronic thermometer
   described in Chapter 7, Section B, Page 27. Output from the thermometer was
   employed to drive a Devices Dc5 Preamplifier coupled to a Dc5 Pen
   Recorder with automatic time signature, and bulb on/off record marker.

   Rise in bulb surface temperature (°C) was plotted as a function
   of duration (sec.) of illumination from a fully cooled, non-illuminated
   baseline of approximately 26.2°C to produce Fig. 42 page 47 (curve A).

   Data points appear for 10°C ascending steps over the 50 sec.
   standard maximum illumination period, with interim values for the
   terminal time point.

   Correction for the small time constant of the thermocouple, includ-
   ing the minimal thermometer circuit latency, was applied to produce
   Curve B in Fig. 42 page 47. This corresponds approximately to the
   common \( y = A(1-e^{-kt}) \) curve description.
FIG. 42

THERMAL STIMULUS (BULBSKIN HEATING UNIT): SURFACE TEMPERATURE TIME CURVE.
(Curve B corrected for Thermocouple time constant)
The curve was replicated twice without significant deviations, and substitution of another skin heating unit produced no marked alteration. Since the primary interest was observation of the time gradient of stimulus intensity rather than its absolute value, no attempt was made to estimate actual skin temperatures. The most relevant stimulus range is covered by the time period 0–20 sec.

B. Neurostimulator Calibration

Stimulation parameters applied to two randomly selected subjects, one from each of the two balanced order experimental groups, were preset and/or monitored exactly as described for Experiment No 2 in Chapter 7, Section (2) Calibration B, Page 305. However, here electrode pairs consisted of two needle electrodes inserted in identical locations bilaterally, whereas in Experiment No 2 electrode pairs were located ipsilaterally, and each consisted of one needle plus one surface electrode. For this reason some differences in power and waveform applied to the electrodes are evident for Experiment No 1. These are presented below. Otherwise all parameters and measurement techniques were as described for Experiment No 2 (Chapter 7, Section (2) Calibration B, Page 305).

1. Voltage and Current: Results are presented in Table 37, page 49.

All measures are peak levels, without analysis over time.

2. Waveform: The voltage waveform showed slight, and probably insignificant, modification under subject load (Fig. 43, page 50) compared to the unloaded form (Fig. 57, page 277). The current waveform (loaded) appears in Fig. 44, page 50.


The complexity of this problem for a mixed radiant and conductive thermal source applied to unblacked skin, together with differences in specific heat capacities, time constants, heat sinking etc. between skin and thermocouples, is beyond appropriate requirements here. Almost certainly, however, skin temperature would be appreciably lower (169,418).
<table>
<thead>
<tr>
<th>Needle Electrode Site (bilateral)</th>
<th>Peak Voltage (v)</th>
<th>Peak Current (mA)</th>
<th>Resistance (\Omega)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>First Dorsal</td>
<td>0.9</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Intercrosseous</td>
<td>3.2</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Pre-Tibial</td>
<td>1.7</td>
<td>1.1</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>0.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Deltoid m.</td>
<td>4.2</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>3.6</td>
<td>1.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Tensor Fasciae</td>
<td>7.2</td>
<td>1.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Latae m.</td>
<td>6.7</td>
<td>1.9</td>
<td>4.6</td>
</tr>
</tbody>
</table>

* Approximate impedance (ohmic)
Fig. 43: Acupuncture Neurostimulator Voltage Waveform Across Subject Load (Bilateral Needle Cathode & Anode Pair).

Fig. 44: Acupuncture Neurostimulator Current Waveform Across Series Resistor (10.5 ohms) Load (Bilateral Needle Cathode & Anode).
TABLE 38: MEAN ELECTRICAL STIMULATION PARAMETERS APPLIED FOR TWO SUBJECTS: NEEDLE ELECTRODE CURRENT AND POWER DENSITIES

<table>
<thead>
<tr>
<th>Electrode Contact Surface Area (mm²)</th>
<th>Deltoid m.</th>
<th>Tensor Fasciae latae m.</th>
<th>1st Dorsal Interosseous</th>
<th>Pre-Tibial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.18</td>
<td>22.13</td>
<td>33.30</td>
<td></td>
</tr>
<tr>
<td>Peak Current (mA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mA)</td>
<td>2.0</td>
<td>3.6</td>
<td>1.0</td>
<td>3.85</td>
</tr>
<tr>
<td></td>
<td>1.65</td>
<td>2.9</td>
<td>0.85</td>
<td>2.6</td>
</tr>
<tr>
<td>Current Density (mA/mm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mA/mm²)</td>
<td>0.18</td>
<td>0.32</td>
<td>0.045</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>0.15</td>
<td>0.26</td>
<td>0.038</td>
<td>0.08</td>
</tr>
<tr>
<td>Peak Power (mW)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mW)</td>
<td>7.8</td>
<td>25.0</td>
<td>2.0</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>5.0</td>
<td>0.54</td>
<td>2.6</td>
</tr>
<tr>
<td>Power Density (mW/mm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mW/mm²)</td>
<td>0.7</td>
<td>2.24</td>
<td>0.09</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>0.18</td>
<td>0.45</td>
<td>0.03</td>
<td>0.08</td>
</tr>
</tbody>
</table>
FIG. 1: ACUPUNCTURE EXPERIMENT NO 1:
Balanced Order Experimental Session Design:

- Adaptation Session (12 subjects)
  - Control Session (12 subjects)
    - 6 subjects (3 male) Genuine Acupuncture Session
    - 6 subjects (3 male) Pseudo-Acupuncture Session
  - 6 subjects (3 male) Pseudo-Acupuncture Session
  - Genuine Acupuncture Session
Method:

Starting two days after their adaptation and training sessions, all subjects passed through three experimental conditions as outlined in Fig. 1, Page 52, with two day intervals between each session. The first experimental treatment for all subjects was a 'Control' session without Acupuncture. For half the subjects, this was followed by a session during which Acupuncture needles were inserted according to current Chinese practice ('Genuine Acupuncture' Session) and then, two days later, by one of simulated Acupuncture ('Pseudo-Acupuncture' Session). Subjects were naturally blind as to this control. The order of the two Acupuncture sessions was reversed for the other six subjects. Both sexes were equally represented in each group in the balanced order design. Subjects attended at the same time of day for all sessions.

The procedural sequence common to all sessions, which lasted approximately 90 minutes, is outlined in Fig. 2, Page 54, and is explained below (items underlined were not included in the 'Control' Session).

(a) Instructions to Subjects:

Upon arrival in the laboratory, subjects were given a standard explanation and instruction sheet (Appendix 3, Page 46) to remind them of the experimental procedures and required responses. Full understanding was ascertained and, where necessary, further explanation given on a basis strictly limited to information already covered by the instruction sheet.

* Henceforth, where reference is made to 'Acupuncture Sessions', this should be taken, unless otherwise stated, to include both 'Genuine' and 'Pseudo-Acupuncture' sessions.
FIG. 2: ACUPUNCTURE EXPERIMENT NO 1:  
90 Minute (approx.) Experimental Procedure for ALL Sessions  
(Items underlined not included in 'Control Session')

(a) : Standard Instructions to Subject

(b) : Subjective Rating Scale (i) Completed

(c) : Attachment of Thermal Stimuli to 6 Body Locations

(d) : Baseline 'Pain Detection Threshold' and 'Pain Tolerance' Values Established for each Body Location

(e) : Insertion of 4 Acupuncture Needles  
(Genuine or Pseudo Acupuncture 'Point' Locations)

(f) : Subjective Rating Scale (ii) Completed

(g) : Electrical Stimulation of Needles  
(Subjective Rating Scale (iii) Completed)

10 min.

(h) : 1st Experimental Trial  
'Pain Detection Threshold' and 'Pain Tolerance' Values Recorded for Each Body Location

10 min.  
(Electrical Stimulation of Needles)

(i) : 2nd Experimental Trial

10 min.  
(Electrical Stimulation of Needles)

(j) : 3rd Experimental Trial  
(Acupuncture Needles Removed)

10 min.

(k) : 4th Experimental Trial  
: 5th " "  
: 6th " "

(l) : Subjective Rating Scale (iv) Completed

(m) : Post-Experimental Interview
(b) Completion of Subjective Rating Scale (i):

A 10cm line visual analogue scale (Fig. 3 (i) Page 56) was completed by all subjects at the very beginning of the 'Genuine' and 'Pseudo-Acupuncture' sessions to indicate the beliefs, and predictions, of the subject as to the efficacy of Acupuncture in affecting pain sensation. Cognitive strategies to be employed by subjects were outlined in their instructions (Appendix 3, Page 44).

(c) Attachment of Thermal Stimuli to 6 Body Locations:

The six Skin Heating Units (S.H.U.) described above (Page 41) were attached to the skin surface of naive subjects, at the body locations illustrated in Figs. 4, 5, 6, 7, Pages 57 and 58 described below.

<table>
<thead>
<tr>
<th>S.H.U. No.</th>
<th>Anatomical Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Antero-medial surface of the left lower leg (Gastrocnemius muscle (Fig. 6, Page 57)).</td>
</tr>
<tr>
<td>2.</td>
<td>Lateral surface of the left upper arm at the approximate level of the Deltoid Tuberosity (Fig. 5, Page 57).</td>
</tr>
<tr>
<td>3.</td>
<td>Central Epigastrium (Fig. 6, Page 58).</td>
</tr>
<tr>
<td>4.</td>
<td>Dorsal right forearm slightly distal to the Pronator Teres impression of the Radius (Fig. 7, Page 58).</td>
</tr>
<tr>
<td>5.</td>
<td>Mid Sternum at a level between the 3rd and 4th ribs (Fig. 5, Page 57).</td>
</tr>
<tr>
<td>6.</td>
<td>Anterior right thigh, over the Rectus Femoris muscle, approximately midway along a line from the Greater Trochanter to the Patella centre (Fig. 7 Page 58).</td>
</tr>
</tbody>
</table>

(d) Baseline 'Pain Detection Threshold' ('P.D.T.') and 'Pain Tolerance' ('P.T.') Values Established for Each Location:

Baseline 'P.D.T.' and a 'P.T.' values were established sequentially for each of the six stimulus sites by the procedure
FIG. 3 : ACUPUNCTURE EXPERIMENT NO 1:
Subjective Rating Scales (i) to (iv):
(Note original scales appeared on separate pages)

<table>
<thead>
<tr>
<th>(i) Acupuncture will have</th>
<th>No Effect at All</th>
<th>A Very Considerable Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>in increasing/decreasing* my sensitivity to pain</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(ii) Sensations arising from the Acupuncture needles are</th>
<th>Hardly Detectable</th>
<th>Extremely Powerful</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(iii) Sensations arising from the Acupuncture needles plus electrical stimulation are</th>
<th>Hardly Detectable</th>
<th>Extremely Powerful</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(iv) Acupuncture has had</th>
<th>No Effect at All</th>
<th>A Very Considerable Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>in increasing/decreasing* my sensitivity to pain</td>
<td></td>
</tr>
</tbody>
</table>

*delete as appropriate

The change in pain sensitivity was greatest at
(tick any box or boxes if appropriate)

<table>
<thead>
<tr>
<th>Left Lower Leg</th>
<th>Right Thigh</th>
<th>Stomach</th>
<th>Chest</th>
<th>Left Upper Arm</th>
<th>Right Forearm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Fig. 4: Location of 'Skin Heating Unit' No. 1 (Left lower leg).

Fig. 5: Location of 'Skin Heating Units' No. 2 (Left upper arm) and No. 5 (Chest).
Fig. 6: Location of 'Skin Heating Unit' No. 3 (Abdomen).

Fig. 7: Location of 'Skin Heating Units' No. 4 (Right forearm) and No. 6 (Right thigh).
The first Skin Heating Unit (S.H.U.) in the first stimulus sequence (see Fig. 40 Page 43) was activated, and automatic timing began. The subject was unaware of the location, or moment of onset, of the S.H.U.* The contact temperature of the S.H.U. thermal stimulus increased regularly over time from onset (as discussed under calibration, Page 46), and the subject was instructed (see Appendix 3, Page 466) to push a button with his left hand immediately the sensation of heat appeared to "focus to a point accompanied by a sharp pricking sensation" at the site of stimulation. This sensory point was defined as the subject's 'Pain Detection Threshold' ('P.D.T.') Threshold descriptions of this type have been used with success in many other studies (179), and appeared to be identified with ease by all subjects here. The logic, and probable neurological substrate, for this threshold definition are discussed elsewhere. Upon depression of the 'P.D.T.' button, a print-out of time elapsed since stimulus onset was recorded and served as the measure of 'P.D.T.'

After this point, the thermal stimulation, now painful, continued to increase in intensity until the subject indicated, by depression of another button with his right hand, that his 'Pain Tolerance' ('P.T.') duration had been exceeded. This button again initiated a print-out of total time elapsed since stimulus onset for use as the 'P.T.' measure, and also terminated the heat stimulus. Instructions

* Subjects were not advised of the stimulus location sequence, and were led to believe it was entirely random. Additionally, subjects were supine, and therefore unable to detect the very slight glow discernible through the skin tissue on close local inspection when an S.H.U. was illuminated. Finally, subjects were alone in an effectively soundproofed cubicle, and therefore could not gain cues from equipment operational noise. No clocks, or other timing devices, were present. Closed circuit television monitoring was employed to observe subjects.
to subjects clearly countermanded any attempts at heretics over the 'P.T.' level, stressing merely the need to adopt a **consistent** painful sensory point at which to terminate the stimulation as being the maximum they were prepared to tolerate. Should a subject fail to depress the 'P.T.' button, an automatic safety cut-out terminated the heat stimulus after a standard 50 second duration.

There then followed an interval of 15 seconds before the next S.H.U., at another body location, (again unknown to the subject), was activated and the sequence of button pushing responses was again completed to establish the 'P.D.T.' and 'P.T.' time values for that body location.

This process continued until all six body locations had been tested. An interval of 3 minutes was then allowed for apparatus and skin cooling, after which the complete process was repeated exactly as before.

The stimulus duration values obtained during the second stimulus series were taken as the baseline (pre-trial) 'P.T.'s and 'P.T.'s for each body location. This decision was based on the findings of pilot work, the results of which are presented and discussed.
ACUPUNCTURE EXPERIMENT NO 1:
Pain Measure Baselines: Pilot Studies

Using exactly the methodology for establishing 'Pain Detection Threshold' ('P.D.T.') and 'Pain Tolerance' ('P.T.') points described above, five subjects were tested to assess the most representative method of establishing baseline values.

From initial trials it quickly became clear that, if multiple successive testing of baselines in close temporal order was undertaken, then considerations of the time scale of the experiment, subject comfort, skin irritation and fatigue and so on, limited the practical number of trials to three at each body location, with a minimum of three minutes recovery time between each trial.

The next concern was to establish whether any particular trial would prove the most representative and reasonable for adoption as baseline, or whether variation from trial to trial was so marked and bidirectional as to require adoption of a mean value.

In general, when tested with three successive trials at three minute intervals, subjects displayed values increasing from trial 1 through to trial 3. This pattern was, of course, subject to a certain amount of variability. Given this pattern, it is not surprising that trial 2 proved to be the single trial most representative of the mean of the trials. Table 39 on page 67 presents values of 'P.D.T.' and 'P.T.' obtained at each body site for 5 subjects in the three individual successive trials, transformed to percent deviations from the mean 'P.D.T.' and 'P.T.' values for the three trials. The pattern of increase across the three trials is evident
TABLE 39: ACUPUNCTURE EXPERIMENT NO. 1:
Baseline 'Pain Detection Threshold' and 'P.T.' Values:
Deviation (%) of Individual Successive Trials from
Mean of Trials

<table>
<thead>
<tr>
<th>Body Location</th>
<th>Deviation (%) of Trials (1, 2, 3) from Mean of Trials (1+2+3)</th>
<th>'Pain Detection Threshold'</th>
<th>'Pain Tolerance'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial 1</td>
<td>Trial 2</td>
<td>Trial 3</td>
</tr>
<tr>
<td>Subject 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-24</td>
<td>-1</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>37</td>
<td>-40</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>-8</td>
<td>-3</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>-15</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>-4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Subject 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>18</td>
<td>27</td>
<td>-37</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>-7</td>
<td>-36</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>4</td>
<td>-5</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>3</td>
<td>-21</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>1</td>
<td>-15</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>22</td>
<td>-46</td>
</tr>
<tr>
<td>Subject 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-10</td>
<td>-5</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>0</td>
<td>-9</td>
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<tr>
<td>3</td>
<td>-10</td>
<td>10</td>
<td>0</td>
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<td>4</td>
<td>-4</td>
<td>7</td>
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<td>5</td>
<td>4</td>
<td>15</td>
<td>-19</td>
</tr>
<tr>
<td>6</td>
<td>-30</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Subject 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-17</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>-25</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>8</td>
<td>-17</td>
</tr>
<tr>
<td>4</td>
<td>-22</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>-11</td>
<td>15</td>
<td>-5</td>
</tr>
<tr>
<td>6</td>
<td>-4</td>
<td>8</td>
<td>-2</td>
</tr>
<tr>
<td>Subject 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-14</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>-19</td>
<td>-16</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>-8</td>
<td>-2</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>-14</td>
<td>-14</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>3</td>
<td>-14</td>
</tr>
<tr>
<td>6</td>
<td>-6</td>
<td>4</td>
<td>-47</td>
</tr>
</tbody>
</table>
from the signs of the values. Raw data is not presented for reasons of space and peripheral importance.

The data of Table 39 Page 62 is summarised in Table 40 Page 64, where the values, irrespective of sign, for all the body locations are grouped, and the means presented. Mean values for the subject group also appear.

Table 41 Page 64 presents the results of a simple count of the number of times each of the trials (1, 2, 3) produced the lowest, and the highest, pain measure values ('P.D.T.' and 'P.T.' grouped together, tied values excluded). From this it can be seen that trial 1 predominantly produced the lowest values, possibly due to initial subject anxiety and greater attention, and perhaps to receptor background effects for novel stimuli. Obviously to take trial 1 values as baselines would aggrandise any possible elevations of values occurring later in the sessions. Selection of trial 2 values is not subject to this criticism. Trial 3 values predominate as the 'highest', but the percentage ratios between the trials are more equal than for 'lowest' values data. It could be argued that selection of trial 3 values as baselines unreasonably reduces the possible range of elevation later in a session, and that trial 3 values were produced during a temporal concentration of successive stimuli which would not be characteristic of the session later.

For all of the above reasons, and in the interests of session length economy and subject comfort, it was decided to take only two measures (trials 1 and 2) for baselines and adopt trial 2 values directly.
TABLE 40: ACUPUNCTURE EXPERIMENT NO 1:
Baseline 'Pain Detection Threshold' (P.D.T.) and 'Pain Tolerance' (P.T.) Values:
Deviation (%) of Individual Successive Trials from Mean of Trials (Summary Table)

<table>
<thead>
<tr>
<th>Subjects (Whole Body Means)</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>8</td>
<td>18</td>
<td>12</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>11</td>
<td>27</td>
<td>6</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>9</td>
<td>10</td>
<td>12</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>9</td>
<td>9</td>
<td>12</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>8</td>
<td>20</td>
<td>11</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Group Mean</td>
<td>14</td>
<td>9</td>
<td>17</td>
<td>11</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

Note: All values rounded.

TABLE 41: ACUPUNCTURE EXPERIMENT NO 1:
Baseline 'P.D.T.' and 'P.T.' Values: Frequency of Occurrence (%) of Highest and Lowest Values in Three Sequential Trials (5 subjects)

<table>
<thead>
<tr>
<th>Lowest Value Occurrence</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64%</td>
<td>7%</td>
<td>29%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest Value Occurrence</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19%</td>
<td>27%</td>
<td>54%</td>
</tr>
</tbody>
</table>

(Note: 'P.D.T.' and 'P.T.' not differentiated. All values rounded. Tied values excluded from count.)
(e) Insertion of 4 Acupuncture Needles ('Genuine' or 'Pseudo Acupuncture' 'Point' Locations):

(i) 'Genuine Acupuncture':

Immediately after completion of the baseline procedures (above), four Acupuncture needles were inserted into premarked locations on the body. Two Acupuncture 'Points' were selected on the basis of current Chinese practice as described by western observers (15, 270, 297). A great variety of 'points' are prescribed for analgesia of the same body regions by different authors. However, there appeared to be almost unanimous agreement as to the use of at least two 'points'.

The 'point' "Ho-ku" (Large Intestine 4) is located in the skin web between the thumb and index finger, about midway between the junction of the first and second metacarpals and the fold (see ringed 'point' Fig. 8 Page 6(a)). This location appears as a fundamental in the 'point' combination formulae for most parts of the body, and may be taken as inducing diffuse analgesia (78, 396, 399).

The exact location was determined by probing around the approximate area, with the subject's thumb fully extended medially, until maximal tenderness was reported. Sensations of increased probe sharpness, internal soreness, numbness, or tingling, dull aching (local or radiating), pressure or fullness, and heaviness, are all characteristically reported when Acupuncture 'points' are probed or punctured, in contrast to their absence or reduction in surrounding tissue (270, 427). Subjects exhibited little difficulty in
Fig. 8 Location of Acupuncture 'Point' 'Ho-Ku' (LI 4).

Fig. 9 Location of Acupuncture 'Points' by Means of Skin Resistance.
differentiating 'point' sensations from surrounding tissue. In cases of some dubiety, location was confirmed by test with a point skin resistance indicator. Reduced electrical resistance over Acupuncture 'points' has been demonstrated and widely reported \(^{(23, 30, 56)}\). However, the technique required is sophisticated and time consuming if it is to be done properly. For quick confirmation, a simple variable trigger threshold indicator (Fig. 9 Page 66) can be useful provided the subject is not overly emotionally aroused. 'Points' were located and marked on the skin surface prior to the beginning of the experiment.

Acupuncture needles of the type described in Chapter 7, Section (3) \(^{282}\) were inserted bilaterally at the "Ho-Ku" point. Insertion was at 90° to the cutaneous surface and to a depth of approximately 2.5 cm. (Fig. 10 Page 68).

Needles were hot air sterilised and inserted through skin cleansed with Isopropyl Alcohol B.P., and briefly sprayed with Ethyl Chloride B.P. to reduce discomfort from penetration. Needles were checked for any malformation or other defect, and then inserted as quickly as possible by applying gentle pressure with simultaneous oscillatory twirling. In this way, the needle tends to insinuate its way through tissue, particularly as it is solid, rather than punch in the manner of a hypodermic needle.

Needles were withdrawn and re-inserted at a slightly different angle if the subject reported excessive discomfort, or else failed to report any of the characteristic sensations of Acupuncture as mentioned above. This was limited to a maximum of one re-insertion. Sterile surgeons' gloves were worn for all needle manipulations, and no complications or side effects were encountered.
Fig. 10: Acupuncture Needle Inserted at 'Ho-Ku' 'Point' and Receiving Electrical Stimulation.

Fig. 11: Location of Acupuncture 'Point' Tsu-San-Li (ST 36).

THE MERIDIANS OF CH'I ENERGY

ANTERIOR MAN
The other 'Genuine Acupuncture' 'point' chosen was "Tsu-san-li" (Stomach 36) (see ringed 'point' Fig. 11 Page 68). This is located one "body inch" distal, and lateral, to the Tibial Tuberosity.

The "body inch" is a proportional body dimension devised by the Chinese, in order to permit description of 'point' locations in terms of a standardised measuring system compensated for individual variation in overall body scale. One "body inch" is the distance between the interphalangeal joints of the subject's middle finger (Fig. 12 Page 70), and is likely to range from about 2.5cm to 4.0cm.

Measurement from the Tibial Tuberosity one body inch distal, and one body inch lateral was undertaken in the manner depicted in Fig. 13 Page 70. The area was again probed, or scanned electrically, as described above, and needles again inserted bilaterally at 90° to the cutaneous surface to a depth of approximately 3.5cm. Insertion was by means of the especially constructed guide tube described in Chapter 7, Section (3), Page 224 (and see Fig. 61 Page 284). All other procedures were exactly as for the "Ho-ku" 'point'. Again no problems were encountered other than occasional harmless bending of needles from forgetful flexion of the leg by the subject.

"Tsu-san-li" is regularly prescribed in manuals (15,270) for all abdominal surgery (particularly epigastric), since this is expected to be the principal locus of its effect. The likely neu-ophysiologically relationship between the needle location and site of effect is discussed elsewhere.

With the selection of these two 'Genuine Acupuncture' 'points' described above, two experimental hypotheses were implicitly generated:

1) There would be a general elevation of 'Pain Detection Thresholds' and/or 'Pain Tolerances' at all the body test locations.
Fig. 12: The Chinese 'Body Inch'.

Fig. 13: Use of the 'Body Inch' to Locate 'Tsu-San-Li' 'Point' by Measurement from the Tibial Tuberosity.
(2) There would be a disproportionately greater increase on the epigastrium compared with all other body test locations.

Hypothesis number two was completely unknown to the physician inserting the Acupuncture needles, and was in no way referred to in the tightly constrained information given to subjects. This control was maintained successfully throughout the complete study (see results section).

(ii) 'Pseudo-Acupuncture':

Needles were again inserted bilaterally at two body locations in the 'Pseudo-Acupuncture' sessions. These locations were selected so as to avoid all recognised Acupuncture 'points', whilst providing a source of suggestion and distraction of comparable psychological potency in the naive subjects.

The first location (Fig. 14 Page 72) was in the Deltoid muscle approximately \( \frac{2}{3} \) body inches (approx. 7-8") along a line directly distal from the Acromio-clavicular joint. Insertion was at 45° to the skin surface penetrating medially to a depth of approximately 1.25c-.

In order to standardise methodology throughout the whole experiment, elaborate measurement using 'body inches', followed by the usual probing, was concocted to simulate the procedure used with the 'Genuine Acupuncture' 'points'. By applying sufficient probe pressure differentially, subjects were induced to report one site as more 'sensitive' than surrounding tissue. The needle was then inserted slightly away from this location just in case a spontaneously tender Acupuncture 'point'\(^{427}\), or myofascial trigger point\(^{439}\) had been inadvertently
Fig. 14: Location of Deltoid 'Neutral' Site for 'Pseudo-Acupuncture' Stimulation.
located. Subjects did not display sufficient cutaneous location awareness to detect this deviation, particularly as a slight delay was allowed between termination of probing and actual needle insertion. All skin preparation and needle insertion procedures were as for 'Genuine Acupuncture'. No complications were encountered.

The second 'Pseudo-Acupuncture' location (Fig. 15 Page 74) was approximately three 'body inches' (about 9cm) distal from the Greater Trochanter, slightly lateral of a line from the lateral extremity of the Greater Trochanter to the lateral border of the Patella. Insertion was at $45^\circ$ to the skin surface, penetrating posteriorly to a depth of approximately 1.25cm. All location procedures were as described above. Occasional withdrawal and reinsertion of needles, for putative improvement of effect, was undertaken for the sake of comparability with the 'Genuine Acupuncture' session procedures. The physician inserting the needles was not informed of the simulated nature of the Acupuncture in these sessions. Subjects naturally were not informed either, and various scales designed to monitor the robustness of this control are described below.

(f) Subjective Rating Scale (ii) Completed:

A 10cm line visual analogue scale (Fig. 3 (i) Page 56) was completed by the experimenter under instruction from the subject, immediately insertion of needles was completed, and prior to any electrical stimulation. Cognitive strategies to be employed by subjects were outlined in their instruction sheets (Appendix 3 Page 466). The scale was intended to provide a comparison of any differences in intensity of sensations at the needle sites during the two Acupuncture treatments ('Genuine' or 'Pseudo').
Fig. 15: Location of Thigh 'Neutral' Site for 'Pseudo-Acupuncture' Stimulation.
(g) Electrical Stimulation of Needles (Subjective Rating Scale (iii) Completed):

Low amplitude, biphasic electrical pulses were applied to the bilateral needle pairs in the manner fully described and calibrated above. During approximately five minutes of adaptation, the intensity of electrical stimulation was gradually increased until stabilised at the maximum, fully adapted, level comfortably tolerable to the subject. The experimenter then completed rating scale (iii) (Fig. 3 (iii) Page 54) under instruction from the subject in the same way as before. By attempting to apply an equivalent level of stimulation, in terms of sensory intensity, during both the 'Genuine' and 'Pseudo-Acupuncture' sessions, it was intended to mask, or compensate psychologically, for the probable slight differences in sensations upon initial insertion of the needles at the different loci. The rating scale was designed to assess the effectiveness of this manoeuvre.

Electrical stimulation thereafter continued uninterrupted* for 10 minutes whilst relaxing music was played to subjects over the intercom until the start of the first experimental trial.

(h) 1st Experimental Trial:

In Acupuncture sessions, electrical stimulation to all needles was turned off, in order to equate conditions with those of the 'Control' sessions where subjects could concentrate on the thermal pain stimuli without distraction from fasciculation of musculature at the needle locations. Sensations emanating from the needles alone,

* The subject was asked to adjust, where necessary, the electrical stimulation intensity to maintain the subjective level constant at the maximum comfortably tolerable level established above.
without electrical stimulation, were minimal (see results). Removal of clonus from hand muscles also facilitated depression of the response buttons.

'Pain Detection Threshold' and 'Pain Tolerance' values (mounting thermal stimulus duration in seconds) were then established once for each body test site in succession. The procedure was identical to that employed for baseline establishment (section (d) above), except that the sequence for activation of 'Skin Heating Units' at the various body locations was now that of Sequence No 2 (see Fig. 40 Page 13). Again subjects were given no cues as to the moment of onset, or sequence, of stimuli at the different locations.

Although the trial had a theoretical maximum duration of 6.25 minutes for completion (50 sec. maximum automatic stimulus times plus 15 sec. interstimulus intervals), a typical maximum time to completion was 3.5 minutes.

Upon completion of the trial, electrical stimulation was resumed at the same intensity as before. Background music was also restarted, and the subject was instructed to relax for a further 10 minutes until the second experimental trial.

(i) 2nd Experimental Trial:

Procedure was exactly as for the first trial, except that the order in which the body locations were tested followed Sequence No 3 (Fig. 40 Page 13).

(j) 3rd Experimental Trial (Acupuncture Needles Removed):

This trial was conducted exactly as the previous trials, apart from the use of stimulus location Sequence No 4 (Fig. 40 Page 13).
In all Acupuncture sessions, immediately upon completion of the third trial, all four Acupuncture needles were removed and the skin checked for injury and cleansed with Isopropyl Alcohol B.P. (Electrical stimulation was not resumed after the trial.) At this point, the needles had been in place for approximately 45 minutes, and electrically stimulated for some 35 minutes of that period. A period of 35 minutes stimulation has been suggested as adequate for the induction of analgesia by 'Genuine Acupuncture', on the basis of evidence reviewed earlier in chapter 2.

(k) 4th, 5th, and 6th Experimental Trials:

The last three trials were completed exactly as the first three, with 10 minute intervals between each trial. The stimulus location sequences Nos. 5, 6, 1 (Fig. 40 Page 43) were utilised for trials 4, 5, 6 respectively.

Subjects were not informed as to the exact number of trials in the session; but were told that there would be a minimum of four, and a maximum of eight, the actual number being determined at random. This was an attempt to avoid a 'last trial', or 'end of experiment', psychological 'set' with possible resulting alteration of response pattern.

(1) Subjective Rating Scale (iv) Completed:

Rating scale (iv) (Fig. 3 Page 56) was completed by the subject immediately following the conclusion of trial No 6, and whilst the 'Skin Heating Units' were being removed. Subjects were reminded that they should neither feel expected to report effects if they did not observe any, nor feel inhibited from expressing any that were observed.

* Subjects were not advised as to exactly when during the session the needles would be removed, in order to reduce the effects of anticipation upon pain response measures.
(m) Post-Experimental Interview:

Finally subjects were interviewed in a structured manner under the following sub-headings:

All Sessions: (Questions relating to Acupuncture not applicable to 'Control' session.)

(i) Attempts to predict onset of thermal stimuli?

(ii) Apparent rapidity of sensory transition through range of hot - 'P.D.T.' - 'P.T.'?

(iii) Consistency and nature of subjective criteria used to determine 'P.D.T.' and 'P.T.' points?

(iv) Relative sensitivity to pain of different body locations?

(v) Anxiety concerning pain stimuli and needles?

(vi) Sensations arising from insertion of needles?

'''' needles alone, once inserted?

'''' plus electrical stimulation?

(vii) Psychological changes, if any, during Acupuncture eg. mood shifts, alertness, reaction to painful stimuli etc.?

(viii) Awareness of changes in 'P.D.T.' and 'P.T.', and locations, during session. Beliefs as to the efficacy of Acupuncture after experience?

Final Session only:

(ix) Awareness of any differences in strength, or quality, of sensation from needle stimulation in the two Acupuncture sessions? Effects on assumptions of potency of stimulation?

(x) Awareness of the simulated nature of Acupuncture in the 'Pseudo-Acupuncture' session?

(xi) Awareness of any particular effect on epigastrium, or of the focus of experimental interest there?
(1) **Baseline Pain Response Measures:**

(a) Differences Between Experimental Treatment Conditions:

For each experimental treatment condition, group mean \(n = 12\) subjects) 'Pain Detection Threshold' ('P.D.T.') and 'Pain Tolerance' ('P.T.') values were calculated for each of the six individual body locations. They are presented in Table 2(a) Page 30 together with their Coefficients of Variance \(\frac{\sigma}{N}\) in parentheses. Mean values for the body as a whole are also included. Although the group means for the different experimental conditions were close, a trend towards slightly higher values in both the Acupuncture sessions compared to the 'Control' condition was evident. It will be recalled from the methods section that, for all subjects, the 'Control' condition was experienced first, with only the two Acupuncture conditions being administered in balanced order. Furthermore some differences in variance between the experimental conditions were noted. Therefore \(t\) ratios for testing the difference between correlated variances \((159)\) were computed for each possible combination pair of experimental conditions, and appear, with associated significance levels, in Table 3 Page 32. Correlation coefficients for each pair of conditions are also presented, with significance levels, in the same table and were derived, like the variances, from a data base of whole body 'P.D.T.' and 'P.T.' values (i.e. mean of the six body locations) for the twelve subjects.

All pairs of conditions displayed significant correlations for both 'P.D.T.' and 'P.T.' baseline measures. There were, however, significant differences in variance between the 'Control' and 'Pseudo-Acupuncture', and 'Control' and 'Genuine Acupuncture' conditions,
**TABLE 2 (a) ACUPUNCTURE EXPERIMENT NO 1:**
Baseline 'Pain Detection Thresholds' and 'Pain Tolerances' (Pain stimulus durations in seconds). Group Mean Values (n = 12) for Different Body Locations and for Whole Body (Coefficients of Variance (CV) in Parentheses), for Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Individual Body Locations*</th>
<th>Whole Body Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Control</td>
<td>9.89(.25)</td>
<td>5.92(.36)</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>9.72(.34)</td>
<td>7.46(.53)</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>10.08(.25)</td>
<td>7.22(.29)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>'Pain Tolerance'</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 1. Left Lower Leg  4. Right Forearm
  2. Left Upper Arm   5. Chest
  3. Abdomen          6. Right Thigh
### TABLE 2 (b) Group Median Values (n = 12) for Different Body Locations and for Whole Body (Ranges in Parentheses), for Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Individual Body Locations*</th>
<th>Whole Body Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Control</td>
<td>10.25 (4.6-14.9)</td>
<td>5.60 (3.8-11.9)</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>9.60 (5.8-16.1)</td>
<td>6.40 (1.9-16.9)</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>10.80 (6.7-14.4)</td>
<td>6.55 (5.2-12.3)</td>
</tr>
</tbody>
</table>

'Pain Tolerance'

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13.25 (7.9-18.3)</td>
<td>8.0 (5.6-13.6)</td>
<td>13.25 (9.2-18.2)</td>
<td>11.35 (8.6-20.3)</td>
<td>11.45 (6.4-17.7)</td>
<td>12.6 (7.3-18.4)</td>
<td>12.07 (8.0-13.25)</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>11.55 (7.4-22.6)</td>
<td>8.7 (4.4-20.4)</td>
<td>14.6 (8.4-21.9)</td>
<td>12.8 (7.4-22.1)</td>
<td>13.55 (7.4-20.4)</td>
<td>12.15 (7.7-17.1)</td>
<td>12.47 (8.9-14.6)</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>12.65 (7.5-16.7)</td>
<td>8.55 (7.0-17.2)</td>
<td>14.95 (6.4-16.2)</td>
<td>12.50 (9.8-30.6)</td>
<td>12.90 (9.1-23.3)</td>
<td>12.25 (6.8-16.8)</td>
<td>12.57 (8.55-14.95)</td>
</tr>
</tbody>
</table>

TABLE 3: ACUPUNCTURE EXPERIMENT NO 1:

Baseline Whole Body 'Pain Detection Thresholds' and 'Pain Tolerances' (Pain: stimulus durations in seconds): Probability of Observed Correlations ($r_*$) Between Each Pair of Experimental Treatment Conditions; and, Probability ($t$ - test) of Differences in Variance Between Each Pair of Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Conditions</th>
<th>'Pain Detection Threshold'</th>
<th>'Pain Tolerance'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline Correlation</td>
<td>Variance Differences</td>
</tr>
<tr>
<td></td>
<td>$r_*$</td>
<td>$P$</td>
</tr>
<tr>
<td>Control v Pseudo-Ac.</td>
<td>0.713</td>
<td>$&lt; 0.005$</td>
</tr>
<tr>
<td>Control v Genuine Ac.</td>
<td>0.757</td>
<td>$&lt; 0.005$</td>
</tr>
<tr>
<td>Pseudo Ac. v Genuine Ac.</td>
<td>0.543</td>
<td>$&lt; 0.05$</td>
</tr>
<tr>
<td>Control v Pseudo-Ac.</td>
<td>0.846</td>
<td>$&lt; 0.0005$</td>
</tr>
<tr>
<td>Control v Genuine Ac.</td>
<td>0.920</td>
<td>$&lt; 0.0005$</td>
</tr>
<tr>
<td>Pseudo-Ac. v Genuine Ac.</td>
<td>0.758</td>
<td>$&lt; 0.005$</td>
</tr>
</tbody>
</table>

* Pearson product moment correlation coefficient.

** $t$ ratio for testing difference between correlated variances (Guilford p193) (159).
for 'P.D.T.' measures; although fortunately this was not the case with the 'Pseudo-Acupuncture' versus 'Genuine Acupuncture' condition comparison. For 'P.T.' measures, only the 'Contr.' and 'Pseudo-Acupuncture' sessions produced a significant difference in variances.

In view of the above findings, the Wilcoxon matched pairs signed-ranks test (391) was applied to test the significance of differences between the whole body baseline values obtained in each experimental condition. Results appear in Table 4 from which it can be seen that the mean differences (seconds) in baselines between different experimental conditions were very small and in no case, for either 'P.D.T.' or 'P.T.' measures, were there significant differences. For interest, matched pairs 't' tests (159) were applied in the same way to the data, and again no significant intersession differences were found. Group median values of baseline 'P.D.T.' and 'P.T.' measures are also presented in Table 2 (b) with ranges, and do not differ significantly from the pattern of means presented above.

(b) Differences between sexes:

Group mean 'P.D.T.' and 'P.T.' baseline values for males (n = 6) and for females (n = 5) were calculated for each experimental condition, using whole body means as the data base. Results are presented in Table 5, from which a clear trend towards greater values for males is evident. When tested (Mann Whitney 'U' test (391)), none of these differences achieved significance. This is not surprising in view of the small sample size.

(c) Differences between body locations:

The group mean 'P.D.T.' and 'P.T.' values for each individual body test location (see Table 2 (a) were ranked in order of
TABLE 4: ACUPUNCTURE EXPERIMENT NO 1:
Baseline Whole Body 'Pain Detection Thresholds' and 'Pain Tolerances' (Pain stimulus durations in seconds): Probability of Observed Differences Between Experimental Treatment Conditions (Wilcoxon matched-pairs, signed-ranks test(391)) and Mean of Differences.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Thresholds</th>
<th></th>
<th>Tolerances</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>P.</td>
<td>Mean</td>
<td>P.</td>
</tr>
<tr>
<td>Control v Pseudo-Ac.</td>
<td>+0.65</td>
<td>N.S.*</td>
<td>+0.76</td>
<td>N.S.</td>
</tr>
<tr>
<td>Control v Genuine Ac.</td>
<td>+0.63</td>
<td>N.S.</td>
<td>+0.48</td>
<td>N.S.</td>
</tr>
<tr>
<td>Pseudo-Ac. v Genuine Ac.</td>
<td>-0.13</td>
<td>N.S.</td>
<td>-0.28</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* p > 0.05

TABLE 5: ACUPUNCTURE EXPERIMENT NO 1:
Baseline 'Pain Detection Thresholds' and 'Pain Tolerances' (Pain stimulus durations in seconds): Group Mean (n = 6 subjects) Whole Body Values for Each Sex in Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Thresholds</th>
<th></th>
<th>Tolerances</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Control</td>
<td>9.86</td>
<td>8.50</td>
<td>12.39</td>
<td>11.87</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>10.37</td>
<td>9.30</td>
<td>13.18</td>
<td>12.61</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>10.55</td>
<td>9.07</td>
<td>13.36</td>
<td>11.73</td>
</tr>
</tbody>
</table>

TABLE 6: ACUPUNCTURE EXPERIMENT NO 1:
Baseline 'Pain Detection Thresholds' and 'Pain Tolerances' (Pain stimulus durations in seconds): Magnitude of Values at Different Body Locations: Mean Rank (1 > 2) For All Experimental Treatment Conditions Combined.

<table>
<thead>
<tr>
<th>Mean Rank (1 &gt; 2)</th>
<th>Body Test Locations</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Thresholds</td>
<td>Left Lower Leg 1</td>
<td>Left Upper Arm 2</td>
<td>Abdomen 3</td>
<td>Right Forearm 4</td>
<td>Chest 5</td>
<td>Right Thigh 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.7</td>
<td>6</td>
<td>1.3</td>
<td>2.7</td>
<td>4</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Tolerances</td>
<td>Left Lower Leg 1</td>
<td>Left Upper Arm 2</td>
<td>Abdomen 3</td>
<td>Right Forearm 4</td>
<td>Chest 5</td>
<td>Right Thigh 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.7</td>
<td>6</td>
<td>1.7</td>
<td>2.7</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
magnitude from greatest (1) to lowest (6) for each experimental condition. Mean (all conditions combined) ranks were then calculated and are presented in Table 6. Clearly location 3 (the abdominal test site) displayed the highest 'P.D.T.' and 'P.T.' values, or in other words was the least sensitive location tested. The implications of this observation are discussed later. The most sensitive location (lowest 'P.D.T.' and 'P.T.' values) was the left upper arm. Although rather more variability of ranking applied to the other locations, a consistent pattern was still evident. The picture is almost identical if the group median values of Table 2 (b) are adopted as the data base.

(2) Session Pain Response Measures:

(a) Shifts in Pain Response Measures WITHIN Sessions: Correction for Baseline Interaction Problems:

Analysis of the session data proceeded through the following stages:-

(i) A measure representative of shifts in 'P.D.T.' during each session was obtained for each body test location, on each subject, during each experimental treatment condition. This was obtained by subtracting the subject's pre-session baseline 'P.D.T.' value from the mean of his six trial values subsequently obtained at the same location during the course of the session.

(ii) A mean representing the magnitude of within-session shift in 'P.D.T.' displayed by the body as a whole was then obtained for each subject, for each session, from his six 'P.D.T.' 'shift-values' (described above).

(iii) 'P.T.' shift-values for each individual body test location, and means for the whole body, were similarly calculated.
(iv) It was clear from an initial examination of all 'shift-values', that progressive increases of both 'Pain Detection Threshold' ('P.D.T.') and 'Pain Tolerance' ('P.T.') measures almost uniformly occurred over time during all three experimental treatment conditions. However, an important problem emerged when the magnitudes of the mean whole-body 'shift-values' for 'P.D.T.', and for 'P.T.', were tested for correlation with baseline heights. As indicated in Table 7, shifts in 'P.T.' correlated significantly with baselines across all three experimental treatment conditions, although only 'Pseudo-Acupuncture' displayed a significant relationship in the case of 'P.D.T.' measures.

It is interesting to note that the correlation is positive, or in other words, the higher the initial baseline the larger the likely subsequent increase in pain response measures. Thus the more initially insensitive a subject, or individual body site, the larger the likely shift towards apparently greater insensitivity during the experimental session. This could be interpreted as indicating that, for thermal stimuli and responses of this type, an initially insensitive (ie. higher baselines) subject, or body site, would require larger shifts (in numerical terms) of 'P.D.T.' or 'P.T.' to reflect the same actual shift in sensitivity as an initially more sensitive (ie. lower baselines) subject, or body site, (displaying smaller numerical shifts in 'P.D.T.' or 'P.T.').

The considerations above become particularly important when it is recalled from Table 6 that the abdominal test site most often displayed the highest baseline values for both 'P.D.T.' and 'P.T.'. Since a major hypothesis of the experiment was based upon disproportionate elevation of pain measures at the abdominal test site, appropriate correction for baseline effects was essential if
<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Thresholds</th>
<th>Tolerances</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r.*</td>
<td>2P.</td>
</tr>
<tr>
<td>Control</td>
<td>0.51</td>
<td>N.S.</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>0.74</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>0.49</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Pearson test
the hypothesis was not to receive artifactual support. Such a correction would also serve to adjust for the small overall differences between the mean baselines of the different experimental treatment conditions.

From this point onwards the data was completely analysed twice by two different methods.

The preliminary analysis proceeded by proportional arithmetic correction of all data from needle sessions. This standardised the baselines of the 'Genuine' and 'Pseudo-Acupuncture' conditions so that they equalled the corresponding baseline values for each body location in the 'Control' session, and thus allowed direct comparison of subsequent trial values at corresponding stages during the three conditions.

Subsequent analysis of differences between the three experimental treatment conditions in terms of shifts of pain response measures was undertaken entirely by non-parametric statistical test procedures. The analysis and results will not be described here, both since they are fully presented elsewhere and because the findings were almost identical to the more sophisticated secondary analysis undertaken, which is described directly below.

(v) Although the 'Control' session data was employed as the standardisation basis for correction procedures in the preliminary analysis, the decision was taken here to exclude these data from consideration for reasons discussed below.

First, with hindsight, the decision to invariantly present the 'Control' condition to subjects first, whilst balancing the order only of the two Acupuncture conditions, was considered methodologically problematic. Despite the fact that a fully balanced order design
would have resulted in cells containing only 4 subjects (2 male), and, of course, the 'Control' procedures could not be considered fully matched to the needle sessions, it would probably have been a preferable procedure. During the preliminary analysis it became clear that significant differences in pain measure shifts between the 'Control' condition and the two needle conditions might be attributable to either treatment or session order effects, without hope of proper differentiation. Certainly the differences were probably too large to be accounted for entirely by order effects, particularly as the 'Control' versus 'Genuine Acupuncture' difference was significantly greater than the 'Control' versus 'Pseudo-Acupuncture' comparison. In addition, the proportional correction procedure would have removed the possible order effect component in baselines which may be indicated by the slightly lower whole body mean baselines evident for the 'Control' condition (see Table 2(a)). Notwithstanding this, tests* for order effects indicated significant differences between the treatments administered first and second for both 'P.E.T.' ($\chi^2 = 0.008$) and 'P.T.' ($p = 0.003$).

Thus, taking data from only the two fully matched, balanced order, Acupuncture sessions for comparison, all 'P.D.T.' and 'P.T.' values were separately adjusted in respect of differences in baselines between the two conditions at each body test location, by application of a regression equation. The procedure of choice was clearly the covariance method available within the Statistical Package for the Social Sciences (S.P.S.S.**) (334). Within this programme, regression

- Wilcoxon Signed-Ranks, Matched-Pairs test (391).

** Programming by kind courtesy of Dr. P. Miller, M.R.C. Unit for Epidemiological Studies in Psychiatry, Edinburgh.
procedures were employed to remove variation in the dependent variable ('P.D.T.' or 'P.T.') due to the baseline covariate, and a conventional analysis of variance was subsequently performed on the corrected scores. 'P.D.T.' and 'P.T.' were, of course, treated separately.

(b) Differences in Pain Response Measures Between Experimental Treatment Conditions: Whole Body Summary Data:

(i) The grand overall output summary for the analysis of covariance appears as Table 8 (a) and (b) Page q1, from which it can be seen that all the main effects (experimental condition, body test location, temporal test point, and subjects) display highly significant differences for both 'P.D.T.' and 'P.T.'. Further detailed analysis was clearly merited.

(ii) First, group (n = 12) mean 'P.D.T.' and mean 'P.T.' values* were computed for the body as a whole, at each of the six post-baseline temporal test points, during the two experimental treatment conditions. These values are plotted in Fig. 16 Page q2, from which a number of preliminary comments can be made. First, as expected from the analysis of covariance, the 'Genuine Acupuncture' treatment produces elevations above 'Pseudo-Acupuncture' levels for both 'P.D.T.' and 'P.T.' measures. These elevations are ubiquitous over time for both measures, although 'P.T.' effects appear more marked.

All curves display relatively smooth progressive increments over time. Since this trend was also evident in all raw data (including the 'Control' condition not included in this analysis), it may be viewed as characteristic simply of the mechanics of the pain generating and measuring methodology employed, rather than as treatment related. Thus, the time course of 'Acupuncture analgesia' must be discriminated against this background.

* After correction.
TABLE 8: ACUPUNCTURE EXPERIMENT NO 1:
Analysis of Covariance: Grand Overall Output
Summary Table:

(a) Pain Detection THRESHOLD

<table>
<thead>
<tr>
<th>Source</th>
<th>S.S.</th>
<th>d.f.</th>
<th>M.S.</th>
<th>F.</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariates:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (Thresholds)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main Effects:</td>
<td>6255.211</td>
<td>22</td>
<td>284.328</td>
<td>18.691</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experimental Condition</td>
<td>104.495</td>
<td>1</td>
<td>104.495</td>
<td>6.869</td>
<td>&lt;0.009</td>
</tr>
<tr>
<td>Body Test Location</td>
<td>507.334</td>
<td>5</td>
<td>101.467</td>
<td>6.670</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temporal Two Point</td>
<td>1616.353</td>
<td>5</td>
<td>323.271</td>
<td>21.250</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subjects</td>
<td>4200.797</td>
<td>11</td>
<td>381.891</td>
<td>25.104</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>35535.449</td>
<td>863</td>
<td>41.177</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(b) Pain TOLERANCE

<table>
<thead>
<tr>
<th>Source</th>
<th>S.S.</th>
<th>d.f.</th>
<th>M.S.</th>
<th>F.</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariates:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (Tolerances)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main Effects:</td>
<td>5917.809</td>
<td>22</td>
<td>268.991</td>
<td>15.050</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experimental Condition</td>
<td>221.600</td>
<td>1</td>
<td>221.600</td>
<td>12.398</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body Test Location</td>
<td>381.349</td>
<td>5</td>
<td>76.279</td>
<td>4.267</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temporal Two Point</td>
<td>1870.388</td>
<td>5</td>
<td>374.078</td>
<td>20.929</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subjects</td>
<td>3104.422</td>
<td>11</td>
<td>283.220</td>
<td>15.790</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>63029.996</td>
<td>863</td>
<td>73.036</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FIG. 16: ACUPUNCTURE EXPERIMENT NO. 1:

WHOLE BODY:
Group (n = 12) Mean Pain Detection THRESHOLD and Pain TOLERANCE (mean stimulus duration in sec.) Over 1 Hour During 'Genuine Acupuncture' and 'Pseudo-Acupuncture' Experimental Conditions.
(Values adjusted for baseline covariate)
Given this, several points may be noted. First, for both pain measures, 'Genuine Acupuncture' curves rise more steeply than 'Pseudo-Acupuncture' curves until removal of the Acupuncture needles. After this the gradients become similar, although residual height differences remain. Secondly, 'P.D.T.' 'Pseudo-Acupuncture' measures exhibit a marked dip at the first test point (40 min.) after needle removal. This may perhaps represent a psychological* response to needle withdrawal, rather than loss of some analgesic effect present, since the curve recovers thereafter. It is interesting, however, that the same effect is not present for the 'P.T.' measure. Similar marginal dips at 40 minutes may perhaps be present in the 'Genuine Acupuncture' curves (especially 'P.T.'), but it is impossible to differentiate these from the general reduction of gradients.

It is also relevant to note the close similarity of curve shape for 'Genuine Acupuncture' 'P.D.T.' and 'P.T.' values.

(iii) Next, differences in the above group mean 'P.D.T.' and 'P.T.' values between the two experimental conditions were calculated for each temporal test point. They appear in Table 9 (a) and (b) Page 94 and, as it is difficult to meaningfully interpret the differences between the conditions expressed in seconds, the values were also converted to percent elevations of 'Genuine Acupuncture' values above the corresponding 'Pseudo-Acupuncture' values at each temporal test point. These results appear both in Table 9(a)(b) Page 94 and are graphed in Fig. 17 Page 95. This figure permits direct comparison of the temporal progression of 'P.D.T.' and 'P.T.' measures, since both are expressed as percentage elevations of 'Genuine Acupuncture' values above the corresponding 'Pseudo-Acupuncture' levels, the latter being adopted as

* This might include distractive or counter-irritation considerations.
TABLE 9: ACUPUNCTURE EXPERIMENT NO 1: WHOLE BODY:

Group (n = 12) Mean 'Pain Detection Thresholds' and 'Pain Tolerances' (adjusted for baseline covariate) Over 1 Hour Experimental Treatment Conditions: Differences Between 'Genuine Acupuncture' and 'Pseudo-Acupuncture' Conditions. (+ve values indicate Gen.Ac. Pseudo-Ac.)

(a) Pain THRESHOLD

<table>
<thead>
<tr>
<th>Test Point (minutes)</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference</td>
<td>0.39</td>
<td>0.51</td>
<td>0.99</td>
<td>1.38</td>
<td>0.41</td>
<td>0.50</td>
</tr>
<tr>
<td>Seconds</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>3.77</td>
<td>4.93</td>
<td>9.12</td>
<td>12.19</td>
<td>3.18</td>
<td>4.16</td>
</tr>
</tbody>
</table>

(b) Pain TOLERANCE

<table>
<thead>
<tr>
<th>Seconds</th>
<th>0.73</th>
<th>1.21</th>
<th>1.42</th>
<th>1.01</th>
<th>0.88</th>
<th>0.79</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>5.68</td>
<td>8.04</td>
<td>8.73</td>
<td>6.17</td>
<td>4.93</td>
<td>4.67</td>
</tr>
</tbody>
</table>
FIG. 17: ACUPUNCTURE EXPERIMENT NO. 1:
WHOLE BODY:
Group (n = 12) Mean Pain THRESHOLD and Mean Pain TOLERANCE Over 1 Hour:
(Values Adjusted for Baseline Covariate).
Plotted as Mean % Elevation of Genuine Acupuncture Values Above Pseudo-Acupuncture "zero" baseline.

---

### Graph Details

- **Y-axis:** Mean difference (\%) between experimental conditions
- **X-axis:** Time (mins)
- **Legend:**
  - Needles inserted
  - Needles removed
  - Pain threshold
  - Pain tolerance

---
zero baselines. Also, in effect, the curves represent visualisation of the time course for 'Acupuncture analgesia' with removal of the effects of suggestive components (as represented by 'Pseudo-Acupuncture'), and routine changes over time independent of treatments.

Several observations may be made from Fig. 17 (Page 95). First, for both 'P.D.T.' and 'P.T.' measures, there is a clear progressive onset of analgesia during the first half of the 'Genuine Acupuncture' condition (i.e. whilst Acupuncture stimulation was in progress) and a progressive** decline thereafter. Interestingly, however, 'P.D.T.' displays peak analgesia at the 40 minute test point, or in other words, 10 minutes after removal of the needles, whilst 'P.T.' elevations are at their maximum immediately prior to removal of the Acupuncture needles.

It is difficult to determine whether this is a mere statistical artifact or represents a meaningful difference between 'P.D.T.' and 'P.T.' responses to Acupuncture, in view of a number of considerations evident from Fig. 16 (Page 92). First, the 'Genuine Acupuncture' 'P.D.T.' an' 'P.T.' curves are extremely similar in shape overall. Thus the major contribution to the peak difference in 'P.D.T.' between the experimental conditions at 40 minutes comes from the sudden dip in 'Pseudo-Acupuncture' values already mentioned, and several interpretations may be placed upon this.

If, as already suggested, it is viewed as a temporary psychological aberration, and a hypothetical line (see Fig. 16 (Page 92) is drawn from the 20 minute to 40 minute points, the curve becomes virtually linear (like the 'Pseudo-Acupuncture' 'P.T.' curve). The largest difference between conditions would then occur at 30 minutes*** (again in line with 'P.T.' results).

** This is precipitate for 'P.D.T.' owing to the aggrandised peak, the origin of which is discussed later.

*** It must, however, be noted that the 40 minute difference value would be only 2% less.
An alternative approach would accept the dip as meaningfully informative of a different 'P.D.T.' and 'P.T.' response pattern. The lack of a similar visual dip for 'P.D.T.' 'Genuine Acupuncture' values might even be viewed as indicative of its analgesic potency since, assuming the same psychological (or other) mechanism applies, the 'Genuine Acupuncture' curve might otherwise display an elevatory salience at 40 minutes (see hypothetical curve Fig. 16 Page 92). As will be seen later there is evidence for this at the most important individual body site. Unfortunately the problem cannot be resolved so readily, as later evidence also indicates that the whole body data is subject to diverse influences which must inevitably generate these problems in assessing the exact time course of 'Genuine Acupuncture' analgesia. It may at least be stated with certainty that in this experiment the peak occurs approximately 30-40 minutes after onset of stimulation. This does not, of course, rule out the possibility of a higher analgesic peak at a later time had Acupuncture stimulation been continued after the third thermal stimulus trial.

On first inspection of Fig. 17 Page 95, it would appear that 'P.D.T.' was the more volatile pain measure in view of its peak analgesic response to 'Genuine Acupuncture'. This would be of interest in terms of traditional assumptions of greater 'P.T.' responsiveness. In fact, however, the differences between percentage elevations of 'P.D.T.' and of 'P.T.' in response to 'Genuine Acupuncture' were not significant (t = 0.109 N.S.), and the overall analysis of covariance reported above suggests that, overall, 'P.T.' was slightly more affected. In addition, the problems discussed earlier concerning the interpretation of the P.D.T. peak elevation, render any suggestion of differences as purely speculative.

Finally it must be said that, although statistically significant overall, the analgesic effects of 'Genuine Acupuncture' beyond those of placebo may be relatively minor, since the largest elevation is only 12.19%.
(c) Differences in Pain Response Measures Between Experimental Treatment Conditions: Individual Body Test Location Data:

Analysis proceeded to investigation of the significant body test location factor reported initially in the overall summary analysis of covariance.

(i) As a preliminary stage in examination of the data for individual body test locations, and to assist in interpretation of later stages of analysis, Figs. 18 (a) and (b) Pages 97 and 100 were prepared. These figures display the group \( n = 12 \) mean 'P.D.T.' and 'P.T.' values respectively, for each 10 minute test point, over the one hour time course of the 'Genuine Acupuncture' and 'Pseudo-Acupuncture' conditions, at each separate body test location.

Several general trends are evident. First, in all cases, both pain measures display the expected gradual increase in values (ie. higher thresholds and tolerances) over the whole time course of the session; but, for some reason, this pattern is rather less pronounced at the thigh location than elsewhere on the body.

Also, with a few notable exceptions, the expected analgesic shifts during 'Genuine Acupuncture' were evident, and the distribution is examined below.

(ii) Group \( n = 12 \) mean (all time points combined) differences in 'P.D.T.' and 'P.T.' between the two conditions were computed, and analysis of covariance completed, for each of the six individual body test locations. The results appear in Table 10 Page (10), in which the different loci are also ranked for overall superiority (taking

* After correction for baseline covariates.

** This was also characteristic of the 'Control' condition, without needle insertion, when examined in the preliminary analysis of the data reported elsewhere [415].
FIG. 18(a) ACUPUNCTURE EXPERIMENT No. 1:
Group (n = 12) Mean Pain THRESHOLDS
(Mean stimulus duration in sec.) Over 1 Hour,
at Different Body Locations.
(Values adjusted for baseline covariate)
(Common scaling)

Key:
- Genuine Acupuncture
- Pseudo-Acupuncture
N.I. = Needles Inserted
N.R. = " Removed

* (Intensity rises with duration)
FIG. 18(b) ACUPUNCTURE EXPERIMENT No. 1:
Group (n=12) Mean Pain TOLERANCES
(Mean stimulus duration in sec.) Over 1 Hour,
at Different Body Locations.
(Values adjusted for baseline covariate)
(Common scaling).

ABDOMEN

CHEST

FOREARM

THIGH

UPPER ARM

LOWER LEG

TIME (1 Hour)

* (Intensity rises with duration) Key: 
• —— Genuine Acupuncture
□ —— Pseudo-Acupuncture
N.I. = Needles Inserted
N.R. = " Removed
**TABLE 10: ACUPUNCTURE EXPERIMENT NO. 1:**

**PAIN THRESHOLD AND PAIN TOLERANCE:**

Group (n = 12) Mean Differences (sec.) Between Genuine and Pseudo-Acupuncture Values at Each Body Location:

(+ ve values Gen. Ac. > Pseud. - Ac.)

(Values adjusted for baseline covariate).

<table>
<thead>
<tr>
<th>Overall Rank</th>
<th>Test Location</th>
<th>Pain Threshold</th>
<th>P*</th>
<th>Pain Tolerance</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abdomen</td>
<td>1.70</td>
<td>0.003</td>
<td>1.96</td>
<td>0.001</td>
</tr>
<tr>
<td>2</td>
<td>Chest</td>
<td>1.02</td>
<td>N.S.</td>
<td>1.38</td>
<td>0.017</td>
</tr>
<tr>
<td>3</td>
<td>Right forearm</td>
<td>1.26</td>
<td>0.020</td>
<td>-0.04</td>
<td>N.S.</td>
</tr>
<tr>
<td>4</td>
<td>Right thigh</td>
<td>1.32</td>
<td>0.008</td>
<td>-0.40</td>
<td>N.S.</td>
</tr>
<tr>
<td>5</td>
<td>Left upper arm</td>
<td>-0.04</td>
<td>N.S.</td>
<td>0.70</td>
<td>N.S.</td>
</tr>
<tr>
<td>6</td>
<td>Left lower leg</td>
<td>-1.08</td>
<td>0.037</td>
<td>0.42</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

*Analysis of covariance*
'P.D.T.' and 'P.T.' together) of 'Genuine Acupuncture' values above 'Pseudo-Acupuncture' values.

It is completely clear from Table 10 that the major hypothesis of the study, namely the predicted disproportionate elevation of pain measures at the abdominal test site, receives highly significant support. The abdomen displays the largest and most significant elevations of both 'P.D.T.' and 'P.T.' during 'Genuine Acupuncture'. Overall, the thoracic location displayed the next largest elevations, although 'P.D.T.' shifts alone just failed to achieve significance. Only one significant negative shift appears at the lower leg, and the bipolar response of this site is examined further later. Again it must be said that even the largest differences are probably rather small in terms of clinical significance, even if statistically significant.

(iii) In order to assist visualisation and interpretation of the above results for individual body sites, the values were converted, as before, to mean percent elevations of 'Genuine Acupuncture' values above 'Pseudo-Acupuncture' levels. Again this also permits direct comparison of effects on 'P.D.T.' and on 'P.T.'.

The results, undifferentiated for points in time, are presented as histograms in Fig. 19, from which the following observations may be derived. The abdomen and chest clearly display the largest 'P.T.' elevations, with smaller analgesic effects on the upper arm and lower leg. The thigh and forearm display negligible reductions below 'Pseudo-Acupuncture' levels.

For 'P.D.T.', again the abdomen exhibits the greatest elevation. However, it is closely followed by thigh values. Forearm 'P.D.T.' measures are clearly elevated, in contrast to their small decrement evident with 'P.T.'; whilst conversion of the chest 'P.D.T.'
FIG. 19: ACUPUNCTURE EXPERIMENT NO. 1:

Pain Threshold and Pain Tolerance:

Group (n = 12) Mean % Differences Between Genuine and Pseudo-Acupuncture at Each Body Location

(+ve values Gen. Ac. > Pse nd.-Ac.)

PAIN THRESHOLD

% difference between conditions

Abdomen Chest Thigh Forearm

0.0

10.0

PAIN TOLERANCE

Abdomen Chest

Upper arm Lower leg

0.0

-5.0

-10.0

Forearm

Thigh

Upper arm Lower leg
elevations to percentage figures in fact generates values larger than those occurring with 'P.T.' (i.e., reverses the order evident from the values expressed as seconds). The lower leg displays marked reduction of 'P.D.T.' compared to the 'Pseudo-Acupuncture' condition, in contrast to a small positive 'P.T.' difference, whilst the upper arm exhibits negligible reductions.

(iv) Abdominal Measures: Time Course of 'Acupuncture Analgesia':

In order to observe the time course of analgesic elevations during the 'Genuine Acupuncture' condition at the test location of focal interest, namely the abdomen, the percent elevations of 'P.D.T.' and 'P.T.' measures above levels prevailing at the corresponding points in the 'Pseudo-Acupuncture' condition were plotted against time, as illustrated in Fig. 20. Again a number of observations may be made.

First, the pattern characteristic for the overall body results, of progressive elevation during the first half of the session, followed by progressive decline in the second half after needle removal, is again evident for both measures. This time, however, it is 'P.T.' which peaks 10 minutes after removal of the needles. However, since a sub-peak, which is only slightly inferior, occurs 20 minutes earlier, and the 'P.T.' maximal elevation for the body as a whole (see Fig. 17) occurs 10 minutes earlier, it is difficult to interpret this observation as meaningful with certainty.

The problem is, however, clarified by the additional information available from the Fig. 18 (b) abdominal 'P.T.' plot. As both 'Genuine Acupuncture' and 'Pseudo-Acupuncture' values (rather

* It should be noted that this graph has a truncated scale at the lower end for space economy.
FIG. 20: ACUPUNCTURE EXPERIMENT NO. 1:

ABDOMEN:
Group (n = 12) Mean Pain THRESHOLD and Mean Pain TOLERANCE Over 1 hour:
(Values adjusted for baseline covariate)
Plotted as Mean % Deviation of Genuine Acupuncture Values Above
Pseudo-Acupuncture Values.
Key: —— = Pain Threshold
     —— = Pain Tolerance
than differences between the two) are simultaneously plotted, it is possible to determine whether apparent elevations of 'Genuine Acupuncture' values evident from Fig. 20 Page 105 might, in fact, derive partially, or wholly, from marked deviations of the 'Pseudo-Acupuncture' curve from its general shape. Furthermore the relative salience of any time point on either curve may be assessed visually in relation to the overall curve shape.

In this case the maximal elevation of 'Genuine Acupuncture' 'P.T.' values above the corresponding 'Pseudo-Acupuncture' levels at the 40 minute point is definitively not attributable to any deviation in the 'Pseudo-Acupuncture' curve, since it is virtually linear at this point in Fig. 18 (b). Similarly the 40 minute 'Genuine Acupuncture' peak appears to represent a salient elevation above the general shape of the curve. For both these reasons, it would appear reasonable to cautiously accept the 'P.T.' peak as providing meaningful information.

It is also important to note from Figs. 18 (a) and (b) Pages 99 and 100, that, viewed in terms of overall curve shape, 'P.D.T.' may also be peaking at 40 minutes in the 'Genuine Acupuncture' condition. As it is plain that the 'P.D.T.' and 'P.T.' curves are virtually identical in shape, the clear cut peaking of 'P.D.T.' at 40 minutes may, therefore, support a similar conclusion for 'P.D.T.'.

In addition, the apparently aberrant dip in 'P.D.T.' values at 30 minutes in the 'Pseudo-Acupuncture' condition must very largely account for the peak difference between the conditions occurring at this time point in Fig. 20 Page 105. The aberrant description receives support from two major considerations evident from Figs. 18 (a) and (b). First, the dip is not evident for 'P.T.' values.
Second it may not be attributed to any change in the experimental environment such as, in particular, removal of the Acupuncture needles. As needles were removed after the 30 minute test point, any psychological effect should be evident at the 40 minute rather than 30 minute test. It will be recalled that this is indeed what occurred with 'P.D.T.' values for the body overall (see Fig. 16 Page 92).

In continuing to describe Fig. 20 Page 105, a sharp fall off in both 'P.D.T.' and 'P.T.' Genuine Acupuncture analgesia is evident at the 50 minute test point. This is particularly precipitate for 'P.D.T.' Both pain measures then display a marked recovery. Again reference to Figs. 18 (a) and (b) suggests that neither the reduced elevation of 'Genuine Acupuncture' above 'Pseudo-Acupuncture' at 50 minutes, nor the major part of the recovery at 60 minutes in Fig. 20 Page 105, may be attributed to aberrations in the 'Pseudo-Acupuncture' curve.

The overall pattern of the 'Genuine Acupuncture' abdominal 'P.D.T.' and 'P.T.' curve shapes (Figs. 18 (a) and (b)) is rather suggestive of a progressively increasing analgesia, peaking at 40 minutes, and followed by a slight oscillatory bounce and level-off, visually reminiscent of the type of record often obtained with electrodermal responses.

Fig. 20 Page 105 also indicates that, although the curves for 'P.D.T.' and 'P.T.' are very similar in shape, 'P.T.' displays a rather larger, and perhaps more rapid, analgesic response to 'Genuine Acupuncture' (in percentage terms) than 'P.D.T.' overall**. The differences are relatively small (mean difference 'P.T.' - 'P.D.T.' = 6.86%),

** This is also evident from Figs. 18 (a) and (b) Page 99 and 100.
but they only just fall short of significance for a two-tailed test ($t = 2.278 \quad P < 0.10$).

Finally, it is important to note that the percent elevations of pain measures during 'Genuine Acupuncture' above 'Pseudo-Acupuncture' levels are much more substantial at the abdominal test site than for the body as a whole. Abdominal 'P.D.T.' and 'P.T.' elevations peak at 25% and 27% respectively, whilst the comparable whole body peak values achieve only 12% and 9%.

(v) Lower Leg Measures:

Of all individual body test sites, only the left lower leg displayed a significant negative (ie. hyperalgesic) shift of a pain measure during 'Genuine Acupuncture' relative to 'Pseudo-Acupuncture'.

The percent elevations, and reductions, for 'P.T.' and 'P.D.T.' respectively, at this site during 'Genuine Acupuncture' are graphed over time in Fig. 21. 'P.T.' values display a progression essentially compatible with changes observed at the other body sites. 'P.D.T.' values, however, display an entirely contradictory pattern of marked hyperalgesia relative to 'Pseudo-Acupuncture' levels, although it is clear from Fig. 18 (a) that the normal progressive increase of 'P.D.T.' over time still occurred.

The effect would appear related to the Acupuncture stimulation since it peaks at 30 minutes (ie. immediately prior to needle removal), and progressively declines thereafter as a virtual mirror image of the normal pattern exhibited by 'P.T.'.

Evidence is reported later which indicates that a local area of hyperalgesia may extend around electrically stimulated cutaneous sites (179). Although this usually, however, develops mainly in a proximal* direction, there is often some distal spread, which is

* With an overlapping area of hypoalgesia extending distally.
FIG. 21 : ACUPUNCTURE EXPERIMENT NO. 1: LOWER LEG:
Group (n = 12) Mean Pain THRESHOLD and Mean Pain TOLERANCE Over 1 Hour:
(Values adjusted for baseline covariate)
Plotted as Mean % Deviation of Genuine Acupuncture Values from Pseado-Acupuncture Values.
Key: ■ = Pain Threshold
□ = Pain Tolerance

MEAN % DIFFERENCE BETWEEN 0.0 EXPERIMENTAL CONDITIONS

PSEUDO-ACUPUNCTURE ZERO BASELINE

Needles Inserted
Needles Removed
TIME (mins)
probably sufficient to take in the only slightly distal placing of the thermal stimulus unit relative to the 'Genuine Acupuncture' needle site in the lower leg. The fact that the effect did not apply to 'P.T.' values could suggest that 'Genuine Acupuncture' had more attenuating effect upon more intense noxious sensations.

This conclusion would not be supported by results for the right forearm (Table 10 Page 10). Although this was the thermal stimulus site next closest to an Acupuncture needle, bipolar effects in the opposite direction occurred. However, since the negative shift is tiny, the latter pattern must be viewed merely as non-supportive, rather than contradictory, to the interpretation.

The only site, other than the lower leg, displaying even moderate negative shifts was the right thigh for 'P.T.' measures. As the right thigh thermal stimulus was close to a 'Pseudo-Acupuncture' needle site, a local hypoalgesic action might have been invoked as an explanation, were it not for the fact that the left upper arm, also close to a 'Pseudo-Acupuncture' needle, displays opposite shifts.

One may only conclude that contradictory and interesting effects occur at the left lower leg thermal stimulus site, but interpretation cannot be assisted by any relevant consistent patterns elsewhere on the body.

(d) Pain Response Measures**: Sex Differences

The covariance method was applied to test for sex differences in the post-baseline mean 'P.D.T.' and 'P.T.' measures for 'Pseudo-Acupuncture' and 'Genuine Acupuncture' conditions. Neither 'P.D.T.' (F = 1.823 d.f. = 1,9, N.S.) nor 'P.T.' (F = 0.088 d.f. = 1,9, N.S.) exhibited significant sex differences.

* Of all thermal stimulus units, this was the most closely placed to a needle during 'Genuine Acupuncture' sessions.
** After baseline correction by the covariance method, male mean whole body baselines and variances for both 'P.D.T.' and 'P.T.' still exceeded those of females. However no significant differences were observed in any case.
(e) Pain Response Measures: Relationship to Subjective Rating Scale Scores and Post-Experimental Interview Reports:

All visual analogue scales appearing in Fig. 3 (i) to (iv) were scored 0-10 (to nearest 0.5) and analysed as below.

(i) Subjects' pre-session predictions of the degree of effect (if any, they expected the Acupuncture procedures to have on their pain sensitivity were scored on scale (i) Fig. 3 and group mean results appear in Table 11 (a).

It is immediately clear that the subject group did not volunteer because they believed greatly in the efficacy of Acupuncture for pain relief. Although these subjects who predicted any change at all as a result of Acupuncture indicated a reduced sensitivity outcome (almost entirely based on media information), the grand mean score for the group, over both experimental conditions, was only 2.56, and there was virtually no difference between the group means for the two different experimental treatment conditions.

There would also appear to be little in the way of order effects, although it is interesting to note that on entering the 'Pseudo-Acupuncture' condition after experiencing 'Genuine Acupuncture', subjects tended to predict slightly more analgesic effect than subjects receiving the opposite sequence. In addition, on entering the 'Genuine Acupuncture' condition, after passing through 'Pseudo-Acupuncture' first, subjects appeared to have slightly reduced expectation of effectiveness. These observations could be indicative of subjects experiencing 'Genuine Acupuncture' as more impressive or potent in some way. However, as these differences are no larger than those between the scores for the two experimental conditions when experienced first, the interpretation is questionable.

* S.D.'s were also uniformly small.
TABLE 11: ACUPUNCTURE EXPERIMENT NO 1:
Subjective Rating Scales:

(a) Group (n = 12) Mean Pre-Session Predictions, and Post-Session Estimates of Analgesia During 'Pseudo-Acupuncture' and 'Genuine Acupuncture' Experimental Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition (Order)</th>
<th>Pre-Session Predictions</th>
<th>Post-Session Estimates</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudo-Ac. (1st)</td>
<td>2.25</td>
<td>1.75</td>
<td>-0.5</td>
</tr>
<tr>
<td>(2nd)</td>
<td>2.75</td>
<td>1.75</td>
<td>-1.0</td>
</tr>
<tr>
<td>Mean</td>
<td>2.50</td>
<td>1.75</td>
<td>-0.75</td>
</tr>
<tr>
<td>Genuine Ac. (1st)</td>
<td>3.00</td>
<td>2.25</td>
<td>-0.75</td>
</tr>
<tr>
<td>(2nd)</td>
<td>2.25</td>
<td>1.50</td>
<td>-0.75</td>
</tr>
<tr>
<td>Mean</td>
<td>2.62</td>
<td>1.87</td>
<td>-0.75</td>
</tr>
<tr>
<td>Grand Mean</td>
<td>2.56</td>
<td>1.81</td>
<td>-0.75</td>
</tr>
</tbody>
</table>

(b) Correlation (rₚ) With Elevations (%) of Whole Body 'Pain Detection Thresholds' and 'Pain Tolerances' Above Baselines, During 'Pseudo-Acupuncture' and 'Genuine Acupuncture' Experimental Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Predictions</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rₛ Threshold</td>
<td>rₛ Threshold</td>
</tr>
<tr>
<td></td>
<td>Tolerance</td>
<td>Tolerance</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>0.43</td>
<td>0.12</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>0.24</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* p < 0.025
** p < 0.001
Pre-session predictions were tested for correlation with percentage elevations of whole body 'P.D.T.' and 'P.T.' values above baselines (corrected data), without significant result (see Table 11(b)). It is, however, interesting, and surprising, to note that 'P.D.T.' values appear to be more related to predictions than are 'P.T.' values. There is also a more expected suggestion of greater relationship for the 'Pseudo-Acupuncture' condition.

(ii) Post-Session Estimates:

Subjects' post-session estimates of the degree of analgesia (if any) they experienced during testing in the two experimental conditions were scored on Scale (iv) Fig. 3, and group mean results appear in Table 11(a). Again it is evident that subjects not only remained unimpressed, but in fact uniformly rated the analgesic efficacy of Acupuncture slightly more poorly (grand mean** 1.81) than at the beginning of the sessions***. Differences between the mean estimates for the two experimental conditions are again negligibly, suggesting, somewhat contrary to indications noted in the previous section (i), that subjects were unable to discern any difference between the 'effects' of the two treatments.

---

* Spearman test.
** S.D.'s were also uniformly small.
*** All subjects (except two after 'Genuine Acupuncture') who indicated any change as a result of the Acupuncture procedures, did at least continue to report reduced, rather than increased, sensitivity. This is not surprising, however, in view of the progressive trend towards higher 'P.D.T.' and 'P.T.' values over time during all sessions (including 'Control' sessions without needles) simply as a result of the mechanics of the pain testing techniques themselves.
No order effects are discernible, and little may be noted from the changes between prediction and estimate scores, other than perhaps again a very tentative indication of more negative appraisal of 'Pseudo-Acupuncture' when experienced after 'Genuine Acupuncture'.

Tests for correlation of post-session estimates with percent changes in pain measures provided significant information (see Table 11(b) Page 12). 'P.D.T.' measure correlations were highly significant, but 'P.T.' correlations, although also displaying larger coefficients than were the case with pre-session predictions, remained smaller than 'P.D.T.' results and failed to achieve significance.

From the overall prediction and estimate correlation pattern a few tentative inferences may be made. As the 'Pseudo-Acupuncture' condition pain measures correlate with both predictions and estimates more highly than do 'Genuine Acupuncture' measures, this may indicate failure of subjects to discern purely sensory analgesic effects of Acupuncture when present. In other words, where attitudinal factors (i.e., suggestion) probably constitute the overwhelming proportion of the effects of a treatment upon pain measures, subjects' predictions and estimates would be expected to be automatically self-fulfilling and hence correlate well with pain measures. There are such indications for 'Pseudo-Acupuncture'.

In the presence of a true sensory component of treatment, predictions would be likely to correlate poorly with pain measures and, although post-session estimates would be more accurate than predictions, they could suffer decrement due either to failure to discern analgesic sensory shifts* if slight, or to monitoring confusion resulting from

* Although these would be expected to be evident from analysis of pain response measures, this does not automatically imply conscious awareness of the changes on the part of the subjects.
the reduced sensitivity of the sensory apparatus itself. It will be noted that 'Genuine Acupuncture' correlations are, in fact, reduced in a pattern appropriate to these interpretations.

It is difficult to know why 'P.D.T.' measures should be assessed much more successfully than 'P.T.'. However, as the 'P.D.T.' point was fairly precisely defined in terms of identifying sensory experiences, compared to the open-ended 'P.T.' point, this may have been of assistance to subjects in monitoring their own progress. There is support for this in section (v)(iii) below.

(iii) Local Maximal Acupuncture Effects: Differences Between Body Test Locations.

Subjects' post-session indications (if any) of individual body test locations displaying most change in sensitivity were obtained from section (iv) Fig. 3 Page 56. Results appear in Table 12 Page 116 as total frequencies of report of maximal effect (analgesic (+) or hyperalgesic (-)) at each body test location during the two experimental conditions.

It appears that subjects were slightly more prepared to report particular local effects (one subject even reported two sites) after 'Genuine Acupuncture' than following 'Pseudo-Acupuncture', and this is suggestive of ability to detect differences of some type in their responses to the two treatments. The origin of these possible differences is unclear, however, since subjects both failed* to significantly increase their mean rating of effectiveness (Table 11 (a)), and displayed reduced predictive and estimative ability (Table 11 (b)) under 'Genuine Acupuncture'.

---

* This is due partly to reports of slight hyperalgesia by two subjects.
TABLE 12: ACUPUNCTURE EXPERIMENT NO 1:
Subjective Rating Scales: Frequency of Report of Maximal Analgesia (+) or Hyperalgesia (-) at Each Body Test Location, During 'Pseudo-Acupuncture' and 'Genuine Acupuncture' Experimental Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Body Test Location</th>
<th>Lower Leg</th>
<th>Upper Arm</th>
<th>Abdomen</th>
<th>Forearm</th>
<th>Chest</th>
<th>Thigh</th>
<th>( \xi )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudo-Ac.</td>
<td></td>
<td>-</td>
<td>-</td>
<td>+1</td>
<td>+3</td>
<td>+2</td>
<td>+1</td>
<td>+7</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td></td>
<td>+3</td>
<td>+1</td>
<td>+2</td>
<td>+3</td>
<td>+2</td>
<td>+1</td>
<td>+11</td>
</tr>
</tbody>
</table>

TABLE 13: ACUPUNCTURE EXPERIMENT NO 1:
Objective Rating Scales: Group (n = 12) Mean Intensity Ratings for 'Pseudo-Acupuncture' and 'Genuine Acupuncture' Stimulation.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Needles Alone</th>
<th>Needles + Electrical Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudo-Ac.</td>
<td>1.2</td>
<td>6.0</td>
</tr>
<tr>
<td>Genuine Ac.</td>
<td>2.8</td>
<td>6.5</td>
</tr>
</tbody>
</table>
There is no evidence to suggest that any local site received a disproportionate number of reports during either experimental condition. This is particularly important for the abdomen, as it indicates the adequacy of subject information controls concerning the importance of this site, in addition to subjects' general failure to discern the disproportionately analgesic shifts present at this site during 'Genuine Acupuncture'. Although three subjects reported maximal analgesia at the abdomen during 'Genuine Acupuncture' compared to only one during 'Pseudo-Acupuncture', the difference probably occurs simply as part of the general body trend towards increased reporting under 'Genuine Acupuncture'.

It is also interesting to note, although rather difficult to interpret, that the two test locations failing to receive any reports of maximal analgesia during 'Pseudo-Acupuncture' are the lower leg and upper arm. Reference to Table 10 Page 101 indicates that these were also the only two sites displaying negative 'P.D.T.' values for 'Genuine Acupuncture' relative to 'Pseudo-Acupuncture'. In addition, two subjects, the same two who estimated slight hyperalgesia as the result of 'Genuine Acupuncture' overall, indicated a maximal hyperalgesic effect on the lower leg. As their 'P.D.T.' responses on the lower leg also exhibited increased sensitivity during 'Genuine Acupuncture', a compatible overall picture emerges. It appears likely that this is a sensory effect reflected in the subjective response ratings, as it is difficult to see why the lower leg should attract such particular psychological importance otherwise.

(iv) Acupuncture Stimulation Intensity Ratings:

The intensity of sensations experienced by the subjects as a result of insertion of Acupuncture needles alone, and then with the
addition of electrical stimulation, were scored on rating scales (ii) and (iii) Fig. 3 Page 56 respectively. The group mean results for the two experimental conditions appear in Table 13 Page 66.

As might be expected from the descriptions in the literature of sensations appropriate to 'Genuine Acupuncture', there is evidence of greater intensity of sensation from the needles alone at the 'Genuine Acupuncture' 'points' compared to the 'pseudo' locations. However, as even the 'Genuine Acupuncture' sensations were very modest in intensity, the mean score falling only approximately one quarter of the way along the scale, the difference appears relatively small.

Electrical stimulation was applied to the Acupuncture needles with little delay after insertion, and continued for the majority of the period until their removal. It appears to have successfully equalised the overall subjective intensities of stimulation within close limits* during the two experimental treatments. This presents an important confirmation of vital psychological matching of stimulation experience during this phase, and almost certainly eliminates it as a significant contributor to the observed analgesic superiority of 'Genuine Acupuncture'.

Electrical stimulation was not, of course, maintained during the actual thermal stimulus trials, and it was impracticable to obtain ratings of residual needle sensations at each trial**. However, evidence presented in the next section suggests that residual needle sensations were virtually non existent at these times, and there were no indications whatsoever of differences between the two experimental treatments.

---

* The difference of 0.5 which still remained may be disregarded as well within chance variation for rating measurements of this imprecise nature.

** It was also considered undesirable in terms of focussing subjects' attention too closely on this factor.
An interpretation of equality of psychological potency for the two treatment forms also receives general support from the similarity of subjects' post-session treatment efficacy estimates (section (ii) above) at the end of the two experimental conditions. It is, however, just possible, if unlikely, that the slight increase in subjects' readiness to report local effects after 'Genuine Acupuncture' (section (iii) above) reflects a psychological rather than analgesic difference between the treatments.

(v) Post-Experimental Interview Reports:

Subjects' reports during the post-experimental structured interviews are summarised below following the scheme laid out in the methods section (m).

(i) Subjects did not report ability to predict the onset of thermal stimuli by time estimation etc. and would appear, as hoped, to have relied purely upon thermal sensory information.

(ii) Most subjects reported relatively rapid transition from sensations of heat through to 'P.D.T.' and 'P.T.' points, and felt that the 'P.D.T.' - 'P.T.' interval remained relatively constant at all times across both conditions. Subjects with very high 'P.D.T.' values, however, reported longer intervals between the measures. This was verified by the actual response measure data which appeared to support a relatively constant proportionality relationship between 'P.D.T.' and 'P.T.' magnitudes.

Apart from one subject who correctly reported an extension of the 'P.D.T.' - 'P.T.' interval during 'Genuine Acupuncture', subjects failed to observe any difference between the two experimental conditions.
(iii) Subjects reported relatively easy and consistent identification of 'P.D.T.' at all times, by virtue of the sensation description given to them in their instructions. 'P.T.' was felt to be much more variable and dependent upon mood, arousal etc. Most subjects indicated that they could probably have tolerated more pain, but in line with the liberal instructions declined to actually test the possibility. Subjects appear to have responded by estimating the rate of pain increase, and then depressing the cut-out button just before the 'P.T.' point, in order to allow for a slight latency evident before sensation reduction after stimulus cancellation.

Again no consistent differences were evident between the experimental conditions.

(iv) It is very difficult to discern any clear pattern of reports concerning sensitivity at different body sites prior to the needle treatments. Although two subjects were able to correctly define their chest and upper arm locations as their most sensitive, many subjects were quite wrong (including two subjects who reported their abdomen as amongst the most sensitive regions). Certainly there is no consistent information available to either contradict the pattern evident from baseline pain measures, or to indicate any differences between the experimental conditions.

(v) Almost all subjects reported some anxiety in anticipation of, and during, the insertion of Acupuncture needles. This appeared to habituate during stimulation and was associated with some interesting mood and arousal shifts. The procedures were not considered overly stressful.

*This probably resulted from residual heat transfer from the contact apparatus rather than any neurological mechanism.*
Subjects appeared much less concerned and anxious with respect to the thermal pain stimuli, presumably as a result of their non-invasive and brief nature.

(vi) Subjects reported relatively mild discomfort associated with insertion of the needles. Comparison of sensations described as emanating initially from the different needle sites clearly indicates that the 'Genuine Acupuncture' 'point' in the hand provided the most intense experiences, with almost all of the 'Te-chi' sensations described as characteristic of Acupuncture stimulation being reported in one case or another. These sensations of numbness, soreness, heaviness or fullness, tingling and radiating sensations etc. were also present to a lesser extent at the other 'Genuine Acupuncture' 'point' in the lower leg. There was a clear, qualitative, and probably to some extent quantitative, difference in the reports at the 'Pseudo-Acupuncture' needle locations, sensations being typically described simply as sharp, pricking, and a little painful, without any of the 'Te-chi' characteristics. This corresponds with the indications evident from the mean rating scale scores in Table 13 and, as already mentioned in the methods section, represents both a confirmation of differences between Acupuncture loci and other putatively neural body areas, and an inevitable problem endemic to attempts to provide controls in Acupuncture experimentation. This concern must, however, be assessed in the light of the supplementary information discussed in part (ix) of this section.

The addition of electrical stimulation appears to have adequately equalised the quantitative intensity of sensation (see Table 13), although interview reports still suggest that some residual
qualitative differences remained between the two treatments. Although both treatments were reported as fairly intense, fortunately not distressingly so, 'Pseudo-Acupuncture' was often described as sharp and burning as opposed to a duller, deep aching, typical for 'Genuine Acupuncture' sites. As in part (ix) below is relevant.

Of particular importance were reports concerning residual sensations at needle sites when electrical stimulation was removed during the pain measure trials. In both conditions equally, subjects appeared to be virtually unaware of the continued presence of needles. This may represent simply a contrast effect, as, even initially, sensations from the needles alone were slight compared to the effects of electrical stimulation. It is also, however, possible that some adaptation or habituation took place.

(vii) Reports of mood, arousal etc. were naturally very mixed. However, a few relatively consistent trends emerged. In both conditions, after an initial period of anxiety and alertness, subjects tended to relax and even become sleepy. This is, of course, not surprising in the presence of regular rhythmic stimulation whilst lying supine in a warm room. Nonetheless, it is interesting to note that these reports were considerably more prominent in association with 'Genuine Acupuncture'.

In addition, 'Genuine Acupuncture' was particularly linked with disassociative reports where subjects typically reported dreamy, distant states, and in two cases slight enhanced visual awareness alterations. They also stated, in several cases, that, although the thermal stimuli remained equally painful throughout the session, they felt rather distant and unconcerned by them. Descriptions of "floating", "headiness", and feeling "high" were also applied.
To be fair, however, it must be said that one subject reported similar experiences equally strongly after 'Pseudo-Acupuncture'.

(viii) Subjects generally indicated that they failed to discern marked changes in either pain measure as a result of either treatment. Where changes were reported they appeared to be virtually randomly attributed to the two conditions and to different body locations.

(ix) Important information was obtained when subjects were interviewed after their final experimental session, and questioned concerning differences between the two experimental treatments in respect of needle sensations.

Only one subject, when pressed, admitted even considering differences between the two treatments in relation to their possible effects upon sensory sensitivity. 'Genuine Acupuncture' was assessed as providing more intense stimulation and therefore to hold the possibility of greater effectiveness. He did not, however, personally discern any such effect, and objectively did not disproportionately contribute to the overall superiority of group mean pain measures during 'Genuine Acupuncture'. Otherwise, subjects were either unaware of any differences between the two treatments (which were, after all, separated by two days), or merely viewed the sensations as qualitatively different as a result of the different needle placements, without extrapolation to any differential effectiveness prediction.

Subjects appeared to largely disregard the pre-electrical stimulation phase of Acupuncture as eclipsed by the very much more impingent subsequent sensations. Residual needle sensations during thermal stimulus trials were also too poorly recalled, particularly in view of distraction by the thermal stimuli themselves, to be assessed retrospectively.
These observations, together with information from part (x) below, appear to strongly discount stimulation sensation differences as major contributors to the analgesic disparity of the two experimental conditions since, although present at various points, they do not appear to have generated unequal suggestive potency.

(x) When directly advised of the deceptive experimental strategy involved in the simulated or 'Pseudo-Acupuncture' treatment, subjects uniformly failed to indicate any spontaneous suspicions along similar lines. This again strongly supports the adequacy of this procedure as a control condition.

(xi) Finally, when advised of the focus of experimental interest on the abdominal test location, all subjects indicated that they were quite unaware of this fact. In particular, when the three subjects reporting predominant analgesia at the abdominal site during 'Genuine Acupuncture' were questioned closely, it became clear that the localisation was tentative to the verge of guess work, and certainly did not result from any specific cueing.
Summary and Conclusions

It is clear from the analysis of covariance for the overall body data (Table 8 Page 9) that, in this experiment, the insertion of needles, together with electrical stimulation, at two Acupuncture 'points' designated by Chinese sources for the induction of analgesia produced significantly greater elevation of both cutaneous 'Pain Detection Threshold' ('P.D.T.') and 'Pain Tolerance' ('P.T.') than similar treatment at putatively 'neutral' sites. There is some indication that this effect was more pronounced for 'P.T.' than for 'P.D.T.' although the difference failed to achieve significance.

Both 'P.D.T.' and 'P.T.' present a generally similar temporal pattern of 'Acupuncture analgesia' (Figs. 16 and 17 Pages 2 and 95), with progressive increase at each test point until removal of the Acupuncture needles, and indications, by extrapolation from the general curve shapes, of potentially greater peak elevations had Acupuncture stimulation been continued longer.

The gradient of elevation was perhaps initially more rapid for 'P.T.', with some signs of deceleration after about 30 minutes of 'Electro-Acupuncture'. There is also a possibility that the peak elevation of 'P.D.T.' actually occurred at the first test after removal of the Acupuncture needles. Whilst this would be particularly important as a contradiction of purely distractive or counter-irritative hypotheses for the mechanism of 'Acupuncture analgesia', the exact timing of this 'P.D.T.' peak is unfortunately questionable for reasons discussed earlier.

* ie. superiority of 'Genuine Acupuncture' values above 'Pseudo-Acupuncture' values.
Of at least equal importance in this connection, however, is the clear-cut persistence of both 'P.D.T.' and 'P.T.' elevations for at least 30 minutes after removal of the needles. Although both measures exhibited decline during this period, approximately one third of the peak 'P.D.T.' superiority of 'Genuine Acupuncture' over 'Pseudo-Acupuncture' still remained at the final test point, and over half of the effect upon 'P.T.' persisted (see Fig. 17 Page95).

These results appear to strongly attribute analgesic effects to Acupuncture beyond those resulting from its suggestive or distractive elements. A certain amount of caution must, however, be attached to this interpretation in view of the small number of subjects, and the limited size of the Acupuncture effect.

In addition certain possible residual problems concerning equality of the sensations elicited by insertion of needles at 'Genuine Acupuncture' 'points' and at 'Pseudo-Acupuncture' sites have been raised. It is just possible that the very slightly more pronounced initial sensations reported at Acupuncture 'points' in some way generated the elevated pain measures associated with the treatment. At a psychological level such an effect would, however, have to be completely subconscious since subjects entirely failed to report any differential assumptions of potency, or realisation of the simulated nature of the 'Pseudo-Acupuncture' treatment. In addition, the two treatments were equally negatively rated for effectiveness. It does appear from the subjective report data that subjects, naive with regard to Acupuncture (particularly when participating in the experiment predominantly for pecuniary reward), may be less sensitive to, or reflective upon, minor experimental differences than might have been feared.

*This, in itself, is supportive for the existence of the putative Acupuncture system.
It is also evident that any initial differences in sensations at needle sites were quickly, and successfully, masked by the application of electrical stimulation to equal subjective intensity under the two experimental conditions. Although electrical stimulation was actually discontinued whilst pain measures were obtained, there is no evidence to suggest that any detectable differences between needle sites remained to provide an unequal suggestive or distractive source. Residual sensations, in fact, appeared to be entirely minimal, indicative of some adaptation or habituation.

Another potential source of subject bias to be considered is the possibility of inadvertent cues from experimenters. This appears most unlikely here for several reasons. First, the physicians inserting the needles were as unversed in Acupuncture theory (other than the techniques for physically inserting needles) as the subjects themselves, and thus were not in a position to provide cues. This barrier did not, of course, apply to the author who performed the task of locating 'points' for both treatments. However, it is not unreasonable to assume that if, despite the careful matching of all verbal communication and location procedures (as described in methods section (e)(ii)), some inadvertent cues were provided, they would be reflected in the rating scales predicting treatment effectiveness (Fig. 3(i) Page 56) which were completed by subjects almost immediately after 'point' location was finished. This manifestly did not occur, since subjects displayed equal, and marked, scepticism as to the likely effects of treatment in both conditions. In addition, correlations between predictions and actual

* It has already been argued in results section (e)(ii) that the pattern of correlation for pain measure changes with both predictions and post-treatment estimates of Acupuncture effectiveness, is incompatible with the hypothesis that the analgesic superiority of 'Genuine Acupuncture' is the result of attitudinal bias effects.
elevations of pain measures were very low for both treatments. It is most improbable that inadvertent cueing occurred after this point in the experiment as the subjects were isolated in a soundproofed cubicle for the remainder of the experiment, and all pain measure procedures were fully automated.

Finally, it is most difficult to reconcile the pattern of gradual onset and offset of the additional analgesic effects of Acupuncture beyond those of 'Pseudo-Acupuncture', with explanations based upon differential sensations at needle sites or inadvertent cues. As already indicated, both the primary opportunity for cues, and the most conspicuous differences in sensations at needle sites, were present in the initial stages of the experimental sessions. One might, therefore, expect any derived suggestive or distractive effects to appear most prominently at the first pain measure test point in the experiment. This clearly is not the case, and it is verging upon the absurd to suggest that 12 non-science subjects, unacquainted with Acupuncture, would assume that the treatment should exhibit gradual progressive onset and offset of analgesic effects, particularly as such a pattern is not evident for the 'Pseudo-Acupuncture' treatment.

In short, it does appear that Acupuncture can significantly attenuate sensory sensitivity to stimulus levels eliciting both minimal and maximal pain sensations, and the first principal hypothesis of the experiment (see page 27) may be considered as confirmed.

The superiority of stimulation at Acupuncture 'points' for the induction of generalised analgesia does, however, appear small, with a peak elevation of only 12-13% above effects produced by supposedly 'neutral' sites. However, general factors may contribute to this apparent paucity of effect. For example, it is generally considered
more difficult to demonstrate effects of even well established analgesic agents upon experimentally-induced pain compared to clinical pain (78).

In addition, as evidence reviewed in the first two chapters indicated, placebo procedures may be quite effective in their own right, and thus a treatment providing significantly better results may, in fact, represent useful pain attenuation.

Although the analysis of data reported here did not include the no-treatment 'control' condition (for strict methodological considerations of comparability), the previous more basic analysis reported elsewhere (415) did indicate significant superiority of 'Pseudo-Acupuncture' over no treatment*. There were also possible indications** that the effects of the supposedly 'neutral' needle locations may have, in fact, included directly physiological (assumedly sensory) elements, in addition to their suggestive and distractive components. This would alter the experimental paradigm to one of comparison of the relative effectiveness of variants upon a fundamentally similar treatment process, and thus emphasise both the need for very precise location, and careful selection, of 'points', and the inevitable limits of possible variance in the analgesic effectiveness of different treatments for the body as a whole.

A final factor limiting the magnitude of mean whole body results was the relative localisation of analgesia induced by Acupuncture. This, of course, simultaneously provides strikingly conclusive support for the third, and most important, hypothesis (see page 37) of the experiment.

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* This appears to support the second major hypothesis (see page 37) of the experiment, although it is unfortunately impossible to confirm the observation through the present analysis.

** By virtue of the anatomical distribution of analgesia in the 'Pseudo-Acupuncture' condition (415). This, however, may have simply reflected baseline interaction effects (as discussed in results section (2)(a)) which were less adequately controlled by correction procedures employed in the preliminary analysis.
As Tables 8 and 10 Pages 91 and 101 respectively indicate, not only were there significant differences in the degree of analgesia induced by Acupuncture at the various cutaneous test locations*, but the distribution conformed exactly to Chinese claims for the specific Acupuncture 'points' selected. 'Genuine Acupuncture' quite clearly exhibited its largest and most significant superiority (27% peak)** over the 'Pseudo-Acupuncture' treatment at the abdominal cutaneous test area. Indeed it was the only individual test site to achieve significant effects for both pain measures.

Although, in line with the overall body results, there was evidence of greater effect upon the 'P.T.' measure, the difference was again not statistically significant. This may be important in so far as 'P.T.' is often considered as more responsive to treatments altering arousal and general psychological variables***, whilst 'P.D.T.' changes are seen as more representative of purely sensory effects (25, 179). The observation of significant effects of Acupuncture upon both abdominal and whole body 'P.D.T.' values, without clear cut superiority of effect upon 'P.T.' levels, may thus provide further support for some directly sensory components in the mechanism of action.

It has also been argued that the time course of 'Acupuncture analgesia' on the abdomen is particularly informative (see Figs. 18(a) (b) and 20), in that, not only is the usual pattern of gradual onset and offset evident, but there are also cogent indications of peak analgesia.

* It will be recalled that possible artifactual contributions from differential baseline sensitivity at cutaneous test locations were corrected within the analysis of covariance process.

** It will be noted that this is more than twice the peak percentage elevation exhibited by the body as a whole.

*** This does not, of course, mean that these variables may not be directly altered by physiological processes.
actually occurring ten minutes after removal of the Acupuncture needles, and hence after removal of most of their presumed suggestive,
distractive, and irritative qualities.

It is exceedingly difficult to conceive of any alternative to a genuine effect of Acupuncture in order to account for these local effects.
The effects of counter-irritation would be expected to be most evident
at the cutaneous test areas on the limbs, as they were closest to the
Acupuncture needles, rather than at the remote abdominal site. It is also important to note that the adjacent thoracic
region, also remote from the Acupuncture points, displayed the next
largest response to genuine Acupuncture rather than any limb site.

Inadvertent release of cues to subjects must be untenable as an
explanation, in view of the exceedingly specific nature of the required
information transmission, the lack of any conspicuous reporting of
analgesia at the abdominal site by subjects, and their unanimous denial
of awareness of the hypothetical importance of this area when directly
interrogated. It is, of course, even more difficult to see how the
temporal pattern of analgesia at this site could be reconciled with
such an explanation, whilst arguments relating to differences in sensa-
tions elicited at needles sites in the two experimental conditions must
be irrelevant.

The conclusion must be that Chinese claims for a relatively
localised analgesic effect induced by Acupuncture stimulation at a
designated remote site are substantiated, and a true sensory effect
probably implicated. The result strongly refutes the negative finding
of the only previously completed study attempting to test localisa-
tion of the Acupuncture effect. The disparity may be related to their

* It will be recalled that again this information was available to
only the experimenter (author), and not to the Acupuncturist.
use of a different noxious stimulus system (pressure), but may also reflect certain evident procedural and analytical weaknesses in their work. A later study by the same authors again employing a different pain stimulus source (contact cold), but with apparently improved methodology, still contradicts the results presented here.

Whilst the study appears generally less carefully controlled and certain specific possible procedural problems have been suggested in earlier discussion of this work, published information is insufficient to permit adequate comparison. One other related study, reported since completion of the author's experiment, employed the same Acupuncture 'points' with the more similar radiant heat type of pain stimuli, and reported exactly the same pattern of maximal analgesia on the abdomen, followed by the chest. The work was, however, most inadequately controlled and must remain suggestive only.

Generally the results of the study appear to equate well with the positive findings of the majority of studies reviewed in chapter 2, particularly with regard to the temporal progress of observed Acupuncture effects. It is difficult to directly compare the results of this analysis with other studies in terms of magnitude of analgesia, since reports are generally presented in terms of percentage elevation of Acupuncture session pain measures above baseline values, rather than the more directly focal and critical elevation above corresponding baseline levels.

* See chapter 2, section (2)(d).
** See chapter 2, section (2)(c).
*** At the present time the authors have failed to supply the necessary information.
**** See chapter 2, section (2)(b).
***** An additional study employing the same Acupuncture 'points' with electrical dolorimetry again reported maximal analgesia on the abdomen. Although this study was also virtually uncontrolled, and uncorrected for baseline effects, it is compatible with results observed here.
'Pseudo-Acupuncture' levels as employed here. Reference to the previous simple analysis of the data does, however, provide a similar results format, and suggests that peak (95%) and mean (45%) elevations may have been less marked than in some studies elsewhere (270% (11, 12) 187% (71)), although improving on other findings (27% (304)). It is, unfortunately, impossible to make fully valid comparisons owing to the host of methodological differences between most studies.

On a more applied descriptive level, it seems probable that the attenuation of sensitivity elicited by Acupuncture in this study, must be considered minor in terms of its clinical usefulness. The descriptive label of analgesia, although applied for conventional convenience (in common with most authors), is clearly a misnomer when applied to the observed effects of Acupuncture. In no case did the treatment result in the complete absence of pain, let alone anaesthesia, and, for what it is worth, neither the author, nor any of the experimental subjects asked, would feel ready to submit to even minor surgical procedures with the degree of pain attenuation obtained.

It would appear most accurate to describe Acupuncture as, at best, a modest hypalgesic agent. This is, of course, in no way to detract from the likely usefulness of the now established phenomenon as a focus for basic research illuminating the mechanisms of pain and its measurement; and it is from this perspective that we now proceed to the second part of this work.

* Application of the Analysis of Covariance package to session data, in order to correct for differential baseline sensitivity, does not permit subsequent access to any simple 'corrected' baseline value.
CHAPTER 4.

PAIN EXPERIMENTATION: THE APPLICATION OF SIGNAL DETECTION THEORY

Introduction:

Perceptual discrimination tasks, for noxious or lower magnitude stimuli of all types, must involve an amalgam of sensory and attitudinal factors in the subject's responses. For example, the traditional 50% "pain threshold" measure is not a pure indicator of sensory sensitivity since it is also influenced by response bias. The same problem naturally applies to rating scale tasks.

That this may be the case would be of little surprise to those involved in clinical work, where it is well known that a patient's report of pain may be as much as expression of anxiety or fear, a call for help or attention, or an attempt to control others, as a sensory state report.

The responsivity of both clinical and experimental pain to covert cognitive factors has been the source of concern leading to the recent application to pain experimentation of Signal Detection Theory (or Sensory Decision Theory).

A description of the underlying statistical theory and mathematics of S.D.T. analysis would not be appropriate here; particularly as excellent reference works (153, 327) are available for the reader not versed in this area. The following sections will therefore be confined to review and discussion of the studies which have now begun to apply the methodology to experimentation on pain and analgesia, and in particular to the investigation of "Acupuncture analgesia".
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(1) Application of S.D.T. to Experiments on Pain and "Acupuncture analgesia": A Review and Methodological Consideration:

The review paper by Lloyd and Appel (1976) (266) divides studies applying S.D.T. to pain research into three categories. Modification, procedural, and normative and comparative areas are covered, and it would appear reasonable to adopt their general organization. Where it is redundant, or impracticable, to describe the experimental work in a manner significantly different from these authors, certain small sections may be adopted direct. This will apply only to this section, and acknowledgement of individual sections will not be made.

(a) Modification Studies (General):

Probably the first study to apply S.D.T. to this area came from Clark (1969) (90). It attempted to determine the origins of the well established elevation of "pain thresholds" following the administration of placebo preparations. 22 paid volunteers served in placebo and control sessions counterbalanced for order effects. The standard Hardy-Wolff-Goodell Dolorimeter (described later) was used to apply radiant heat stimuli, of a standard 3 second duration, to the volar forearm. On the basis of the subject's predetermined pain threshold, a randomised series of five fixed stimulus intensities were presented, ranging from 0-309 mcal/sec⁻¹/cm⁻². Subjects rated the intensity of sensory experience induced by each stimulus on a 13 category descriptive scale ranging from "nothing" to "extremely painful". In the placebo
sessions subjects were monitored for "drug reaction" symptoms in response to the inert substance, and marked effects were noted.

S.D.T. rating scale methods were applied to estimate the discriminability (d') between each adjacent stimulus pair, the lower serving as the noise distribution for the higher level. Sensitivity indices did not alter in value under either experimental condition, although the criterion (B) was significantly elevated for each stimulus pair with the administration of the placebo. The observed reduction in the disposition of subjects to report pain, heat, or warmth was therefore attributed to nonsensory psychological factors.

A virtual replication of this study was undertaken by Feather, Chapman, and Fisher (1972). This time only two stimulus intensities were applied to multiple spots on the forearm, and a four point rating scale was employed. This permitted presentation of twice the number of stimuli at each level as was possible with the design of Clark (1969). Side effects were also monitored, with significant positive findings. Results again indicated significant response criterion increases with placebo administration for the 'painful' response category, although not for the heat and warmth ranges. The sensitivity index remained unchanged throughout the study. One apparent methodological weakness derived from the probable opportunity for subjects to obtain visual cues as to the intensity of the radiant heat stimuli.

S.D.T. has been applied to evaluate the effects of pharmacological agents assumed to be active analgesic, or anaesthetic, agents. Chapman et al. (1973) administered randomised series of 50 radiant heat stimuli at each of four different intensities, including zero, to 14 male volunteers. The stimulus levels were adjusted to suit each individual on the basis of his predetermined pain threshold. A six
category response scale ranging from "nothing" to "strong pain" was employed, whilst subjects inhaled either pure room air, or a 33% Nitrous Oxide mixture, in two separate, balanced order, sessions. Owing to the definite side effects of the gas, and the sophistication of the subjects, no attempt was made to introduce 'blind' controls. Analysis indicated a significant reduction in willingness to report moderate and faint pain under Nitrous Oxide as measured by the percent response bias (200). This did not apply to the "hot" response category. The authors interpreted this finding as indicating a "significant change in cognition" under the gas. This conclusion must, however, be questioned in view of the interaction between bias and sensory indices discussed earlier; since the study also reported significant shifts in sensory sensitivity under Nitrous Oxide. Absolute discriminability between the zero stimulus and each non-zero stimulus level was significantly reduced by Nitrous Oxide. An important additional result, however, was the failure to find a similar significant attenuation in differential sensitivity, that is the ability to discriminate between adjacent stimuli.

This last finding raises an important methodological consideration. It is vital to include a zero stimulus in the series, in order to provide an anchor for the distributions of sensory experience generated by the non-zero stimuli above (186). It is possible for induced analgesia to pass undetected, if the sensory distributions for all the stimulus levels move equally towards zero. This would leave the interstimulus discriminability between adjacent stimuli (i.e. differential sensitivity) unchanged, and a failure to induce analgesia would be deduced. Comparison of each non-zero stimulus distribution with zero (i.e. absolute sensitivity) would illuminate the shift, and amend the conclusion drawn.
This procedure does impose the additional analytical requirement that each pair of adjacent stimulus levels, across the whole sensory range, be fixed sufficiently close as to ensure overlap of the sensory experience distributions they generate. If any pair of stimuli should be perfectly discriminable, no meaningful sensory sensitivity index can be derived at that point. This produces a break in the sensory continuum from zero to the most intense sensation, with subsequent loss of both a differential sensitivity measure at the break, and the ability to compare more intense sensory levels with the zero level.

Practical problems, however, abound (as discussed further in Chapter 7, Studies section). To ensure overlap, stimulus levels must be close set, or else presented many times; or even possibly both. This means it is difficult to cover the entire sensory continuum up to the very painful categories (which are obviously of prime interest in analgesic studies), whilst minimising the number of noxious stimuli subjects must endure. Clearly a risky compromise must be made to minimise the likelihood of failure to detect analgesia through inadequate coverage of higher stimulus sensory levels, or through inability to detect absolute sensitivity shifts due to breaks in the sensory continuum.

It is important to conceptually separate absolute and differential sensitivity as above, since they may not safely be assumed to represent two aspects of a single sensory capability. For example, manipulation of sensory adaptation (227), and physical damage to a receptor (451), can cause differential sensitivity to increase, with a simultaneous decrease in absolute sensitivity. The distinction must, however, be made even more finely, and certain additional controls introduced, if improper comparisons of sensitivity measures are to be avoided.

Table 14, modified from Clark et al (1975) (101), is employed to illustrate the various categories of sensitivity. In
TABLE 14: DISTINCTION OF THE VARIOUS CATEGORIES OF ABSOLUTE AND DIFFERENTIAL SENSITIVITY (after Clark et al. (1972))

<table>
<thead>
<tr>
<th>Background</th>
<th>Discrimination Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Sensitivity (Surround = 0)</td>
<td>Absolute Sensitivity</td>
</tr>
<tr>
<td></td>
<td>( \frac{A}{N_1 \text{ versus } N_1 + S_1} )</td>
</tr>
<tr>
<td></td>
<td>Differential Sensitivity</td>
</tr>
<tr>
<td></td>
<td>( \frac{B}{N_1 + S_1 \text{ versus } N_1 + S_2} )</td>
</tr>
<tr>
<td>Differential Sensitivity (Surround &gt; 0)</td>
<td>( \frac{C}{N_2 \text{ versus } N_2 + S_1} )</td>
</tr>
<tr>
<td></td>
<td>( \frac{D}{N_2 + S_1 \text{ versus } N_2 + S_2} )</td>
</tr>
</tbody>
</table>

\( N \): indicates Noise distribution.

\( S \): "signal".

Numerical subscript: indicates amount of activity in sensory system \((1 \leq 2)\)

Versus: indicates physical states to be discriminated in the task.
cell A the discrimination is made between neural noise alone (hence $N_1$ rather than the absolute silence implied by $N_0$), and that noise plus a target signal. This is the strict "absolute sensitivity" state where the background surround intensity, against which the signal is detected, is at its physiological minimum. Cell B indicates the differential task of discriminating between two levels of stimulus against the minimum surround noise. It is quite legitimate to compare type A measurements with type B, since both are absolute sensitivity with respect to background.

Cell C indicates a situation where the background surround noise has itself become elevated, and the added signal is to be detected against this higher noise level. Although this would commonly be termed an 'absolute sensitivity' task, it is strictly a differential situation, since the background surround is now effectively a signal with respect to its baseline. This situation might occur where, for example, previous thermal stimuli had elevated the baseline temperature of a skin test site, to which a further stimulus was to be applied as a detection task.

The final condition in cell D simply indicates the differentiation of two different levels of stimulus intensity against this elevated background noise/signal. Comparison of C and D type measurements is clearly correct. However comparison of either with type A measures is invalid. The problem calls for careful monitoring and stabilising of baseline skin temperature in order to maintain a single adaptation level.

*This was undertaken, and reported, by Chapman et al (1973)(75), and their failure to observe any significant deviation between average skin temperature under Nitrous Oxide, and during the control condition, eliminated drug induced changes in skin temperature as a factor in the etiology of the significant perceptual changes. Clark et al generally report similar monitoring in their studies; but where it is absent, vascular changes resulting from the drug, or treatment administered, can not be ruled out as a source of possible artifactual analgesia.
It is interesting to note, however, that Clark (71) obtained 17 sensory sensitivity values ($d'$) for thermal stimuli at intervals of $25 \text{ mcaldcm}^{-2}\text{sec}^{-1}/\text{cm}^{-2}$ from 0 to $425 \text{ mcaldcm}^{-2}\text{sec}^{-1}/\text{cm}^{-2}$, and observed that the "absolute sensitivity point" at $0 - 25 \text{ mcaldcm}^{-2}\text{sec}^{-1}/\text{cm}^{-2}"
was not unique and fitted the $d'$ versus thermal intensity function. Defined in terms of discrimination but not in terms of surround, absolute and differential sensitivity are, indeed, related aspects of a single sensory capability".

Considerable care in the use of terminology is required if red herring criticisms of S.D.T. application to pain experimentation are not to arise. For example, McBurney (1975) suggests that S.D.T. may not be applied to "absolute sensitivity for pain" since it is impossible to present a stimulus which is either painful, or not perceived at all (blank). Weak stimulus intensities evoke warmth or heat reports, not pain reports. The problem arises from illegitimate use of the response term 'pain' as if it were also a stimulus term. This use is analogous to the different and legitimate situation where the subject is presented with various intensities of light (stimulus term), and uses the same term as a response, 'light' or 'no light'. Clearly different intensities of thermal radiation, not pain, constitute the independent variable in pain experimentation. It is incorrect to refer to 'absolute sensitivity to pain', since the phrase assumes pain to be a stimulus. Fortunately from the point of view of S.D.T. analysis, it really does not matter what terms the subject uses for response categories, since he is not scored as correct or incorrect in the transition from cold to hot, or not painful to painful. The experimenter need only know which stimulus he presented on each trial, and measure the ability of the subject to discriminate between stimulus quantifiable states of the world. The subject's observation may be
regarded as unidimensional, even when the sensory system has many dimensions, since it may be represented in m-dimensional space, and a likelihood ratio exists for each such point.

A series of three double-blind experiments conducted by Chapman and Feather (1973) evaluated the effects of 10mg. diazepam on pain report. The first two studies employed the "submaximum effort tourniquet technique" which is felt to more accurately mimic the physical and emotional characteristics of clinical pain. Diazepam significantly increased pain tolerance and reduced anxiety, relative to aspirin or placebo.

In order to apply S.D.T. analysis to these results, a third study was undertaken presenting five levels of radiant heat, including zero, to the volar forearm. The levels were again based on each individual's pain threshold, and presented in random order. Each level occurred 50 times in each session, with subjects responding on a six point rating scale ranging from "Nothing" to "Strong Pain". Interstimulus (differential) discriminability (d') was estimated for each adjacent stimulus pair, and the effects of placebo and diazepam compared. No significant effects of the drug upon sensory sensitivity were detected, and, most interestingly, the response criterion also remained unchanged. The authors concluded that diazepam has no effect upon pain sensations, "i.e. it does not affect the sensory-discriminative aspect of the pain experience. Neither does it function as a placebo to reduce willingness to report pain". They introduce the further conceptual category of a motivational-emotional aspect to the pain experience in order to explain the results of their first two studies. The apparently analgesic effect of the drug in extending pain tolerance is attributed to reduced "aversive drive associated with continuing pain".
If anxiety, as a crucial component of the motivational-emotional aspect of pain, may affect pain reports independently of the S.D.T. measures, it is clearly an element to be stabilised and minimised by the experimental pain methodology employed*. This is particularly true if the drug, or treatment, under evaluation is intended to be a true sensory analgesic. This is discussed further in later sections of this work.

The effects of suggestion upon pain report have been investigated using S.D.T. methods. Clark (1974)[91] applied six stimulus levels of radiant heat ranging from 0 - 435 mcal/sec^-1/cm^-2, with 12 presentations at each level, in randomised order. Subjects (n = 10) responded on an 11 point rating scale ranging from "Nothing" to a timed latency "Withdraw".

After an initial series of stimuli to establish baselines, standardised suggestion was given to the effect that "previous thermal stimulation has fatigued your skin receptors and made them less sensitive". This, it was suggested, would permit the toleration of more pain, and subjects were urged to "endure maximal pain". The second thermal stimulus series was then administered.

Analysis focused upon the differential discriminability of the most intense stimulus pair to which "withdrawal" responses (tolerance) were occurring, and the stimulus pair below which located reports of "very faint pain" (threshold). Discriminability remained unaffected.

* The radiant heat dolorimeter is generally claimed to have the advantage of producing a distinctive sensory experience without the emotional reaction of the tourniquet technique. This, of course, immediately carries the inherent disadvantage of reduced comparability with clinical pain [275].
by the instructional 'set' for both pairs. However, the criterion for "Withdrawal" was significantly raised, although not for "Very Faint Pain". Clark concluded that, although pain intensity reports were reduced, sensory experience ($d'$) was not altered by suggestion or permissiveness of instructions.

In a similar, larger study, Clark and Goodman (1974) applied suggestion for both raising and lowering pain reports. The manipulation was separately directed at pain threshold responses and at pain tolerance responses in different groups. Again, although pain intensity reports responded as expected, sensitivity measures remained unchanged in all groups. Suggestion of decreased sensitivity significantly raised response criteria for both "Very Faint Pain" and "Withdrawal"; however changes following suggestion of increased sensitivity, although in the right direction for both ranges, failed to reach significance levels. There was some indication, although non significant, of greater responsiveness of the "Withdrawal" criterion to suggestion. This is in line with other authors who have promoted pain tolerance as being more heavily loaded with psychological or attitudinal variables than pain threshold responses (38, 39, 179, 481). Results suggested that part of this difference may be attributed to a more potent arousing effect of the inevitably more dramatic instructions relating to pain tolerance.

The study also reported some interesting sex differences. Although sensory sensitivity did not differ, males displayed significantly more reduction in their pain tolerance criteria to the appropriate suggestion; whilst females exhibited significantly greater increase in tolerance criteria in response to the suggestion that more pain could be accepted. These differences were not evident for pain threshold levels.
In contrast to the study above, Craig and Cohen (1975) report significant increases in sensory sensitivity ($d'$) to electrical shock stimuli* when subjects were exposed to the suggestive influence of an intolerant modelling group, compared to control and tolerant model groups. The tolerant model group displayed significantly different pain ratings from the control group, and in the expected direction. These latter differences were attributed to criterion shifts (although the methodology employed precluded direct estimation of bias), since no significant difference in differential sensitivity was evident. The authors reached the important conclusion that "the sensory qualities of the experience can change as the result of social experiences, and that it is not just public expressions that vary in response to changes in social contexts".

It is difficult to reconcile the results of the last two studies discussed, especially as the host of procedural and experimental manipulation differences which doubtless generate the discrepancy, probably render comparison invalid. This problem will be discussed further at the end of this section.

(b) Modification Studies (Acupuncture 'Analgesia'):

A major influential study in this area was undertaken by Clark and Yanp (1974) using a modified Hardy-Wolff-Goodell dolorimeter as the noxious stimulus source.

Radiant heat stimuli at six intensities (0, 120, 240, 305, 370, 435 mcal/sec/cm²) were applied to six india inked patches on each volar forearm of 12 subjects. Twelve presentations at each intensity

* 12 shocks at each of five intensity levels were delivered in randomised order. Levels were tailored to suit individuals and responses were selected from a 10 category scale ranging from "Undetectable" to "Painful".
were applied in random order in a stimulus test series, with subjects responding on a 12 category intensity scale ranging from "Nothing" through various degrees of warmth, heat, and pain to "Withdrawal" (timed latency). Three test series (ie. 3 x 72 stimuli) were applied to each arm in the complete experimental session. After an initial test series to establish baseline values for each arm, one arm (the left arm for half the subject group) was electrically stimulated via Acupuncture needles at sites said to be standard for analgesia of the arm (42). Biphasic stimulation at 88 Hz, with current ranging from 1.8 - 4.0 mA, and mean peak to peak voltage from 360 - 600 mV, was applied for 15-20 minutes, during which the second test series of radiant heat stimuli was applied. The needles were then removed, and a final test series conducted. Treatment of the control arm was identical apart from omission of the Acupuncture stimulation. Skin temperature was monitored every 15 minutes throughout the experiment but no changes were observed.

Analysis of variance for period versus treatment revealed no significant differences for d' (differential) for any stimulus pair between the Acupunctured and control arms, or between the periods before and after Acupuncture*. However, a significantly higher pain criterion was set for the Acupunctured arm during the stimulation phase**. The authors concluded that, although the proportion of withdrawals and pain reports were reduced by Acupuncture, S.D.T. analysis revealed that this was merely the result of the suggestive element of the treatment without any underlying alteration of the sensory system.

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* These results appeared against the background of a slight increase (non significant) in discriminability, attributed by the authors to practice.

** The similar increase in criterion was attributed to progressive reduction in fear of possible skin damage, and hence in the need to use pain responses to discourage the experimenter from application of extreme stimulus intensities. Similar phenomena have been observed in other work (90, 227).
The study has been criticised on the grounds of inadequate stimulus presentations at each level, with the possible result of variability of S.D.T. measures, and hence reduced power of the statistical tests to detect differences in the conditions (73). In their defence, the authors reasonably point to the limitations on the endurance of subjects, but also underline the "remarkable" uniformity of mean d' at both test sites, and under all conditions. Clark and his co-workers repeatedly use this very small number of presentations together with the parametric measure of sensitivity (d') (90, 91, 94, 95). Their results are indeed remarkably reliable with very low variance*. This lowers the likelihood of failure to detect condition differences due to reduced test power. Also, it is unlikely that tests which detected criterion shifts would be insufficiently powerful to illuminate sensitivity changes. Finally, Clark and his colleagues have employed up to 25 stimuli at each level without any marked change in variability. Even using less than 12 presentations, the authors found a dose-related decrease in d' following a median nerve block with dilute Carbocaine (120).

These points would seem reasonable in view of the fact that the researchers were simply concerned as to whether sensitivity and bias differed in control and experimental conditions. In such cases the paucity of stimulus presentations would be much less important than in studies attempting to determine precise normative data. Nevertheless, McNicol (1972) (327) argues that at least 50 presentations are needed to realistically estimate R.O.C. curves in any design, and where this is not possible, the nonparametric measures of P(A) for sensitivity, and B for bias, are strongly advocated.

* It proved impossible to replicate this standard in this laboratory, as can be seen from the results section for Experiment No 2 and the report on pilot work in Chapter 7.
The study has also been criticised on the grounds of possibly inadequate duration of Acupuncture stimulation. Chinese researches have reported negatively accelerated growth of analgesia, stabilising only after approximately 50 minutes, whilst most of the western studies reviewed in chapter 2 observed a gradual increase, typically peaking after 30 minutes stimulation. The results of Acupuncture Experiment No.1 in this laboratory accord with these results in that, although there were some signs of gradient deceleration, analgesia was still clearly developing progressively when the needles were removed after approximately 35 minutes.

On the other side it should be said that some analgesia was evident at 20 minutes, and generally the studies reviewed in chapter 2 also report some effect within this time period, even if peak shifts were achieved later. In addition, very rapid effects (within 10 minutes) have been reported.

It does, however, appear that analgesia of the extremities may be more difficult, as it require longer stimulation, to induce than for the head and trunk and generally the evidence suggests that Clark and Yang (1974) may have, to some extent, reduced the likelihood of positive results. It would have been preferable to allow at least 30 minutes for development of 'Acupuncture analgesia', as the effect appears at best weak, and the S.D.T. testing procedure may be insufficiently sensitive to detect its presence at an early stage of development. It is also interesting to assess their observation of altered bias without sensitivity change in the light of all the evidence for progressive onset and offset of the effects of

* Dental analgesia, the objective of many of the other experimental studies, appears to be particularly easy to induce.
Acupuncture on pain reports. It is difficult to see why criterion shifts should be subject to latency effects of this type if underlying physiological events were entirely absent.

A final criticism of their technique concerns the employment of high frequency (88Hz) electrical stimulation as opposed to the normal low frequency 1 - 2Hz practice. Evidence suggests that not only may low frequency stimulation be more effective overall, but, in fact, it may have a different mode of action since it provides more widespread analgesia with slow onset and offset, unlike the lesser high frequency effects which are very short-lived and strictly segmental (220,221). This, coupled with their failure to mention employment of the careful techniques recommended for Acupuncture 'point' location, suggests that Clark and Yang may have failed to apply a treatment directly comparable with Chinese practice.

Clark et al (1976) employed an almost identical methodology to compare Acupuncture with Transcutaneous Electrical Stimulation (T.E.S.) of the median nerve. Careful stabilisation of limb temperature was required in the latter case, since vasomotor fibre stimulation decreased the hand temperature. Again, although reducing pain reports as before, Acupuncture failed to affect discriminability, whilst producing significant elevation of criteria. Surprisingly, T.E.S. was effective in reducing pain at all thermal intensities except the highest, although this did not outlast stimulation cessation for

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* Study of the effects of Acupuncture stimulation on evoked potentials in the cat thalamus and cortex clearly observed low frequencies as most effective in reducing evoked potentials associated with noxious sciatic stimulation (274). In addition EEG slowing effects characteristic of Acupuncture are elicited only by low frequency stimulation (426).
longer than 30 minutes. The distraction and discomfort of T.E.S. did not affect $d'$ values for the control arm tested concurrently. Criterion elevation was evident for the stimulated arm only during the passage of current. The obvious conclusion is that T.E.S., but not Acupuncture, suppresses experimental pain.

The findings above are in direct opposition to the results of another important study by Chapman et al (1975) (74). Forty-two male volunteers were assigned to three groups, Control, 33% Nitrous Oxide, and Acupuncture (20 minute induction period). Noxious stimulation was generated by pulsed, constant current, electrical stimulation of the tooth pulp with careful controls for constancy of electrode contact. Four stimulus intensities were applied, ranged around each individual's detection threshold, and including a zero value. In each session, 75 stimuli at each level were presented in randomised order, with subjects employing a seven category sensory intensity scale ranging from "Nothing" to "Strong Pain".

Baseline sessions were compared with subsequent treatment sessions for changes in discriminability ($d'$) between each stimulus pair, after the methods of Richards and Thornton (1970) (363) which provide for the averaging of data with the slope of the double probability plot taken into account. Bias was estimated as percent bias, a nonparametric index based on the geometry of the unit square of the ROC (200). Compared to the control session*, Acupuncture

* Controls exhibited a slight increase in sensitivity similar to that reported by Clark and Yang (1974) (100) and Clark (1969) (90). This can probably be attributed to practice effects (327).
and Nitrous Oxide significantly reduced sensitivity and, although for all levels combined the two treatments did not differ, Acupuncture consistently lowered sensitivity at all three levels, whereas Nitrous Oxide primarily affected the lowest level. The two treatments also differed significantly from controls, but not from each other, by their increase in attitudinal bias against reporting pain. The authors concluded that Acupuncture produces true sensory deficits, but described it as hypoalgesia, rather than analgesia, comparable to that produced by 33% Nitrous Oxide which is known to be insufficient for surgical procedures.

A second study by Chapman et al (1976) compared controls with genuine Acupuncture treatment, a "placebo" Acupuncture, and with Transcutaneous Electrical Stimulation (T.E.S.) at an Acupuncture site. Sixty male volunteers were carefully trained in response procedures, and the noxious dental electrical stimuli were administered exactly as in the first study. Each of the four groups (n = 15) received an identical baseline test series of stimuli followed by the different experimental treatments, and then a second stimulus test series for comparison. Needles were not inserted into the control subjects, although 'points' were located and palpated in a similar manner to the other groups. In the case of the other groups, sites in the hand designated for dental analgesia by Chinese sources, were stimulated electrically for 20 minutes by either Acupuncture needles or surface electrodes (T.E.S.). Alternatively, in the placebo Acupuncture group, the needles were inserted in a slightly removed, supposedly neutral, site in the hand; all procedures otherwise being identical.
Although it has been convincingly argued that Acupuncture analgesia studies cannot be run strictly 'double blind' (293), it is nonetheless desirable to reduce experimenter effects as far as possible. To this end, a 'pseudo-double blind' procedure was employed whereby the principal experimenter and the subject were visually screened so they could not tell which treatment was being administered. Naturally, tactile clues were still available to the subject.

Analysis revealed the usual significant reduction in pain reports under all treatments compared with controls. Interstimulus discriminability measures, however, revealed that only the Acupuncture and T.E.S. groups differed significantly from controls. Thus Acupuncture and T.E.S. developed a small, but significant, sensory decrement, whilst placebo Acupuncture did not. Changes induced by treatment, especially Acupuncture, were greater at the lower levels of stimulation. The Acupuncture and T.E.S. groups also differed significantly from controls by their alteration of response bias towards greater reluctance to label the strongest stimuli as painful.

In a novel analytic departure, the authors employed multiple regression methods to estimate the proportions of variability among the rating scale change scores which could be accounted for by changes in the sensitivity and criterion components*. They concluded that the apparently analgesic

* Although adequate approximations are possible as indicated by the methodology and results of Acupuncture Experiment No.1 in this laboratory.

** In principle the idea is useful. In practice, however, given a shift in sensitivity, one may merely be measuring the effects of that shift upon bias. Again it comes down to a question of defining what is meant by bias.
effects of Acupuncture at the higher levels of stimulation were primarily due to response bias shifts, whereas the effects were primarily sensory at the lowest stimulus intensity. In the case of T.E.S., however, sensitivity and bias shifts appeared as equal contributors to response changes at the highest stimulus level. At the medium and lowest stimulus levels, sensitivity effects outweighed bias, although this was not as marked as the effect of Acupuncture at the lowest level of stimulation. Subsequent application of the regression analysis to the data of the previous study (Chapman et al (1975) (74) revealed the similar pattern of the effect of Acupuncture predominating at lower intensities, in a manner very similar to the effects of Nitrous Oxide.

The results of the criterion analysis must be strongly questioned in view of the probable lack of orthogonality of the bias measure in the presence of sensitivity shifts (210). Chapman et al (1976) (77) attribute the failure of placebo Acupuncture to significantly alter response bias, to the possible absence of the characteristic sensation of "te chi" which is reported to accompany stimulation at Acupuncture "points" (382). Subjective awareness of this sensation may, they say, produce response bias changes. The alternative explanation of a directly physiologically mediated effect on cognition might also be preferred. The most parsimonious resolution of the problem, however, would probably attribute the lack of bias shift simply to the fact that the placebo Acupuncture treatment was also the only condition which failed to alter sensitivity.

A later study by Chapman et al (1977) (71) employed a similar methodology for noxious dental stimulation with 20 male volunteers. Control and Acupuncture treatments were again compared, but this time 80 minutes of electro-Acupuncture stimulation at submaximal tolerance levels was applied to intrasegmental points in a manner similar to other researchers (10). In addition to the S.D.T. six category rating
task, threshold measures were established at 10, 20 and 80 minutes after onset of stimulation.

Results indicated that the Acupuncture group gradually increased thresholds significantly compared to controls, and stabilised after 20 minutes. S.D.T. analysis for differential sensitivity employed the nonparametric index $A(327)$, and indicated significant sensory decrement at both high and low stimulus levels following Acupuncture. Response bias, measured as percent bias $(200)$, was not significantly different for the two groups. These results stand in contrast to the earlier S.D.T. studies of this research group, and the conclusion is drawn that inter-segmental stimulation produces a stronger, and more reliable, true sensory sensitivity effect, than extrasegmental meridian 'point' locations. Despite the significant result, it should be noted that the Acupuncture group were still able to detect and discriminate stimuli of intensities well below their supposed thresholds at the 20 minute point in the treatment sessions. This not only depreciates Acupuncture as a genuinely useful therapy, but also further indicates the weakness of the traditional all or none threshold model.

It is difficult to resolve the disparities in findings between the respective research groups of Clark and Chapman. A number of possible problems concerned with the Acupuncture techniques employed by Clark have been discussed earlier, together with other criticisms. As far as S.D.T. methodology is concerned, it would seem that the work of Chapman is more adequate in terms of the number of stimulus presentations, and numbers of subjects, although the defense offered by Clark (as discussed earlier) would appear cogent. The use of nonparametric S.D.T. measures, where assessed as appropriate, must also tell in favour of Chapman, as does the general agreement of his results with
the majority of non S.D.T. studies of Acupuncture analgesia. Beyond this, the methodologies employed are too dissimilar to enable proper comparison. The field is clearly open for a definitive study of the Acupuncture phenomenon, employing S.D.T. analytical methods in an attempt to resolve the presently confused state of knowledge.

In conclusion, it is worth mentioning another smaller, and less controlled, S.D.T. study of Acupuncture by Lloyd and Wagner (1976)\(^{267}\). Radiant heat stimuli at four levels, including zero, were presented as combinations of adjacent pairs (total 150 pairs), in randomised order, for a binary* decision by the subject. Stimuli were applied to the dorsal hand of right subjects, and a baseline test session of 45 minutes was immediately followed by 45 minutes of Acupuncture stimulation to points in the hand and forearm. During the stimulation, a further series of ratings was obtained. No attempt to balance the order of presentation is reported. This appears important in order to compensate for progressive improvements in discriminability resulting from practice effects alone, as reported elsewhere\(^7\),\(^9\),\(^10\). The procedure might, therefore, be expected to reduce the visibility of any possible sensory decrement following Acupuncture. This may be contributory to the finding that Acupuncture only significantly reduced discriminability for the lowest stimulus intensity pair, which were well below painful levels. The results are interesting in that they are similar to the findings of one of the studies by Chapman et al (1976)\(^7\) using both a different noxious stimulus source and different S.D.T. methodology.

* The authors hoped to improve the sensitivity of the S.D.T. measure at the expense of information right across the sensory spectrum. The failure of Clark and Yang (1974)\(^{100}\) to find Acupuncture effects on sensory dimensions, was hypothesised as resulting from the lower sensitivity of the rating scale method.
(c) Procedural Studies:

Three studies have been concerned largely with assessment of the relative merits of different S.D.T. procedures for analysis of pain modification data (93, 98, 101a). The work has already been discussed in section (1)(b)(ii).

(d) Normative and Comparative Studies:

An important, but unpublished, normative study conducted by Clark (1971) systematically investigated thermal discriminability across the whole range of sensory intensity up to the barely tolerable (0 - 425 mcal/sec\(^{-1}\)/cm\(^{-2}\)). Highly trained subjects were used in a series of sessions in each of which two stimuli, 25 mcal/sec\(^{-1}\)/cm\(^{-2}\) apart, were discriminated. Following each stimulus presentation, multiple sensory decisions were obtained from the subject: (a) one-interval binary d' (response "high or low"), (b) one-interval confidence ratio R.O.C.-curve, (c) one-interval sensory magnitude rating R.O.C.-curve, (d) two-interval binary d', and, following an additional observation interval, (e) forced-choice judgment of which interval contained the higher stimulus.

Slopes of the linear R.O.C. curves were plotted on double probability axes, and did not differ significantly from unity. Analysis of variance revealed significant differences in d' with respect to method and to intensity, but no method by intensity interaction was evident. A weighted mean discriminability index for the four d' estimates was therefore calculated and plotted against intensity for each stimulus pair across the range. Discriminability improved between 0 - 75 mcal/sec\(^{-1}\)/cm\(^{-2}\) (i.e. "just detectable" or "faintly warm"), then decreased to the initial level and remained there between 150-225 mcal/sec\(^{-1}\)/cm\(^{-2}\).
Thereafter it increased with an approximately linear slope to the highest intensity \(425 \text{ mcal/sec}^{-1}/\text{cm}^{-2}\) (pain reports beginning above approximately \(300 \text{ mcal/sec}^{-1}/\text{cm}^{-2}\)). A least squares fitting curve described a parabola up to \(150 \text{ mcal/sec}^{-1}/\text{cm}^{-2}\), and was linear thereafter with a slope significantly different from zero.

Since one \(d'\) (mcal/sec\(^{-1}\)/cm\(^2\)) is analogous to the 'just noticeable difference' of classical psychophysics, but with response bias removed, the Weber ratio could be plotted across the range. The ratio decreased rapidly until it reached a constant (0.25) between 75 - 175 mcal/sec\(^{-1}\)/cm\(^2\). After this initial plateau, it again decreased down to a second constant value (0.45) between 300 - 425 mcal/sec\(^{-1}\)/cm\(^2\).

Several comparative studies have been completed by Clark and his colleagues. Clark and Marmor (1969)\(^{(96)}\) provide the only S.D.T. study to use a physiological measure in conjunction with verbal reporting. Valmar skin potential responses above a set criterion were compared with pain magnitude estimates for eight intensities of electric shock, with eight subjects. The sensitivity index derived from the verbal reports proved significantly more sensitive to changes in shock intensity than were skin potential responses\(^*\).

Another paper by Clark and Rubin (1969)\(^{(99)}\) reports the use of S.D.T. to compare the sensitivity of various diagnostic categories of psychiatric patients with normal student controls. Noxious thermal stimulus procedures similar to other studies\(^{(93)}\) were employed, and values of \(d'\) and \(\beta\) were obtained for each stimulus intensity compared to zero. Sensory sensitivity did not significantly differ for

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\(^*\) Values of \(d'\) for the S.P.R. were calculated from the absolute sums of the largest negative and positive deflections occurring within 10 sec. of a stimulus presentation.
the two groups at any stimulus intensity, or with any order of stimulus presentation. Nor did knowledge of results have any effect. However, the older patient group, which displayed comparatively elevated thresholds, did set a significantly higher criterion than normals or younger patients, for the highest stimulus level. It was further observed that subjects experiencing the higher stimulus first, set a lower criterion which was reflected in their apparently lower thresholds. Since the older psychiatric patients differed significantly from all the other groups, it is unfortunate that the supposed "older" student control group was only half their mean age.

The effects of age and sex on $d'$ for adjacent radiant heat stimuli, and various measures of bias, have been investigated in 64 normals\(^{(97)}\). To summarize, the results indicated that older females had significantly reduced sensitivity for noxious stimuli compared to all males, although both sexes in the older age group tended to set more stringent criteria for reporting pain. In general, over almost all intensities, females set a more stringent criterion. It appears that many of the reported age and sex differences in pain thresholds may be caused by variation in the criterion for pain rather than by differences in sensitivity. This study is discussed further in the next chapter.

Summary and Conclusions:

Subject to certain discussed limitations upon interpretation of results, application of the methodology of S.D.T. to
pain experimentation appears valid, both theoretically and practically, in view of the demonstrated ability of the measures to discriminate between active analgesics inducing sensory modification and placebos or suggestion associated with purely attitudinal shifts. Results of the few S.D.T. studies of "Acupuncture analgesia" are, however, highly contradictory concerning possible sensory attenuation, and the need for a definitive experiment employing suggested methodological improvements is evident.
The Mechanics of The Pain Experiment

Stimulus Systems

Introduction:

Hardy, Wolff & Goodell (1952) (179) list the following requirements for an adequate noxious stimulation system:

(a) The measurable aspect of the stimulus should be closely associated with changes causing pain, i.e. with noxious stimulation.

(b) The stimulus should be one for which, under the same conditions, reproducible quantitative measurements of the pain threshold are obtained.

(c) The intensity of the stimulus should be controllable and measurable to a degree higher than the difference between two stimuli which evoke a just noticeable difference in pain sensation.

(d) The stimulus should be one for which the ability of the subject to discriminate differences in pain intensity can be ascertained throughout the effective range of the stimulus, i.e. from threshold to 'ceiling' pain.

(e) The stimulus should cause minimal tissue damage at pain threshold, and should be a minor hazard to the subject even at higher intensities.

(f) The stimulus should be capable of evoking separately one of the qualities of pain - burning, pricking, aching.

(g) The stimulus should be one which can be conveniently applied.

(h) The stimulus should be one for which the perception and identification of pain is clear cut, whether or not other sensations are evoked prior to, concurrent with, or following the pain.
Many stimulus variants have been employed over the years with varying advantages and problems.

(1) Types of Noxious Stimuli:

(a) Mechanical Stimuli:

A wide variety of stimuli have been devised in this class including pressure from sharp bristles \((^452)^\), spherical beads \((^36)^\), or needles \((^228)^\), mounted on various gauges of stiff hairs and applied to the skin. Also employed were plungers applied under pressure \((^114, ^490)^\), compression of blood vessels by a sphygmomanometer cuff accompanied by constant rate isometric contractions by subjects \((^29)^\), distention of the viscus by inflation of a swallowed balloon \((^48, ^80)^\), dropping fixed weights on to the skin from varying heights \((^470)^\), and application of supersonic oscillation \((^207)^\).

Hardy, Wolff and Goodell \((1952)^{179}\) reviewing many of these methods describe several problems. Firstly, the reactivity of tissue to pressure is highly variable, and hence it can be inferred that noxious stimulation is variably related to pressure. Also, the range of measurable stimulus values between threshold pain and maximal discernible pain is relatively small and highly variable. In the case of distensible hollow organs, normal threshold variations may include stimuli which induce high intensity pain in the same individual at another testing. Obviously also the sheer mechanical problems of this procedure render it most unsuitable for large scale testing.

An improved technique has been used in a few studies \((^92, ^140, ^141)^\) whereby ultrasound applied to the skin induces periosteal pain. Fixed intensities were used, and the duration of the stimulus to pain threshold noted. The method suffers from practical problems of
application since it requires an oil coupling medium, displays the common wide variability in relationship between pressure and noxious stimulation, and most of all offers exceedingly limited comparability with the rest of the literature.

A number of studies have induced ischemic pain with tourniquets (396, 399). The method is claimed to produce deep aching pain with slow onset, very similar to much clinical pain (399), and it has been used to evaluate 'Acupuncture analgesia' in one study (397). Again the method is difficult to quantify, unsuited to rapid multiple measures, and is difficult to compare with the more common methods.

In general, therefore, the mechanical approaches appear obscure or cumbersome, difficult to scale in valid units, and too variable in the relationship between stimulus strength and pain intensity, to be adopted here.

(b) Chemical Stimuli:

Several approaches have again been employed, including stimulation of the nasal mucosa with epinephrine packs (323), and intramuscular injection of hypertonic saline (392). The application of corrosive, or irritative, mixtures on and into the skin has also been utilised (14, 112, 367, 482), whilst two studies of 'Acupuncture analgesia' in China have employed potassium iontophoresis dolorimetry (348, 359).

All these methods suffer from the problem of quantification of the relationship between stimulus and pain, and are generally rather crude. In addition, many preparations may themselves interfere with normal nerve processes and induce confusing sensations of contact (243). Again these approaches seem quite unsuited to large scale, reproducible, experimental pain assessment using repeated measures.
(c) Electrical Stimuli:

Faradic current for the stimulation of pain sensations has a long history (151, 295, 453), and has been applied as a calibrated system since the 1940s, particularly for the testing of analgesic agents on animals (282). In humans, the effects of skin temperature upon pain threshold were assessed using single break shocks (468); interestingly, pain threshold decreased as temperature increased.

Some researchers have applied electrical currents to metal fillings in teeth, and noted the voltage at which pain was reported (145). The authors claim that pain was the only definite sensation which could be produced in a tooth by this stimulus. It is not, therefore, suitable for providing a sensory continuum below pain threshold down to no sensation.

A recent study by Chapman et al (1975) (74) (1976) (76) applied the method to the evaluation of 'Acupuncture analgesia' with positive results. In this case, constant current dental stimulation was applied through a hand held probe with preset current levels based on the subject's previously established threshold. The tooth was kept dry by an air jet, and abnormalities of contact between the tooth and probe were detected by observing the stimulus waveform on an oscilloscope. The authors contend that variations in waveform clearly identify conditions of both moisture on the dental surface (which would carry current into the soft tissue rather than through the pulp), and of inadequate pressure. Although trials characterised by these problems had to be aborted, a low failure rate is reported. Notwithstanding this report, clearly either at least some responses were lost, or additional discomfort for the subject was incurred.
Other authors (366) ascertaining pain thresholds in teeth found considerable variation from tooth to tooth, and at various sites on the same tooth. They also found no uniformity for the same tooth and site across different individuals. Obviously the requirement for use of subjects as their own controls may be considerable. (Chapman et al (1975) (74) (1976) (76) incidentally did not use this procedure.)

Electrical procedures suffer from problems concerning the first requirement of Hardy et al (1952) (179) for a satisfactory method, i.e. that the stimulus be closely associated with specific tissue changes causing pain. This leads to dispute (131) as to which stimulus parameter should be measured as indicative of 'stimulus intensity'. At one time or another e.m.f., current, frequency, power*, and even waveform have been proposed as the important variable for control. Furthermore, holding any of these factors constant, especially when stimulating the skin, and even with theoretically constant-current devices, is almost impossible.

Another major consideration, particularly when stimulating the skin, is the likelihood of directly inducing hypoalgesia as a result of the electrical stimulus itself, since it is unlikely to excite pain afferents alone (389). The technique of Transcutaneous Electrical Nerve Stimulation (T.E.N.S.), and allied methods** for the relief of local and distal pain are fully discussed elsewhere, but similarly involve the application of electrical stimulation to the skin surface aimed at stimulation of large afferents. Intensities are normally, of course, below pain threshold, and the duration normally much more prolonged than

* Power probably emerges as the most important complex parameter (195).

** T.E.N.S., and Electro-Acupuncture, as employed in experiments in this laboratory bear many close similarities (132, 310).
the brief noxious shocks used as pain stimuli. Nonetheless, reduced
pain experience has been demonstrated with electrical stimulation
durations of only two minutes\(^{(460)}\), and there may well be appreciable
effects from very much briefer applications, particularly when at high
intensity. Other authors\(^{(179)}\) have also reported secondary areas of
hyperalgesia, in addition to the zones of hypoalgesia in the area of the
electrical stimulation. Whilst these considerations are of less
importance provided exactly the same stimulus site is used on all
tests, and an intra-subject comparative design adopted, it would appear
inadvisable to investigate a putative analgesic technique which may be
slight in itself, with a stimulus testing procedure which may also
alter sensitivity. There is no certainty that the two effects should
be additive, and the end result may merely be the masking, or reduced
scope for visibility, of induced analgesia due to an already truncated
response range.

A final major consideration concerning electrical stimulation of
the teeth is the possible hazard to subjects. Prolonged stimulation
at high intensities results in irreversible damage to the tooth\(^{(179)}\).
This again limits the range of pain sensation which may be examined.
It is also worth noting that many subjects find this form of stimulation
most psychologically distasteful due to association with previous life
experience of acute dental pain. This additional stress would not be
conducive to accurate responding.

These limitations apart, electrical stimulation does meet many of
the criteria for a laboratory stimulus. It is easily applied to any
part of the body through simple electrodes, without undue constraint of
the subject. It can also be calibrated, turned on and off instantly at
any intensity, and can produce clear cut pain which may briefly be
extreme without irreversible tissue damage. Furthermore, many recent advances in calibration and stabilisation of the stimulus parameters have recently been made (146). For these reasons many investigators have employed the technique; a number in the field of Acupuncture research (10, 85, 201, 262, 304, 406, 441A). Only one group of investigators has applied a 'Signal Detection Theory' analysis to the evaluation of the effects of Acupuncture on electrically induced pain, although they have completed several studies with generally positive findings (71, 74, 77).

(d) Thermal Stimuli:

Thermal stimuli have been employed overwhelmingly by investigators over the past 25 - 30 years, a fact which alone prompts their use on the grounds of permitting direct comparison of results with other work.

An early attempt at pain threshold measurement applied an electrically heated thermometer bulb to the skin (123). The system was subject to considerable inaccuracy. Others employed instruments in which hot or cold water, or alcohol, flowed within a metal surface applied to the skin (375). Again, considerable problems were involved in maintaining constant temperatures, the cumbersome nature of the apparatus, and confusion with other sense modalities of touch and pressure. One study applied cold pain stimulation in this manner, for the study of Acupuncture effects (280).

A few studies have lowered tissue temperature to induce pain by immersion in circulating ice water (cold pressor pain) (194, 47C), at least two of which applied the technique to evaluating 'Acupuncture analgesia' (0, 238). The method is obviously not suited to response analysis approaches requiring multiple repeated measures, or stimulus
pair discrimination. Test sites are also virtually limited to the limbs.

By far the bulk of work has been undertaken using radiant heat stimulation, the best known, and most extensively investigated system being the Hardy-Wolff-Goodell Dolorimeter first described in 1940 (174). Their apparatus focuses the radiant output from an incandescent bulb (usually 500 watt) with a condensing lens, and the beam emerges through a fixed circular aperture in contact with the india-ink blackened forehead of the subject. The aperture is contained within low heat transmission material, and incorporates an electronically activated, and timed, polished metal shutter mechanism. The device is aligned, and calibrated, for standard exposure times with a radiometer in the manner described in their publication (1952) (179).

The authors claim that the approach almost ideally meets their prescription (see above) for the optimal pain stimulus. It can be calibrated precisely for intensity and temporal parameters, and the resultant pain can be associated with particular tissue changes of a non, or minimally damaging, nature, even when repeated in rapid succession. The stimulus can be conveniently applied to large, small, or irregular skin areas, and can produce separate qualities of clear-cut pain, as well as being discriminable into many just noticeable differences across the effective range from a reproducible well defined pain threshold to ceiling pain.

The list of authors that have accepted radiant heat dolorimetry as the optimal pain stimulus for general pain investigation is well beyond the scope for discussion of this section. More directly applicable, however, are the many studies of 'Acupuncture analgesia' which have also employed the technique (33, 86, 87, 109, 111, 209, 333, 353)
In particular, the study by Clark and Yang (1974)\(^{(100)}\), one of the few, and more carefully designed, investigations employing "Signal Detection Theory" analysis, also used radiant heat dolorimetry. This study, and the other radiant heat/S.D.T. investigation by Lloyd and Wagner (1976)\(^{(267)}\), found negative, or equivocal, results compared to the generally positive outcomes of the studies using conventional approaches. In an attempt to resolve this disparity it would seem, therefore, important to adopt a pain stimulus system as comparable as possible to the S.D.T. studies. It would also seem desirable, in order to maintain some comparability with the first study by the present author, which also employed a thermal stimulus, although of a mixed radiant and conductive type. This, in addition to the objections raised above to alternative stimuli, prompts adoption of a radiant heat stimulus system. The precise details of the optimal stimulus parameters are discussed below.

Radiant Heat Stimulation Procedures: Optimal parameters

(1) Radiant Beam Area:

Certain practical limitations clearly limit the maximum stimulus aperture area. The larger the aperture, the greater is the required wattage of the incandescent source. This magnifies both the enclosure casing size and problems of dissipating unwanted residual apparatus heat. Hardy et al (1952)\(^{(179)}\) report that initial experiments with an aperture of 3.5 cm\(^2\) were mechanically practical, but this was later reduced to 0.5 - 1.0 cm\(^2\) since stimulation of warmth and heat sensations (which display spatial summation\(^{(172)}\)) was thus reduced, and a more clear transition from heat to pain occurred at the threshold point.

The aperture may not be reduced below 0.1 cm\(^2\), since lateral conduction of heat from the edges of the irradiated skin area becomes
sufficient to appreciably reduce skin temperature at the centre of the exposed area for a given intensity of radiation \(^{(179)}\). This produces an apparent increase in the pain threshold due solely to rapid cooling of the stimulated area. This artefact becomes insignificant with stimulation areas above \(0.15 \text{ cm}^2\), at which point the heating effect of the radiation reaches a 100\% plateau.

The next major consideration is the possibility of spatial summation for thermally induced pain sensation. Thresholds for warmth and cold display clear-cut spatial summation \(^{(172,173)}\), but variation of the skin area exposed to intense radiant stimuli from \(0.07 \text{ cm}^2\) through to \(28.30 \text{ cm}^2\) fails to produce significant evidence of summation for pain \(^{(174)}\). This failure appears to be singular to pain sensation, and applies to both pricking and aching qualities, and to both threshold and supra-threshold pain \(^{(478)}\).

These findings were later re-examined using considerably more sophisticated procedures and equipment \(^{(154)}\). This time care was taken to test the uniformity of the radiant beam applied to the skin, since Weddell \((1955)\) \(^{(465)}\) had implied that possible "hot spots" within the radiant field might produce pain at a point within the stimulated area, regardless of the decrease in local area. Considerable care is required to ensure uniformity, and a solution to this problem is fully discussed in Chapter 7, Section (1), Collaboration Section 5, Page 298.

Using an acceptably uniform beam, Greene and Hardy \((1958)\) \(^{(154)}\) applied apertures of \(16 \text{ cm}^2\), \(7.85 \text{ cm}^2\), and \(2.5 \text{ cm}^2\) to the blackened forehead, and measured the 'pricking pain' threshold in terms of induced skin temperature. A significant, although small \((1.1 \text{°C})\), degree of spatial summation occurred upon increasing the area from \(2.5 \text{ cm}^2\) to \(7.8 \text{ cm}^2\), but none thereafter. The result was independent of edge
effects or warmth summation. The use of a smaller aperture, therefore, may require the application of slightly higher intensities of stimulation, although not to a problematic degree. Smaller areas are much easier to maintain with even energy distributions, but there are indications that a lower limit of 1 cm^2 is required to ensure representative sampling of pain fibres, and avoid a statistical variation in fibre sensitivity (191,192).

The selection of a beam area of 1.0 cm^2 would therefore seem to represent an optimal compromise for the provision of a uniform beam (as discussed in Chapter 7, Section 4) without edge effects, or requirement for an excessive provision of radiant source, whilst ensuring a representative skin receptor distribution, and clear separation of heat and pain sensation due to minimised heat sense summation.

(2) **Stimulus Intensity and Duration:**

Traditionally, two approaches have been used for stimulus application. The stimulus level may be fixed and the duration of exposure until the subject's report of pain threshold, tolerance, or various points on the scaling system employed, noted. Alternatively, the stimulus exposure duration may be fixed, usually at 2 or 3 seconds, and intensity varied in small steps until the desired report is obtained. Both of these methods derive from the narrow concern with pain thresholds, or the use of j.n.d. scaling.

Neither approach is particularly suited to the use of a Signal Detection Theory (S.D.T.) type of rating scale experiment for which, as has been discussed elsewhere, multiple, well spaced, fixed intensities of a standard duration, are probably optimal. Many of the considerations vital to the accurate establishment of thresholds, become much less important with the adoption of an S.D.T. approach, whilst many new
problems arise. For example, a factor such as the physical intensity interval between stimuli, important for the pain threshold point, becomes important in the different way discussed in Chapter 7, Introduction (Pilot Studies), which covers pilot work towards the establishment of a stimulus interval scale suitable for S.D.T.

Certain information derived from threshold studies is of help in scaling stimuli. It appears clear, for example, that for most of the cutaneous surface an induced temperature of approximately 45°C is critical for the perception of 'pricking pain', and also that, with normal basal skin temperatures, this will be induced by a 3 second exposure to a radiant intensity of approximately 220 mcal/sec⁻¹/cm⁻² (60,170,178,472). Furthermore, intensities of approximately twice this level will usually induce blistering and intense pain from a 3 second exposure (174), with a ceiling level of approximately 680 mcal/sec⁻¹/cm⁻² beyond which discrimination of different intensities becomes impossible. This sets the probable useful range of intensities from approximately 220 - 440 mcal/sec⁻¹/cm⁻² for experimentation without injury, and with good discriminability. Information derived from study of j.n.d. intervals and the Weber ratio is of some assistance in setting minimum inter-stimulus intervals, and this is fully discussed in Chapter 7, Introduction (Pilot Studies), Page 223.

As already mentioned, as discussed further elsewhere, absolute skin temperature appears to be the critical parameter for thermal pain. Since the object of experimentation here is to produce pain with minimal tissue damage, high radiant levels with short exposure times are optimal, since tissue temperature is thus rapidly raised to the critical protein inactivation rate with minimum nett breakdown. It has been demonstrated that, for both radiant and conduction heat, high energy inputs produce
higher thresholds for skin flare than for pain, whilst the converse is true for low energy application. Short exposure times also minimise cues from the rise time of pre-pain warmth sensations, and ensure that skin heating is local, and that edge conduction effects may be ignored.

A three second duration has been adopted as standard by Hardy et al, Clark et al, and most other researchers employing radiant heat dolorimetry, as the most suitable intersect on the intensity/duration curve in respect of the above considerations. Adoption of the same duration obviously provides the additional advantage of study comparability.

(3) Interstimulus Interval and Sensitivity Variation:

Repeated brief thermal stimulation of the same area of skin in quick succession may reduce the pain threshold as a result of skin temperature elevation, and an induced local hyperalgesia. This is especially important when applying suprathreshold stimuli, particularly when hyperaesthesia or erythema occurs.

Neisser (1959) on the other hand, claims that changes occur in quite the opposite direction for stimuli repeated at 15 second intervals; or in other words that pain adaptation occurs. From details supplied in the two publications it is difficult to unequivocally resolve this contradiction. However, it would appear that Neisser is correct if very high stimulus levels, long durations, or both are applied, apparently reduced pain sensitivity will result due to destruction of sensory fibres. At pain threshold levels, even long exposures (25 minutes) do not elicit adaptation, and indeed sub-threshold stimuli tend eventually to become painful. Warmth sensation does exhibit adaptation, although slow and often incomplete. There is also evidence suggesting adaptation of pain sensation elicited by other non-radiant heat forms of noxious stimulation.
referring to an elevation of pain threshold in terms of the required skin temperature. Since he also indicates that, due to warmth retained in the tissues from the previous stimulation, the now 'higher' temperature threshold is attained more quickly, or with less stimulus energy, this seems quite compatible with Hardy et al (1952) (179) reporting 'reduced' thresholds in terms of stimulus energy requirements.

However the shift is described, Hardy et al (1952) (179) found that an interval of 60 seconds between successive stimuli at pain threshold level was required to avert this complication. Other authors observing the rate of dissipation of heat imparted to the skin by the heat stimulus indicate a requirement for an interval of at least 2 minutes (35). Clearly such intervals are time consuming and, whilst acceptable for threshold estimation, are not practical for long series of repetitive stimuli.

One economical solution to the problem may be adopted when the precise responding of the threshold studies is not essential. Multiple skin test areas may be tested sequentially, thereby permitting the presentation of many stimuli in a short space of time, whilst allowing adequate cooling time before each individual site is restimulated. Pain thresholds for adjacent areas of normal skin correlate adequately (0.79 - 0.93) (330), and the approach has been applied with apparent success in an S.D.T. general pain assessment model by Clark (1974) (91), and specifically to 'Acupuncture analgesia' by Clark and Yang (1974) (100), and Lloyd and Wagner (1976) (267); and to Nitrous Oxide effects by Chapman et al (1973) (75).

With this technique, stimuli presented in pseudo-randomised order of intensity, could be delivered every 15 seconds whilst allowing 3 minutes before restimulation of each skin area. This would avoid any
significant general basal skin temperature increase (91). Apart from these inherent advantages, the desirability of comparability with these studies again prompts adoption of a similar procedure.

The method is, of course, subject to certain criticisms. Adjacent skin areas can differ at least slightly in sensitivity (see above), preparation of the skin may be unequal (see below), application of the apparatus aperture may differ in pressure, and so on (186, 325). However, it would appear that, whilst these factors may be important for ideal threshold measurements, they do not seem to present a significant barrier to acceptably reliable sensation intensity estimates in an S.O.T. rating scale experimental situation (see Chapter 7, Introduction (Field Studies), Page 223).

(4) Skin Conditions:

(a) Skin temperature, perspiration, and environmental control:

It has been observed that the mediating variable in the determination of pain threshold for radiant heat stimuli is the final skin temperature. This holds true for a wide range of combinations of stimulus intensity and exposure duration (170). Hardy et al (1951) (178) report that "the relationship between levels of skin temperature and pain threshold is characterised by a straight line passing through zero stimulus at a skin temperature of 44.9°C, which suggests that the skin in the areas tested must be raised to this temperature before stimulation becomes noxious, regardless of the initial level of skin temperature ....... It follows that .. it is necessary to make correction for the initial temperature of the skin being tested". The finding has been closely agreed by both direct radiometer measures, and
application of the equations of Buettner (59) for calculation of skin temperature achieved following irradiation with a nonpenetrating radiation. It also agrees closely with the skin temperature at which reflex responses were elicited in guinea pigs and rats (170). Further confirmation in humans also comes from other independent authors (472).

The temperature of 45°C appears critical not only for eliciting pain but also for onset of reversible thermal denaturation of vital cellular proteins (58, 190), probably of the pain fibre endings (170, 268, 325). It is, perhaps, important to point out that pain is dependent solely upon the skin being raised to the critical temperature, whereas tissue damage also depends upon duration. Thus high intensity pain may be induced briefly with little or no injury. It also implies that noxious stimulation derives from the rate, rather than total amount, of protein inactivation. The threshold is then the lowest rate of inactivation which will cause damage if the stimulation is sufficiently prolonged. Comparison of pain intensity ratings with protein denaturation rate supports this conclusion (170). Indeed Stoll and Greene (1959) (417) found that pain intensity was linearly related to the log of the damage rate throughout the entire range of pain sensation.

In view of the above information, it is not surprising that alteration of basal skin temperature will alter the threshold stimulus intensity, and the pain induced by higher levels (35, 166, 178, 250, 472).

\[ T_s = T_0 + Qk \sqrt{t} \]

where \( T_s \) = Final skin temperature (°C)
\( T_0 \) = Initial skin temperature before irradiation (°C)
\( Q \) = Intensity of radiation (mci/sec \( \cdot \) cm \( ^{-2} \))
\( k \) = Constant = 0.032 (determined empirically)
\( t \) = Time of exposure (seconds).
Cooling or heating the skin of the forehead by 10°C induces elevation and reduction respectively of the pain threshold by 200 mcal/sec^-1/cm^-2 (178). There are also effects on warmth and cold sensation, although they are rather different (88, 117, 249). Similar results were reported by other authors (35) with manipulation of skin temperature, and even diurnal variations may have an effect, as do 'affective' states (319).

The effect of painful stimulation per se upon general skin temperature in non-irradiated areas would appear small, and in a downward direction indicative of vasoconstriction (166). This stress response is consistent with other studies, but is unlikely to significantly affect sensory pain sensitivity. It is interesting to note that the effects of any vascular changes on pain sensitivity are probably mediated entirely by their effect upon skin temperature. Hardy et al (1952) (179) surprisingly infer from their experimental evidence that "neither the amount of blood flowing to the skin, nor the degree of vasoconstriction and dilation of the blood vessels themselves have any direct effect upon the pain threshold".

Clearly there is a requirement for careful control of environmental temperature fluctuations between test and retest periods. Hardy et al (1953) (179) suggest that, for measurement on the forehead, room temperatures should not be outside the range of 20 - 30°C, and there should be little departure from the selected optimal temperature within that range.

An important consideration in selection of the forehead as a test site has been its constancy of temperature, reported as 34°C (+0.5°C) by Hardy et al (1951) (178), and 33.8°C (+0.6°C) by other authors (35). In warm rooms of 30°C to 35°C, although the forehead temperature will not increase greatly (385), sweating may occur and interfere with measurement. Moisture prevents the usual rise in skin temperature
during exposure to radiation, due to increased vaporization\(^{36, 179}\). Hardy et al (1952)\(^{179}\) indicate increases up to 40% in pain threshold for subjects with warm water sprinkled on the forehead. Dry skin is thus desirable for testing, and should be ensured by environmental control and examination of the skin. For most likely test areas of the body, sweating will not begin below air temperatures of 29 - 30°C \(^{193}\). This suggests that a draught-free air temperature of approximately 27 - 28°C might represent a desirable compromise between comfort for supine partially clad humans, whilst remaining below the average sweating threshold.

Many carefully controlled threshold studies provide for a long period of adaptation and skin temperature stabilisation prior to testing. One hour has been claimed as the requirement\(^{325}\), but most subjects will stabilise within 10 minutes\(^{166}\) under controlled conditions. Naturally, even when subjects are maintained at a constant environmental temperature (e.g., 25°C) for long periods (1 hour), variation in skin temperature can still amount to nearly 1°C\(^{385}\), whilst inter-subject range may be ten times that size if volatile body locations are employed\(^{325}\). Again the constraints are somewhat less pressing for an S.T. rating scale type of experiment. Allowance of 10 - 15 minutes pre-test adaptation, close control of temperature and humidity in the experimental room, and skin temperature monitoring for gross variation would appear adequate.

Some authors, concerned primarily with threshold study of the forehead, have monitored pre-stimulus skin temperature at each presentation, and corrected for departures from the baseline mean temperature when quoting threshold or injury points\(^{178, 417}\). This can become very complicated indeed when it is realised that the thermal inertia of the
skin itself varies over a wide range and increases with level of irradiance\(^{(417)}\). The procedure, although undoubtedly correct, would, however, be inappropriate to the large number of stimulus presentations, and less defined sensory points, of the S.D.T. rating scale experiment. In addition, much larger fluctuations in skin temperature are to be expected when testing cutaneous areas other than the forehead\(^{(166,179,325)}\).

As a final footnote to the consideration of environmental control, there is a clear need to avoid all distractions in the visual or auditory field likely to reduce concentration. For example, a clanging noise during testing is capable of elevating pain threshold by 38\% \(^{(186,485)}\). The effects of distraction on pain judgements are fully discussed elsewhere.

(b) Regional skin variation:

As mentioned above, most studies of thermal pain sensitivity have tested the forehead, with most of the remainder employing the volar forearm or dorsal hand. Several advantages have been proposed for the forehead. In addition to convenience of access, it exhibits the least range of temperature variation within and between subjects \(^{(35,166,178)}\). The forehead also displays minimal variation (\(\pm\) 8\%) in epidermal and subcutaneous thickness \(^{(80,487)}\), although this is probably a minor source of inter-subject threshold variability.

Skin thickness is, however, probably an important contributor to the differences found in pain thresholds at different body sites \(^{(178,487)}\). Hardy et al \(^{(1952)}\)\(^{(180)}\) concluded that, although variations in "pricking pain thresholds" were to be found on different areas of the body surface, they were generally small, and the body, with the exception of the plantar surface of the heel, the lower back, buttocks, and thighs,
could be treated as uniform. It should be pointed out that this conclusion was based upon standardisation of all measurements to a pre-stimulus skin temperature of $34^\circ C$ (the mean forehead temperature). Even then, variations in the pain threshold skin temperature are in the order of $2^\circ C$ or 4 - 5%, and there is no evidence to suggest greater uniformity of threshold for the forehead than elsewhere, despite its desirable qualities mentioned above.

An average basal skin temperature of $33^\circ C$ is quoted for the remainder of the body surface. In threshold studies, the use of other body areas would appear perfectly reasonable provided correction for skin temperature is made before comparison with forehead studies. For an S.D.T. rating scale experiment, close comparison of thresholds could not be made, and it is, therefore, important merely to avoid the areas of great sensitivity abnormality mentioned above. Use of the volar forearm would provide comparison with the S.D.T. studies of Clark et al. However, more compelling logic dictates selection of the abdomen on the grounds of compatibility with the first Acupuncture study conducted by the present author, in which a relationship between certain Acupuncture loci and localised analgesia of the abdomen was established. It is also interesting to note that the data of Hardy et al (1952) show the abdomen to have the least variability of average pain threshold of any area of the body tested including the forehead. In addition, the stimulus energy required to elicit threshold pain was slightly lower than that required for the forehead or volar forearm. Another study, although unfortunately not including the abdomen, clearly indicated larger intra and inter-subject variability of the forehead.

*This finding is, however, contradicted by Marechaux and Schafer (1949), and by the results of Acupuncture Experiment No. 1 in this laboratory.
than the volar forearm (33). Another problem concerned with the forehead appears in the work of McKenna (325). Monitoring of subjects' electroencephalograms during forehead stimulation indicated that subjects responded to the light immediately the shutter was open. Many also reported conscious cues to the intensity of stimulation from the relative brightness of the light which transilluminated the frontal sinuses.

It would seem, therefore, that use of the abdomen as a test site meets little criticism, and may even represent a positive improvement on previous practice.

With regard to sweating thresholds, the abdomen is at a slight disadvantage. Air temperatures for onset of sweating are 29 - 30°C abdomen, 32 - 33°C forearm and forehead, but the critical skin temperatures are rather more equal, being abdomen 34.3°C, forehead 34.8°C, forearm 35.2°C (193). With a closely controlled environment at 27°C, the brief 3 second stimulus exposures, long intervals between restimulation of each skin patch, and the relatively slow response time of the sudorific system, these differences should not prove problematic.

(c) Skin preparation:

The surface of normal skin is partially reflective in the visible and infra-red regions of incident radiation. A common procedure has been to coat the skin surface with a dense blackening agent in order to increase radiation absorption and hence the skin heating effect (445). This effectively lowers the applied energy requirements for warmth and pain thresholds, and increases the magnitude of sensations evoked by stronger stimuli (491).
Oppel and Hardy (343) found that, for the important penetrating infra-red range, with allowance for reflected energy, 53% more energy had to be absorbed by unblackened skin to elicit threshold sensation. Wright (1958) observed that, for both the hand and abdominal wall, blackening almost exactly doubled the median sensitivity for warmth sensation. Approximately the same proportional change is reported by Hardy et al (1952) (179) for the effect of blackening upon "pricking pain threshold".

Blackening can also reduce variation in pain thresholds (as measured by stimulus intensity) due to skin pigmentation. Negro subjects initially exhibited significantly lower thresholds, but came within the normal range for white subjects when both groups were blackened at the test site (143, 179). It should also be mentioned that skin calluses, lesions, or sunburn can markedly affect sensitivity and such areas should, therefore, be avoided whether blackened or not (175, 377).

The effect of blackening the skin is to ensure absorption of virtually all radiation, irrespective of wavelength, entirely at the skin surface (491). Without preparation, perhaps half the incident energy will be absorbed in the corium, with a quarter reaching yet deeper tissues. Once absorbed, energy is distributed by conduction in the avascular epidermis, and by forced convection via blood vessels in the dermis. The amount of this blood flow is, incidentally, important in determining the final skin surface temperature (250), a factor already identified as crucial for pain sensation intensity.

It appears likely that the essential thermal stimulus is generated close to the skin surface, and certainly at a depth which is slight compared to the total penetration of radiant energy in unblackened skin (248).
An appreciable proportion, therefore, passes into tissues too deep to significantly stimulate thermal receptors. This, together with the loss of approximately 25% of incident energy due to reflectance, probably accounts for much of the lesser sensitivity of unblackened skin for thermal sensation. It is not unreasonable to suppose that this contributes to differences in pain sensation also.

A small (1°C), but significant, increase in pain threshold measured as final skin temperature, has been reported simply as a result of the blackening process (330). This has been attributed to either inadvertent shifts in judgement due to the more rapid heating of the skin, or to the effectiveness of the ink layer in preventing incident radiation from reaching deeper skin layers. This is not a significant problem, particularly for an S.D.T. experimental situation, since, from the equations of Buettner (1951) (59), this would require only the application of an additional 15 mcal/sec\(^{-1}\)/cm\(^{-2}\) stimulus energy to raise the skin to the required threshold temperature. If this applies throughout the range of pain sensation, the extra requirement is very small in comparison with the reduction of nearly 200 mcal/sec\(^{-1}\)/cm\(^{-2}\) in the stimulus energy for pain threshold in blackened skin (179).

There would seem to be strong incentives in terms of stimulus intensity economy, and hence reduced risk of tissue damage, for the adoption of skin blackening. Most authors have prepared the skin and again comparability is desirable. A common treatment consists of dense, multiple coats of india ink applied as uniformly as possible. Even with this coating, a reflectance of 6% (170) to 10% (179) has been reported; and, for study comparability, correction for this should be

* Varied density of blackening has been observed to alter pain thresholds (186).
made when reporting applied stimulus levels. Unfortunately many authors fail to follow this practice. It is also important to allow thorough drying of the application, since evaporation temporarily lowers skin temperature (325). Any blackening skin preparation may be used provided its reflectivity is not too high, and a uniform coating is possible (179). In practice, when coating multiple areas of skin, India ink is extremely slow, messy, and laborious, and the use of a stage blacking preparation appears preferable. The preparation can be quickly applied and removed, and will not stain or mark. It is non-irritative to the average skin, and can be applied to match a reference standard kept in the laboratory. Its reflectance is slightly higher at 12-15% (414) of incident energy. This implies correction when comparing with studies using India ink, and the application of very slightly higher stimulus energies. Neither of these factors are significant practical difficulties.

(5) **Cyclic variations: test/retest reliability:**

Variation in skin temperature has been discussed as an important determinant of pain sensation and individual diurnal fluctuations, even under conditions of constant environmental temperature, of up to 1.5°C have been reported (385). This may partially explain the circadian rhythm in pain threshold and perception reported by some authors, with the acrophase in the early morning (80, 355). This is refuted by other authors (174, 175) for pain threshold, as distinct from the reaction to pain, provided concentration is maintained (486). Fatigue and irritability over 24 hours without sleep, did not alter thresholds beyond ± 12% of the usual mean (179).
Whether variations are genuinely sensory, or due to concentration deficit, there would seem to be a case for testing and retesting subjects always at the same time of day. This is particularly true in an S.D.T. testing situation, where pain thresholds are rather less important than the pain reaction, or 'alarm' reaction, components given the number of suprathreshold stimuli to be administered. The reaction component is agreed by all to vary widely from subject to subject, and with time of day (488).

Menstrual rhythms have also been reported (355). In young women with normal menstrual periods, and pregnant or menopausal women, a 30 day rhythm is present in pain thresholds. Deviations of approximately ± 7% from the mean are evident, and it would seem preferable, therefore, to test only young women receiving oral contraceptives since they are not subject to this fluctuation. The lesser rhythm observed in men would appear to be unavoidable, and might prompt selection of an all female subject pool were it not for other sex related considerations discussed below.

As far as "pricking pain threshold" studies are concerned, good reliability over weeks can be obtained with very carefully controlled conditions, unbiased, intelligent, highly trained and practiced subjects (476). Results within -16% to +13% have been obtained under these conditions, even without control for the rhythms discussed above. Other authors have reported a correlation of 0.86 between thresholds on different days for 50 subjects, and learning or experience effects were not evident (35). With less carefully controlled conditions, variation has been observed. Some differences may doubtless be attributed to variations in the physical condition of the skin, but others may well
be due to a "training effect". Intersession correlations, however, seem to be reliably in excess of 0.80, and almost all authors have concluded that the measure is useful and representative.

Suprathreshold pain has been little investigated, but is usually reported as more variable, generally owing to a wide range of subject "reaction" variables discussed below. Clearly thresholds can be reliable from day to day, but the demands of an S.D.T. rating scale procedure with many suprathreshold stimuli are likely to produce a much less precise response outcome. Little information on the day to day reliability of the S.D.T. measures is available in the studies surveyed earlier. This is due to the fact that repeat testing without the compounding factor of an experimental treatment was not reported. Furthermore second testing was usually undertaken, with little delay, on the same day. Pilot work reported fully in Chapter 7 indicates the reliability of the S.D.T. measure for testing on successive days (Table 44). The measure appears acceptably reliable, and representative, across the full range of stimulus intensities and sensations.

With regard to consecutive test/retest reliability on the same day, reports from conventional threshold studies again indicate acceptable repeatability. Chapman and Jones (1944) report a range of variation from ± 2% to ± 6% for individuals during testing, whilst Hardy et al (1942) observed a range of ± 5%. Neisser (1959) reports no change in thresholds with massed practice testing on the same day. These results appear typical for carefully conducted experiments and indicate a good validity.

* Distributed practice (i.e. separate days) may raise thresholds slightly. This is non-significant for individuals, although evident for the group. Massed practice (i.e. same day) has no effect.
Pilot studies with the S.D.T. methodology were conducted for test/retest without intervening variables on the same day (see Chapter 7 Table 44 (b) Page 235). Results appear to be usefully reliable, and even improve upon those obtained by other authors (91), thus supporting the validity of the technique.

Subject variables:

(1) Sex differences:

The first Acupuncture experiment reported here indicated clear trends towards higher pain threshold and pain tolerance baselines for male subjects. Owing to the small sample, this did not reach significance levels. There did not, however, appear to be a differential response to Acupuncture once the data was corrected for the effects of initial baseline differences.

Results with similar non-significant trends have been very widely reported in the literature (80, 166, 325, 387, 475). The sex related effect has been significant for pain sensation in some studies (97, 167, 231, 355) using radiant heat stimulation, and has also been reported using other stimuli such as pressure to induce pain (314, 490) and also for warmth sensation (88). Of the authors (103, 179, 337) who failed to find sex related differences, Hardy et al (1952) (179) attributed the positive results above to differences in the reaction component of the pain response, rather than to differing thresholds. It is claimed that careful instruction to "purify" the response can remove sex effects. There is support for their 'reaction component' hypothesis (39, 166, 167, 378), although their secondary explanation of skin differences is not supported (231).
One S.D.T. study has reported significant sex differences in discriminability for older subjects, females being less sensitive. Averaged over all stimulus intensities, women set a significantly higher response criterion, except at noxious intensities, where younger women lowered their criterion and emitted more pain responses.

In view of all the above findings, it is of interest to include both sexes within the study design, with the possibility that an S.D.T. analysis might shed light upon the origin (sensory or bias) of the observed sex differences in baselines of Acupuncture experiment No 1; and perhaps reveal sex related differences in response to the various experimental treatments proposed.

(2) **Age differences:**

Age differences in pain responses have also been widely reported (44, 80, 97, 104, 217, 355, 490). Both pain perception, and pain reaction, are generally reported to decrease with increasing age (80, 128, 355, 388). Hardy et al (1952) (179), however, again failed to find any effect, subject to the ability of the volunteer to "maintain a detached, unprejudiced attitude". Hall (1955) (166) similarly failed to note age differences provided skin temperature was maintained constant.

The S.D.T. study of Clark and Mehl (1971) (97) is, however, particularly revealing since highly significant age differences were observed for both sensitivity and bias.

Whilst interactions of pain variables with age are of interest, the slightly stressful nature of the proposed pain experimentation, and the perhaps undesirable stoicism and management problems of the older

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* One study using a pressure, rather than thermal, stimulus, reported decreasing pain tolerance with age (490). The discrepancy with other studies was attributed to the unusual stimulation.
subject (97), prompt exclusion of age grouping from an already multi-
cellular design, and selection of a narrow youthful age group of
18 - 30 years.

(3) **Education and socio-economic group:**

Individual variation in pain thresholds has been linked to
educational achievement or verbal intelligence (103, 165, 374), although
the S.D.T. study of Clark and Mehl (1971) (97) suggests that the lower
thresholds of their non-college group was due only to a lower criterion
induced by anxiety, without any true sensitivity difference. The
relatively higher social status of the experimenter, and the
institutional setting were seen as anxiety generators*. This negative
finding is in line with one conventional study which failed to
correlate pain thresholds and Wechsler scores (167).

Hardy et al (1952) (179), and many other authors, stress the need
for motivated, but detached, concentration if pain response variance is
not to be considerable. This, together with the comprehension demands
of the complex proposed experimental procedure, suggest the desirabil-
of a homogeneous subject group with a similar educational and socio-
economic background to the experimenter. If, in addition, subjects
are selected for expressed interest, as well as pecuniary motivation,
then responding should achieve maximal reliability, and anxiety levels
remain low.

(4) **Race:**

Differences in the reaction to pain between various racial and
cultural groups have been extensively studied, and the results are

* A relevant finding relating clinical pain report predominance to
Social Class 5 (Hall-Jones scale) may temper this conclusion (404).
reviewed by Weisenberg (477)\(^{(467)}\). He concludes that the major group differences derive from the 'reaction' or 'tolerance' component of pain, influenced by attitudinal and anxiety factors, rather than from thresholds\(^{(409)}\). Some of the earlier work\(^{(80)}\) was methodologically poor, and led to unfortunate stereotypes of low thresholds and tolerances for negroes and "mediterranean types". Such differences have not been substantiated in more recent studies\(^{(314)}\), although it would appear that negroes fall within the more sensitive end of the 'normal' european range\(^{(179)}\), and that thermal sensitivity does increase with skin pigmentation\(^{(163)}\).

Generally, it would be most difficult to include racial or cultural variables in the proposed experimental design for reasons of the very limited suitable subject availability in the local populace of Scotland. Additionally, their inclusion would merely add sources of variance outside the scope of the small sample analysis. Inclusion of oriental subjects, if practical, would have been of interest, in view of the origin and support for the viability of Acupuncture analgesia from China. The stereotype of the stoic oriental has often been evoked in explanation of the phenomenon; but even this is questioned by experimental reports indicating orientals to be less tolerant of pain than either blacks or whites\(^{(238,490)}\).

(5) Personality and anxiety:

Lynn and Eysenck (1961)\(^{(281)}\) report a 0.69 correlation for extraversion (M.P.I.) with radiant-heat pain tolerance, whilst neuroticism correlated at -0.36. Reduced anxiety concerning the noxious stimulation due to the poorer conditioning of extraverts is suggested as a basis for the first relationship. Increased autonomic lability, and
associated anxiety, in neurotics is thought to underlie their lower pain tolerance. Haslam (1967) (184) also observed a significantly lower forehead pain threshold to radiant-heat induced pain for introverts, and attributed the result to the effect of a higher arousal level, in a manner similar to the lowering of threshold found with the administration of caffeine.*

Similar relationships failed to emerge in some studies for the M.P.I. (252) or the 16 P.F. (322) personality questionnaires when correlated with electric shock pain stimuli. However, overall, a paper presenting analysis of pooled data from nine comparable studies by different authors, heavily supports the posited relationship between pain threshold and tolerance and extraversion, although unfortunately neuroticism is not included in the analysis (22).

In clinical studies, the relative presence of pain in women with advanced cancer of the cervix appears to relate to neuroticism; whilst the response bias towards reporting pain symptoms can relate to extraversion (45). Other authors have also reported a correlation of acute and chronic pain with neuroticism (344, 489).

To some extent, the self-selecting subject pool for experimental pain studies tends to be extraverted and liable, so there are problems in obtaining a range of scores. Nevertheless, it would seem of interest to administer the E.P.I. test with a view to illuminating, if possible, the relationship of personality to pain responding by means of an S.D.T. analysis. The origin of subject differences might be attributed

* It is of relevant contributory interest to note that significant S.D.T. differences in both sensory sensitivity, and response criterion, have been demonstrated for extraverts and introverts in vigilance tasks (182).
to sensory sensitivity or attitudinal bias, and comparison with a conventional analysis of the pain reports also undertaken. There is also the possibility of a relationship between personality and beta-endorphin blood levels, or the response to Acupuncture or the opiate antagonist naloxone.

Whilst a range of 'normal' personality is desirable in the subject pool, exclusion of any volunteers exhibiting psychiatric tendencies would appear advisable. Psychoneurotic patients may display significantly earlier pain reaction points, greater range, and have a bimodal tendency rather than the normal distribution for pain perception threshold which is characteristic of normal (79). This is almost entirely accounted for by the early reactions of anxiety and hysteria cases. Differences extend into a wide range of motor and autonomic responses (285). Psychotics and depressives, not to mention individuals with specific abnormal psychological attitudes to pain, similarly exhibit abnormal pain reactivity (189, 284). Although the S.D.T. study of Clark and Rubin (1969) (99) discussed in the previous chapter indicates that many of these findings may be largely attributed to bias rather than sensitivity abnormalities, it would seem advisable to exclude such a clearly problematic group as outside the scope of the present study.

For both normal and abnormal subjects, in the clinic or laboratory, a major intervening variable in the pain response is anxiety. An extensive review by Sternbach (1968) (408) of related studies, concludes that the greater the anxiety, the greater, and more variable, will be the 'reaction' to painful stimulation. The requirement for thorough preparation of subjects, with explanation of procedures prior to experimentation, and a feeling of control over threatening noxious stimulation,
is clearly vital for objective responding and reduced distress. In addition, close comparability of procedures, and a balanced order of presentation, for the different experimental conditions are important to avoid both localised anxiety 'incidents', and progressive anxiety habituation* effects.

Consideration of anxiety variables suggests monitoring one of the electrodermal measures, such as G.S.R., both for basal levels (for possible use as a weighting factor when comparing overall verbal pain response ratings for the subject on different days), and as an alternative measure of response magnitude to each stimulus. G.S.R. response criteria have been used in several studies as a measure assumed to relate more directly to the "sensory pain threshold" as conceived in the traditional all or none sense by classical psychophysics. There are, however, problems of oversensitivity of the response. Maximum reactions tend to occur at low stimulus intensities, leaving no scope for discrimination at high levels. Hardy et al. (1952) refer to the first marked G.S.R. excursion accompanying increasing stimulus intensity, as the 'alarm', or reaction threshold, and report its extreme day to day variability. Almost exclusively, the 'alarm' response occurs at intensities well below (up to 85%) the verbal pain threshold report. The 'alarm' reaction is considerably elevated above pain threshold by ingestion of ethyl alcohol.

Notwithstanding the problems mentioned above, Hardy et al. (1950) have, subject to elaborate methodological rigour, felt

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* This is not to imply habituation, or adaptation, of pain sensation which has been discussed earlier.

** This assumption is highly questionable in view of one study which found no relationship between stimulus intensity and P.G.R. magnitude, although P.G.R. did discriminate between verbal reports of pain and no pain irrelevant of the stimulus level.
the method to be usable, and valid as a direct sensory sensitivity measure probably less contaminated by attitudinal bias*. The technique is of further interest since Day et al (1975) failed to find any effect of 'Acupuncture analgesia' upon G.S.R. responses to noxious radiant stimuli. For these reasons, the measure was initially included in pilot runs of the experimental design. However, the response range and pre-stimulus levels, despite a lengthy adaptation period, were found to be so variable during the course of an experimental session, as to require constant attention to the only available recording apparatus which was not of the auto-ranging type.

Regrettably, there was not sufficient manpower available to meet this demand and the measurement was therefore discontinued.

Summary and Conclusions:

The mechanics of the second Acupuncture experiment (chapter 7) are determined from review of the literature in this chapter, and on the basis of pilot work, Chapter D.

From consideration of the requirements for an optimal experimental pain stimulus source, noxious radiant-heat is selected as providing most calibration precision, suitability for the desired type of investigation of 'Acupuncture analgesia', and comparability with relevant studies elsewhere.

* In fact, a later study which applied S.D.T. methodology to compare electrodermal responses (Palmar skin potential) with verbal ratings to noxious stimuli, indicated the latter to be significantly better indicators of sensory sensitivity(96).
Precise stimulus parameters are selected for radiant beam area, stimulus intensities and duration, and interstimulus interval, in addition to choice of pain test site location, skin preparation, and stabilised environmental conditions.

Consideration of subject pain response characteristic variables leads to composition of an all caucasian subject group with equal sex representation, limited youthful age range, more advantaged educational and socio-economic background, and normal psychiatric profiles.
CHAPTER 6.

'ACUPUNCTURE ANALGESIA': HUMORAL AND NEUROPHYSIOLOGICAL MECHANISMS

Introduction:

The principal focus of investigation in this work is directed towards the application of new methods of pain measurement to behavioural rather than physiological aspects of 'Acupuncture analgesia'. However, the positive, and highly specific, results of Acupuncture Experiment No.1 deserve some consideration in terms of likely neurophysiological and humoral substrates.

(1) Localisation of Acupuncture 'Points':

The results of the first experiment suggest, first of all, the relative specificity of Acupuncture 'point' locations. The traditional 'point' and meridian theory as conceived historically by the Chinese (see chapter 1 (introduction)) is generally discounted as without substance, despite the description of a corpuscle and duct system corresponding to these structures claimed by a Korean author (46). These observations were later firmly dismissed as histological artifacts (229), but it is interesting to note that more recently various histological differences such as thickening of the epithelium, realignment of collagen fibrils, perfusion of cholinergic nerve endings, and vascular spirals, have been reported at 'points' compared to surrounding areas (356). There is also considerable evidence that 'points' correspond to areas of low electrical skin resistance, although the techniques required to demonstrate this adequately are highly sophisticated (23, 30, 358), and it is of importance to note that peripheral nerves may be located in a similar manner (307).

This latter correspondence is hardly surprising when it is observed that the main Acupuncture 'points' are usually located near branches of
cutaneous or deep muscular nerves. Indeed, surveys have indicated that 'points' either correspond to known anatomical entities such as the motor point of a muscle, the focal meeting of superficial nerves in the sagittal plane, or lie over superficial nerves or plexuses (162, 276).

This also applies to the two Acupuncture 'points' selected for use in the experiments in this laboratory*, whilst the 'Pseudo-Acupuncture' locations selected for stimulation were deliberately neutral in these respects. Given this observation, it is hardly surprising that Acupuncture 'points' should give rise to more powerful, and different, sensations, as well as eliciting fasciculation at much lower current levels (398).

It is also interesting to note the high degree of correspondence between Acupuncture 'points' and the well known western 'myofascial trigger point' system which has long been used for both diagnostic and pain relief purposes (402, 439, 440).

The 'trigger points' represent small areas of muscular spasm and, like Acupuncture 'points', yield intense radiating pain when palpated strongly**. The zones of referred pain and 'trigger points' are linked to the primary lesion site by spinal reflexes of a viscerocutaneous or viscerosomatic type (290). The cutaneous zone is usually in the same embryological segment as the related organ, although examples of intersegmental reflexes are known (290, 306). Not only the 71% 'point'

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* 'Ho-Ku' corresponds to the first dorsal interosseus motor point. 'Tsu-San-Li', " " " tibialis anterior " "

** Acupuncture also probably both prolongs stimulation around the point as well as inducing a host of other reported effects by virtue of local tissue-injury/inflammatory products (51, 350).
location agreement, but also the fact that both systems may employ dry needling, intense cold, electrical stimulation, or injection of saline or local anaesthetics at 'points', together with the coincidence between 'points' and their related pain patterns in the two systems, suggests a fundamental unity of mechanism (134,310).

There have been attempts to identify receptors, and types of afferent nerve fibres, activated by Acupuncture, with indications that group 2 afferents, particularly those carrying impulses from deep pressure receptors and muscle stretch receptors, provide maximal effects when stimulated (379). This type of afferent input is firmly implicated in the induction of 'Acupuncture analgesia' by experimental work which has demonstrated abolition of the effect following 2% procaine injection of 'points' or the nerves innervating the site, whilst similar injection of saline was without effect (85,348,359). Spinal block or nerve section proximal to the 'point' also abolishes, or prevents, the effect (255,333). In addition, 'Acupuncture analgesia' fails to develop in paralytic and hypesthetic limbs of hemiplegic or paraplegic patients (348,359).

Furthermore, it has been demonstrated that selective block of the cutaneous nerve (superficial branch of the radial nerve) from the 'Ho-Ku' 'point' in the hand fails to abolish the effect, whereas procaine block of the deep muscular nerves (deep branches of the ulnar and median nerves innervating deep fasciae, tendinous sheaths, muscles, periosteum, bursae etc.) can achieve this result (85)*. It is also relevant to note that the characteristic 'Te-chi' sensation at

* Some caution must be exercised before assuming that Acupuncture effects depend upon an intact nervous system in view of one report of induced analgesia at levels above a traumatically transected spinal cord as a result of needling 'points' below the section (134).
Acupuncture 'points' is abolished by the nerve block procedures. The sensation appears to be related to a spinal reflex contraction of the muscles in the punctured region, since the resistance to needle insertion, and the characteristic E.M.G. and subjective responses, disappear under lumbar anaesthesia(2).

Finally with regard to the apparent specificity of Acupuncture 'point' location it is interesting to note that, in addition to the numerous human studies reviewed in chapter 2 supporting this contention, there are also indications for such specificity in animals(68,333,338).

(2) Localisation of Referred Acupuncture Effects:

The most important observation of the first Acupuncture experiment in this laboratory was the relationship established between Acupuncture stimulation of two selected 'points' and abdominal analgesia. There was support for such a relationship in humans in two papers(85,209) reviewed earlier, although the methodology employed was considerably less than optimal. There is, however, evidence from animal studies to suggest predominantly localised action for many 'points'(296,298,333,435).

In general, effects appear to be largest when the Acupuncture 'point' and target zone are segmentally related(12,71), and increasingly Chinese 'prescriptions' follow this pattern(85,359,379). This is hardly surprising in view of the growing body of western evidence for the effectiveness of electrical and other counter-irritation stimulation treatments within the same or adjacent segments generally subsumed under spinal "gate control" theories(311,312).

It would be quite redundant to review the now vast body of literature relating to this theory when excellent presentation is available elsewhere(457,458). In short, the theory proposes that noxious stimulation carried to the spinal cord by small C-fibres, and
A-delta fibres, may be blocked at their synapses in the dorsal horn by the simultaneous stimulation of convergent large A-fibres.

Recent evidence has strongly indicated that segmental stimulation of the type involved in Acupuncture may indeed activate a spinal inhibitory mechanism by repetitive stimulation of large (group I\(\text{a}\) and III) myelinated A-fibres\(^1\)\(^{168,352}\). In addition, various electrical stimulation procedures via cutaneous surface electrodes (transcutaneous nerve stimulation), needles, or direct dorsal column implants, have been spawned by the theoretical model and are now firmly established in Western treatments for not only somatic, but also visceral pain\(^{62,63,72,15,383,384,460}\).

As one group of authors has stated "there is no dispute that Acupuncture works within the same segment"\(^368\). They continue, however, by stating that "our present knowledge of anatomical and physiological pathways within the nervous system is inadequate to explain the heterosegmental analgesic effects of Acupuncture". This is not entirely true for a number of reasons. First, although the best effects from counter-irritation treatments are obtained within the same segment, the primary afferent fibres dichotomise and distribute impulses to neighbouring segments, whilst proprioceptive fibres interconnect across several spinal segments, and this may readily give rise to effects in, or when stimulating, more distant dermatomes\(^454\). Although transmission cells in the dorsal horns have restricted receptive fields, they are affected by electrical stimulation of

\(^\ast\) The sensations associated with needling Acupuncture 'points' such as fullness, warmth, pressure, numbness, etc. with little or no pain, certainly suggest stimulation of large cutaneous fibres rather than small units.
afferent nerves that cover a much greater body-surface \(^{(311)}\), and the substantia gelatinosa (a suggested site for the gating mechanism) at any level receives inputs from both sides of the body (and via Lissauer’s tract) from the substantia gelatinosa in neighbouring segments \(^{(310)}\). One Chinese study \(^{(321)}\) specifically investigated the morphologic relationship between Acupuncture 'points' of the lower limb and their target sites of the abdominal viscera using degeneration and electron microscopy techniques. Their results indicated that impulses generated from 'points' in the lower limb could be transmitted to as many as six segments (T11-L5) via the ascending and descending collateral branches of the somatic course fibres entering the spinal cord, and to numerous small cells in the substantia gelatinosa by way of the large endings of the collateral branches. The authors also concluded that

"since the few fine fibres which supply the tract of Lissauer can only connect with the large cells of layer IV or V through the media of the small cells occupying layers I, II, and III (most of the fine fibres of Lissauer's tract are of intraspinal origin), the latter are believed to play a very important regulating role in the conveyance of the impulse produced by needling certain points on the lower limb. Thus in the presence of an inhibitory synapse, a regulating activity is already established in the posterior horn of the spinal cord. In the light of the specific connection of the segmental reflexes, it can be judged that it is through this complex process that needling at certain points on the lower limb induces analgesic action on the abdominal viscera."
Rapid inhibition of pain impulses in the spinal cord by Acupuncture (manual or electrical), or direct repetitive electrical stimulation of afferent cutaneous or deep muscle nerves, has been demonstrated although attenuation of the effect was evident when distant 'points' were employed(379). In addition, it was shown that a lesion placed in the ventral two thirds of the lateral funiculus on the contralateral side to stimulation could abolish the analgesic effects of Acupuncture, whilst section of the dorsal column alone at T12-L1, or superficial lateral cordotomy, were without effect.

Inhibition of pain impulses at thalamic and midbrain levels by Acupuncture has also been demonstrated in animals. Acupuncture was found to reduce responsiveness to noxious peripheral stimulation for neurons in the nucleus parafascicularis (medial thalamus) in a similar manner to intravenous morphine (69, 381). In addition, convergence of afferent impulses from different regions on the same medial thalamic neurons was demonstrated. Although Acupuncture stimulation of any body area (including the trigeminal area) resulted in some inhibition, there was again more effect from segmentally related 'points', and one study (265) demonstrated that site specificity may operate for certain nucleus ventralis posterolateralis neurons which are differentially responsive to painful stimuli, and show restricted peripheral sensory fields. For such neurons, Acupuncture stimulation is effective only when applied within the boundaries of the sensory field. Consistent with the clinical and experimental observations that Acupuncture produces hypoalgesia, rather than complete analgesia or anaesthesia, thalamic

* Or low frequency stimulation of the relevant peripheral nerve.
neuronal responses to noxious peripheral stimulation are attenuated rather than abolished, and responses to innocuous stimuli remain essentially unchanged\(^{(265)}\). It is also interesting to note that the effects of Acupuncture are reduced under conditions of increased background thalamic neuronal activity, a factor suggested in explanation of the poor results obtained with anxious, tense, or apprehensive patients\(^{(15,69)}\).

Whilst all these findings are informative in relation to segmental or generalised effects of Acupuncture, it is a little difficult to apply them to the specific relationship observed in this laboratory. Neither of the Acupuncture 'points' employed in the study bear a direct segmental relationship to the abdominal cutaneous area located within the T9 cutaneous dermatome\(^{(226)}\). The supposedly specifically related Acupuncture 'point' 'Tsu-San-Li' lies approximately within the L5 cutaneous dermatome and provides stimulation primarily to the Anterior Tibial nerve (L4/5) proceeding via the lumbo-sacral plexus\(^{(276)}\). Even allowing for the considerable normal variations in anatomical location, and segmental overlap, the Acupuncture stimulation must enter the cord several segments distal of the target zone. This makes it a little difficult to attribute the disproportionate abdominal effect entirely to propriospinal mechanisms**.

It is likely, however, that the analgesic effects on the thoracic (T1/2) cutaneous test area, which were second in order of magnitude in the experiment, may relate in a direct segmental manner to stimulation, by Acupuncture at the 'Ho-Ku point', of the radial, median and ulnar nerves (1st dorsal interosseus, adductor pollicis, T1/C8) proceeding via the brachial plexus, although it is surprising that the cutaneous

* This is also true for lamina 5 dorsal horn neurons\(^{(352)}\).

** There are additional possible autonomic factors to consider in that the 'point' has also been shown to specifically alter stomach and intestinal functions\(^{(110,246,339,380)}\).
test sites on the upper limb (C6, C7) should be so little affected.

Another mechanism to explain the relief of pain by stimulation at distant 'points' has been suggested. Various brain stem areas are known to exert powerful inhibitory control over pain information transmission, and have been described as constituting a "central biasing mechanism" which receives inputs from diffuse body areas with subsequent widespread descending or ascending projection to the spinal cord or brain. The local stimulation of particular nerves or tissue by Acupuncture might increase input to the "central biasing mechanism" which, in turn, could close gates to inputs from selected body areas.

Certainly Acupuncture of the 'Tsu-San-Li' 'point' has been shown to produce inhibition (with gradual onset and offset) of single unit responses in the midbrain reticular formation to noxious stimulation of various body sites of guinea pigs in a manner similar to morphine; and there is also some support for possible localisation in observations that cells of the midbrain reticular formation (R.F.) have large receptive fields, and stimulation of particular sites within the R.F. can produce gradients of analgesia with disproportionate effects in relatively discrete areas of the body. In addition, these effects may often outlast the period of stimulation by as long as 20 minutes. Consistent evidence is also available from patients who have undergone anterolateral spinal cordotomy and may exhibit unusual spatial pain report patterns. For example, pain at abdominal or thoracic locations may be elicited when the patient is pricked in analgesic leg areas.

Finally, there is also a recent investigation of normals demonstrating reliable complex patterns of referred cutaneous sensation.

* It should, however, be noted that at least the forearm test site was third in order of analgesic effect.

** It is also relevant to note that damage or anaesthetisation of the R.F. can abolish the specific analgesic and stomach/intestinal regulatory effects of the 'Tsu-San-Li' Acupuncture 'point'.
completely outside the stimulated dermatome (407). Although the
description of these relationships is too inadequate to permit proper
comparison with the Acupuncture system, certain ressemblances are
evident, and the author concludes with the relevant comment that "the
failure of a sensory phenomenon to be distributed in a dermatomal
fashion should not be grounds for dismissing it".

(3) Humoral Mechanisms in Acupuncture:

A major problem remains unexplained by all the potential
mechanisms so far discussed, in the observation, both in this labora-
tory and in all studies monitoring the time course of 'Acupuncture
analgesia', of a gradual onset of the effect over at least 30 minutes,
and its persistence for minutes, hours, or even days (448) after
termination of stimulation. The neuronal mechanisms discussed so far
do not satisfactorily explain this without postulation of reverberatory
activity or similar ad hoc mechanisms*, and a humoral factor is strongly
implicated. Although vascular occlusion** above standard Acupuncture
'points' in the forearm failed to prevent or abolish*** the analgesic
effect (85), this appears to merely indicate that the principal site
of release of the humoral agent is not at the site of stimulation, in
view of several cross perfusion animal studies.

* This is not to say that very prolonged effects cannot arise from
these mechanisms (306), merely that such instances are largely
confined to pathological conditions and do not appear to produce
reliable, generalised effects, with the temporal pattern shown
to be characteristic of Acupuncture.

** Confirmed by blockage of injected radioactive I131 uptake by the
thyroid.

*** Although there were slight, non significant, reductions.
Acupuncture at sites in the hindlimbs of 36 rats provided significant elevations (Peak 140%) of withdrawal latency to contact heat applied to the tail\(^{(277)}\). Onset of analgesia was progressive until cessation of treatment after 60 minutes with gradual offset thereafter. These effects were significantly superior to untreated control animals. 75% of animals paired with the Acupuncture group and linked by the common carotid artery developed a similar significant analgesic response. This finding has been replicated elsewhere in rats and rabbits\(^{(333,379)}\).

Further work has indicated that Acupuncture may alter the EEG of the brainstem, diencephalon, and cerebral cortex (integrated \(\theta\) wave decreased several minutes after onset of stimulation followed by \(\delta\) wave increase, both effects persisting after cessation of Acupuncture) of not only the treated animal but also in the cross circulated recipient animal\(^{(426)}\). It was also noted that 5-HTP potentiated these effects, whilst PCPA inhibited the changes.

Extremely important transfusion studies in France indicated that a humoral factor released into the blood stream could exert its effect upon the specific target area for analgesia, even in the recipient animal\(^{(356,435)*}\). This work also demonstrated not only production of the humoral factor in rabbits with the spinal cord severed behind the medulla oblongata, but also that effects in the donor and recipient animals developed in the target zone on the same side of the body. These findings appear particularly important in the explanation of extra-segmental effects of Acupuncture which are more difficult to reconcile with known neuronal mechanisms.

* This has also been confirmed elsewhere\(^{(275)}\).
Similar results have been observed when ventricular CSF was withdrawn from donor rabbits after 30 minutes of Acupuncture stimulation and injected into the third ventricle or the anterior horn of the lateral ventricle in recipient animals. Finger-Acupuncture (ie. low frequency rhythmic application of pressure at Acupuncture 'points') produced significant elevation (133%) of withdrawal latency to radiant heat stimuli in 16 rabbits compared to baseline levels or to untreated controls. Analgesia persisted for 40 minutes after treatment. Rabbits receiving CSF from Acupuncture-treated partners also exhibited similar, if slightly attenuated, analgesic shifts (82%) which significantly exceeded the minimal changes observed for control pairs of animals not receiving Acupuncture stimulation.

Several studies in man not only point towards a humoral factor in Acupuncture analgesia, but suggest certain candidates for the active agent. However, before discussing these studies, it is relevant to outline recent developments in our understanding of opiate action which have directed Acupuncture research along new, and fruitful, lines of enquiry.

The demonstration, several years ago, of the existence and characterisation of highly specific opiate receptor binding sites in the synaptic plasma membranes, suggested a functional receptor unit. The receptors were located in a large number of vertebrate species with marked regional variation in density. The regional localisation is highly informative in relation to known opiate actions. For example the periaqueductal gray, one of the four regions in which morphine microinjection elicits analgesia, and where focal electrical stimulation produces naloxone-reversible analgesia, is also particularly rich in opiate receptors. Also, the medial thalamus (mediating * A highly specific opiate antagonist apparently otherwise neutral).
poorly localised and emotionally influenced deep pain of the type most affected by opiates) exhibits considerably greater receptor density than the lateral thalamus (which deals with highly localised somatotopic pain such as pinprick).

The limbic system in general seems to contain the greatest proportion of rich binding sites, and it is particularly interesting to note that many of these areas are not directly associated with sensory analgesia. The amygdala and septal nuclei, for example, appear to be involved in production of fear or aggression reactions, both of which are modified by opiates. The latter may also contain opiate modifiable "pleasure centres". It therefore seems likely that receptors in these and other limbic areas may be more associated with influences of opiates on emotional behaviour, and the response to pain.

The receptors are also localised densely within the substantia gelatinosa of the spinal cord, a finding with clear implications for spinal as well as higher centre direct opiate effects.

The demonstration of the receptors, of course, logically promoted a search for an endogenous ligand and evidence for the existence of such natural substrates in the brain and pituitary was soon forthcoming with results indicating that a complete group of high-molecular weight peptides with opiate-like properties were, in fact, present. They are now collectively termed 'Endorphins' and it appears that β-lipotropin is the pro-hormone for all endorphins (except leucine-enkephalin).

The two pentapeptides, leu-enkephalin and met-enkephalin, were originally isolated from the brain but appear to be widely distributed throughout the C.N.S. in a manner paralleling the opiate receptor distribution, although localised to nerve terminals suggesting intraneuronal synthesis. The enkephalins do not seem to be present in appreciable amounts in the pituitary, gland or peripheral nerves,
although the longer, and considerably more analgetically potent, \( \beta \)-endorphin\(^{(260)} \) (and other less potent or neutral long endorphin chains) are concentrated there\(^{(160)} \). It is not known to what extent the large pituitary endorphins enter the brain (hypophysectomy does not significantly alter brain endorphin content\(^{(147)} \)) or the general circulation, but the present weight of evidence does suggest a functional division of more brain specific enkephalins as neurotransmitter candidates, and more pituitary specific larger peptides (such as \( \beta \)-endorphin) as hormonal agents.

The pharmacologic properties of the endorphins in animals are similar to those of morphine. Neurones typically activated by noxious stimuli can be inhibited by application of met-enkephalin iontophoretically\(^{(197)} \), and mild analgesia may be induced in vivo by intraventricular administration of enkephalin\(^{(27)} \), or much more potently* by \( \beta \)-endorphin\(^{(160)} \), which may also be effective when given intravenously\(^{(443)} \). Enkephalin effects are short lived (<5 min.) but changes induced by the larger endorphins may persist for several hours\(^{(160)} \). This does not, of course, necessarily exclude enkephalins from an important role when endogenously stimulated.

These reported effects are reversible by the specific opiate antagonist naloxone and cross tolerance with morphine has been demonstrated for both met-enkephalin and \( \beta \)-endorphin\(^{(132,442,463)} \)\(^{**} \). Unfortunately, although the development of tolerance and dependence for endorphins has not been completely conclusively established, it does also appear likely from the results of chronic perfusion of rat cerebral ventricles or repeated injections of \( \beta \)-endorphin\(^{(269,466)} \).

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* Intravenous \( \beta \)-endorphin was some 3–4 times more potent than morphine on a molar basis but has been reported as 17–48 times more potent when applied centrally\(^{(269)} \).

** Cross dependence has also been demonstrated for \( \beta \)-endorphin and morphine\(^{(442)} \).
Further functions of endorphins are suggested by the demonstration that stress from acute pain can produce naloxone reversible elevation of brain enkephalin levels \(^6\), and in one long term study this was also associated with naloxone reversible analgesia \(^{283}\)*. It has also been found to concomitantly increase \(\beta\)-endorphin and ACTH circulating concentrations \(^{161}\)*. This significant, and reliable, effect has been proposed as indicative of a neurotropic regulatory role for the circulating pituitary \(\beta\)-endorphin, and could be particularly relevant in pain experimentation with high stress loading. It does seem likely, however, that although \(\beta\)-endorphin has profound behavioural and physiological (morphine-like) effects** when administered centrally \(^{41,213}\), these effects (except perhaps analgesia) are not generally evident with intravenous injection \(^{160}\), and the targets for pituitary secretion are probably peripheral in view of the lack of evidence for retrograde flow to the brain. In addition, the circulating levels of \(\beta\)-endorphin induced by stress were very much lower than plasma concentrations associated with the reported successful induction of analgesia by intravenous injection \(^{443}\). Since the pituitary itself possesses opiate receptors, similar in their properties to the brain receptors, it is even possible that important effects are mediated locally.

Although many of the behavioural effects of endorphins mimic those of morphine in animals, little is known of the likely results in normal humans. There are, however, tentative indications of mild cognitive impairment, drowsiness, and feelings of perplexity, following \(\beta\)-endorphin administration \(^{234}\) and there may also be effects inhibiting

* This effect was abolished by hypophysectomy.

** Profound sedation or catalepsy, wet-dog shakes, also rectal hypothermia (>2\(^0\)C) and loss of corneal and tail-pinch reflexes. All effects are rapidly reversed by naloxone.
anxiety, tension, and hostility (156). This could extend to frank depression if observations of abnormally high CSF endorphin levels in depressed patients prove meaningful (43). It has been suggested by a number of experiments that the endorphin system is not continuously active at anything beyond a minimal level, a not unreasonable possibility in view of the biological advantages of relative arousal and responsivity to noxious stimulation. Rats, for example, treated with doses of naloxone sufficient to block morphine analgesia have failed to display altered threshold for escape from foot shock (149). It does, however, appear as though care must be exercised in the choice of noxious stimuli, as one study demonstrated naloxone-induced hyperalgesia for tail-flick, but not for tail-pinches tests (34), whilst others observed significant hot-plate test results without effect upon paw-lick latency (157, 212). Interestingly, mice have also been shown to take longer to enter a dark box after administration of naloxone (157), a finding perhaps compatible with the possible anti-anxiety effects of endorphins in humans referred to above. Small hyperalgesic responses to naloxone were also evident for "squeak latency" with radiant heat stimulation (353). Overall, the results suggest that naloxone effects are more likely where the animals have experienced more prolonged exposure to the noxious stimulus source. This is quite consistent with other evidence discussed above indicating that prolonged pain or stress may be necessary to activate the endorphin system. It might then be seen as an adaptive mechanism initiated by longer exposures to less immediately imperative noxious stimulus sources. Clearly it would be biologically disadvantageous for such mechanisms to activate with very short latencies.

* It is interesting to note evidence that brain enkephalins may have euphoric or drive-reduction characteristics as it is reinforcing to rats (28).
In humans, again normal clinical doses of naloxone failed to alter electric shock pain (124), ischemic pain, coli pressor pain, or mood-state (156,158), whilst one well controlled study of post-operative pain observed significant increase in pain sensitivity after naloxone compared to placebo controls (254). It seems likely that the increased anxiety, stress, and prolonged nature of the clinical pain testing situation contributed to this positive finding by permitting slow development of an adaptive endorphin response.

Another study (253) by the last group of authors is of particular interest and importance, in that the results indicate that the analgesic effects of placebos may be endorphin dependent. Patients (n = 52) with post-operative dental pain were randomly allocated, under double-blind conditions, to balanced order groups receiving placebo and naloxone*. Results indicated that naloxone induced a significantly greater increase in pain ratings in placebo responders than in non-responders, and also that prior administration of naloxone reduced the probability of a positive placebo response. These effects of naloxone were significant after 5 minutes, peaked after 20 minutes, and persisted for over 60 minutes. The astonishing implications of this experiment do seem consistent with other evidence, usually interpreted entirely within a psychological** framework, that placebo responders get significantly more post-operative pain relief from

* Patients were told they might receive either morphine, placebo, or naloxone (described as an agent which might increase their pain). Knowledge of potential receipt of placebo does not appear to reduce response likelihood and naloxone has not been reported as providing any effect discernible to subjects, provided they are opioid-naive (214).

** In the sense of being entirely without physiological substrate.
narcotic analgesics, and that tolerance and abstinence syndromes may occur with placebos, whilst they may partially reverse withdrawal symptoms in narcotic addicts (cited in 253).

Finally, in connection with this study, it is interesting to note elsewhere the failure of naloxone to modify hypnotically induced analgesia (148, 304). This might appear as a contradictory finding were it not for evidence of poor correlation between responses to placebos and to suggestion or hypnosis, possibly indicative of different underlying modes of action (126, 127).

A number of studies directly implicate endorphin mechanisms in the phenomenon of 'Acupuncture analgesia'. A well controlled animal study (353) applied noxious radiant heat stimuli to the noses of 70 mice with measurement of squeak latency. Matched groups of 10 animals received different treatments as follows: Acupuncture ('Ho-Ku' point', 20 min. electrical stimulation), 'sham' Acupuncture (deltoid region), Acupuncture plus naloxone, Acupuncture plus saline, naloxone, saline, and no treatment. Injections were given in a blind protocol.

Acupuncture, with or without saline injection, provided significant elevations of response latency above baselines, and above all other groups, with progressive ascent, a peak at 40 minutes**, and gradual offset over 2 hours. Naloxone thus completely antagonised the development of 'Acupuncture analgesia' and this together with the time course of analgesia strongly implicates a humoral opiate-like mechanism. In fact, the injection of naloxone combined with Acupuncture, or alone,

* It is also relevant to note the increased effectiveness of both placebos and 'active' drugs under conditions of increased stress (26).
** i.e. 20 minutes after termination of Acupuncture.
provided significant hypalgesic shifts compared to no-treatment or saline injection controls (which exhibited negligible departures from baseline levels). Contrary to indications from studies discussed earlier, this appears to suggest some ongoing baseline endorphin secretion. However, it is likely that the animals were initially stressed by the experimental situation and thus endorphin baselines may have already been artificially elevated.

A similar methodology was employed in a second study from the same laboratory with hypophysectomised mice (n = 15). This time, however, noxious electrical stimulation was delivered near the intercostal nerves at T5 to T10, and Acupuncture 'points' recommended by Chinese sources for thoracic surgery were electrically stimulated for 30 minutes. The effects of identical treatment upon squeak threshold voltages in sham operated animals (with intact pituitaries) were compared as control measures. Hypophysectomised mice exhibited a mean elevation of only 7% after Acupuncture compared to the significantly greater mean value of 56% obtained with the intact animal group.

These results strongly suggest that a pituitary peptide mediates the major proportion of the Acupuncture effect, and therefore that further investigation might most profitably look for manifestation of effects characteristic of the larger endorphins in association with Acupuncture.

An alternative animal model has been employed in studies by two separate groups, whereby the effects of Electro-Acupuncture upon the morphine withdrawal syndrome have been observed. Rats or mice were rendered physically dependent upon morphine by subcutaneous pellet implantation over several days, and then the withdrawal syndrome was precipitated by naloxone after pre-treatment with Acupuncture.
stimulation of the ears. Both studies reported reduced severity and
frequency of withdrawal symptoms* as a result of the Acupuncture pre-
treatment compared to untreated control animals**.

One study (331) further indicated that without Acupuncture, rectal
temperature of morphine-dependent rats, originally higher than that of
sham-implanted controls, fell significantly below that of these controls
at 30 minutes after naloxone injection. This descent was limited by
Acupuncture.

The other study (199) sacrificed the animals and observed signifi-
cant elevation of one opiate-like peptide in whole brain extracts from
the Acupuncture group compared to the untreated controls. Proper
identification of the fraction obtained was not undertaken but similari-
ties to β-endorphin were noted. A second fraction, suggested as
corresponding to met-enkephalin, was also identified but without
significant difference between the animal groups. Although the result
is rather imprecise, it is yet another indication of the probable
involvement of β-endorphin in the mechanism of 'Acupuncture analgesia'.

In humans, increased levels of endorphins have been observed in
C.S.F. after Electro-Acupuncture (395). Nine patients actively suffering
from chronic painful conditions underwent lumbar puncture procedures
before*** and shortly after 45 minutes of Electro-Acupuncture via surface
electrodes. C.S.F. was analysed for endogenous opioids by ultrafiltra-
tion and fractionation by Sephadex G10 column. The first fraction (I)
collected remains unidentified, whilst the second (II) was apparently

* ie. restlessness, hypothermia, wet-dog shakes, and squeaking.
Negative signs such as salivation and/or lacrimation, and diarrhoea
were unimproved.

** It is particularly relevant to note reports of successful alleviation
of opiate withdrawal syndrome by similar Acupuncture treatment
applied to the ears (256,346,347,471). In addition Acupuncture has
been shown to provide profound sedative effects in man and animals
(346,426). This aspect of the treatment is now in current use for
psychiatric problems (347,390).

*** Analgesics were not taken for 12-18 hours prior to this point.
identical to met-enkephalin. On analysis the lumbar C.S.F. concentra-
tions of fraction I were found to be unusually low in all patients
experiencing pain. During stimulation analgesia a marked rise in
this fraction level was noted in only the four patients undergoing
stimulation of lumbar segments for lumbar regional pain. The remain-
ing patients were stimulated close to their painful areas and, with
one exception, obtained good to full pain relief, but did not show
increased lumbar C.S.F. endorphin levels. The authors suggest that a
local release of endorphins is implicated, and that effects might have
been observed in other patients if fluid at appropriate segments had
been analysed. Again, in line with the last study reviewed above,
fraction II (met-enkephalin) did not display any systematic change
during treatment and appeared unrelated to analgesia.

A study (305)* in humans, of major importance, investigated the
effects of naloxone (0.8mg i.v.) administered after significant
successful induction of 'Acupuncture analgesia' from 30 minutes of
manual stimulation of needles inserted in the hands. Eleven subjects
received naloxone, and nine subjects an equal volume of saline, five
minutes after termination of 30 minutes of Acupuncture stimulation.
Pain thresholds were then measured at 5, 10, and 15 minutes after
injection. Naloxone reduced pain threshold to approximately the level
of the placebo control group after five minutes. This effect was
highly reliable (within-group t-test) and was maintained at ten minutes
post-injection. Pain thresholds then returned to pre-injection levels
five minutes later. Saline injection had no effect on pain threshold
at any test point. Potential contributory effects of naloxone upon
baseline pain thresholds were discounted by administration of 0.8mg i.v.
naloxone, or saline, to two further control groups under 'double-blind'

* As already reviewed in chapter 2.
conditions with pain testing over 15 minutes. Pain thresholds remain unaltered in both groups at all temporal points.

These observations, together with very similar findings for clinical pain elsewhere (394) must be taken as strongly implicating endorphin mechanisms in the mode of action of Acupuncture for analgesia in humans. In addition, it greatly supports the likely applicability of information from all the animal work reviewed.

Additional support for the role of endogenous opiates in 'Acupuncture analgesia' comes from its considerable similarity with other forms of stimulation analgesia which appear to involve such mechanisms.

For example, numerous studies have demonstrated that focal electrical stimulation of various brain structures* can produce powerful analgesia in animals (150, 263, 299, 301, 341, 403), and in man (5, 164, 203, 364, 365) for a wide range of noxious stimulus sources including electrical shock, electrical stimulation of the tooth pulp, and thermal stimulation (299, 301, 403), as well as various clinical pain syndromes in man (5, 364).

The effects do not appear to result from generalised sensory, motivational, emotional, attentional, or motoric deficits, since the field of analgesia can be extremely restricted and other sensory modalities remain unaffected (299, 301, 403). In addition, the phenomenon displays a prolonged period of onset and offset (299, 309), and although stimulation of the brain areas involved is often intrinsically rewarding, there is clear evidence that this is neither a necessary, nor sufficient, condition for analgesia (299, 301).

* From a review of available evidence the anatomical substrate for analgesic effects appears concentrated in the medial brain stem structures extending from the medial diencephalon caudad to the medullary raphe nuclei with particular implication of the periaqueductal gray regions, and sites adjacent to the third ventricle (303).
Endogenous mechanisms are suggested in stimulation analgesia by a number of observations. First, spinal cord nociceptive responses such as the rat tail flick and flexion reflexes, which are resistant to all but narcotic analgesics, are readily suppressed by the treatment (299,301). In addition, electrolytic or chemical lesions at the stimulation site do not produce analgesia, whilst the behavioural expression of analgesia can be abolished by the interruption of neural pathways descending to the spinal cord dorsal horn (303). If stimulation was directly incapacitating some link in a pain pathway, there would be no reason for the lesion of a descending pathway to block its analgesic action. There is also ample behavioural and electrophysiological evidence for activation of a descending inhibitory system in the action of morphine (303).

Endogenous opiates (endorphins) are particularly implicated in the effects of focal electrical stimulation of the brain by the fact that it is antagonised in both animals and man by naloxone (5,7,203, 342,365), although not always entirely (7). Furthermore, development of tolerance, and cross tolerance with morphine has been demonstrated for human and animal stimulation analgesia (203,300). Finally analgesia produced by stimulation of the human periaqueductal gray, in patients with chronic pain, has been directly associated with increased β-endorphin concentrations in ventricular c.S.F. (204).

It is clear from the above discussion that very substantial correspondences are evident between the characteristics of Acupuncture and focal electrical stimulation analgesias, and endogenous opiates are clearly implicated in both processes.

There have, however, been suggestions of possible differences in action. For example, although both treatments are modulated by monoaminergic transmission, it appears that stimulation analgesia
particularly facilitated by serotonin, and further facilitated by dopamine, but antagonised by norepinephrine (303). 'Acupuncture analgesia' on the other hand has been reported as enhanced and prolonged by intraventricular reserpine, and restored to its original level by replacement of the monoamines (NE, DA, 5-HT), whilst atropine inhibits the effect (360). Whilst it is true that different antinociceptive tests reflect the function of different centres (81), and the influence of reserpine may vary for different tests (370), in addition to the usual problems of species specificity, this could suggest a very complex and somewhat contradictory relationship between the two forms of analgesia, and indeed between Acupuncture and morphine.

This picture is certainly further confused by evidence suggesting that Acupuncture actually increases serotonin content in the lower brainstem (3), whilst treatment with 5-HTP enhanced the EEG slowing effects of Acupuncture associated with induced analgesia, and PCPA antagonised the effect (426). The problem is fully discussed elsewhere (220, 303).

A final interesting correspondence between Acupuncture and other analgesic agents is worthy of mention in view of the similarity of analgesic pattern of effect reported by some authors for nitrous oxide and Acupuncture (74, 75). It appears that this may not be so surprising, in view of evidence elsewhere to demonstrate that, like 'Acupuncture analgesia', nitrous oxide relief of pain is antagonised by naloxone, again possibly implicating endorphin mechanisms (31, 32).

* It is unfortunate in this context that no controlled studies have yet examined, or reported, the possibility of cross tolerance for Acupuncture and stimulation analgesia or morphine; or the development of tolerance to Acupuncture. There are indications from clinical studies reviewed in chapter 2, but their design makes it impossible to discriminate between potential extinction of placebo effects and development of tolerance to Acupuncture. In addition, since placebo mechanisms may also involve endogenous opiates (253) such distinctions are further complicated. There are possible indications of cross tolerance for opiates and Acupuncture from use of the treatment for withdrawal syndrome, which is less effective when opiates are taken in conjunction with Acupuncture (387).
Summary and Conclusions:

The results of the first Acupuncture experiment in this laboratory are placed in the context of potential neurophysiological and humoral substrates.

The relative anatomical and functional specificity of the Acupuncture 'points', and their correspondence to well known western systems of myofascial 'trigger points' is suggested from reviewed evidence in the literature. The integrity of proprioceptive input from the 'point' is also particularly implicated in the analgesic and subjective effects of Acupuncture.

Consideration is given to the relationship between Acupuncture 'points' and their analgesic target loci. The specific relationship observed in this laboratory, although not strictly segmental (like many other Acupuncture or counter-irritation treatments) may be compatible with current "gate control" theories of pain in view of evidence for propriospinal interactions, and suggestions for a brainstem "central biasing mechanism" with possible descending selective inhibition of inputs from relatively discrete body areas as a result of Acupuncture.

Powerful evidence implicates an endogenous opiate (endorphin) humoral mechanism in 'Acupuncture analgesia'. The time course of Acupuncture effects, and the results of cross-perfusion (circulation and CSF) experiments support humoral components; and the latter may be particularly important in view of the development of target specific analgesia in recipient animals. Endorphins are specifically implicated by the reversal of 'Acupuncture analgesia' by naloxone, and the relief of opiate withdrawal syndromes by Acupuncture in man and animals.
Results from hypophysectomised animals, various brain and systemic endorphin assays, the observed sedative behavioural effects of Acupuncture, and the known analgesic potency and other properties of the various endorphins, strongly point to \( \beta \)-endorphin as the principal humoral agent.

Finally, indirect support for endorphin involvement in 'Acupuncture analgesia' is provided by its similarities with analgesia induced by focal electrical stimulation of the brain. Considerably more research evidence is available for the latter treatment in man and animals, and endorphins have been firmly implicated.

All the available evidence suggests that further investigation of Acupuncture with respect to the likely involvement of endorphins, \( \beta \)-endorphin in particular, may prove fruitful.
CHAPTER 7.

ACUPUNCTURE EXPERIMENT NO. 2

Introduction:

Evidence provided in the first pilot study (ref. chapter 3) strongly discounts purely psychological factors as an explanation of 'Acupuncture analgesia', and suggests the potential value of investigation directed at underlying physiological mechanisms.

Chapter 6 indicates the likely involvement of endogenous opiates (β-Endorphin in particular), and the major follow-up study to be reported below attempts to test this possibility by administration of the opiate antagonist Naloxone, direct radioimmunoassay of systemic Endorphin content, and monitoring of temperature and subjective side-effect reports. It is also, naturally, hoped that the findings of the first study may be confirmed on a larger scale by replicating treatment and control conditions, in addition to the new measures.

This investigation of 'Acupuncture analgesia' also serves as the simultaneous focus for the equally important concern of the study, namely validation of the novel methodology of 'Signal Detection Theory' as applied to pain experimentation. The weaknesses of traditional approaches were discussed in chapter 4, and it is clear that, if S.D.T. can be successfully implemented, greatly increased information concerning the relative importance of direct inhibition of sensory transmission or of higher centre responses to pain during 'Acupuncture analgesia' may be forthcoming. Although the localisation of analgesic effect in the first experiment implies some
specific sensory effect, it is not clear how much bias or attitudinal shift may also be physiologically* induced by the treatment.

The review of S.D.T. studies of 'Acupuncture analgesia' undertaken in chapter 4 indicates marked conflict as to the existence of bias or true sensory effects of the treatment. This clearly requires resolution by a definitive study avoiding many of the methodological criticisms which were raised against these experiments.

It is hoped that a combination of optimal S.D.T. procedures as suggested in chapter 4, together with optimal pain stimulus, subject, and ambient condition, parameters (as outlined in chapter 5) will permit the required resolution of the problem.

Review of S.D.T. studies elsewhere (chapter 4) also appears to imply that the methodology may be easily, and successfully, applied with considerable reliability. It should, however, be noted that this did not appear to be the case during the very extensive pilot work undertaken in this laboratory prior to the main experiment.

* This could be indicated by Naloxone antagonism of bias shifts, and perhaps by differential shifts under 'Genuine Acupuncture' compared to the 'Pseudo-Acupuncture' treatment.
ACUPUNCTURE EXPERIMENT NO 2

Pilot Studies

Introduction

For the reasons discussed in chapter 4, the Signal Detection Theory model (principally the rating scale experiment) was to be adopted for the analysis of responses to pain inducing radiant heat stimuli, applied to the subject's abdomen. Extensive pilot trials were run in an attempt to build upon the methodologies employed in some of the other studies discussed in chapter 4. For reasons of limited direct relevance and space, these are not fully described here. Only a summary outline of some of the model variants assessed, and the problems leading to their rejection, are presented. An attempt is, however, made to discuss the final design adopted within the framework of conventional approaches to pain measurement, and in relation to other studies employing S.D.T. methodology.

Methods Assessed

Subjects were to receive an adaptation and training session, as described below, two days prior to the first experimental session.

The form completed during these sessions indicates the sequence of events and is reproduced as a sub-section at the end of this section, together with the standardised instructions given to subjects.

Essentially all experimental procedures were demonstrated during an adaptation phase. Then the subjects 'Pain Detection Threshold' and 'Pain Tolerance' points were established as stimulus intensities (watts/cm\(^2\)) by the method of limits (437). On the basis of these

* Instructions were for pricking pain threshold after Hardy et al 1952 (179).
values, a series of six stimulus levels (labelled A-F) was set up ranging from zero (A) to the 'Pain Tolerance' intensity plus 10% (F). Two log* interval-stimulus levels (D,E) were interposed between the threshold + 10% (C) and tolerance + 10% (F) points, and one level (B) set midway between zero and the threshold + 10% level.

The stimulus series was presented to the subjects in ascending order (A-F), followed by descending order (F-A), twice. Subjects were instructed to identify each of these stimuli with a number (0,2,4,6,8,10) in order of intensity. These numbers were then to be used by the subjects for their responses to stimuli. A heat sink at equilibrium temperature with thoracic skin was applied to the subjects' epigastrium after each series to return the cutaneous temperature to the previous baseline.

Next, the stimulus series was presented in a pseudo-random order over a series of trials, with subjects identifying the stimulus presented by number. Two trials with feedback were followed by two without, and the hit percentage was monitored throughout. Subjects were motivated by knowledge that a good hit rate was required for continued participation in the experiment, and by ongoing contingent verbal reinforcement.

Incremental stimulus levels increasing logarithmically were established using the formula below:

\[ \log e_n = n \times \left( \frac{\log e_\omega - \log e_\alpha}{N} \right) + \log e_\alpha \]

where \( e \) = energy (watts/cm\(^2\) or mcal/cm\(^{-1}\)/sec\(^{-2}\)) cf. \( e_1, e_2, e_3 \)

\( n \) = number of the stimulus point the 'e' value of which is to be established, eg. \( e_1, e_2, e_3 \)

\( e_\omega \) = Highest energy value of the range to be established

\( e_\alpha \) = Lowest " " " " " " " " " "

\( N \) = Number of divisions required in the interval between the lowest and highest energy levels, ie. \[ e_1 \; e_2 \; e_\omega \; N = 3 \]
from the experimenter. Finally, if the subject obtained a sufficiently high hit rate (~60%), the pseudo-random series was readministered with the subject employing a full range response scale from 0, 1, 2, 3-10 under a misleading instruction set to the effect that a totally random, infinite variety, of stimuli were to be presented. Subjects were instructed merely to report the response number (0-10) which most closely approximated the sensation experienced, using the remembered sensations induced by the six 'fixed' stimuli of the training session for comparison.

The goals of this design were multiple. First to attempt to tie the stimulus series to each individual subject in a meaningful way by basing levels on his demonstrated threshold and tolerance points. Other workers (70,93) have similarly attempted to use individual pain thresholds to locate stimulus intensity ranges, with claimed success. The addition of 10% to these levels was intended to compensate for the psychological set, doubtless due to attentional and anxiety factors, whereby subjects tended to report lower thresholds and tolerances on their initial visit to the Laboratory than subsequently. Since the focal interest of the study was on alteration of pain sensitivity, it was important that at least the higher intensity stimuli should evoke pain whatever the later psychological set of the subject. The elevation of intensities was also intended to compensate for, and aid the visibility of, any analgesia induced by the Acupuncture stimulation in the experimental sessions to come.

The use of a numerical response system and training was intended to produce educated observers unbiased by differing or changing internal definitions of descriptive response categories such as 'very painful' etc.
Most important, however, was the intention to produce an inter-
stimulus interval of approximately equal discriminability ($d'$) 
between adjacent stimuli, at least over the range of focal interest 
between threshold and tolerance. (A $d'$ discriminability between 
adjacent stimuli with large numbers of presentations would be ideal.) However, limitations as to the maximum number of stimuli one might 
reasonably deliver to a subject, compromised with the number of 
presentations required at each intensity for an adequate S.D.T. 
analysis, suggested a maximum of six levels. Threshold to tolerance 
could be adequately covered by four stimulus intensities; with an 
additional intensity interspersed between zero and threshold to provide 
continuity of overlap between the sensory magnitude distributions of 
adjacent stimulus levels across the entire range. This would serve to 
anchor the entire sensory continuum to the pure neural noise distribu-
tion of the zero stimulus. It was again hoped to produce approximately 
equal discriminability ($d'$) between zero (A) and the first stimulus 
intensity (B), and between threshold (C) and the first stimulus 
intensity (B).

The use of a logarithm interval scale for the higher levels (C-F) 
of the series was based upon reports of gradual increase in the Weber 
ratio for radiant heat pain over these levels\(^{18}\).

Expansion of the rating system to 11 numerical categories in the 
experimental sessions was intended to permit subjects to fully exploit 
their ability to hold multiple criteria, and thus expand the number of 
points available for the R.O.C. curve. Care was taken not to imply to 
the subjects that there were ten different stimulus levels when, in 
fact, only six were present. That might be criticised on the grounds 
of introducing artificial variance into subjects' responses which did 
not necessarily reflect a true variance in sensory experience. The
implication of a very great number of stimulus intensities, with use
of the rating categories as best approximations (based on a standard-
ised training) to a very great range of sensory experience, might be
argued as permitting subjects to respond largely on the basis of
sensory experience. Response variance should, therefore, largely
represent true sensory variance. The importance for S.D.T. analysis
of overlap between response distributions for adjacent stimuli across
the whole stimulus range has already been mentioned above.

Results

Subjects successfully defined threshold (eight trials) and
tolerance (four trials) points by the method of limits with remarkably
small standard deviations. Typical results appear in Table 42 page 228
and fit the uniformity reported elsewhere (487) quite acceptably for
within session testing on individuals, and across subjects for their
initial session. A number of variables may account for the slightly
higher threshold values observed here compared to some studies (174,188,378),
although not all (80,373), using similar instruction 'sets' for
'pricking pain'. The forehead test site employed by these authors
appears to be more sensitive than the abdomen (292), and certainly the
latter clearly displayed the highest threshold and tolerance values
of any body site in the first Acupuncture experiment. Hardy et al
(1952) (179) would not, however, agree with this finding. In addition,
the forehead is subject to cues due to light transmission through the
tissues (325). Also, in view of evidence for slight spatial summation
for pain (154), the rather small area of cutaneous stimulation (1.0 cm²)
employed here may contribute marginally to elevated thresholds.
Certainly one study employing a similar aperture area, although testing
the dorsal hand, also found slightly higher thresholds than usual (325).
Most important, however, is probably the difference in skin blackening
preparation employed and this is discussed fully later.
TABLE 42: ACUPUNCTURE EXPERIMENT NO 2: PILOT STUDIES:
Pain Detection Threshold and Pain Tolerance
Stimulus Intensities (mcal/sec\(^{-1}\)/cm\(^{-2}\)) for 6 Typical Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean Threshold</th>
<th>S.D.%</th>
<th>Mean ** Tolerance</th>
<th>S.D.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>262.8</td>
<td>3.6</td>
<td>353.6</td>
<td>0.7</td>
</tr>
<tr>
<td>2</td>
<td>274.8</td>
<td>1.2</td>
<td>353.6</td>
<td>0.5</td>
</tr>
<tr>
<td>3</td>
<td>305.8</td>
<td>2.3</td>
<td>367.9</td>
<td>1.3</td>
</tr>
<tr>
<td>4</td>
<td>277.1</td>
<td>3.4</td>
<td>322.5</td>
<td>2.2</td>
</tr>
<tr>
<td>5</td>
<td>229.4</td>
<td>3.1</td>
<td>344.0</td>
<td>1.4</td>
</tr>
<tr>
<td>6 (Day 1)</td>
<td>212.6</td>
<td>5.2</td>
<td>293.9</td>
<td>4.8</td>
</tr>
<tr>
<td>Day 2)</td>
<td>215.0</td>
<td>6.3</td>
<td>315.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Day 3)</td>
<td>279.5</td>
<td>1.7</td>
<td>351.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Day 4)</td>
<td>267.6</td>
<td>1.0</td>
<td>353.6</td>
<td>1.3</td>
</tr>
</tbody>
</table>

**Group Means**

<table>
<thead>
<tr>
<th>Mean Threshold</th>
<th>S.D.%</th>
<th>Mean ** Tolerance</th>
<th>S.D.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>258.3</td>
<td>3.1</td>
<td>339.5</td>
<td>1.7</td>
</tr>
</tbody>
</table>

* 8 trials (method of limits)
** 4 trials ascending

Note: 1 mcal/sec\(^{-1}\)/cm\(^{-2}\) = 1 x 4.1855 x 10\(^{-3}\) watts/cm\(^{2}\).
Much greater variability was evident for subjects given repeat tests on separate days. A typical example appears as subject 6, tested on four occasions, in Table 42 page 228. This was evident to the extent that a subject might entirely fail to report pricking pain to a stimulus level reliably producing pricking pain on a previous occasion. As an extreme example, one subject with a reliably established pain threshold in the training session failed to report any pain to a stimulus level 40% greater than that level on a subsequent day. The notorious unreliability of thresholds in all but the most rigorous conditions, and for highly trained subjects, was perhaps becoming evident. Interestingly, much less variance was attached to pain tolerance levels although many authors have regarded this element as especially subject to psychological variables.

Although considerable variability was present between subjects, the majority proved able to successfully identify the six stimulus levels in the training session to the required approximately 60% hit rate criterion. In general, subjects most successfully identified the zero and maximal stimuli (0 and 10 respectively), achieving 100% hit rates in some cases. Intervening stimuli were much less successfully identified. Rather disturbing variability was, however, often present, with subjects displaying sudden lapses in scoring. There appeared to be little difference between trials with, or without, feedback of results.

Despite success in the training session, subjects proved unable to carry responding success rates over adequately to the subsequent experimental sessions on later days. Fatigue effects were also clear after extensive test series. Most important, however, were problems concerning comparability of discriminability between adjacent stimulus
pairs across the series, and of ensuring overlap of the response distributions across the series. A considerable variety of inter-stimulus intervals were assessed towards this goal. Initially good discriminability equality appeared to be produced by the logarithm interval scale, and overlap was continuous once the stimulus (B) between zero and threshold was moved up to the three-quarter interval point. In many cases (see Subject 1, Table 43 page 1), setting this level (B) at the half or two-thirds position in the interval produced a more equal discriminability between the two pairs of stimulus levels. However, since the interval from zero to threshold evidently could not be adequately covered by only one intervening level, and additional stimuli could not be added because of limitations on total stimuli in the experiment; a decision was taken to ensure overlap of the threshold stimulus (C) and the one below it (B). For most subjects little response variance to the zero stimulus was evident anyway, and lowering the stimulus (B) above did not increase the response tendency to label the zero stimulus as higher. Provided the first stimulus level (B) above zero never elicited pain, it was viewed as representing an acceptable pure noise distribution for the pain distributions above.

This scaling system could, for some subjects, produce reasonable interstimulus discriminability equivalence (e.g. Subject 2, Table 43 page 23) and could be acceptably reproducible on retest. The d' values were also often agreeably close to d' = 1.0 with this series. Typical intensity increments of 25-30 mcal/sec⁻¹/cm⁻² at the higher levels were observed under this scaling system. Some workers (18) have indicated j.n.d's of around 15-20 mcal/sec⁻¹/cm⁻², whilst elsewhere (91) reports suggest approximately 50 mcal/sec⁻¹/cm⁻², for noxious stimulus ranges
### TABLE 43: ACUPUNCTURE EXPERIMENT NO 2: PILOT STUDIES:

Discriminability (d') of Pairs of Adjacent Stimulus Levels (log interval scale).

<table>
<thead>
<tr>
<th>Stimulus Pair</th>
<th>A-B (0-2)</th>
<th>B-C (2-4)</th>
<th>C-D (4-6)</th>
<th>D-E (6-8)</th>
<th>E-F (8-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.</td>
<td>153</td>
<td>153</td>
<td>26</td>
<td>29</td>
<td>32</td>
</tr>
<tr>
<td>d' test 1</td>
<td>1.08</td>
<td>0.95</td>
<td>1.81</td>
<td>2.74</td>
<td>0.85</td>
</tr>
<tr>
<td>d' test 2</td>
<td>1.15</td>
<td>0.99</td>
<td>1.90</td>
<td>0.67</td>
<td>0.54</td>
</tr>
<tr>
<td>Subject 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.</td>
<td>210</td>
<td>72</td>
<td>26</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>d' test 1</td>
<td>2.01</td>
<td>1.14</td>
<td>1.18</td>
<td>1.11</td>
<td>0.87</td>
</tr>
<tr>
<td>d' test 2</td>
<td>2.08</td>
<td>-</td>
<td>1.40</td>
<td>1.50</td>
<td>0.94</td>
</tr>
<tr>
<td>Subject 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.</td>
<td>200</td>
<td>105</td>
<td>24</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>d' test 1</td>
<td>1.93</td>
<td>1.83</td>
<td>0.82</td>
<td>0.95</td>
<td>0.70</td>
</tr>
<tr>
<td>d' test 2</td>
<td>2.60</td>
<td>1.40</td>
<td>0.66</td>
<td>0.94</td>
<td>0.88</td>
</tr>
<tr>
<td>Subject 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.</td>
<td>193</td>
<td>113</td>
<td>17</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>d'</td>
<td>1.70</td>
<td>1.50</td>
<td>0.73</td>
<td>0.94</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* S.I. = Stimulus Interval (mcal/sec\(^{-1}\)/cm\(^{-2}\))

** d' = Interstimulus Discriminability (S.D.T.)
of the order employed here (see Table 43 page 23). Values found here seem quite compatible with this range.

Unfortunately, the pattern was unreliable from one subject to the next, even when interstimulus intervals were very similar. Only the highest pair of stimulus levels produced reasonably consistent discriminability values across subjects.

With the evident variability of discriminability measures between subjects and even within subjects the reliability of the S.D.T. model was in doubt. It was therefore decided to include a descriptive category response scale upon which a conventional analysis for changes in pain reporting might be applied if S.D.T. analysis failed to prove possible. The additional advantage of interpretability was also obviously available. Several abbreviations of the scale employed by W. Crawford Clark (91) (Nothing - Detect something - Faintly warm - Warm - Hot - Very hot - Very faint pain - Faint pain - Painful - Very painful - Withdraw) were assessed. Immediately it became clear that subjects could not hold numerical and descriptive multiple criteria simultaneously. The numerical system was therefore abandoned and the number of descriptive categories expanded to that of Crawford Clark (91) less the 'Faintly warm' response which appeared to be redundant.

A similar problem was encountered when an attempt was made to combine both a binary decision with a rating scale decision after each stimulus presentation, as advocated by Clark & Dillon 1973 (93) and discussed in chapter 4. In addition, the required interstimulus interval became inordinately lengthened if the subject was not to feel stressed by the response demands of the experiment. This would expand the time taken for a complete stimulus test series prohibitively in terms of the likely durations of the hypothesised analgesic actions of Acupuncture and the antagonist drug Naloxone.

Furthermore, none of the Acupuncture/S.D.T. studies reviewed in chapter 4, including that by Clark & Yang 1974 (100), involved concurrent decision tasks. Adoption of a rating scale only design would ensure greatest comparability with the other available studies. As discussed in chapter 4, it would appear that the rating scale is the most important and useful single task for the establishment of the S.D.T. measures.
Trials with this response system further highlighted the problem of the variability of threshold displayed by subjects from session to session. The simplifying solution adopted was the use of standard stimuli for all subjects, with the upper levels set at sufficient intensities to reliably elicit definite pain in all subjects of 'normal' sensitivity. The safety factor of a stimulus cancel or 'withdraw' button was, of course, available. Subjects at either extreme of sensitivity were excluded from the study. The use of standard stimuli has the advantage of allowing direct comparison of d' discriminability measure for different subjects rather than employing unit-d' which is required otherwise (51).

Use of the descriptive category response scale improved intra-subject sensitivity reliability on test-retest, with perhaps slightly improved inter-subject comparability. Further efforts were, however, made to fine tune the interstimulus discriminability towards equality across the range by manipulation of the stimulus level intervals. A ratio scaling based on Stevens power law (410,418) was attempted, and even a 1-antilog incremental system was assessed. These systems were, however, even less successful.

Next a long series of adjustments up, or down, of individual stimulus levels was undertaken on a trial and error basis, whilst the effects on the discriminability of each adjacent stimulus pair were assessed. Eventually it became quite clear that, although the scale could be adjusted for equality to suit individuals quite well, there was no universal formula whatsoever.

This given, it appeared reasonable to simply adopt the same intervals and levels used in the most directly comparable study of Crawford Clark (100). These levels, with the minor amendment of an upward shift of the second stimulus level (B), for reasons already
discussed above, were as follows:

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clark et al</td>
<td>0</td>
<td>120</td>
<td>240</td>
<td>305</td>
<td>370</td>
<td>435 mcal/sec$^{-1}$/cm$^{-2}$</td>
</tr>
<tr>
<td>Stewart</td>
<td>&quot;</td>
<td>175</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

$^{+1}$ mcal/sec$^{-1}$/cm$^{-2} = 1 \times 4.1855 \times 10^{-3}$ watts/cm$^2$.

Trials with four subjects produced the surprisingly acceptable mean interstimulus discriminability (d') figures presented in Table 44 a page 235. It can be seen that there is good equality of discriminability between pairs of adjacent stimuli across the stimulus range, and that the measures remain reasonably stable when tested on four separate days. It seems likely, therefore, that the measure, as a group mean, may be reliable enough for comparison of the effects of different experimental treatments applied on different days. Similar conclusions may be drawn from the data in Table 44 b) page 235, where the changes in group mean d' between tests on the same day, at an interval of 40 minutes, are presented for four subjects. Although, as already indicated, there are large differences between subjects, hence the large standard deviations, the test/retest reliability of the group mean d' appears acceptable at a mean change of 12.5% (correlation 0.67). These figures are typical for instructed subjects without extensive practice. There was evidence of improved reliability with practice, a factor which makes a balanced order design for experimental treatments imperative.

The uniformity obtained in these results equalled any produced by other stimulus intervals assessed and it was not possible, given the extensive requirements of experimental time, subject availability, and finance, to evaluate further modifications.

*This is in view of the variability of individuals, and between individuals, in discriminability and the Weber ratio at these stimulus intensities (179).*
TABLE 44: ACUPUNCTURE EXPERIMENT NO 2: PILOT STUDIES:

a) Mean Discriminability ($d'$) of Pairs of Adjacent Stimulus Levels for 4 Subjects Tested on 4 Days.

<table>
<thead>
<tr>
<th>Stimulus Pair</th>
<th>A-B</th>
<th>B-C</th>
<th>C-D</th>
<th>D-E</th>
<th>E-F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus Interval (mcal/sec cm$^{-2}$)</td>
<td>175</td>
<td>65</td>
<td>65</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Mean $d'$</td>
<td>1.6</td>
<td>1.1</td>
<td>1.3</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Breakdown Day 1</td>
<td>1.70</td>
<td>1.26</td>
<td>1.46</td>
<td>1.23</td>
<td>1.10</td>
</tr>
<tr>
<td>Mean $d'$ Day 2</td>
<td>1.33</td>
<td>0.99</td>
<td>1.10</td>
<td>1.15</td>
<td>1.65</td>
</tr>
<tr>
<td>Day 3</td>
<td>1.40</td>
<td>0.96</td>
<td>1.27</td>
<td>1.31</td>
<td>1.01</td>
</tr>
<tr>
<td>Day 4</td>
<td>1.83</td>
<td>1.10</td>
<td>1.41</td>
<td>1.06</td>
<td>1.43</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.24</td>
<td>0.14</td>
<td>0.16</td>
<td>0.11</td>
<td>0.30</td>
</tr>
</tbody>
</table>

b) Mean Discriminability ($d'$) of Pairs of Adjacent Stimulus Levels for Test and Retest (40 Minute Interval, 4 Subjects).

| Mean $d'$ test 1 | 1.70 | 1.26 | 1.46 | 1.23 | 1.10 |
| S.D. | 0.25 | 0.14 | 0.80 | 0.31 | 0.27 |
| Mean $d'$ test 2 | 1.69 | 0.97 | 1.07 | 1.37 | 1.09 |
| S.D. | 0.59 | 0.53 | 0.23 | 0.49 | 0.46 |
| Change $d' 1$ - $d' 2$ | -0.01 | -0.29 | -0.39 | +0.14 | -0.01 |
Apart from a possible reference in an unpublished paper, Clark et al. do not report on background studies to evaluate the reliability of their measures, or the equivalence of discriminability between adjacent pairs of stimuli with the physical intervals employed. However, from the data provided by Clark (1974), values have been calculated as before and appear in Table 45. The values derive from means of ten subjects and it can clearly be seen that the test reliability is, if anything, slightly poorer than the results obtained here, yet the method has been considered viable by Clark et al. and many other authors. Table 45 also indicates slightly different interstimulus discriminability ($d'$) values across the range from those found here. However, the differences are relatively small in view of the size of subject pools under comparison, the distribution patterns are similar, and greater equality of discriminability between the various stimulus pairs is evident in this laboratory.

In practice, the stimulus levels appeared to elicit less intense sensations than those reported by the subjects of Clark. For example, Clark reports predominantly 'Withdrawal' responses to 4.5 mcals/cm$^2$, whereas the modal response amongst pilot subjects here was 'Very Painful', with relatively few withdrawals. Similar scaling down was evident to the other stimulus levels.

A considerable number of explanations are suggested by the literature in this area. Most important probably, is the effect of thickening the skin surface. Clark, and most other authors, have applied a 'uniform' coating of india ink to the skin principally to ensure absorption of radiant energy only at the cutaneous surface (this is discussed fully in Chapter 5). However, losses due to the reflecting power of the blacking must be taken into account.
**TABLE 45:** CLARK (1974)(91)

Mean Discriminability (d') of Pairs of Adjacent Stimulus Levels for Consecutive Test/Retest (10 Subjects).

<table>
<thead>
<tr>
<th>Stimulus Pair</th>
<th>A-B</th>
<th>B-C</th>
<th>C-D</th>
<th>D-E</th>
<th>E-F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus Interval mc/s cm^-2</td>
<td>120</td>
<td>120</td>
<td>65</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Mean d' test 1</td>
<td>1.38</td>
<td>1.21</td>
<td>0.75</td>
<td>1.51</td>
<td>1.09</td>
</tr>
<tr>
<td>&quot; test 2</td>
<td>1.12</td>
<td>0.97</td>
<td>0.54</td>
<td>1.02</td>
<td>1.04</td>
</tr>
<tr>
<td>Change d'1-d'2</td>
<td>-0.26</td>
<td>-0.24</td>
<td>-0.21</td>
<td>-0.49</td>
<td>-0.05</td>
</tr>
</tbody>
</table>
India ink is variously reported as averaging 6%\textsuperscript{(169)} to 10%\textsuperscript{(179)} reflectivity, whilst the stage make-up preparation used here has been assessed as ranging from 12% to 15%\textsuperscript{(414)} reflectivity to the total energy applied within the spectral output of the Dolorimenter bulb source. Table 46 page\textsuperscript{239} presents the calibrated stimulus intensities applied to the skin in row no. 1, and the values obtained after correction for a mean reflectance loss of 13.5% appear in row no. 4. The correction immediately comes close to resolving the anomaly evident from the calibration of the six stimulus levels by the induced temperature of a blacked thermocouple on the skin surface under the radiant beam (see calibration section Table 49b) page\textsuperscript{303} and Fig. 69 page\textsuperscript{304}).

Even allowing for problems of comparability of thermocouple measures with skin temperatures due to divergence of specific heat capacities, time constants, heat sinking etc., the temperatures obtained by such measurement (row no. 3 of Table 46 page\textsuperscript{239}) appear too low for the applied stimulus intensities (row no. 1) on two counts. Firstly, application of the equation evolved by Buettner (1951)\textsuperscript{(59)}, and adopted by Hardy et al (1953)\textsuperscript{(170)} and other authors\textsuperscript{(325)}, for the calculation of final skin temperature resulting from the application of known, non-penetrating, radiant energies, produces rather higher expected values (see row no. 2 Table 46 page\textsuperscript{239}) than those found in practice. The formula appears below:

$$Ts = To + Qk \sqrt{t}$$

Where $Ts$ = Final (maximum) skin temperature ($^\circ$C).

$To$ = Initial Skin Temperature before Irradiation ($^\circ$C).

$Q$ = Intensity of Radiation (mcal/sec\textsuperscript{-1}/cm\textsuperscript{2}).

$k$ = Constant (0.032).

$t$ = Time of Exposure in Seconds.
<table>
<thead>
<tr>
<th>Stimulus Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Stimulus Intensity™ Applied</td>
<td>0</td>
<td>175</td>
<td>240</td>
<td>305</td>
<td>370</td>
<td>435</td>
</tr>
<tr>
<td>2 Final Skin Temperature (°C) Calculated*</td>
<td>0</td>
<td>42.9</td>
<td>46.5</td>
<td>50.1</td>
<td>53.7</td>
<td>57.3</td>
</tr>
<tr>
<td>3 Final Skin Temperature (°C) Measured**</td>
<td>0</td>
<td>39.2</td>
<td>43.1</td>
<td>46.9</td>
<td>50.8</td>
<td>54.4</td>
</tr>
<tr>
<td>4 Stimulus Intensity™ Applied (Corrected for Losses i.e. x 0.865)</td>
<td>0</td>
<td>151.4</td>
<td>207.6</td>
<td>263.3</td>
<td>320.0</td>
<td>376.3</td>
</tr>
<tr>
<td>5 Final Skin Temperature (°C) Calculated* for Corrected Stimulus Intensities</td>
<td>0</td>
<td>41.5</td>
<td>44.6</td>
<td>47.8</td>
<td>50.9</td>
<td>54.0</td>
</tr>
</tbody>
</table>

™ mcals/sec⁻¹/cm⁻².

* Ts = To + Qk √t
Where Ts = Final Skin Temperature °C
To = Initial Skin Temperature (33.19°C average) before Irradiation
Q = Intensity of Radiation (mcals/sec⁻¹/cm⁻²)
k = Constant (0.032)
t = Time of Exposure in seconds (standard 3.0 sec.)
Buettner (1951)(59)

** Direct Measurement by Thermocouple (see Chapter 7, Section 2 Calibration, Page 300)
The formula has been validated by measurement of end point temperatures by radiometer\(^{(169)}\), and the value of the constant verified experimentally\(^{(329)}\). To was determined for the abdominal test site from four baseline measures for each of 16 subjects, to produce a mean value of 33.19\(^{\circ}\)C (S.D. = 1.109) for the 64 data points. This concords with other reports indicating an average value of 33\(^{\circ}\)C\(^{(173)}\). \(t = 3.0\) sec. as standard for all stimuli. When the expected temperatures are recalculated using the reduced stimulus intensities after correction (row no. 4) the results (row no. 5) are much more in line with the measured values (row no. 3).

Secondly, based on the findings of many authors\(^{(60,170,178,472)}\), an induced skin temperature of approximately 45\(^{\circ}\)C appears critical for the pricking pain threshold, and the onset of reversible tissue damage\(^{(58,190)}\), with little deviation over different body areas\(^{(180)}\).

On the basis of calculated skin temperatures (row no. 2) for the applied stimulus intensities (row no. 1), this would place the pain threshold somewhere between stimulus B and stimulus C. In practice normal subjects completely failed to report any pain to either of these stimuli, the threshold appearing to be approximately around stimulus level D. Again the measured skin temperature (row no. 3) for stimulus D approximates the expected pain threshold temperature more satisfactorily. The calculated skin temperature for corrected stimulus intensities (row no. 5) likewise provides a value (47.0\(^{\circ}\)C) which is closer to the 45\(^{\circ}\)C expected from the work of the authors cited above.

* Another equally meticulous study\(^{(329)}\), testing the dorsal hand, instead of the usual forehead, found an even closer critical temperature of 48.6\(^{\circ}\)C. The author implicated tissue transmission of intensity cues on the forehead as a factor likely to lower threshold report levels in other studies. Such cues were not available to subjects tested here on the abdomen and visually screened.
Since the methodology employed here does not measure pricking pain threshold per se, but merely allows observation of the first, fixed intensity, stimulus to which subjects begin to report 'Very Faint Pain', it is difficult to estimate how far, if at all, pain thresholds exceeded the skin temperatures expected. There were indications that the stimulus intensities for first report of pain were slightly elevated, but this may be attributable to numerous factors. First, the intensity at which subjects report 'Very Faint Pain' is almost certainly higher than that required to elicit the 'pricking sensation' conventionally employed as a definition of pain threshold, since the latter, although a clearly defined sensation, may not, in fact, be painful in the everyday sense \(^{(325)}\). Certainly, it is also interesting to note that the mean abdominal pricking pain threshold for the six subjects tested earlier using the traditional Hardy et al (1952)\(^{(179)}\) methodology in this laboratory, was 258.3 mcal/sec\(^{-1}/cm^{-2}\) (see Table 42 page 228). This figure is already substantially lower than the stimulus level D intensity and, when corrected for reflectance losses (i.e. x 0.865), produces a value of 223.4 mcal/sec\(^{-1}/cm^{-2}\) which is remarkably similar to the values reported by Hardy et al (1940)\(^{(174)}\) and many others, using the same type of instructions to subjects for 'pricking pain'. The calculated temperature for 223.4 mcal/sec\(^{-1}/cm^{-2}\) is 45.5\(^{\circ}\)C, which again is very close to the critical temperature variously reported around 44.8\(^{\circ}\) ± 0.5\(^{\circ}\)C\(^{(178)}\) and 45.5-45.7\(^{\circ}\)C\(^{(170)}\).

The mean pain tolerance intensity of 339.5 mcal/sec\(^{-1}/cm^{-2}\) shown in Table 42 page 228 seems very low also, particularly when corrected for losses to 293.7 mcal/sec\(^{-1}/cm^{-2}\), with a calculated skin temperature of 49.5\(^{\circ}\)C. It will be recalled that hardly any withdrawals were occurring to the considerably more intense fixed stimulus F- of
appears that the method of limits, which provides subjects with more discretionary scope, produces much more conservative tolerances than a higher fixed intensity stimulus which forces subjects to test its actual painfulness.

Other factors possibly contributing marginally to differences in values for pain thresholds found here, and by other authors, have been mentioned earlier. There is evidence to suggest lesser sensitivity of the abdomen than of the forehead which is normally used, although this is not supported by Hardy et al. It was not possible to empirically test this factor, but, as already mentioned, the abdomen was clearly shown in the previous Acupuncture experiment to be less sensitive than all other body areas tested.

The small stimulus area (1.0cm$^2$) employed here may also have a slight influence, in view of some reporting of spatial summation for pain.

The use of suprathreshold stimuli repetitively can also raise thresholds abnormally. However, this should not apply here, owing to the use of multiple patches of skin for testing, and the long intervals between irradiation of the same patch.

Since Hardy et al 1953 clearly state that correction is made for surface reflectance losses when reporting stimulus intensities, direct comparison is possible, at least on that point. However, the differences in the subject response system employed, and other major methodological departures required for the signal detection theory analysis, severely limit other comparisons.

The methodologically directly comparable studies by Clark et al suffer from a failure of the authors to state in
publications, or to respond to written enquiry, as to whether
correction of the reported stimulus intensities was made. As already
mentioned, the reported responses of the subjects of these authors
indicated more intense sensations than those expressed by subjects
in this laboratory to supposedly the same stimulus intensities.

Clark et al were, of course, testing the volar forearm rather
than the abdomen, but slight differences in sensitivity of these
areas are insufficient to account for this discrepancy (180).

If Clark et al have corrected for the approximately 8% mean loss
attributable to india ink, prior to reporting stimulus intensities,
the discrepancy is clearly resolved by the fact that the Americans
employed higher stimulus intensities. Even if they did not do so,
and in the absence of contrary evidence this is perhaps the safest
assumption, the differences in response magnitudes might still be
explained by the higher relative skin temperatures induced on the
American subjects due to the lower reflectance of india ink compared
to the skin preparation used in this laboratory. The corrected
stimulus intensities for both preparations are presented in Table 47
page 244 which indicates the higher stimulus levels likely to apply
in the Clark et al studies.

Clark (1974) (91) reports the criterion for onset of 'Very Faint
Pain' at 323.1 mcal/sec\(^{-1}\)/cm\(^{-2}\) and for 'Withdrawal' at 374.5
mcal/sec\(^{-1}\)/cm\(^{-2}\). He also reports a virtually unchanging volar forearm
skin temperature* of 31.0-31.2°C during testing. This seems rather
\(t_{cw}(171)\), and even more remarkably, stable in view of the findings in
this laboratory.

* Presumably group mean temperature, although this is not stated.
### TABLE 47: ACUPUNCTURE EXPERIMENT NO 2
Radiant Heat Stimulus Intensities: Correction for Reflectance Losses at the Skin Surface with Different Blackening Preparations (after Clark et al and Stewart).

<table>
<thead>
<tr>
<th>Stimulus Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal Intensity †</td>
<td>0</td>
<td>120/175</td>
<td>240</td>
<td>305</td>
<td>370</td>
<td>435</td>
</tr>
<tr>
<td>Corrected Intensity † × 0.865 (D. Stewart)</td>
<td>0</td>
<td>-151.4</td>
<td>207.6</td>
<td>263.8</td>
<td>320.0</td>
<td>376.3</td>
</tr>
<tr>
<td>Corrected Intensity † × 0.92 (Clark et al)</td>
<td>0</td>
<td>110.4</td>
<td>220.8</td>
<td>280.6</td>
<td>340.4</td>
<td>400.2</td>
</tr>
<tr>
<td>Final Skin Temperature (°C) Calculated* for Corrected Intensity (Clark et al)</td>
<td>0</td>
<td>37.2</td>
<td>43.3</td>
<td>46.6</td>
<td>50.0</td>
<td>53.3</td>
</tr>
</tbody>
</table>

† mcal/sec⁻¹/cm⁻².

* Buettner (1951) (59).
If both the stimulus intensities, and basal skin temperatures, are accepted as reported, and the Buettner (1951) formula applied, the criterion for 'Very Faint Pain' appears at 49.0°C and for 'Withdraw' at 51.9°C. The 'V.F.P.' criterion at least is clearly rather high indeed. Correction of stimulus intensities, as described earlier, produces a 'V.F.P.' criterion of 297.2 mcal/sec⁻¹/cm⁻² or 47.6°C which, although still higher than some findings, more closely approximates expected values.

The 'Withdraw' criterion becomes 344.5 mcal/sec⁻¹/cm⁻² or 50.2°C. This appears rather low from observations in this laboratory, but the initial instructions given to subjects by Clark were much more vague and permissive. The use of more demanding instructions later by Clark is reported to have raised the 'Withdrawal' criterion to 422.6 mcal/sec⁻¹/cm⁻² (or 54.6°C) which, when corrected, becomes 388.8 mcal/sec⁻¹/cm⁻² (or 52.7°C). These figures are more in line with experience here.

A further quite likely source of this discrepancy between the two studies may lie in possible non-uniformity of the radiant beam of the Dolorimeter used by Clark. The possibility of a 'hot spot' within the radiant field, which might produce apparently higher subjective responses, is a criticism raised against the early work of Wardy et al in 1940 by Weddell (1955) and for which later work carefully controlled. Extensive pilot construction modification and calibration was also undertaken in this laboratory (see Calibration Section page 298) to control for this factor, but no reference to similar procedures appears in the publications of Clark et al.

It is clear, therefore, that there are numerous problems encountered when attempting to compare other studies in the literature with each other and with the present design. Fortunately this, of course, does not detract from the internal validity of the design to
test the specific hypotheses concerning Acupuncture analgesia.

The basic stimulus structure was maintained in the final form described above. Although, as already mentioned, there was some evidence of underscaling of stimulus intensities these were not increased for several reasons.

First, evidence from the first Acupuncture experiment and from pilot work here indicated a tendency for subjective responses to increase in intensity with repeated testing over time even without any other experimental treatment. This is consistent with other reports on the interaction between pre-stimulus skin temperature and pain threshold levels \( \text{(178, 472)} \). Pain thresholds are reduced as initial skin temperature is elevated, since it appears that maximum skin temperature (and hence rate of inactivation of tissue proteins) is the most critical factor in the experienced intensity of noxious thermal stimuli \( \text{(170)} \). Notable increases of 1-2°C in temperature of the general abdominal test area were observed here and must, therefore, contribute to the increased magnitude of responses elicited by the fixed stimuli.

This effect is not to be confused with the lowering of pain thresholds which can result from repeated stimulation of the same skin spot with interstimulus intervals below 60 seconds \( \text{(416)} \). It will be recalled that in the procedure adopted here, twelve different skin areas were sequentially tested with an interval of approximately two minutes between stimulations of the same area of skin. This interval has been reported as adequate for the various physiological effects of stimulation to subside and to permit dissipation of the heat imparted \( \text{(35)} \).

A further consideration is derived from the considerable number of stimuli \( n = 108 \) to be presented to subjects in each stimulus test series. Since about half of these might be painful in some degree,
and the complete series was to be repeated twice within an experimental session, careful limitation on the amount of stress to subjects was desirable. It was, for example, found that, even with the facility of a 'withdraw' button, some subjects could become agitated after many exposures if the stimulus levels were set much higher.

The usual necessary compromise between the experimentally ideal and the practically attainable was made, and the experiment proceeded accordingly.
ACUPUNCTURE EXPERIMENT NO 2:
Pilot Studies: Initial Experimental Model

Data Collection Procedure Format and Instructions to Subjects

Subject Name ..................... Code No ........ Date ...........
Sex .............................. Group .......... Time ..........
Address .......................... M.C.W. ......... Special Conditions.....
Tel. .............................. Con. .................

ADAPTATION SESSION

1. General Medical Questionnaire completed       ☐ Completed ✓
2. Needle insertion and sites demonstrated       ☐
3. Electrical stimulation demonstrated           ☐
4. Heat Stimulus demonstrated and Pain Sensitivity found within normal range ☐
5. Apparatus for blood samples and injection displayed and nature of drug described ☐
6. Outline of experiment, attendance requirements, payment terms etc. ☐
7. Consent Form signed                           ☐
8. E.P.I. completed                              ☐

TRAINING SESSION

1. Ensure subject is in suitable physical and mental condition to proceed ☐
2. Abdominal Test Sites blackened                  ☐
3. Baseline Resting Temperature °C Abdominal ☐ Oral ☐
    Room Temperature °C ☐ Relative Humidity % ☐
4. PAIN THRESHOLD ESTABLISHMENT (see prepared subject instruction sheet(a)(1))

Note: (↑ = Ascending Series of Stimulus Intensities)
       (↓ = Descending
       (Th = Threshold Value (Watts/cm²))

Initial Approx. Value (I.A.V.) W/cm² (↑ steps of 0.01 W/cm²)

Test Series Values W/cm² (↑ and ↓ steps of 0.01 W/cm²)

Th₁ ↓ Th₂ ↓ Th₃ ↓ (Th₄ ↓)
(Th₁ ↑) ↓ (Th₂ ↑) ↓ (Th₃ ↑) ↓

Th₁(Mean) Th₂(Mean) Th₃(Mean) Th₄(Mean)

Mean Th. Mean Th. + 10% S.D.

5. PAIN TOLERANCE ESTABLISHMENT (see prepared subject instruction sheet(a)(2))

Note: (↑ = Ascending series of stimulus intensities)
       (T = Tolerance Value Watts/cm²)

I.A.V. W/cm² (↑ steps 0.01 W/cm²)

Test Series Values W/cm² (↑ steps 0.01 W/cm²)

T₁ ↑ T₂ ↑ T₃ ↑ T₄ ↑
(IAV-6) (T₁-3) (T₂-5) (T₃-4)

Mean T Mean T + 10% S.D.
6. **STIMULUS SERIES**

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power (W/cm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Description</td>
<td>Zero</td>
<td>½ interval</td>
<td>Pain threshold</td>
<td>Log interval</td>
<td>Log interval</td>
<td>Pain tolerance</td>
</tr>
<tr>
<td>Calibration (Volts)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response label required</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>10</td>
</tr>
</tbody>
</table>

7. Explanation of response procedures to subject (see instructions to subjects (b))

8. Demonstration Series (Abdominal points 1→6) □ Completed

   - □
   - □
   - □

9. Heat sink (H.S.) applied □ Completed ✓

   Temperature °C Abdominal □

10. **TRAINING TRIALS** /
10. **TRAINING TRIALS**

H.S. = Heat sink applied

<table>
<thead>
<tr>
<th>Stimulus level</th>
<th>Trials WITH Feedback</th>
<th>% Correct</th>
<th>Trials WITHOUT Feedback</th>
<th>% Correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>F10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. → 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
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<td></td>
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<tr>
<td>10</td>
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<td></td>
</tr>
<tr>
<td>2</td>
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</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. → 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
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<tr>
<td>4</td>
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<td></td>
</tr>
<tr>
<td>2</td>
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<tr>
<td>8</td>
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<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. → 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
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<td>8</td>
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</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. → 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6</td>
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<td>8</td>
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<td></td>
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<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. → 10</td>
<td></td>
<td></td>
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<tr>
<td>8</td>
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<td>4</td>
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</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.S. →</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Temperature °C (Abdominal) at end of trial.
(Instructions to Subjects)

Please read these instructions very carefully and ask the experimenters any questions you wish until you fully understand everything you will be required to do in the experiment.

The study in which you are about to participate is concerned with the possible effects of Acupuncture upon your sensitivity to painful stimulation. Some points on the body, when needled, are claimed to make one less sensitive to pain, others to make one more sensitive to pain, whilst others may have no effect at all. You should not therefore predict changes in any particular direction and would be safest to assume that no change at all will occur.

During the experiment you will be required to give ratings as to how intense or painful are various levels of heat applied to your abdomen by means of the apparatus which has been demonstrated to you. Some of these levels of heat will elicit pain, others will not. In order to tailor the levels of heat to suit you individually, we now wish to establish the following points:

(1) Your 'PAIN THRESHOLD' - in other words the level of heat which just elicits very faint pain and no more by the time the shutter closes. The indicator above you will tell you the moment when the shutter opens and closes. The sensation you should look for is the feeling of heat focusing down to a point followed by a sharp pricking sensation just before the shutter closes. Once you start to feel the pricking sensation appreciably before the shutter closes your 'Pain Threshold' has been exceeded.

We will try to establish your 'Pain Threshold' point over a number of trials. On half the trials we will begin at low levels of heat and gradually increase the heat in small amounts each time the shutter opens until your 'Pain Threshold' point is reached. On the other half of the trials we will begin at higher levels of heat, decreasing a little each time the shutter opens, until you just fail to experience the pricking sensation by the time the shutter closes. At the higher levels of heat you should press the button to close the shutter IMMEDIATELY that you experience the pricking sensation. Do NOT allow the stimulus to continue (i.e. the shutter to remain open) for its normal 3 second period once you are certain that the pricking sensation has occurred. You may find it easier to let the series go one heat level past the point at which you think the pricking sensation has just started or just stopped, in order to be sure, and then tell the experimenter that it was the previous heat level which should be noted as your threshold.

The heat level will start at a different point in every single series so make your reports of the 'threshold' point entirely from the sensations you feel, and do not try to count any standard number of stimulus presentations from the start of the series to the point at which you say 'threshold'.

Do your best to be consistent, and once you have decided what the 'threshold' feels like, try to remember it throughout the whole experiment.
(2) Your 'PAIN TOLERANCE' point - in other words the level of heat which elicits an amount of pain which you can just bear without pushing the button to close the shutter before the normal 3 seconds period has elapsed. It is emphasised strongly that THIS IS NOT A TEST OF ENDURANCE - DO NOT BE HEROIC. All that is required is that you select a level of pain which you feel is the maximum you can CONSISTENTLY tolerate without having to push the button.

You should not worry about suffering any burns as a result of this painful stimulation. The whole design purpose of the apparatus is to produce pain without tissue damage other than a possible slight redness and tenderness which will soon disappear after the session is over.

In order to minimise your discomfort, your 'Pain Tolerance' point will only be tested a few times and always with the series of heat levels starting from a level below your 'tolerance' point and increasing each time the shutter opens. Again the series will start at a different heat level each time, so do not try to count any standard number of increments from the starting point to the level at which you say 'Tolerance'. You may again find it easier to be absolutely sure by letting the heat level go one increment higher than your 'Tolerance' point (i.e. so that you just have to push the withdraw button) and then telling the experimenter that it was the previous heat level which should be noted as your 'Tolerance' point.

Remember, it is very important that you are CONSISTENT in the 'Tolerance' point you adopt. Once you have decided upon the level of pain which is the maximum you can consistently tolerate, try to remember how it feels and stick to it throughout the whole experiment.
(b) TRAINING SESSION

(Instructions to Subjects)

Over the next week or two you will be required to attend on four occasions for experimental sessions. During each session a great variety of different intensities of heat will be applied to your abdomen. You may, however, rest assured that the programmes will be tailored to suit your own particular sensitivity to pain as indicated by your 'Pain Threshold' and 'Pain Tolerance' points which we have just established. This means that you should not experience any levels of pain far beyond your capacity to withstand. It is possible, however, that you may find that the highest levels of heat seem slightly more, or slightly less, painful than those you have just experienced, since many people's sensitivity to painful stimulation varies slightly from moment to moment and from day to day. If they are less painful you have obviously nothing to worry about, whilst if they are slightly more painful you may push the withdraw button to terminate the heat whenever you wish. Just try to remember how much pain you decided was the most you could consistently tolerate earlier, and stick to that throughout all the sessions.

During the experimental sessions to come you will be asked to express the maximum intensity of sensation you have experienced by the time the shutter closes, in terms of a number from 0-10. 0 should be used to describe the situation when you fail to detect any change in sensation on your abdomen by the time the shutter closes. 10 should be used to describe the most intense painful sensations of all those you experience. In other words, those which you can just tolerate and no more, and also any for which you have to push the 'withdraw button'.

In between these extremes will be a whole variety of sensations of different intensities some painful, others not, to which you will be asked to assign numbers.

In order to help you report the intensities of your sensations in a meaningful and reliable way across the whole range, we are now going to train you to identify sensations until you reach the required standard of reliability.

Once you have reached this standard it will be essential that you concentrate and try very hard to maintain that standard throughout the whole experiment. An appreciable fall in your performance below this standard at any time could jeopardise your suitability to continue with the rest of the study.

To make it easier for you just now you will only be required to identify the sensations we want you to call 0, 2, 4, 6, 8, and 10. However, try to imagine during the training just what all the intervening sensations would feel like so that you will be prepared when you have to use all the numbers.

We are now going to apply a series of increasing levels of heat to your abdomen. The first level you should call 0, the second level you should call 2, the third level you should call 4, the fourth call 6,
the fifth call 8, and the sixth call 10 (accompanied by the word 'withdraw' should you have to push the 'withdraw button').

These levels will be demonstrated to you twice in ascending order, and twice in descending order. You should try to memorise the way each number 'feels' and use it during the rest of the experiment whenever you feel the same sensation.

Don't worry if at first you find it very difficult to distinguish between the numbers or to note any specific sensation for each. You will improve during the rest of the training session and people usually do better than they think possible.

Next, a whole series of these same levels of heat will be presented to you but this time in randomised order. All you have to do is say which number you think it was. You will be told after each stimulus which number you should have used to describe your sensation.

Following this you will receive a further series of these levels of heat in random order but this time you will not be told whether the number you used was correct or not. You may think this is very difficult, but if you just try to keep relaxed and concentrate you should do perfectly well.

If you achieve a sufficiently high success rate during the above tests you will then move on to a full trial series where conditions will be identical to those in the four experimental sessions to come.

You will then receive a variety of different levels of heat in random order, and will have to use all the numbers from 0-10 to describe the intensity of the sensations you experience.

Try to remember, for example, the kind of sensation which you learned in earlier training to call 6 and, if the sensation feels exactly the same, then report the number 6. If, however, you think it feels just a little less intense than a 6 but not low enough for a 4 you should report the number 5. Use this same approach for all the other intervals.
Hypotheses

On the basis of the stated aims of the study, and the evidence reviewed in the previous three chapters, a number of principal operational hypotheses were generated for testing:

(1) Acupuncture will reduce pain intensity reports to noxious thermal stimuli significantly compared to placebo treatment, or no treatment.

(2) This effect will reflect a true sensory-sensitivity decrement, as assessed by S.D.T. analysis.

(3) This effect will be cancelled, or reversed in direction, by the administration of Naloxone.

(4) Acupuncture will have analgesic, rather than anaesthetic effects, and therefore will not significantly affect intensity reports, or sensory sensitivity, to low stimulus intensities.

(5) Placebo treatment (Pseudo-Acupuncture) will significantly reduce pain intensity reports compared to no treatment.

(6) This effect will reflect a shift in response criterion only, as assessed by S.D.T. analysis.

Experimental Design

(1) Subjects:

Sixteen paid volunteers (8 male), aged 18-35 years, and mainly students (non-science) were selected. None participated in the previous experiment.

The same medical questionnaire (Appendix 1 Page 458) was employed as in the first study, with the addition of questions
designed to ensure that the subject was not receiving narcotic drugs of any type. (Subjects could be assumed to answer truthfully since they were advised that "blood tests" would be undertaken during the experiment.) Two other unusual physical requirements were included. First, the exclusion of males with hairy abdominal regions, since this was to be the cutaneous test area in the experiment; and second, the selection of only females taking oral contraceptives, in an effort to stabilise the cyclic fluctuation in pain sensitivity of the female population (see Chapter 5, part 2, section (5)).

Ignorance, apart from the vaguest general public knowledge, of the details of acupuncture procedures, and likely effects, was again a selection prerequisite, as was a 'normal' psychological motivation for participation in the experiment.

A complete practical demonstration of ALL stimulus and response systems to be used in the experiment was given to subjects in an extensive initial adaptation and training session. If the subject exhibited both sufficient acuity to deal with the complex experimental situation, and a pain report pattern within the desired range (see pilot work above, Page 223), he was offered the opportunity to participate in the study.

An 'Experimental Consent Form' (Appendix 4, Page 770) was then signed. It will be noted that again this form did not obviate the subject's right of claim against the medical defense insurance of the physicians involved in the study. Again all procedures were also approved by the Royal Edinburgh Hospital Ethics Committee prior to the beginning of any experimental work.

To avoid confusion, it should be noted that for the purposes of various 'Controls' discussed in section (c) below, the consent form...
contains reference to insertion of needles at two sites which were never, in fact, used.

Subjects were strictly instructed, on penalty of their continued participation in the study, not to discuss any aspect of the experiment with anyone, especially other subjects, and to make no attempt to acquire knowledge, or information, concerning Acupuncture until the experiment was completed.

Finally, subjects completed the Eysenck Personality Inventory (Form B) (129).

(2) Experimental Equipment System:
ACUPUNCTURE EXPERIMENT NO 2

EXPERIMENTAL EQUIPMENT SYSTEM
(Description and Calibration)

General System Description

A. Radiant Heat Stimuli

1. Generation (The Dolorimeter, Fig. 45 Page 260).

A sequential channel selector with a pseudo-random hard-wired programme was used to select six different 'control' reference voltages in a Dolorimeter Power Supply Unit. These 'control' voltages were converted to proportional current duty cycles in a Triac circuit, thereby producing six different intensities of radiation from a 150 watt projector bulb powered from the Triac. Feedback of the bulb output was derived from an adjacent Phototransistor which supplied automatic DC stabilising circuitry for the Triac.

The projector bulb was mounted in a ventilated and heat-sinked Dolorimeter handset held in contact with the subject's skin. Radiant output from the bulb was directed onto the skin via a shuttered aperture. Shutter opening was powered automatically for standard periods of 3.0 seconds by the channel programmer unless the subject activated his 'withdraw' cut-out button to close the shutter earlier. The duration of shutter opening was automatically timed and recorded on punch tape.

An illuminated visual display indicated the status of the shutter to subjects and cued responses.

2. Calibration (Fig. 46 Page 261).

Radiant output from the Dolorimeter handset was determined by a laser thermopile sensor head coupled to an integrated power meter with
FIG. 46

ACUPUNCTURE EXPERIMENT NO. 2
DOLORIMETRY CALIBRATION SYSTEM
shutter power (attenuated)

Shutter Power Supply

TRIAC

DOLORIMETER HANDSET

THERMOPILE SENSOR

DOLORIMETER HANDSET

THERMOCOUPLE

shutter power (attenuated)

digital voltmeter

d.c. 6 pk.-pk. amplifier

pen recorder (with shutter status marker)

digital voltmeter microprocessor

electronic thermometer
output to a DC amplifier and pen recorder. Output wattage was determined as a function of 'control' voltage present in the Dolorimeter Triac circuit as measured by a high resolution digital voltmeter.

B. Miscellaneous Monitoring and Stimulation Systems (Fig. 45 Page 160).

1. Neurostimulator - A purpose-built device was connected to electrode pairs consisting of one surface electrode and one active acupuncture needle electrode to provide low current, low repetition frequency, biphasic electrical stimulation to the subject.

2. Thermometer - A three channel thermistor/electronic thermometer was used to monitor the subject's abdominal, thoracic, and oral temperatures.

3. Tape Recorder - A tape recorder was used to record subject's verbal ratings of radiant heat induced sensations, and also to play background music during the inactive periods.

4. Environmental Control Unit - A thermostatically controlled air conditioning/heating system maintained the experimental cubicle at approximately 27°C. A maximum-minimum thermometer recorded the deviation limits for each session.

5. Experimenter Cue Projector/Monitor - A projector/monitor display, automatically stepping on after each radiant heat stimulus presentation, was used to cue the experimenter to move the Dolorimeter handset to a new, numbered and blacked test site on the subject's abdomen.
Construction Design Specifications

A. Radiant Heat Dolorimeter

1. Handset (Figs. 47, 48 Pages 264, 265)

A hand held radiant heat device was constructed to produce an approximately uniform intensity output beam falling, via a shuttered aperture with timer control, on to the cutaneous surface.

Inside a vented, black anodised aluminium casing (14 x 8 x 8cm) with padded rubber grip handle, was mounted a projector bulb encased in a further anti-glare aluminium housing. The bulb was mounted and supported by a heat resistant ceramic valve base and brass barrel connectors were machined to completely encase the bulb connecting pins, thereby preventing arcing with subsequent carbon deposit and variable contact resistance present with the standard fixture. All wiring carried high temperature resistant sleeving. A phototransistor sensor head was mounted in the base of the internal bulb housing to supply feedback for stabilising circuitry (see power supply below). Normally, forward radiant output to the skin was completely occluded by a spring returned shutter. Shutter opening was controlled by a 20V solenoid which was externally, automatically, timed (see power supply below). The inner surface of the shutter blade was silvered for reflectance.

Radiant output to the skin was via a machined PTFE funnel barrel with a silvered interior to enhance diffusing of any non focused diverging rays. The barrel was mounted in a solid aluminium heat sinking bezel with finned mounting studs supporting a low thermal transmission PTFE disc in actual contact with the subject's skin. The use of heat sinking and PTFE contact areas reduced conduction of heat from the handset chassis to negligible levels, thus maintaining output as a relatively pure radiant source.
Fig. 47: Radiant Heat Dolorimeter Handset and its Application to Prepared Abdominal Cutaneous Test Sites.
FIG. 48. RADIANT HEAT DOLORIMETER (Handset)

- Shutter Solenoid Mechanism
- Aluminium Heat sinking
- Bulb Housing

- P.F.T.E. Skin Shield (low thermal transmission plastic)
- Photoelectric Sensor (stability feedback)

Note: Not exactly to scale

- All dimensions in cm.
- Filament to Aperture 5 cm. approx. (i.e. Principal Focus of Bulb)
- Handle
- Power Cable

Venting (Cut away for illustration only)
The PTFE disc in contact with the skin had an outside diameter of 5cm and was 0.3cm thick. The central aperture was of 1.128cm diameter producing an exposure area of 1.0cm². The outer edge of the central aperture was approximately 5cm from the centre point of the projector bulb. A principal focal point of 5cm was quoted by the manufacturers for the bulb used.

The barrel was internally funnelled to approximate the beam shape of the focused rays and coated with a silver preparation.

2. Bulb (Fig. 48 Page 265).

The Dolorimeter energy source was a projector bulb of the following specification:

- **Type:** Atlas Projector Bulb Model A1/184.
- **Rating:** 150 watt, 21.5v A.C. recommended supply.
- **Reflector:** Elliptical Nickel/Silver plated of short focal length.
  (Note obsolete reflector type required since modern dichroic reflectors are designed for transparency and emission to the rear in the infrared wavelengths. Forward energy loss is significant.) Principal focal point 5cm (approx.) from bulb centre point. Image diameter and focal luminance area approximately 1cm and circular at focal point.
- **Colour Temperature at 21.5v:** 3,400°K.
- **Bulb Glass Transmission:** Effectively transparent (surface losses only) to 2.7µm, 40-50% loss plateau thereafter to approximately 4.0µm with precipitate fall to 1% by 5µm (see absorption spectrum graph Fig. 49 Page 267).
- **Mounting Base:** 4 pin valve type configuration with locating lug.
3. Power Supply (Fig. 45 Page 260).

A variač transformer running at 110% of mains supplied a 10 ampere (maximum), 21.5v AC fully stabilised power supply to the projector bulb. Current supply to the bulb could be attenuated continuously over 100% of the supply range by a variable phase triggered triac. A photo-transistor was incorporated in the Dolorimter handset for DC feedback stabilisation circuitry to ± 1% accuracy.

Six remotely selectable triac level control channels (labelled A-F) were available. Locking spindle 10 turn wirewound potentiometers (10K Log ± 5%) were employed to preset control reference voltages (0-10v) on these channels. The reference voltages were automatically monitored sequentially by screened connection to six input channels of a Solartron Digital Voltmeter/Data Logger and resolved to two decimal places. The relationship between reference voltage and power output from the bulb is discussed in detail in the calibration section below. In summary the six channels were calibrated and checked daily to supply the following output levels:

<table>
<thead>
<tr>
<th>Dolorimeter Channel</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watts/cm²</td>
<td>0</td>
<td>0.73</td>
<td>1.00</td>
<td>1.28</td>
<td>1.55</td>
<td>1.82</td>
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<tr>
<td>m.cal.sec⁻¹ cm⁻²</td>
<td>0</td>
<td>175</td>
<td>240</td>
<td>305</td>
<td>370</td>
<td>435</td>
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</table>

B. Channel Selector/Programmer (Fig. 45 Page 260).

A custom designed programmer was constructed. Three GPO type, six bank, 48v uniselectors were used to hardwire a pseudo-random programme of sequential selection of six different output channels (labelled 1-6). A total sequence of 36 channel selections comprised a complete cycle which could be reset to the beginning at any point by a 'reset' control. The complete programme cycle appears in Fig. 50 Page 269
FIG. 50: PROGRAMMER-SEQUENTIAL CHANNEL SELECTION PROGRAMME

Programmer
Channel Nos. → Start 1 2 3 4 5 6 → Auto-continue

6 5 4 3 2 1 → " "
3 1 5 2 6 4 → " "
2 4 6 1 3 5 → " "
5 3 1 6 4 2 → " "
4 6 2 5 1 3 → Stop

It will be noted that each channel was selected once in each sub-cycle and therefore each channel appeared six times in the complete programme cycle. Each programmer channel, when selected, provided voltage to operate a relay interface, which in turn selected the appropriate channel on the Dolorimeter power supply unit (see above). The programmer channel matching with the Dolorimeter power supply channels was as indicated in Fig. 51 below.

FIG. 51: PROGRAMMER-DOLORIMETER CHANNEL MATCHING LINKAGE

Programmer
Channel Nos. → 1 2 3 4 5 6

Dolorimeter
Control Channel → D F A B C E

It should be noted that Dolorimeter channel output intensities increase progressively from A through to F (see calibration section below).

This matching therefore produced a programme on the Dolorimeter as per Fig. 52 below.
FIG. 52: DOLORIMETER-SEQUENTIAL CHANNEL SELECTION PROGRAMME

<table>
<thead>
<tr>
<th>Channels</th>
<th>Start →</th>
<th>D</th>
<th>F</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>E</th>
<th>Auto-continue</th>
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</thead>
<tbody>
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<td>→ E</td>
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<td>F</td>
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<td>D</td>
<td>C</td>
<td>F</td>
<td>E</td>
<td>B</td>
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<td>&quot; &quot;</td>
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<td>→ F</td>
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<td>D</td>
<td>A</td>
<td>C</td>
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<td>→ B</td>
<td>E</td>
<td>F</td>
<td>C</td>
<td>D</td>
<td>A</td>
<td>→ Stop</td>
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</table>

A front panel L.E.D. display indicated, at any time, which channel was currently selected and in which subcycle it lay. Additionally any channel could be engaged by means of a manual control switch, again with the appropriate L.E.D. display, and a master disarm switch was available to deprive all channels of their voltage supply, if required.

Monolithic digital timer circuits accurate to + 0.01% with fully stabilised power supply were used to control all uniselector stepping functions and dependent relay interfacing, to provide a fully automated, integrated system. Control of all hardware associated with the presentation of EACH stimulus and associated functions to the subject, was divided into three cyclical timed steps as presented in Fig. 53 Page 271.

The duration of Steps 1 and 2 was determined by stabilisation period requirements for the Dolorimeter (see Calibration section), whilst that of Step 3 was determined by requirements for stimulus duration equivalence with comparative studies elsewhere (see main text). Step durations were controlled by locking spindle 10 turn wirewound potentiometers (10K Log + 5%) and calibration was completed as described below.
### Fig. 53: Programmer Unit - Experimental Equipment

**Coordination Sequences**

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<thead>
<tr>
<th>Step 1 (2.0 sec.)</th>
<th>Step 2 (5.0 sec.)</th>
<th>Step 3 (3.0 sec.)</th>
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At the very beginning of a complete stimulus cycle the programmer, upon the start command, would enter Step 1 and select the first Dolorimeter Power Supply channel, Channel D (see Fig. 52 Page 270). This channel would remain engaged throughout Steps 2 and 3, whereupon the programmer would return to Step 1 and select the next channel, F. The process would continue automatically through the complete cycle of 36 channel selections.

The stimulus was not actually delivered to the subject until Step 3, which was the only period when the Dolorimeter Handset shutter could be open. Unless prematurely closed by the subject depressing his 'Withdraw' response button, the shutter remained open for the full 3.00 second duration of Step 3. A Digital Timer, reset to zero in Step 2, started timing at the onset of Step 3. It was stopped, and a paper tape print-out ($\leq 3.00$ sec.) of time elapsed initiated, when either the subject depressed his 'Withdraw' button, or automatically upon return of the programmer to Step 1 (print-out = 3.00 sec.). To prevent accidental print-out from the Digital Timer the subject's 'Withdraw' button was only armed during Step 3. Also, for identification purposes, a print-out of 0.00 sec. was initiated by the programmer at the end of each subcycle of six stimuli presentations. The subject's illuminated indicator would automatically cue as appropriate in each Step, and the experimenter's monitor would display the number of the abdominal site on the subject to which the stimulus should be applied. This would automatically change to the next number at the onset of Step 1.

C. Digital Timer/Logger (Fig. 45 Page 260).

An SE(LABS)LTD Timer-Counter Series SM200 Mk2 was utilised to time and log stimulus presentation times. This is a high noise rejection unit and was set for the timer mode, range 0-99.999 seconds $\pm$ 1.00m.sec.
Fig. 54: Subject's 'Withdraw' (Thermal Stimulus Cancel) Response Button (Acupuncture Experiment No.'s 1 & 2).

Fig. 55: Neurostimulator Employed for Electro-Acupuncture Stimulation (Acupuncture Experiment No.'s 1 & 2).
The remote start/stop/reset gating and B.C.D. time output and print command facilities were employed in connection with the Programmer unit and subject 'Withdraw' button as indicated in Figs 45, 53 Pages 260, 271.

The B.C.D. output was logic interfaced for compatibility to a SOLARTRON Punch Drive Unit LU1967 driving an ADDO Model 5 (LX1995) Paper Punch Unit in a sound-proofed case. Word length was set for the required five timer characters, and a 'new line' character appended after each print. This produced a scan/print time of 400m.sec., during which the timer gate was held closed by circuitry in the logic interface. A print was initiated for every stimulus, either by depression of the subject's 'Withdraw' button, or automatically by the master programmer (see above). The punched tape produced was reprinted on a teletype and any 'Withdraw' times (ie. <3.0 sec.) could be assigned to the appropriate stimulus presentation manually. This was facilitated by the division of print-out words into groups of six corresponding to each subcycle on the master programmer; by the insertion of a 00.000 print-out initiated from the programmer after every six stimulus presentations.

D. Subject's 'Withdraw' Response Button (Figs. 45, 53, 54 Pages 260, 271, 273)

This consisted of a pair of miniature bounce-free S.P.D.T. lever microswitches with momentary, spring return action mounted in an aluminium case 18cm x 13cm x 6.5cm. A large red padded finger-pressure plate was attached across the levers of both switches to activate them simultaneously. The mounting was engineered to permit switch activation by slight lateral motion to the right of the subject's little finger whilst the hand rested on the upper surface of the case. Depression of this button disconnected power to, and hence closed, the Dolorimeter handset shutter. It simultaneously held the digital timer count, and initiated
a print command. Circuit design in these dependent systems ensured logic activation and hold, however briefly the 'Withdraw' button was depressed. False triggering due to switch-return noise was fully suppressed, and the button was disarmed by the Programmer, except when the Dolorimeter handset shutter was open, to prevent print-out from inadvertant switch depression by the subject.

The switch case was secured to the subject's couch by means of a specially machined bracket such that the case position could be adjusted in all planes to suit the comfort of the subject.

E. Subject Cue Display (Fig. 45 Page 260).

A three window illuminated display was employed to cue subjects during each phase of a stimulus cycle. The 55 x 17 x 5cm display was mounted on the ceiling directly in line with the gaze of the supine subject. The list of response categories was mounted immediately adjacent and illuminated from below. Each message panel was illuminated from the rear. An internal 12v A.C. supply rail was supplied to the panels by remote relay switching controlled from the Programmer as outlined in Fig.53 page 271. During presentation of the radiant heat stimulus to the subject's abdomen the 'Shutter Open' display only was illuminated. Immediately upon shutter closure on the Dolorimeter handset, this was replaced by illumination of the 'Rate Sensation Now' display with the addition two seconds later of the alerting cue display '15 sec. to Shutter Open'. The subject thus had 7.0 sec. in which to give a response before the 'Shutter Open' display was again illuminated and the other displays simultaneously extinguished. Display lettering was large and clear, and subject's ability to read and understand the display was confirmed in each case.
F. Neuro-Stimulator (Figs. 45, 55 Pages 260, 277).

A slightly modified and more robust version of an electrical stimulator (G6805), in standard use in Chinese hospitals for the induction of analgesia via acupuncture needles, was constructed with the following specification:

1. Waveform (Open circuit Fig. 57 page 277):
   
   Biphasic: Positive Phase: Modified Rectangular Wave  
   : Negative Phase: Asymmetrical Spike

2. Continuous Pulse Train:
   
   Repetition Frequency: 21Hz - 90Hz continuously variable
   
   Pulse Width: Positive Phase 0.5m.sec.  
   : Negative Phase 0.75m.sec.

   Voltage: Positive Phase 0 - 100v (unloaded)  
   : Negative Phase 0 - 90v

3. Variable Repetition Rate Pulse Train: (not used in experiment)
   
   Gate Open/Close Duration: 2.5 - 4.5 sec.
   
   Repetition Frequency: variable
   
   Pulse Width: as above
   
   Voltage: as above

4. Interrupted Pulse Train: (not used in experiment)
   
   Gate Open/Close Duration: 1.5 - 5.0 sec.
   
   Repetition Frequency: 60 Hz
   
   Pulse Width: as above
   
   Voltage: as above

5. Number of Outputs: 5 pairs, independently variable voltage

6. Circuitry: All silicon semiconductor

7. Power Source: 5 Nickel Cadmium Rechargeable Cells (6.25v total)

8. Dimensions: 282.9mm (Width) x 60.7mm (Ht.) x 235.0mm (Depth)
FIG. 56: G. 6805. CHINESE ACUPUNCTURE STIMULATOR:
ELECTRICAL CIRCUIT SCHEMATIC

(1) (2) (3) (4)

FIG. 57: ACUPUNCTURE NEUROSTIMULATOR VOLTAGE WAVEFORM
(Open Circuit)
The circuit diagram for this device appears in Fig. 56 Page 277 for which the following explanations apply:

1. Variable frequency oscillator for pulse gating.
2. Output buffer for above.
3. Pulse oscillator (relaxation type).
4. Output monitor (neon).
5. Output.

A list of parts and specification for the output transformers which required special prototype manufacture are available on request.

G. Thermometer and Probes (Figs. 45, 58 Pages 260, 274).

A thermistor balanced wheatstone bridge thermometer of the following specification was utilised:

Yellow Springs Instrument Co. U.S.A.

Tele-Thermometer YSI Model 44TA, 12 channel.


Accuracy : 0.2°C.

Readability : 0.1°C.

Metering : 4½" taut band 50uA in-built calibration source.

Probes : YSI Model 409 Skin surface probe. Diameter ½", depth ½", stainless steel, epoxy backed, electrically insulated. Thermistor resistance range 2.8K (20°C) - 1.1K (42°C). Response time 1.1 sec.

: YSI Model 408 Oral probe. Diameter 13/32", depth 5/64", stainless steel, response time 0.6 sec., otherwise as Model 409.

Oral Probe : placed beneath tongue, central and maximally posterior, and with the mouth closed. Subjects were required to verify probe similarity of position at each reading.
Fig. 58: Cutaneous Temperature Monitoring by Thermistor Probes (Abdominal and Thoracic) *

* Oral Probe not shown.
Abdominal Probe: placed immediately superior (approx. 1-2cm) to the umbilicus and hence approximately central to the abdominal stimulation grid. Held in place with Micropore surgical tape.

Thoracic Probe: placed approximately 1-2cm directly inferior and central to the suprasternal notch, held as above.

II. Tape Recorder (Fig. 45 Page 260).

A Uher Universal two track tape deck was used to present background music of a restful nature during the period of Acupuncture stimulation (or alternative control procedure) in each experimental session. The spare track was used to record subject's verbal rating responses to the radiant heat stimuli, for verification against manual recording if required. Subjects were reminded by the cue display to speak clearly and the M153 microphone/remote control was suspended close to the subject's mouth. Recording level was automatically adjusted.

I. Environmental Control/Monitor Unit (Fig. 45 Page 260).

A Rootes 'Tempair' air conditioner and heater unit under thermostatic control was used to maintain the experimental cubicle at approximately 27°C in line with the requirements for the comfort of inactive, partially clad humans. Deviations were monitored by a 'Speediset' Maximum-Minimum alcohol/mercury thermometer.

J. Experimenter Cue Projector/Monitor (Fig. 45 Page 260).

An Electrohome 10" monitor/projector system was used to display sequentially to the experimenter, slides printed with the numbers 1-12 in ascending order. Each number indicated a blackened disc abdominal test site on the subject as shown in Fig. 59 page. The sequence of numbers from 1 through to 12 was repeated three times for a complete stimulus series cycle of 36 stimuli.
FIG. 59: SUBJECT'S ABDOMINAL TEST SITE GRID - NUMERICAL IDENTIFICATION CODE AND DIMENSIONS

Dimensions:

- $a = 2.0 \text{ cm}$
- $b = 2.5 \text{ cm}$
- $c = 5.0 \text{ cm}$
Slide changing was triggered by relay contact closure initiated by the Programmer Unit at the beginning of each Step 1 (see Fig. 53 page 283). This cued the experimenter to move the Dolorimeter handset to a new abdominal test site for each successive stimulus and identified the site number required. The display was not visible to the subject.

K. Electrodes and ancillary equipment

1. Acupuncture Needle Electrodes (Fig. 60 Page 283).

These were supplied direct by

The East Wind Medic-l Instrument Co Ltd,
Kwantung Provincial Bank Building 11/5,
589 Nathan Road,
Kowloon, Hong Kong.

Handle lengths (excluding needle):
- 2.2cm, 2.7cm, 3.5cm.

Needle lengths:
- 1.27cm (0.5 inch), 2.54cm (1.0 inch),
- 3.81cm (1.5 inch).

Needle Diameter: 0.28mm.

Material: Stainless steel with spiral handle.

Sterilisation: Hot air, in sealed aluminium containers.

2. Acupuncture Needle Inserter (Fig. 61 Page 284).

Barrel: Clear Pyrex tube, length 12.75cm, diameter (external) 7mm, diameter (internal) 3mm.

Plungers: Brass rods, length 1.25cm (1.5 inch needles), 10.05cm (1.0 inch needle).

Sterilisation: Hot air, in sealed aluminium containers.

These devices provided support during insertion of longer needles, thus preventing kinking or bending. They also provided for more accurate angle of insertion. End stops on plungers prevented any accidental insertion beyond the required depth.
Fig. 60: Acupuncture Needle Stimulation Electrodes.
Fig. 61: Acupuncture Needle Insertion Device and its Operation.
3. Cutaneous Surface Electrodes (Fig. 62 Page 285).

Supplied by Beckman Instruments Inc., California, U.S.A. 92634.

Type : 650944 Biopotential Electrodes.

Diameter : Electrical contact area 9mm; total including casing 16mm.

Material : Silver/Silver Chloride.

Attachment : Double adhesive sided circular collars.


'Synapse' Conductive electrode cream, non-ionic, hypo-allergenic base, buffered to skin pH.

Fig. 62 : Cutaneous Surface Stimulation Electrode.
Calibration

A. Radiant Heat Dolorimeter

1. Energy Source

As described above (Construction Design Specification A2 page 26).

2. Calibration Sensor

A laser Power Meter of the following specification was employed:

Make: Coherent Radiation Ltd.
Model: 210 Power Meter.
Sensor type: Direct absorption head with thermopile element connected via 10K calibration resistor to an operational amplifier.
Active Sensor Area: 2.54cm².
Maximum Power Dissipation: 3 watts continuous.
Maximum Power Density at Sensor: 200 W/cm².
Spectral Sensitivity: 300.0mm to 30μm.
Sensor Output: 1mv/watt.
Operational amplifier: Type A1-uA725.
Meter Ranges: 300mW, 1W, 3W, (10W).
System Response Time: <0.5 sec., Meter damping circuit.
System Accuracy: ± 5%.
Calibration: Automatic calibration by cross range zero control.
Pen Recorder Output: 1mv/watt.

3. Source/Scisor Spectral Compatibility

Sensor Spectral Sensitivity: 300.0mm to 30μm.
Dolorimeter Bulb Source: Minimum colour temperature above zero used as a stimulus in the experiment >1,000°K (visible filament emission point). This produces <1% energy output cut-offs at 1μm and at 30μm (see
black body radiation curve calculated for $T = 1,000^\circ K$, Fig. 63 page 288.
The relative radiated energy density peak at $3\mu m$ is well within the sensor spectral sensitivity, as is the curve spread. Furthermore the filtering effect of the bulb glass above $5\mu m$ limits the longer wavelengths to well within the range of the sensor.

The upper limit colour temperature used as a stimulus in the experiment could not be directly measured owing to the lack of suitable calibration apparatus. However the duty-cycle of the current supply to the bulb from the Triac, at the maximum stimulus intensity, was well below that required at the manufacturer's recommended supply levels for 6.97 amperes at 21.5V. Recommended supply levels produce a colour temperature of $3,400^\circ K$ for which the black body radiation curve was calculated and appears in Fig. 64 page 289. At this level the power output from the Dolorimeter handset equalled 4.20 Watt/cm$^2$ as measured by the Coherent Radiation Power Meter described above. From this, using Stefan's law, it is possible to estimate the temperature applying at the maximum stimulus intensity used in the experiment from the relationship $M = \sigma T^4$ (where $M$ = total power radiated from a black body, $T$ = absolute temperature, $\sigma$ = constant).

Thus, if the power output of the Dolorimeter at full supply levels = 4.20W and colour temperature = $3,400^\circ K$, then $\sigma = \frac{M}{T^4} = \frac{4.20}{3,400^4}$. From the value $\sigma$ we may calculate the temperature corresponding to any output power since $T = \sqrt[4]{\frac{M}{\sigma}}$.

The maximum stimulus intensity in the experiment was set at 1.82 watt/cm$^2$ from which the derived temperature = $2,758^\circ K$. The black body radiation curve for this figure rounded to $2,800^\circ K$ appears in Fig. 64 page 289 from which it may be observed that peak emission occurs at approximately $1.04\mu m$ with a $<1\%$ tail-off at $300nm$. With the bulb glass filter cut-off at $5\mu m$ it is found that the sensor spectral sensitivity is again quite adequate.
FIG. 63. BLACK BODY RADIATION AT DOLORIMETER LOWER COLOUR TEMPERATURE LIMIT

\[ \frac{dE}{d\lambda} \text{ relative} \]

\[ T = 1,000^\circ \text{K} \]

\[ \lambda \mu m \]

3\mu

350

300

200

100

0

0

10

20

30

40
FIG. 64. BLACK BODY RADIATION AT DOLORIMETER UPPER COLOUR TEMPERATURE LIMITS

\[
\frac{dE}{d\lambda} = \frac{1}{\lambda^5 \left( \text{antilog} \frac{\lambda}{kT} - 1 \right)}
\]

\(\lambda_{\text{max}} = 860\,\text{nm}\)
\(\lambda_{\text{max}} = 1,040\,\text{nm}\)

\(T = 3,400^\circ\text{K}\)
\(T = 2,800^\circ\text{K}\)

NOT TO
(Scale for different temps.)
4. **Dolorimeter Power Output Calibration Procedure** (Fig. 46(a) Page 261)

In order to equate with radiation and conduction levels at the cutaneous surface, the power meter sensor was similarly placed centrally, over, and in contact with, the Dolorimeter handset output aperture. The Dolorimeter output nozzle was machined for exact diameter and depth fit into the well in which the sensor surface was mounted in the power meter head block. The thermopile sensor head element and amplifier circuitry provided an integrated output of 1mv/watt for direct meter drive and pen recorder output with a response latency of <0.5 second. Since the Dolorimeter output aperture was 1cm² power readings could be made directly in Watts/cm².

Calibration of Dolorimeter 'control' voltages against output in Watts/cm² was made in incremental steps of 0.01 W/cm², this being the minimum accurate meter resolution. This represents increments of 2.39m.cal.sec⁻¹ cm⁻² (the units employed in other relevant studies (see main text)) and produces an acceptable error limit of <0.01% of the stimulus levels used in this study.

The following procedure was adopted (using the automated programmer for all sequencing and timing):

a) Power meter set to zero in accord with manufacturer's instructions whilst set up in contact with the Dolorimeter handset.

b) Room temperature was maintained at approximately 27°C ± 1°C (as during all experimentation) by the Rootes Tempair unit.

c) The Dolorimeter bulb 'control' reference voltage across the wirewound potentiometer was monitored by a Digital Voltmeter of the relevant specification below:
Make: Solartron Type LM1426.
Range: 10v DC.
Input Impedance: >10 GΩ.
Accuracy: ± 0.01% of reading (24 hour).
Readings per second: 33.
Calibration: Internal Weston standard cell (unsaturated) calibrated to four decimal places after 30 minute stabilisation.

d) The 'control' voltage was set to the approximate level for the required bulb output wattage and a stabilisation period of seven seconds allowed (the stabilisation period was predetermined on the basis of the bulb manufacturer's data and the tolerances of the Dolorimeter Power Supply circuit design).

e) The Dolorimeter handset shutter was opened for the standard, automatically timed, three second period (ie. stimulus duration) and the maximum power meter reading was noted. This reading was also recorded by coupling (see Fig. 46(a) Page 261) to a Devices D.C.6 preamplifier (range 1mv/cm) and a Devices D.C.5 pen recorder (paper speed 10mm/sec.). The Dolorimeter shutter open/close function was automatically marked alongside the record, a typical example of which appears in Fig. 05 Page 292.

It will be noted that after approximately 2.75 seconds of sensor exposure a, presumably conductive, element of output produces a slow, and slight, meter drift upwards from the previously stabilised reading. This drift proved to be a very small proportion of total output, and certainly too small to measure with accuracy within the limitations of the sensor and meter sensitivity. For this reason, and since the skin would also be subject to this element of heating, reading measurement
FIG. 65. TYPICAL POWER METER RECORD FOR DOLORIMETER HANDSET CALIBRATION.
was made at the maximum level, occurring immediately prior to shutter closure, rather than at the stabilised point which appeared after cessation of the initial overshoot and rebound. f) The bulb was then extinguished and cooling of the sensor and Dolorimeter handset allowed to proceed, via their intrinsic heat sinking, until the initial baseline zero was re-established. g) Procedures d) - f) inclusive were then repeated, adjusting the 'control' voltage as required until the exact power requirement was achieved and replicated over three successive readings. By this method the Dolorimeter Calibration Table appearing as Table 48 page 294 was produced in steps of 0.01 watt/cm² up to 2.5 watt/cm². When power output is plotted against 'control' voltage as in Fig. 66 a, b, c, it can be seen that, at least in the range used in the experiment (0.73 - 1.82 watts/cm²), the expected linear relationship is fulfilled. The departure above this level appears to result from saturation of the phototransistor in the Dolorimeter handset. The above procedure was used to set up power levels on the six dolorimeter channels (stimuli) as follows:

<table>
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<th>Stimulus</th>
<th>Channel</th>
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<tr>
<td>Watts/cm²</td>
<td>A</td>
</tr>
<tr>
<td>0.00</td>
<td>0.73</td>
</tr>
<tr>
<td>'Control' Voltage (v.)</td>
<td>0.00</td>
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</table>

Calibration of these levels was checked daily during the experimental series but showed no discernible drift over the six month period. The system showed calibration stability for mains variation of 110% - 85% as verified by test with the variac transformer coupled to the Dolorimeter power supply. This more than allows for any likely alteration in mains supply during the course of experimentation.
<table>
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<tr>
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<th>Watts</th>
<th>Volts</th>
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TABLE 48: DOLORIMETER CALIBRATION (continued) (Range: 2.08 - 2.50 watts/cm²)

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<td>2.18 - 8.00</td>
<td>2.35 - 8.75</td>
<td></td>
</tr>
<tr>
<td>2.19 - 8.03</td>
<td>2.36 - 8.77</td>
<td></td>
</tr>
<tr>
<td>2.20 - 8.07</td>
<td>2.37 - 8.80</td>
<td></td>
</tr>
<tr>
<td>2.21 - 8.13</td>
<td>2.38 - 8.82</td>
<td></td>
</tr>
<tr>
<td>2.22 - 8.18</td>
<td>2.39 - 8.84</td>
<td></td>
</tr>
<tr>
<td>2.23 - 8.23</td>
<td>2.40 - 8.85</td>
<td></td>
</tr>
<tr>
<td>2.24 - 8.28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: 1 mcal/sec⁻¹/cm²⁻² = 1 x 4.1855 x 10⁻³ watts/cm²
5. Dolorimeter Output Beam - Uniformity of Radiant Intensity

In order to ensure uniformity of intensity in the Dolorimeter output beam, the beam area of $1\text{cm}^2$ was scanned by a $1.5\text{mm}^2$ sampling aperture, being 1.5% of total area. Fig. 67 page 299 illustrates the black PTFE template of $1\text{cm}^2$, which was fitted exactly to the Dolorimeter output aperture, with three $1.5\text{mm}^2$ holes spaced equidistantly from the centre to the perimeter. A standard Dolorimeter output of 1.5 Watt/cm$^2$ was selected for all sampling measurements since this provided sufficient output through the sampling holes to provide reasonable drive for the pen recorder preamplifier from the power meter and avoided the use of noise prone higher sensitivity ranges. The dimension of the sampling aperture was selected on a trial and error basis using successive size increments, for an optimum compromise between division of the Dolorimeter output beam into an adequate number of sampling areas whilst retaining sufficient size to transmit adequate energy levels for measurement.

Initially the two outer sampling apertures (Fig. 67 page 299) were blocked off and the power meter output recorded for the central aperture. The same procedure, as described above for the whole aperture, of taking repeated measures followed by cooling to baseline after reading, was adopted. The central hole was then blocked and the perimeter hole exposed and readings recorded. The template was then rotated through seven successive $45^\circ$ arcs, a reading being taken at each point. A similar procedure was then completed for the remaining sampling aperture.

The central aperture produced the highest reading since the Power Meter and discs of heat sensitive paper had been used to align the bulb beam peak energy zone centrally to the Dolorimeter output aperture. This value was therefore taken as 100% and all other values obtained were expressed as percentages of this value to produce Fig. 68 Page 299.
FIG. 67 DOLORIMETER BEAM SAMPLING
APERTURE TEMPLATE (BLACK PTFE)

All dimensions $\rightarrow 0.7 \text{ mm}$

FIG. 68 DOLORIMETER OUTPUT BEAM - RELATIVE
INTENSITY PLOT

All sampling apertures $1.5\text{mm}^2$ (1.5% of total area)
Fig. 68 indicates that, apart from deficits of approximately 25% at the 90° and 270° outer perimeter positions due to design of the bulb reflector, there was acceptable uniformity of the beam output intensity. These figures represent the best obtainable uniformity as a result of substantial pilot tests with varying combinations of Dolorimeter output aperture diameters and barrel lengths, subject to the restriction of producing the required output energy levels.

Measurement of pen deflection could not be made with an accuracy beyond approximately 0.5 mm (i.e. ± 3% of maximum deflection taken as the 100% standard), and the preamplifier sensitivity range could not be increased without incurring noise problems. The apparent, rather than actual, uniformity of readings expressed in Fig. 68 reflects this limitation. Allowing for error limits of ± 3%, we find a maximum range of 72% - 103% (31%) in energy distribution relative to the central standard across the output beam. Exclusion of the two peripheral cold spots narrows the range to 84% - 103% (19%). Discussion of the likely significance of cold spots in the beam appears in Chapter 5.

Actual data values are not presented here since it was the relative intensities of different segments of the beam which were of interest.

6. Dolorimeter Induced Temperature Calibration Procedure
(Fig. 46(b) Page 26)

An approximation to the induced temperature (°C) on the cutaneous surface beneath the Dolorimeter output beam was obtained as below.

A NiCr/NiAl point Thermocouple was blacked with the usual preparation and taped in the centre of a similarly blacked abdominal test site on a volunteer subject. The Dolorimeter handset was now applied to the test site in the normal manner. Ambient air
temperature was maintained at approximately $27^\circ$C. The thermocouple, together with an identical reference unit immersed in melting ice, was connected to an electronic thermometer of the specification below:

- **Make**: Comark Electronics Ltd Electronic.
- **Thermometer Type**: 1604.
- **Accuracy**: (at $23^\circ$C) $\pm 0.5^\circ$C.
- **Resolution**: $0.1^\circ$C per division.
- **Range**: $-60^\circ$C to $+170^\circ$C in 23 steps of $10^\circ$C.
- **Cold Junction Deviation with Ambient Temperature**: $0.5^\circ$C at 0 to $+40^\circ$C ambient.
- **DC Output**: 1 volt for F.S.C.

The DC Output was connected to a Solartron Digital Voltmeter/Microprocessor of the relevant specification below. This device was not yet available on the market during previous calibration and the experimental work.

- **Make**: Solartron Type 7C55.
- **Range Selected**: 1v DC.
- **Input Resistance**: 10 G.
- **Limits of Error**: 0.002%.
- **Readings per second**: 33G (scale length 3 x 9).
- **Calibration Balance**: Automatic drift correction. Internal zero and positive/negative reference potentials corrected every 10 seconds.

The microprocessor was programmed to store and display the maximum input voltage applied from the thermometer during each three second period (990 readings) when the Dolorimeter shutter was open.
Readings were recorded at an Electronic thermometer-range plus Digital Voltmeter maximum reading eg. $40^\circ C + 0.15v = 41.5^\circ C$.

The Dolorimeter 'control' reference voltage was again monitored by the Solartron Digital Voltmeter type LM1426 as outlined above (section 4(c) page 290).

'Control' voltage was plotted against thermocouple temperature for the range 1 - 6.5 v.d.c. in incremental 0.5v. steps. A mean of three successive readings with cooling to baseline between each measurement were taken to produce Table 49(a) page 303. In no instance did the values deviate beyond $\pm 0.5^\circ C$; figures are rounded to one decimal place. Graphic presentation of these results appears in Fig. 69 page 304 (small dots).

Next the Dolorimeter handset was applied to the abdomen to deliver the six different radiant heat power levels used as stimuli in the main experiment. Temperature measurements were made as outlined above and appear in Table 49(b) page 303. They are plotted graphically in Fig. 69 page 304 (triangles). The temperature increment between each successive stimulus displays the uniformity to be expected from the equal power increments set up for the stimulus series. A least-squares linear regression was performed using all 17 data points and is graphed on Fig. 69 page 304. The data display the expected approximate linearity of relationship between induced temperature and 'control' voltage. Comparability with actual skin temperatures is, of course, subject to the assumptions that the same fraction of energy
TABLE 49: INDUCED THERMOCOUPLE TEMPERATURE (°C) AS A FUNCTION OF DOLORIMETER 'CONTROL' VOLTAGE (v.)
(Standard 3 second exposure)

<table>
<thead>
<tr>
<th>'Control' Voltage (v.)</th>
<th>1.00</th>
<th>1.50</th>
<th>2.00</th>
<th>2.50</th>
<th>3.00</th>
<th>3.50</th>
<th>4.00</th>
<th>4.50</th>
<th>5.00</th>
<th>5.50</th>
<th>6.00</th>
<th>6.50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Temperature (°C) (approx.)</td>
<td>37.8</td>
<td>40.1</td>
<td>41.4</td>
<td>44.0</td>
<td>45.8</td>
<td>46.6</td>
<td>48.7</td>
<td>50.0</td>
<td>51.4</td>
<td>52.3</td>
<td>53.8</td>
<td>54.6</td>
</tr>
</tbody>
</table>

b)

<table>
<thead>
<tr>
<th>Stimulus Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>C</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Control' Voltage (v.)</td>
<td>0.00</td>
<td>1.29</td>
<td>2.22</td>
<td>3.48</td>
<td>4.89</td>
<td>6.38</td>
</tr>
<tr>
<td>Maximum Temperature (°C) (approx.)</td>
<td>0.00</td>
<td>39.2</td>
<td>43.1</td>
<td>46.9</td>
<td>50.8</td>
<td>54.4</td>
</tr>
<tr>
<td>Temperature Increment (°C)</td>
<td>3.9</td>
<td>3.8</td>
<td>3.9</td>
<td>3.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INDUCED THERMOCOUPLE TEMPERATURE (°C) AS A FUNCTION OF VOLTMETER CONTROL VOLTAGE

THERMOCOUPLE TEMPERATURE (°C)

Intercept = 35.89

Stimulus Level

0 1.29 2.22 3.48 4.89 6.38
A. B. C. D. E. F.

A. 33.5
B. 39.2
C. 43.1
D. 46.9
E. 50.8
F. 54.4
impinging is absorbed irrespective of wavelength, and to the limitations of divergences in specific heat capacities and time constants etc.

B. Neurostimulator calibration

Stimulation parameters applied to four experimental subjects were preset and/or monitored as follows:

1. Pulse Frequency: The 'continuous pulse train' mode of operation was selected and calibrated to a rate of 2.5Hz using the S.E. Labs Ltd Counter/Timer described above. Calibration was checked daily but showed negligible drift independent of subject load.

2. Pulse Width: Standard Positive Phase 0.5m.sec. Negative Phase 0.75m.sec. as monitored by a Telequipment D61A Oscilloscope. Input impedance 1MΩ, 30pF. Pulse width showed no measurable variation at any time independent of subject load.

3. Voltage and Current: These parameters were monitored with the D61A Oscilloscope across each Acupuncture needle/surface electrode pair in series with a 10.5Ω resistor (nominal 10Ω) which was negligible as compared with subject impedance. Twin channel simultaneous monitoring of the oscilloscope input was undertaken (with or without X10 attenuation probe as required) across the subject load (voltage waveform) and series resistor (current waveform). All stimulation during experimentation was carried out with the resistor in circuit.

Owing to the time consuming nature of these measures during the extremely tight experimental session time scale, they were completed for only 4 of the 16 experimental subjects. One subject was randomly selected for measurement from the four sub-groups in the balanced order design of the main experiment. This should compensate, in the main experiment, for possible effects on subjects resulting from the additional procedures.
The results for two subjects are presented in Table 50. Data from the other two subjects does not appear owing to their loss but were very similar. Anatomical locations are more fully described in the main text.

Readings were taken at the maximum comfortably tolerable level of stimulation for the subject after a five minute adaptation and habituation period. Paraesthesias were present in all cases, at all sites, usually involving tingling, throbbing, formication, and often discernible fasciculation.

Current and resistance were determined by application of Ohm's law. The temporally coincident current and voltage waveforms did not differ markedly; thus it seems justifiable to neglect the capacitive (and inductive) components of tissue impedance. The undoubted capacitive element of skin resides mainly in the superficial layers of the stratum corneum (447) and is removed by skin drilling. It obviously still applies to the present situation with the use of surface electrodes. A capacitive bridge was not available for measurement, but evidence suggests that it is a small and stable element. At low currents, and low frequencies, the skin does, in fact, behave as a true ohmic resistance (447). Linearity, however, would appear unlikely to remain operative much above 75µA/cm² (447), and reference to section 5 below indicates densities of much greater magnitude were involved in this study. However, in view of the somewhat peripheral importance of knowledge of precise levels of tissue stimulation and resistance in this study it would seem justifiable to ignore this last point. For the same reason all stimulation levels are presented as peak measures without attempt to analyse over time.
**Table 50: Electrical Stimulation Parameters Applied to Two Typical Subjects**

<table>
<thead>
<tr>
<th>Electrode Pairs*</th>
<th>Peak Voltage (v.)</th>
<th>Peak Current (mA)</th>
<th>Resistance of Tissue (Ω)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+     -</td>
<td>+     -</td>
<td>+     -</td>
</tr>
<tr>
<td>Needle - Surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Dorsal A. Pollicis Interosseous Brevis m.</td>
<td>14</td>
<td>7</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>4</td>
<td>1.4</td>
</tr>
<tr>
<td>Pre-tibial Gastrocnemius m.</td>
<td>30</td>
<td>15</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>7.5</td>
<td>2.1</td>
</tr>
<tr>
<td>Deltoid m. - Biceps m.</td>
<td>12</td>
<td>5.5</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Tensor Fasciae Rectus Femoris m. Latae m.</td>
<td>22</td>
<td>10</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>8.5</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* Surface Electrode - Pulse output ('live')
Needle Electrode - Return ('ground')

** Approximate impedance (ohmic)
4. Waveform: The voltage waveform was only slightly modified across the subject load (Fig. 70 page 309) as opposed to the unloaded form (Fig. 77 page 277). The current waveform (loaded) appears in Fig. 71 page 309.

5. Current/Power Density at Electrodes: Current and power densities were calculated for needle and surface electrodes, at all anatomical locations, from the means for the two subjects' peak current and voltage measurements (Table 50 page 307).

a) Needle Electrodes: Three lengths of needle electrode were inserted to full depth at the various body sites and stimulated at a level producing current and power densities as presented in Table 51 page 310.

b) Cutaneous Surface Electrodes: A standard size cutaneous electrode was used at all body locations and produced current and power densities as presented in Table 52 page 311.
Fig. 70: Acupuncture Neurostimulator Voltage Waveform Across Subject Load (Unilateral Needle Cathode & Surface Anode Pair).

Fig. 71: Acupuncture Neurostimulator Current Waveform Across Series Resistor (10.5 ohm) Load (Unilateral Needle Cathode & Surface Electrode Anode Pair).
### TABLE 51: MEAN ELECTRICAL STIMULATION PARAMETERS APPLIED FOR TWO TYPICAL SUBJECTS: NEEDLE ELECTRODE CURRENT AND POWER DENSITIES

<table>
<thead>
<tr>
<th>Needle length (excluding tip)</th>
<th>Deltoid n./Tensor Fasciae latae m.</th>
<th>First Dorsal Interosseous</th>
<th>Peroneal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 inch (12.45 mm)</td>
<td>1.0 inch (24.9 mm)</td>
<td>1.5 inch (37.6 mm)</td>
</tr>
<tr>
<td>Radius (mm)</td>
<td>0.14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rod Surface Area (mm²)</td>
<td>10.95</td>
<td>21.90</td>
<td>33.07</td>
</tr>
<tr>
<td>Cone (tip) Height (mm)</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cone Slant Height (mm)</td>
<td>0.52</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cone Surface Area (mm²)</td>
<td>0.23</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Contact Surface Area (mm²)</td>
<td>11.18</td>
<td>22.13</td>
<td>33.30</td>
</tr>
<tr>
<td>Peak Current (mA)</td>
<td>2.4</td>
<td>2.8</td>
<td>1.65</td>
</tr>
<tr>
<td>Current Density (mA/mm²)</td>
<td>0.2</td>
<td>0.25</td>
<td>0.07</td>
</tr>
<tr>
<td>Peak Power (mW)</td>
<td>20.0</td>
<td>50.0</td>
<td>18.0</td>
</tr>
<tr>
<td>Power Density (mW/mm²)</td>
<td>1.79</td>
<td>4.47</td>
<td>0.81</td>
</tr>
</tbody>
</table>
TABLE 52: MEAN ELECTRICAL STIMULATION PARAMETERS APPLIED FOR TWO TYPICAL SUBJECTS: CUTANEOUS ELECTRODE CURRENT AND POWER DENSITIES

<table>
<thead>
<tr>
<th>Cutaneous Electrode Location</th>
<th>Biceps m.</th>
<th>Rectus Femoris m.</th>
<th>A Pollicis Brevis m.</th>
<th>Gastrocnemius m.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface Area (mm²)</td>
<td>63.62</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Peak Current (mA)</td>
<td>2.4</td>
<td>2.8</td>
<td>1.65</td>
<td>3.25</td>
</tr>
<tr>
<td></td>
<td>3.35</td>
<td>3.85</td>
<td>2.35</td>
<td>4.60</td>
</tr>
<tr>
<td>Current Density (mA/mm²)</td>
<td>0.034</td>
<td>0.044</td>
<td>0.026</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>0.053</td>
<td>0.060</td>
<td>0.037</td>
<td>0.072</td>
</tr>
<tr>
<td>Peak Power (mW)</td>
<td>20.0</td>
<td>50.0</td>
<td>18.0</td>
<td>70.0</td>
</tr>
<tr>
<td></td>
<td>16.0</td>
<td>35.0</td>
<td>13.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Power Density (mW/mm²)</td>
<td>0.31</td>
<td>0.78</td>
<td>0.28</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>0.25</td>
<td>0.55</td>
<td>0.20</td>
<td>0.78</td>
</tr>
</tbody>
</table>
Method: Starting about 5 days after adaptation and training, all subjects participated under four different experimental conditions at approximately five-day intervals. All sessions were conducted at the same time of day. Female subjects were scheduled so as to begin and complete the whole experiment in the interval between successive menses.

As depicted in Fig. 22, subjects were divided into four groups with equal sex representation, to pass through the four experimental conditions in fully balanced order. The concepts and procedures of the different conditions were largely identical to those of the first experiment. Genuine Acupuncture was to be compared for its analgesic potency (with respect to intense radiant heat stimuli applied to the alaminal region only), with the effects of a simulated or Pseudo-Acupuncture, and an otherwise identical 'Control' condition without insertion of Acupuncture needles. In addition, however, a further treatment of identical 'Genuine Acupuncture', with the addition of an injection of Naloxone, was included to test the Endorphin mechanism hypothesis. Subjects, and the physician inserting needles, were, of course, blind as to the differences between the types of Acupuncture performed, and the injections given in the four sessions.

It will be noted in Fig. 22 that there are no conjunctions of the two Genuine Acupuncture sessions. This was not only to avoid traumatising the same loci in close succession, but also to weaken the

* A shorter interval might have been desirable to maintain familiarity with experimental conditions, and possibly to increase similarity of the physiological and psychological background state of the subject during different sessions. In practice, the first concern did not prove problematic, since subjects were all intelligent and recalled the requirements of the experiment well. The latter consideration was controlled for gross changes by a questionnaire (section (j)*) and may otherwise probably be assumed as either random, or controlled by the balanced session order design. In any event, this delay was felt to be beneficial in reducing cumulative stress from the lengthy multiple pain testing sessions, allowing full recovery from the multiple needle insertions, particularly the blood samples, and finally to slightly weaken recall of the finer differences between the various Acupuncture, or Acupuncture-like, procedures.
FIG. 22: ACUPUNCTURE EXPERIMENT NO. 2:
BALANCED ORDER EXPERIMENTAL SESSION DESIGN

Adaptation and training session
16 subjects (8 ♂)

- 4 subjects (2 ♂)
  - Genuine acupuncture session
  - Pseudo-acupuncture session
  - Genuine acupuncture + Naloxone session
  - Control session

- 4 subjects (2 ♂)
  - Control session
  - Genuine acupuncture + Naloxone session
  - Control session
  - Control session

- 4 subjects (2 ♂)
  - Genuine acupuncture session
  - Pseudo-acupuncture session
  - Genuine acupuncture session
  - Genuine acupuncture + Naloxone session

- 4 subjects (2 ♂)
  - Pseudo-acupuncture session
  - Control session
  - Control session
  - Control session

- 4 subjects (2 ♂)
  - Control session
  - Genuine acupuncture + Naloxone session
  - Control session
subject's memory for the exact sites of insertion, and to reduce undesirable pondering as to the reason for duplication of one treatment only.

The procedural sequence common to all conditions is outlined in Fig. 23, together with a guide to the time course of the various stages in the sessions which lasted approximately 2½ hours in total. Items boxed or underlined with dotted lines were not included in the 'Control' session, although a similar time allocation was allowed, and other appropriate events substituted where indicated in the explanations below.

(a) : Pre-Session Assessment Questionnaire:

The simple questionnaire appearing in Appendix 5 (i) was completed prior to each experimental session. This ensured that subjects had not taken any drugs likely to affect their pain sensitivity, mood, or otherwise alter their performance, or negatively interact with the experimental procedures in any way.

Subjects were requested to attend experimental sessions in only the best physical and mental condition. Heavy drinking was to be avoided for at least one day prior to attendance, and illness or other physical problems were to be reported, and the session date preferably amended. Subjects were also requested to report any life conditions, or events, which might render them especially intolerant of experimental demands and stresses, or excessively anxious or agitated.

(b) : Surface Temperature Thermistors Attached (Abdominal, Thoracic, Oral):

Skin temperature monitoring equipment as described in Chapter 7, Section (c) was attached (Fig. 58 Page 279) and allowed to stabilise,
FIG. 23: ACUPUNCTURE EXPERIMENT NO. 2:
2 1/4 Hour (approx.) Experimental Procedure for ALL Sessions:
(Items boxed [ ] not included in 'Control Session')

<table>
<thead>
<tr>
<th>Time Scale</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) 1 min.</td>
<td>Pre-Session Assessment Questionnaire.</td>
</tr>
<tr>
<td>(b) 9 min.</td>
<td>Surface Temperature Thermistors Attached (Abdominal, Thoracic, Oral). Epigastrium Blackened (12 Discs). Standardised Instructions to Subject. Subject Screened from Visual Contact.</td>
</tr>
<tr>
<td>(c) 7 min.</td>
<td>Genuine or Pseudo-Acupuncture 'Points' Located, Palpated, and Marked. Baseline Surface Temperatures(°C) Recorded. Thermal Stimulus Practice Trial (One stimulus at each level).</td>
</tr>
<tr>
<td>(d) 23 min.</td>
<td>1st (Baseline) Thermal Stimulus Series (3 Blocks of 36 Stimuli with Intervening 2 min. Rest Periods and Surface Temperatures Recorded After Each Block).</td>
</tr>
<tr>
<td>(e) 2 min.</td>
<td>Blood Sample (10 ml.) Taken.</td>
</tr>
<tr>
<td>(f) 5 min.</td>
<td>Break/Rest Period</td>
</tr>
<tr>
<td>(g) 2 min.</td>
<td>Mood Rating Scales Completed.</td>
</tr>
<tr>
<td>(b) 10 min.</td>
<td>4 Acupuncture Needles Inserted and Electrical Stimulation Started. Intensity of Stimulation Predicted for Prediction of Analgesic Potency</td>
</tr>
<tr>
<td>(i) 35 min.</td>
<td>Electrical Stimulation of Acupuncture Needles.</td>
</tr>
<tr>
<td>(j) 2 min.</td>
<td>Electrical Stimulation Reduced to Subliminal Level Mood Rating Scales Completed.</td>
</tr>
<tr>
<td>(k) 2 min.</td>
<td>Blood Sample (10 ml.) Taken.</td>
</tr>
<tr>
<td>(l) 5 min.</td>
<td>Injection (2 ml) of: Saline or Naloxone (0.8 mg). Acupuncture Needles Removed. Baseline Surface Temperatures(°C) Recorded.</td>
</tr>
<tr>
<td>(m) 23 min.</td>
<td>2nd Thermal Stimulus Series (3 Blocks of 36 Stimuli with Intervening 2 min. Rest Periods and Surface Temperatures Recorded After Each Block). Injection (1 ml.) During First Rest Period: Saline or Naloxone (0.4 mg)</td>
</tr>
<tr>
<td>(n) 4 min.</td>
<td>Rating Scales Completed for Effect of Acupuncture Effect of Injection Mood</td>
</tr>
<tr>
<td>(o) 5 min.</td>
<td>Post-Experimental Structured Interview.</td>
</tr>
</tbody>
</table>
together with the subject, in a 27°C, humidity controlled, environment.
This was intended principally to monitor background temperature of the
*general* abdominal area for possible progressive changes, against which
subjects would have to discriminate radiant heat stimuli applied to
adjacent specific abdominal test sites. The importance of this was
discussed in chapters 4 and 5. The thoracic thermistor was intended
to permit comparison of skin temperatures at a non-stimulated site;
whilst the oral probe was designed to monitor hypothesised Endorphin
induced changes comparable to the effects of opiates (as discussed in
chapter 6).

*Epigastrium Blackened (12 Discs):*

12 small discs of skin in the abdominal region were blackened
for use as radiant heat stimulus test sites, as described in *Chapter 7, Section (2)*
Page 25, and for reasons discussed in chapter 5 page 180. It should
be noted that the abdomen was the only area of the body to be employed
for sensory testing.

*Standardised Instructions to Subjects:

Instructions to subjects appear in Appendix 6 Page 183.
Volunteers should have been fully familiar with all experimental
procedures and response requirements from the training session. However,
full understanding was reascertained, and, where necessary, further
explanation given on a basis strictly limited to information already
covered by the instruction sheet. Subjects were also tested at this
point for their ability to remember all the response scale categories
until 100% recall was attained with ease.

*Subject Screened from Visual Contact:*

In order to remove visual cues as to the intensity of the
radiant heat stimuli which the subject was to rate, a thick dark
curtain was used to completely partition the experimental cubicle (Fig. 24 Page 317). The subject's head was thus contained in one compartment, together with a response cueing display (see Chapter 7, Section 2 of Page 275), and his or her body on the other side of the screen for the application of the thermal stimuli and the various Acupuncture procedures. The side of the curtain containing the subject's head was brightly illuminated to further reduce transmission of light cues. This arrangement afforded excellent protection against all types of inadvertent cues to the subject, since strict limitation of verbal and tactile communication to a pre-arranged programme was easily arranged.

(c) 'Genuine or Pseudo-Acupuncture' 'Points' Located, Palpated, and Marked:

Exactly the same 'Genuine Acupuncture' 'points' in the hand (Figs. 8, 10, 28 Pages 62, 62, 327) and leg (Figs. 4, 11, 29 Pages 57, 68, 327) were employed as in the first study. Since a relationship between Acupuncture of the leg 'point' and the induction of abdominal analgesia was strongly established in that study, the testing of skin sensitivity could now be restricted to the abdomen only. This allowed application of S.D.T. methodology to the study, since otherwise, for a multiple body area S.D.T. analysis, the considerable number of noxious stimulus presentations required at each body site would be prohibitive.

These same 'Genuine Acupuncture' 'points' were, of course, also used in the 'Genuine Acupuncture plus Naloxone' sessions, although the subjects were induced to believe that 'points' at slightly removed sites were employed. The neutral placebo, or 'Pseudo-Acupuncture', 'points' in the thigh (Figs. 15, 27 Pages 74, 326) and upper arm (Figs. 15, 26 Pages 74, 326) of the first study were again utilised;
Fig. 24: Application of the Radiant Heat Dolorimeter to Test Sites on the Subject's Abdomen: Prevention of Visual Intensity Cues by Screening.
and, to aid the symmetry of the design, areas very close to these 'points' were also located, palpated, and marked in the 'Control' sessions, although, of course, needles were not later inserted at these sites. * Both the above additional safeguards were included in an effort to reduce the likelihood of undesirable speculation by subjects as to reasons why Acupuncture was performed twice at one set of loci, and only once at the other. All procedures for location and palpation were as described for the first experiment.

: Baseline Surface Temperatures (°C) Recorded:

At this point sufficient time had elapsed in the controlled environment for the subject's various surface temperatures to have reached adequate stabilisation, and for the recording apparatus to reach equilibrium. These abdominal, thoracic, and oral baseline values were, therefore, recorded.

: Thermal Stimulus Practice Trial (One stimulus at each level):

In order to maximise responding efficiency right from the first block of stimuli, subjects were given one presentation of each of the six radiant heat stimulus levels to be used in the study as a practice run. The apparatus employed was a modified version of the Hardy, Wolff, Goodell Dolorimeter(179), a gun-like projector, hand held by the experimenter, and moved to a new blackened test site on the subject's abdomen with each stimulus presentation, following a pre-programmed pattern (see Chapter 7, Fig. 59 Page 281). The skin was exposed to stimulation every 7 seconds by a shutter timed to open automatically.

* It was also considered useful as a control against the slight possibility of a direct physiological effect of the palpation itself. As discussed in an earlier chapter, some practitioners of Acupuncture merely massage or palpate the 'points' in their treatments, without inserting needles.
for a standard three-second duration, unless pro-empted by the subject depressing his safety stimulus cancel button.

Six stimulus intensities of 0, 175, 240, 305, 370, 435 mcal/sec\(^{-1}\) cm\(^{-2}\) were delivered in the randomised order of the final sequence in Fig. 52 Page 270 to abdominal test sites 6-12 (Fig. 59 Page 28\(^{1}\) ). The selection of these optimal stimulus intensities, the duration, and the intensity and temporal intervals between them, were determined by the extensive pilot study work reported above and considerations discussed in chapters 4 and 5. For reasons also discussed in the pilot section, subjects were induced to believe that an effectively infinite number of random stimulus intensities were available. These would generate a wide variety of sensory experiences, and the subject was provided with the response rating scale shown in Fig. 25 Page 32\(^{1}\) to indicate the closest, or most appropriate, description. If the subject depressed his 'Withdraw' response button to terminate the stimulus, this response latency was automatically timed and recorded. The selection of this response system as optimal was again discussed principally in the pilot section above and Chapter 4.

(d) 1st (Baseline) Thermal Stimulus Series:

Using exactly the same stimulus procedures outlined above, a complete test series of 108 thermal stimuli in total was administered. The six stimulus levels (again the subject believed the number was effectively infinite), were presented in a row, following a different sequence order each time (see Fig. 52 Page 270), and again the
FIG. 25: ACUPUNCTURE EXPERIMENT NO. 2:

Subjects' Sensation Report Scale

| Nothing | Something | Warm | Hot | Very Hot | Very Faint Pain | Faint Pain | Painful | Very Painful | Withdraw* |

* Withdrawal latency timed (secs)
Dolorimeter was moved to a new abdominal test site, in the sequence described in Fig. 59, following each stimulus. An extra five-second interstimulus delay was interspersed after every sixth stimulus, for the application of a rectangular, light aluminium, heatsink to the stimulated area. The heatsink was maintained at an appropriate 'adapted' temperature by resting in contact with the uppermost abdominal region of the subject when not in use.

Upon completion of a block of stimuli (i.e., six presentations at each level), a two minute rest interval was allowed, during which the subject's abdominal temperature was recorded. This entire block of stimuli was exactly repeated twice more, with a further two minute interval between each block to complete the series. After the final block, thoracic and oral temperature were recorded in addition to the usual abdominal measure.

The measures derived from responses in this complete series were designed to serve as baseline values for comparison with a later identical series following the various different experimental treatments.

(c) Blood Sample (10ml) Taken:

Using completely standard procedures, a 10ml sample of venous blood was drawn off from the subject's left arm for later Beta-Endorphin content assay. The site employed does not correspond to any listed Acupuncture 'point'. The sample was processed as described below.

(f) Break/Rest Period:

The subject was then permitted a few minutes to get up, stretch, quietly walk about the laboratory, and generally rest or refresh himself.
as desired for the next session. During this time, and as quickly as possible, the blood sample was high-speed centrifuged, and the plasma drawn off with a pipette for transfer to a storage tube. The sample was labelled for storage with a single numerical coding, derived from a separate index recording the name, sex, number, and experimental group of the subject, and the point in the experiment at which the sample was taken (e.g. 1st sample). Storage conditions were maintained at -30°C.

Upon return of the subject to the experimental cubicle, the blacking preparation on the abdominal test sites was checked for density uniformity against the reference standard, and any evidence of wear was repaired.

(g) Mood Rating Scales Completed:

In view of indications of changes in subjective state or mood, during Acupuncture stimulation in the first experiment, it was of interest to monitor such factors under all the various treatments of the present study. This was especially true since S.D.T. analysis should indicate whether changes accompanied a real sensory sensitivity reduction, or were simply contributory factors in a reduced pain report pattern resulting from bias shifts alone.

A series of bipolar 10cm. line visual analogue scales as presented in Appendix 5 (ii) Page 475 were devised. Subjects were introduced to these scales in their initial training session, and full understanding of the response requirements was ascertained. Subjects were strictly instructed not to discuss their subjective feelings with anyone, and especially other subjects, until the study was completed.
In view of the hypothesised Endorphin mechanism of Acupuncture analgesia, the scales were directed at alterations in mood typical following the administration of opiates\(^{(244)}\). An open ended section for other spontaneous observations was also, of course, included.

These scales were to be administered three times in the course of each experimental session (including the 'Control' session), with slightly different attached instructions for completion on the first occasion compared to the second two occasions. This initial administration of the scales was intended to provide a mood baseline for comparison with later states following the various treatments. Subjects were therefore instructed to indicate their present mental state compared to their normal, or average, feelings (see set of instructions Appendix 5 (ii) Page 475). Clearly subjects' moods would be likely to alter from day to day, and session to session, quite spontaneously. Only within-session mood change scores would therefore be of any value.

(h) Acupuncture Needles Inserted and Electrical Stimulation Started:

Immediately the rating scales were completed, four Acupuncture needles were inserted in the 'Genuine' (Figs. 28, 29 Page 327) and 'Pseudo' (Figs. 26, 27 Page 326) 'point' locations marked out earlier. Neither the subject, nor the physicians inserting the needles, were aware of the significance of the differences between loci employed in the different sessions. The needles and their manner of insertion, (involving especially devised equipment for longer lengths), have been discussed extensively above, section k, Page 282.

* Physicians involved in the study were largely naive with regard to Acupuncture loci and their significance. They were trained merely in techniques for insertion of needles into sites pre-marked for them by the author.
and in chapter 3 (c) Page 65 describing the methods for Acupuncture Experiment No. 1.

Once inserted satisfactorily, the needles were electrically stimulated in the manner described, and fully calibrated, in the technical section (Calibration section B, Page 305). It will be noted that the procedures were identical to those of the first experiment, with the exception, for preferred safety considerations, of the use of a separate silver-silver-chloride surface electrode (Fig. 62 Page 285) as the anode for each needle electrode. This introduced minor modifications to the electrical stimulation parameters as discussed under calibration.

The surface electrodes were placed directly adjacent (Figs. 26, 27 Page 226) to the needles in the Pseudo-Acupuncture sessions, in order to reduce and localise current flow through neural tissue by providing a lowered resistance direct cutaneous pathway. In addition, as in the first experiment, the needles employed were shorter and inserted obliquely into the tissue to reduce penetration for the same reasons. Conversely, during Genuine Acupuncture stimulation, the surface anodes were placed on the opposite side of the limb to their respective needle cathodes (Figs. 28, 29 Page 327), in order to promote passage of current through deep tissue. Needles were full length and inserted perpendicularly to the cutaneous surface.

It may be argued that these differences reduce the comparability of stimulation under the two conditions. However, the major concern was only for comparable subjective suggestive potency, and control monitors for this are described later in this section. If, as has been suggested in earlier chapters, Acupuncture is to be viewed as a comprehensible neurophysiological mechanism, then it is perfectly reasonable to attempt to maximise its effectiveness in these terms, whilst minimising this component in a placebo treatment included entirely as a
Fig. 26: Needle Cathode and Adjacent Surface Electrode Anode for 'Pseudo-Acupuncture' Stimulation at the 'Neutral' Deltoid Location.

Fig. 27: Needle Cathodes and Adjacent Surface Electrode Anodes for 'Pseudo-Acupuncture' Stimulation at the 'Neutral' Thigh Location.
Fig. 28: Needle Cathode and Surface Electrode Anode Pair for Acupuncture Stimulation at the 'Ho-Ku' 'Point'.

Fig. 29: Needle Cathode and Surface Electrode Anode Pair for Acupuncture at the 'Tsu-San-Li' 'Point'.

control for psychological factors. As was seen in the first experiment, it is possible with electrical stimulation to produce sensations at 'Pseudo-Acupuncture' 'points' which are equally intense as those at 'Genuine' 'points'. Whatever the qualitative differences that may exist, they can probably be safely disregarded if subjects do not report any differences in subjective intensity, or expected analgesic potency, on appropriate rating scales (see below).

Once initiated, the amplitude of electrical stimulation was gradually increased over approximately five minutes, until the subject stabilised at his maximum, comfortably tolerable, level after full adaptation.

Rating Scales Completed for

- Intensity of Stimulation
- Prediction of Analgesic Potency

10cm-line visual analogue scales (iii)(a) and (b) Appendix S were next completed by the subject, or by the experimenter under his instruction.

Scale (a)* was designed to indicate the relative intensity of sensations resulting from Acupuncture plus electrical stimulation, for all stimulation sites taken together, under each experimental condition. The need for equivalence has already been discussed above. Ratings of sensations emanating from the needles alone, without electrical stimulation, were not obtained. This decision was taken since, although information derived from the first experiment indicated probable differences in needle sensation between 'Genuine' and 'Pseudo' 'points', the electrical stimulation was initiated almost immediately the needles were inserted; its intensity provided the overwhelming component of total sensation, and its duration far exceeded the pre-

* Not included in 'Control' session.
electrical stimulation phase. In view of this, the electrical stimu-
lation phase may safely be assumed to dominate the subjects' subject-
ive appraisal of the intensity of Acupuncture stimulation for the
session as a whole, and hence indicate its relative suggestive force.

The suggestive force of the stimulation was also directly moni-
tored by scale (b), where the subject was simply required to indicate
his beliefs or predictions as to its likely effects, if any, on his
sensitivity to the noxious thermal stimuli. In line with earlier
instructions, the scale was bipolar with a 'no change' centre point
to reduce the likelihood of automatic assumptions that analgesia was
the only available outcome. In the 'Control' session the subject was
alternatively asked to complete the same rating scale for predicted
effects, if any, resulting simply from the passage of time.

(i) Electrical Stimulation of Acupuncture Needles:

Electrical stimulation of all the Acupuncture needles now con-
tinued for a further approximately 35 minutes**, during which time
relaxing taped music was played to the subject. He was instructed to
adjust the intensity of electrical stimulation at all body sites as
necessary to maintain a constant level of sensation. Usually this
required occasional slight current increases, although in some cases,
fatigue from the paraesthesias and slight fasciculation prompted
reduction.

Subjects were asked in all sessions to monitor their subjective
feelings, mood etc, particularly any strong and/or unusual experiences

* This was clearly supported by the reports and ratings obtained from
subjects in the first experiment.

** The theoretical adequacy of this duration for the establishment of
'Acupuncture analgesia' is indicated in chapter 2 and supported by
the empirical findings of the first experiment.
during this period, for later report. They were also asked to assess their visual acuity at regular intervals by reading the response scale above them. This concern was based on several spontaneous reports of visual changes in the first experiment.

It should be noted that, although, of course, needles and electrical stimulation were not employed in the 'Control' session, an equal time period to that involved for procedures (h) and (i) was allowed to elapse, with subjects similarly lying quietly in a relaxing musical background.

(j): **Electrical Stimulation Reduced to Subliminal Level:**

Upon completion of the allotted stimulation period, current applied to all needles was reduced to subliminal levels, but the needles were not removed. The residual sensations emanating from the needle sites were sufficiently slight as to be considered negligible, and conditions were thus acceptably comparable in terms of distraction to those of the 'Control' session during completion of the scales below.

: Mood Rating Scales Completed:

Essentially the same series of subjective-state rating scales used earlier (section (g)) were again completed by the subject in all sessions. This time, however, the instructions (see Appendix E iv) asked the subject to compare his present mood state with the way he was feeling when he completed the form earlier. The wording of the scales was thus aimed at eliciting ratings of changes, if any, directly.

The procedure was conducted as quickly as possible without disturbing the subject, in order to reduce the standing time between reduction of Acupuncture stimulation and testing with the thermal stimuli.

* Again this contention is supported by the results of the first experiment.*
A 10ml sample of venous blood was again obtained as quickly as possible in a manner similar to that of the earlier sample (section (e)). This time, however, the subject's right arm was used in order to reduce discomfort. Processing and labelling of the sample were exactly as described earlier in section (f).

Capture: Injection (2ml) Saline or Naloxone (0.8mg)

Whilst the processing of the blood sample was underway, a Butterfly-21 cannula was introduced into a vein in the subject's left arm, close to the site used earlier, and then taped in place. Again the site did not correspond to any listed Acupuncture 'point'.

In the 'Genuine Acupuncture plus Naloxone' session, 0.8mg in 2ml of Naloxone Hydrochloride (Narcan*), an opiate antagonist, was injected gradually via the cannula. The reasons for this, in terms of the hypothesised Endorphin mechanism of Acupuncture, are fully discussed in chapter 6.

In the other Genuine Acupuncture session, identical in all other ways, 2ml of Sodium Chloride EP (0.9%) was injected in a similar manner as a control. The subject had been advised, when signing the form consenting to participate in the experiment, only that a drug "affecting the central nervous system" would be administered at some point during the experiment. The hypothesised effects were not elucidated, and indeed, in line with the clinical reports discussed in chapter 6, he was advised that discernible effects were most unlikely. Questionnaire controls (see section (n) below) were included to verify whether injections of saline or of Naloxone were subjectively indistinguishable to the subjects.

* Winthrop Laboratories, Surbiton-upon-Thames, Surrey KT6 4PH. This represents normal clinical dosage for reversal of opiate effects within approximately 2 minutes. It has also been shown as fully adequate for reversal of Acupuncture analgesia(305), and focal brain stimulation analgesia(5).
In addition, administration of the drug or saline was conducted fully double blind. Prior to the beginning of the entire experiment the labels were blanked out, and the identical ampoules of saline or Naloxone placed in coded envelopes. These were synchronised with the desired order of sessions in the balanced study design and allocated to subjects identified numerically, and by required sex. Equal numbers of male and female subjects were later randomly allocated to the two anonymous groups. Although it was practically impossible for the author to remain blind as to the nature of the different types of Acupuncture stimulation applied in the study, these controls at least ensured that investigation of the Endorphin hypothesis remained uncontaminated by the potential for inadvertent suggestive cues to the subject.

Saline (2ml) was also administered in the 'Pseudo-Acupuncture' and 'Control' sessions. The injection content was, of course, known to the author, although not to the physician giving the injection, or to the subject.

Acupuncture Needles Removed:

Whilst the injection was being administered, the remaining low level electrical stimulation to the Acupuncture needles was fully turned off, the needles quickly removed, and the area checked for injuries (none were noted).

Baseline Surface Temperatures (°C) Recorded:

New baseline abdominal, thoracic, and oral temperatures were also recorded, as previously, whilst the injection was given. This was also intended to indicate any possible effects (particularly oral) of the Acupuncture treatments upon body temperature (see chapter 6).
The complete thermal stimulus series was run again, exactly as described in section (d) above, this time, however, without a prior practice trial (see section (c)). This was based on the assumption that subjects would retain adequate recall of stimulus-response conditions from the first test, and there was no wish to add to the effects of practice upon sensory sensitivity which were already likely to accrue to the second test, on the basis of evidence discussed in chapter 5.

The series was intended to provide measures for comparison with the first (baseline) series to enable detection of any differential changes under the different conditions. The subject was advised that the stimulus series would be generally similar to the first, but it was not described as identical. This was intended to avoid inhibiting the subject from expressing an altered response pattern, if appropriate.

Two minute rests, with recording of body temperature, were included after blocks of stimuli as before.

- Injection (1ml)
- Saline or Naloxone (0.4mg)

During First Rest Period:

The Butterfly cannula remained in place during the first block of 36 thermal stimuli, and, during the two minute rest period before the start of the second block, a further 1ml infusion was given. This contained either 0.4mg Naloxone Hydrochloride in the 'Genuine Acupuncture plus Naloxone' sessions, or normal saline in the other conditions. The procedure was again double-blind as described above. This additional infusion was given both to compensate for the possibly

* This could not safely be assumed for the first test since several days elapsed between each session for the subject.
relatively short duration of action of Naloxone with respect to antag-

oneism of Acupuncture analgesia\(^{(305)}\), and in an attempt to equalise

levels in the brain over the 23 minute thermal stimulus series as a

whole\(^{(214)}\).

Upon completion of the infusion the cannula was withdrawn, and

an airstrip patch applied to the site.

\[ \text{Effect of Acupuncture/time} \]
\[ \text{Effect of Injection} \]
\[ \text{Mood} \]

Immediately upon conclusion of the full thermal stimulus series,

the rating sections appearing in Appendix 5 (v)(a)(b)(c)(d) Pages\(^{472}\)

and 479 were completed by the subject.

Scale (a) simply required the subject to rate any effects that

Acupuncture, or simply the passage of time in the 'Control' session,

had induced upon his pain sensations.

In section (b) the subject was asked to indicate his beliefs as

to whether the injection was 'active', and if so, to describe the

sensations experienced or other reasons for reaching this conclusion.

Next, scale (c) requested the subject to rate any effects he

believed the injection to have had upon his pain sensation. Normally,

of course, if the subject believed the injection to be inert, this

scale would be centre marked. However, it was just possible that a

subject might feel that any injection was sufficiently disturbing to

alter his sensitivity.

Finally, in section (d), the subject again completed a set of the

same comparative mood rating scales employed earlier in the session.

\[ \text{(o) : Post-Experimental Structured Interview:} \]

The last procedure after every session consisted of filling out

a post-session assessment questionnaire (Appendix 5 (vi) Pages 480 to 482)
The first section was directed towards eliciting the presence of any physical side effects resulting from the Acupuncture and/or injection procedures. Although an open question was included for spontaneously observed effects, the checklist generally corresponded to the more common physical side effects occurring with opiate administration. Subjects were asked to describe the nature of any effects reported, and to indicate their severity, and points of onset and offset in the session. In line with earlier instructions, they were also asked to assess realistically whether the effects were really very marked or unusual, or whether they might expect such results anyway from the other general physical conditions of the experimental situation.

The last portion of the questionnaire was a guided free-response section. Subjects were asked to describe, and comment upon, the efficiency of their mental processes, their relative arousal and mood, and their general responses or reactions to the various experimental procedures, throughout the session.

In the final session for each subject, the experimental strategy of the use of pseudo or placebo Acupuncture 'points' was explained carefully at this juncture. The subjects were asked outright whether they were aware of, or suspected, the deception involved. Although none reported such realisation, they were also asked if they found the needle sensations to differ in any important and suggestive way. Finally, they were told which session included the active injection, and asked whether this accorded with any experiences they had already reported, or if they now had any new observations to make.
Analysis* and Results

(1) Conventional Analysis:

(a) Rating Scale Responses (Descriptive Analysis):

Initial examination of the data collected proceeded through the stages outlined below:

(i) Subjects' rating category responses to the six stimulus levels were recorded from left to right in the rows on the left side of Table 15, in order as they were emitted, and then arranged as shown in the right hand columns of the Table.

(ii) The raw data were then transformed to a stimulus-response frequency matrix, a typical example of which appears as Table 16. Cell entries in Table 16 represent the frequency of emission of each response category to each stimulus level, in a complete stimulus series of 18 presentations at each level.

(iii) For descriptive information purposes only, the modal response category for each stimulus intensity level in the first (baseline) stimulus series, was extracted from each stimulus-response matrix, for each subject, under each experimental treatment condition. The total number of times which each response category appeared as the modal response to each of the six stimulus levels was then calculated. Bimodal responses were double counted. The results appear in Table 17, and are intended merely as a crude guide to the range of, and predominant, response categories associated with each stimulus level. This should assist in interpretation of the meaning, in sensory quality terms, of changes in responses to the different stimulus levels resulting from the experimental treatments, when they are presented in solely numerical terms in later sections.

* Computer programming by kind courtesy of Dr D Millar, Dept. of Psychology, University of Utrecht, Netherlands.
### TABLE 15: ACUPUNCTURE EXPERIMENT NO 2:
Rating Scale Response Record Form (Example)

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Sex          Date          Time
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**Table 15:** ACUPUNCTURE EXPERIMENT NO 2:

**Rating Scale Response Record Form (Example)**

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**Test Series**

**TRIAL 1**

Baseline Temps (°C)

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<td>VP</td>
<td>N</td>
<td>Wm</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>Wm</td>
</tr>
<tr>
<td>Wm</td>
<td>N</td>
<td>VP</td>
<td>VP</td>
<td>S</td>
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<td>S</td>
<td>S</td>
</tr>
<tr>
<td>N</td>
<td>P</td>
<td>VP</td>
<td>VII</td>
<td>VP</td>
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<td>N</td>
<td>N</td>
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</tr>
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</table>

**TRIAL 2**

Baseline Temps (°C)

<table>
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<th>Stimulus</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>Abd.</th>
<th>Thor.</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td>Response</td>
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<td>Wm</td>
<td>H</td>
<td>H</td>
<td>F</td>
<td>P</td>
<td>P</td>
<td>VP</td>
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<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>Wm</td>
<td>P</td>
</tr>
<tr>
<td>N</td>
<td>VII</td>
<td>H (2.9)</td>
<td>VP</td>
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<td>N</td>
<td>N</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>VP</td>
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<td>3.0</td>
<td>VP</td>
<td>N</td>
<td>Wm</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>Wm</td>
</tr>
<tr>
<td>S</td>
<td>N</td>
<td>VP</td>
<td>VII</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
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<td>S</td>
<td>S</td>
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</tr>
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<td>N</td>
<td>P</td>
<td>VP</td>
<td>VII</td>
<td>VP</td>
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<td>N</td>
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</tr>
</tbody>
</table>

**TRIAL 3**

Baseline Temps (°C)

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Sec Code Sheet</th>
<th>Stimulus</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>Abd.</th>
<th>Thor.</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response</td>
<td></td>
<td>Response</td>
<td>N</td>
<td>Wm</td>
<td>H</td>
<td>H</td>
<td>F</td>
<td>P</td>
<td>P</td>
<td>VP</td>
<td>P</td>
</tr>
<tr>
<td>H</td>
<td>VF</td>
<td>N</td>
<td>S</td>
<td>Wm</td>
<td>P</td>
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<td>P</td>
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<td>P</td>
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<td>P</td>
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<td>VII</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>VP</td>
<td>N</td>
<td>S</td>
<td>N</td>
<td>3.5</td>
<td>VII</td>
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<td>N</td>
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<td>P</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>N</td>
<td>H</td>
<td>VF</td>
<td>VP</td>
<td>N</td>
<td>Wm</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
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<td>Wm</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>Wm</td>
</tr>
<tr>
<td>S</td>
<td>N</td>
<td>Wm</td>
<td>VP</td>
<td>N</td>
<td>VP</td>
<td>P</td>
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<td>N</td>
<td>P</td>
<td>Wm</td>
</tr>
<tr>
<td>S</td>
<td>P</td>
<td>2.9</td>
<td>VP</td>
<td>N</td>
<td>VP</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>Wm</td>
</tr>
</tbody>
</table>

Stimulus duration = 3 secs

**Inter-stimulus interval = 7 secs

n at each level = 18

Test Site - Epigastrum
(12 blacked discs)

**Stimulus A B C D E F Post Trial Temp (°C)

<table>
<thead>
<tr>
<th>Levels</th>
<th>0 175 240 305 370 435 495</th>
<th>Abd.</th>
<th>Thor.</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>mcal. sec⁻¹/cm⁻²</td>
<td>36.0 34.4 37.3 37.3</td>
<td>36.0 34.4 37.3 37.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Responses = N = Nothing, S = Something, Wm = Warm, H = Hot, VH = Very Hot, VFP = Very Faint Pain, FP = Faint Pain, P = Painful, VP = Very Painful, W = Withdraw (latency in brackets)**
### TABLE 16: ACUPUNCTURE EXPERIMENT NO 2:
Response Processing Matrics (Example)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Group</th>
<th>Sex</th>
<th>Code No</th>
<th>Date</th>
<th>Time</th>
<th>Special Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>D LAKE</td>
<td>PAcF</td>
<td>F</td>
<td>4F</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**1st/2nd TEST SERIES**

#### Stimulus-Response Matrix

**Total Number of Responses in each cell**

<table>
<thead>
<tr>
<th>Responses</th>
<th>N</th>
<th>S</th>
<th>Wm</th>
<th>H</th>
<th>VH</th>
<th>VFP</th>
<th>FP</th>
<th>P</th>
<th>VP</th>
<th>W3</th>
<th>W2</th>
<th>W1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>level*</td>
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<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>F</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>12</td>
<td>5</td>
<td>-</td>
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<td>-</td>
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</tr>
<tr>
<td>E</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D</td>
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<td>1</td>
<td>5</td>
<td>2</td>
<td>1</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>C</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>1</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
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<td>6</td>
<td>2</td>
<td>1</td>
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<tr>
<td>A</td>
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<td>-</td>
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<td>-</td>
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</tr>
</tbody>
</table>

**NB Mode boxed in red**

#### Cumulated Conditional Probability of Responses to the Right of a Particular Category

<table>
<thead>
<tr>
<th>Responses</th>
<th>N</th>
<th>S</th>
<th>Wm</th>
<th>H</th>
<th>VH</th>
<th>VFP</th>
<th>FP</th>
<th>P</th>
<th>VP</th>
<th>W3</th>
<th>W2</th>
<th>W1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus</td>
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<td></td>
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</tr>
<tr>
<td>level*</td>
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<td></td>
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</tr>
<tr>
<td>F</td>
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<td>-</td>
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</tr>
<tr>
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<td>0.92</td>
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<td>0.54</td>
<td>0.49</td>
<td>0.49</td>
<td>0.27</td>
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<td>-</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>0.91</td>
<td>0.75</td>
<td>0.31</td>
<td>0.15</td>
<td>-</td>
<td>0.10</td>
<td>0.35</td>
<td>0.05</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>0.49</td>
<td>0.16</td>
<td>0.05</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>A</td>
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<td>0.05</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Stimulus levels* 0 175 240 305 370 435

**Stimulus duration** = 3 secs
**Inter-stimulus interval** = 7 secs
**mcal. sec^-1/cm^2**

**Response categories**

- N = Nothing, S = Something, Wm = Warm, H = Hot, VH = Very Hot, VFP = Very Faint Pain, FP = Faint Pain, P = Painful, VP = Very Painful, W3 = Withdraw 2-3 secs, W2 = Withdraw 1-2 secs, W1 = Withdraw 0-1 secs.

**Group/Session coding**

- NAcF = No Acupuncture Session First
- PACF = Pseudo coding
- GAcF = Genuine coding
- GAc + NF = " + Naloxone "

Subject M = Male coding F = Female
TABLE 17: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS.
Baseline Stimulus Series (1) Responses (all experimental conditions (4) included):
Range of Modal Response Categories to each Stimulus Intensity Level (A - F):
(Total frequency of occurrence, sum of all subjects (n = 16))

<table>
<thead>
<tr>
<th>Stimulus Level*</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
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<tbody>
<tr>
<td><strong>Modal Responses</strong></td>
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<td></td>
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</tr>
<tr>
<td>W</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>VP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5 30</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>FP</td>
<td></td>
<td></td>
<td>8</td>
<td>20</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>VFP</td>
<td></td>
<td></td>
<td>14</td>
<td>21</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>VH</td>
<td></td>
<td>2</td>
<td>9</td>
<td>9 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>3</td>
<td>20</td>
<td>16</td>
<td>9 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wm</td>
<td>33</td>
<td>39</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>13</td>
<td>26</td>
<td>6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>55</td>
<td>14</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A < B

Key: N = Nothing, S = Something, Wm = Warm, H = Hot, VH = Very Hot, VFP = Very Faint Pain, FP = Faint Pain, P = Painful, VP = Very Painful, W = Withdraw.
It will be noted that there is some evidence of under-setting of the stimulus intensity levels. The necessity for this was fully discussed above, and, as will be seen later in this results section, in three experimental treatment conditions out of the four, there is a clear increase in the intensity of ratings associated with the stimuli during the second (post-treatment) stimulus series.

(iv) Cell entry values from Table 16 where next summed for the complete subject group (n = 16) to produce eight separate group stimulus-response matrices, corresponding to the first and second thermal stimulus series under each of the four experimental conditions. Obviously this procedure to produce an 'artificial subject' does not supply properly representative population results to which statistical procedures may usefully be applied. However, it was considered useful to obtain a rapid impression of the data for such factors as the adequacy of matching of the experimental conditions, strong differences between the experimental treatment effects, and sex related factors.

(v) The response categories from 'Nothing - W1' were then substituted with numbers 1 - 12 as shown below:

<table>
<thead>
<tr>
<th>Response</th>
<th>N</th>
<th>S</th>
<th>Wm</th>
<th>H</th>
<th>VH</th>
<th>VFP</th>
<th>FP</th>
<th>P</th>
<th>VP</th>
<th>W3</th>
<th>W2</th>
<th>W1</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

Ratio scaling is naturally not implied by this substitution. The response category Withdraw 0 - 1 sec. (W1) was later deleted from the scale since it was not employed by any subject, at any point in the experiment.

(vi) The group median response value for each stimulus
intensity, in each of the two stimulus series, of each of the four experimental conditions was then computed. These values appear in Table 18 (a) Page 342 together with the calculated change in values occurring between the first stimulus series (baselines) and the second stimulus series (post-treatment). They are also plotted in Fig. 30 Page 343.

As a guide to the meaning of these values in terms of sensory quality, Table 18 (b) Page 342 presents the group mean (all experimental treatment conditions) median response ratings to each stimulus level (A - F), in the first stimulus series (baselines), together with their associated descriptive categories. Table 18 (c) Page 342 provides the categories for the post-treatment stimulus series in each experimental treatment condition.

The figures in Table 18 (a) Page 342 generally increase confidence in the vital matching of the three Acupuncture experimental treatment conditions during the baseline stimulus series. The 'Control' condition, however, exhibits very slightly lower baselines than the other conditions. It would appear that simply the knowledge* that Acupuncture needles were not to be inserted later was sufficient to lower baselines. Certainly, subjects generally experienced the Acupuncture procedures as rather unpleasant and their absence might be expected to reduce anticipative anxiety and stress. This certainly accords with the

* Ethical requirements imposed on the experiment necessitated that subjects be advised on the consent form as to exactly how many needles would be inserted, where they would be inserted, and on how many occasions in order that they might assess the discomfort and risk to which they were consenting. Since the four subjects passing through the 'Control' condition last would be able to deduce that no needles were to be inserted later anyway, it seemed better to equalize subjects by advising them all at the start of the 'Control' condition. It was also of interest to know whether the anxiety associated with Acupuncture was artificially elevating rating response intensities.
# ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS (Descriptive)

## (a) Group (n = 16) Median Response Ratings to each Stimulus Level (A - F) for each Stimulus Series, of each Experimental Condition.

<table>
<thead>
<tr>
<th>Stimulus levels*</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>( \xi )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condition CON</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.22</td>
<td>2.25</td>
<td>3.17</td>
<td>4.29</td>
<td>6.64</td>
<td>7.88</td>
<td></td>
</tr>
<tr>
<td>Series 2</td>
<td>1.22</td>
<td>2.20</td>
<td>3.17</td>
<td>5.04</td>
<td>7.28</td>
<td>8.55</td>
<td></td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-</td>
<td>-0.05</td>
<td>-</td>
<td>0.75</td>
<td>0.64</td>
<td>0.67</td>
<td>( \xi = 2.01 )</td>
</tr>
<tr>
<td><strong>Condition PAC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1</td>
<td>1.24</td>
<td>2.30</td>
<td>3.21</td>
<td>4.69</td>
<td>6.66</td>
<td>8.11</td>
<td></td>
</tr>
<tr>
<td>Series 2</td>
<td>1.17</td>
<td>2.23</td>
<td>3.29</td>
<td>5.04</td>
<td>6.96</td>
<td>8.44</td>
<td></td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.07</td>
<td>-0.07</td>
<td>0.08</td>
<td>0.53</td>
<td>0.30</td>
<td>0.33</td>
<td>( \xi = 1.10 )</td>
</tr>
<tr>
<td><strong>Condition GAC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1</td>
<td>1.27</td>
<td>2.41</td>
<td>3.09</td>
<td>4.50</td>
<td>6.72</td>
<td>8.19</td>
<td></td>
</tr>
<tr>
<td>Series 2</td>
<td>1.14</td>
<td>2.03</td>
<td>2.93</td>
<td>4.31</td>
<td>6.46</td>
<td>7.76</td>
<td></td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.13</td>
<td>-0.38</td>
<td>-0.16</td>
<td>-0.19</td>
<td>-0.26</td>
<td>-0.43</td>
<td>( \xi = -1.55 )</td>
</tr>
<tr>
<td><strong>Condition GAC + N</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1</td>
<td>1.27</td>
<td>2.42</td>
<td>3.25</td>
<td>4.97</td>
<td>6.61</td>
<td>8.09</td>
<td></td>
</tr>
<tr>
<td>Series 2</td>
<td>1.18</td>
<td>2.18</td>
<td>3.23</td>
<td>5.07</td>
<td>7.22</td>
<td>8.40</td>
<td></td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.09</td>
<td>-0.24</td>
<td>-0.02</td>
<td>0.10</td>
<td>0.61</td>
<td>0.31</td>
<td>( \xi = 0.67 )</td>
</tr>
</tbody>
</table>

## (b) Group (n = 16) Median Response Ratings to each Stimulus Level (A-F) in First Stimulus Series (Baseline), with Associated Sensory Quality Descriptive Categories.

<table>
<thead>
<tr>
<th>Stimulus levels*</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series : (Baseline)</td>
<td>1.25</td>
<td>2.34</td>
<td>3.18</td>
<td>4.61</td>
<td>6.66</td>
<td>8.07</td>
</tr>
<tr>
<td><strong>Descriptive Categories</strong></td>
<td>N-S</td>
<td>S-Wm</td>
<td>Wm-H</td>
<td>H-VH</td>
<td>VFP-FP</td>
<td>P-VP</td>
</tr>
</tbody>
</table>

## (c) Second Stimulus Series (Post Treatment): Descriptive Categories in each Experimental Treatment Condition.

<table>
<thead>
<tr>
<th>Descriptive Categories</th>
<th>Condition CON</th>
<th>PAC</th>
<th>GAC</th>
<th>GAC + N</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-S</td>
<td>N-S</td>
<td>N-S</td>
<td>N-S</td>
<td>N-S</td>
</tr>
<tr>
<td>S-Wm</td>
<td>S-Wm</td>
<td>S-Wm</td>
<td>S-Wm</td>
<td>S-Wm</td>
</tr>
<tr>
<td>Wm-H</td>
<td>Wm-H</td>
<td>Wm-H</td>
<td>Wm-H</td>
<td>Wm-H</td>
</tr>
<tr>
<td>H-VH</td>
<td>H-VH</td>
<td>H-VH</td>
<td>H-VH</td>
<td>H-VH</td>
</tr>
<tr>
<td>VFP-FP</td>
<td>VFP-FP</td>
<td>VFP-FP</td>
<td>VFP-FP</td>
<td>VFP-FP</td>
</tr>
<tr>
<td>P-VP</td>
<td>P-VP</td>
<td>P-VP</td>
<td>P-VP</td>
<td>P-VP</td>
</tr>
</tbody>
</table>

*A*B

FIG. 30: ACUPUNCTURE EXPERIMENT NO. 2:
Group (n = 16) Median Response Ratings to Each Stimulus Level (A-F), for Each Stimulus Series, of Each Experimental Condition.

Key: N. = Nothing, S. = Something, Wm. = Warm, H. = Hot, V.H. = Very Hot, V. F. P. = Very Faint Pain, F. P. = Faint Pain, P. = Painful, V. P. = Very Painful. S1, S2 = Stimulus Series 1 or 2.
subjective reports of subjects as discussed later in this results section. The difference must result purely from these psychological anticipative factors since 'points' were located and palpated at the beginning of the 'Control' sessions, exactly as during needle sessions, on account of the remote possibility that these procedures might have effects upon sensitivity (see Methods section (3)(c) above).

It must be said that the above considerations may slightly weaken the 'Control' condition as a comparative base for the other three conditions. As later measures use shift in pain responses as an indicator of treatment effect magnitude, it is possible that lower baselines may artificially aggrandise elevation of 'Control' condition responses during the second stimulus series. It is much more likely, however, that the anxiety and stress effects would affect responses during both stimulus series equally, and thus leave shift measures unaffected.

Even adopting the exceedingly unlikely assumption that these psychological factors served only to lower baselines in the 'Control' condition, without lowering of values at the second stimulus series, a correction might be made to the data as follows. If baseline values in the 'Control' condition are raised to the mean baseline values of the other three conditions and then subtracted from the second stimulus series 'Control' condition values, similarly to Table 18 (a) Page 342, the figures below are obtained.

<table>
<thead>
<tr>
<th>Stimulus Level</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change (2 - 1)</td>
<td>-0.04</td>
<td>-0.18</td>
<td>-0.01</td>
<td>0.32</td>
<td>0.62</td>
<td>0.42</td>
<td>≤1.13</td>
</tr>
</tbody>
</table>

It can be seen that, not only does the 'Control' condition still
produce the largest elevation of responses overall, but much more importantly, the difference is mainly evident for the two most intense (or pain-inducing) stimulus levels (E,F). It seems most unlikely that any of the differences between the 'Control' condition and the other treatments which are presented later in this results section, may be explained away as an artifact produced by the very slightly lower 'Control' condition baselines.

Comment: The above preliminary examination of the data* indicated the likely usefulness of an extensive statistical analysis, since almost all of the principal hypotheses of the experiment seemed clearly supported. Only the 'Genuine Acupuncture' condition shows an overall decrement in intensity reported after treatment, whilst the 'Control' condition shows the largest increase, followed by 'Pseudo-Acupuncture' (in line with its predicted suggestive effect). Administration of Naloxone also appears to counteract the analgesic, and possibly even anaesthetic, effects of Acupuncture, although not entirely.

It should be noted, however, that the effects are very small, and in no case is there even a shift of one complete category.

(b) Rating Scale Responses - Sex Differences (Descriptive Analysis):

The data were examined for sex related differences in response patterns as outlined below:

(i) Stimulus-Response matrix cell values (see (a)(ii) above) were summed for all males, to produce eight separate group stimulus-response matrices, corresponding to the first and second stimulus test series under each of the four experimental conditions. Females were similarly treated.

* Excluding sex differences.
(ii) The procedures outlined above ((a) (v) ar- (vi)) were then employed to compute male and female group median response values for each stimulus intensity, in each stimulus series, of each condition. These values are presented in Table 19 Page 347, and are plotted in Fig. 31 Page 348.

It would appear from Table 19 Page 347 that females may report slightly more intense sensations to all stimulus levels except zero. This is in line with their lower pain thresholds and pain tolerances observed in the first experiment. They also appear to display less increment in median response ratings from the first to the second stimulus series, in the 'Control' and 'Pseudo-Acupuncture' sessions. This may simply be a limiting effect of the higher initial baseline, analogous to many measures subject to the law of initial values (496).

A high initial value may also account for their tendency apparently to exhibit greater analgesic changes in the 'Genuine Acupuncture' session, although Naloxone may not reverse this analgesia as completely as in the case of the male group.

In order to obtain an impression as to where in the sensory spectrum these apparent sex differences might predominate, grand mean values at each stimulus level, were derived for males and for females, from the median response ratings of both stimulus series of all sessions combined. These values appear at the bottom of Table 19 Page 347 and are plotted in Fig. 32 Page 349, from which it would seem that men and women really differ only as to how they define 'Hot' or 'Very Hot' categories. This probably means little, since use of the categories around the middle of the response scale appears more variable than for extreme responses, in the case of both males and females.
## Table 19: Acupuncture Experiment No 2: Conventional Analysis (Descriptive):
Male (n = 8) versus Female (n = 8) Group Median Response Ratings to each Stimulus Level (A-F),
for each Stimulus Series, of each Experimental Treatment Condition.

<table>
<thead>
<tr>
<th>Stimulus Levels*</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>Σ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Sex Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition CON.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.32</td>
<td>1.14</td>
<td>2.22</td>
<td>2.29</td>
<td>3.04</td>
<td>3.29</td>
<td>3.88</td>
</tr>
<tr>
<td>Series 2</td>
<td>1.27</td>
<td>1.19</td>
<td>1.99</td>
<td>2.51</td>
<td>2.22</td>
<td>3.46</td>
<td>4.75</td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.05</td>
<td>0.05</td>
<td>-0.23</td>
<td>0.25</td>
<td>-0.12</td>
<td>0.15</td>
<td>0.87</td>
</tr>
<tr>
<td>Condition PAC.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.35</td>
<td>1.15</td>
<td>2.21</td>
<td>2.42</td>
<td>3.16</td>
<td>3.27</td>
<td>4.07</td>
</tr>
<tr>
<td>Series 2</td>
<td>1.24</td>
<td>1.11</td>
<td>1.05</td>
<td>2.43</td>
<td>3.08</td>
<td>3.52</td>
<td>4.37</td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.11</td>
<td>-0.04</td>
<td>-0.16</td>
<td>0.01</td>
<td>-0.08</td>
<td>0.25</td>
<td>0.30</td>
</tr>
<tr>
<td>Condition GAc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.45</td>
<td>1.14</td>
<td>2.50</td>
<td>2.42</td>
<td>2.93</td>
<td>3.26</td>
<td>3.90</td>
</tr>
<tr>
<td>Series 2</td>
<td>1.23</td>
<td>1.07</td>
<td>2.02</td>
<td>2.04</td>
<td>2.82</td>
<td>2.94</td>
<td>3.71</td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.22</td>
<td>-0.07</td>
<td>-0.37</td>
<td>-0.38</td>
<td>-0.11</td>
<td>-0.22</td>
<td>-0.19</td>
</tr>
<tr>
<td>Condition GAc. + N.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.34</td>
<td>1.21</td>
<td>2.30</td>
<td>2.55</td>
<td>3.04</td>
<td>3.43</td>
<td>3.95</td>
</tr>
<tr>
<td>Series 2</td>
<td>1.20</td>
<td>1.09</td>
<td>2.12</td>
<td>2.26</td>
<td>2.82</td>
<td>2.55</td>
<td>4.24</td>
</tr>
<tr>
<td>Change (2 - 1)</td>
<td>-0.04</td>
<td>-0.12</td>
<td>-0.18</td>
<td>-0.29</td>
<td>-0.06</td>
<td>0.12</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean of ALL conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1 (Baseline)</td>
<td>1.36</td>
<td>1.16</td>
<td>2.28</td>
<td>2.42</td>
<td>3.04</td>
<td>3.31</td>
<td>3.95</td>
</tr>
<tr>
<td>Series 2</td>
<td>1.26</td>
<td>1.11</td>
<td>2.05</td>
<td>2.32</td>
<td>2.95</td>
<td>3.39</td>
<td>4.27</td>
</tr>
<tr>
<td>Grand Mean</td>
<td>1.31</td>
<td>1.13</td>
<td>2.16</td>
<td>2.37</td>
<td>2.99</td>
<td>3.35</td>
<td>4.11</td>
</tr>
</tbody>
</table>

* A&B Key: CON. = 'Control', PAC. = 'Pseudo-Acupuncture', GAc. = 'Genuine Acupuncture',
GAc. + N. = 'Genuine Acupuncture + Naloxone'.
FIG. 31: ACUPUNCTURE EXPERIMENT NO. 2:
Male (n = 8) versus Female (n = 8) Group Median Response Ratings to Each Stimulus Level (A–F). For Each Stimulus Series of Each Experimental Condition.

Key: 1, 2 = Stimulus Series 1 or 2,
M = Nothing, S = Something, Wm = Warm, H = Hot, VH = Very Hot, VFP = Very Faint Pain, FP = Faint Pain, P = Painful, VP = Very Painful

Control  Pseudo-Acupuncture  Genuine Acupuncture  Genuine Acupuncture + Naloxone
FIG. 32: ACUPUNCTURE EXPERIMENT NO. 2:
Male (n = 8) Versus Female (n = 8) Group Median Response Ratings to Each Stimulus Level (A-F).
(Grand Mean Values for All Sessions, All Stimulus Series, Combined)

Key: N. = Nothing, S. = Something, Wm. = Warm, H. = Hot,
V. H. = Very Hot, V. F. P. = Very Faint Pain, F. P. = Faint Pain,
P. = Painful, V. P. = Very Painful.
(c) Rating Scale Responses (Statistical Analysis):

Given the complexity, and number of possibly interacting variables, within the experimental data, clearly the statistical method of choice in terms of sensitivity and comprehensiveness, was multi-factorial ANOVA. A split-plot factorial - pr. qu design analy-is of variance (233) was therefore computed in the following stages.

(i) The data base was derived from the stimulus-response frequency matrices (see Table 16 Page 38) of each subject as outlined in section (a)(ii) above. This time, however, the cell values were not summed for all subjects as in the preliminary examination of the data (see (a)(iv)). since obviously this does not provide properly representative data to which statistical procedures may usefully be applied*.

(ii) The rating scale categories of the stimulus-response matrix were converted to a numerical series as before (see section (a)(v) above). This, of course, does not imply ratio scaling.

(iii) The median response value for each of the six stimulus intensities was computed for each stimulus series, in each experimental session, cr. an individual subject basis.

(iv) For each individual subject, the median response value for each stimulus intensity in the first stimulus series of each session, was subtracted from the corresponding value for the second stimulus series in the same session. This change, or shift, in median pain intensity report during each session, was to serve as the basic dependent variable, or measure of the effect of the different treatments administered, and was employed for subsequent analysis.

* The focus of interest is clearly on populations rather than individual subjects (artificial or otherwise).
The split-plot factorial - pr. qu design ANOVA (233), with subjects nested within sex and within balanced order group, was next applied with the following organisation of factors.

**Factor A = Balanced Order Treatment Group (1 - 4)**
1. 'Control' Session First.
2. 'Pseudo-Acupuncture' Session First.
3. 'Genuine' Session First.
4. 'Genuine' Session First + Naloxone First.

**Factor B = Experimental Treatment Condition (1 - 4)**
1. 'Control' Condition.
2. 'Pseudo-Acupuncture' Condition.
3. 'Genuine' Condition.
4. 'Genuine' Condition + Naloxone Condition.

**Factor C = Sex (1 - 2)**
1. Male.
2. Female.

**Factor D = Stimulus Intensity Level (1 - 6)**
1. Stimulus F (highest - 435 mcal/sec\(^{-1}\)/cm\(^{-2}\))
2. " E
3. " D
4. " C
5. " B
6. " A (lowest - 0 mcal/sec\(^{-1}\)/cm\(^{-2}\))

**Factor S = Subject in Cell (1 - 2)**
1. Odd number subjects.
2. Even "

The file organisation will not be further described.

(vi) The multifactorial ANOVA output summary appears as Table 20 Page 352, from which it can be seen that there are four significant variance components B, D, CD, and BD. These may be interpreted as follows.

**B** - There are highly significant differences between the four experimental treatment conditions, disregarding, for the present, the relative proportions of this effect contributed at the different stimulus intensity levels (see BD below).
### TABLE 20: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS

Analysis of Variance (type S.P.F. - 42.46(233)),
Output Summary Table for Within-Session SHIFT in Median Response Ratings, All Experimental Treatment Conditions.

**Key:**
- A is Treatment Order Group.
- B is Experimental Treatment Condition.
- C is Sex of Subject.
- D is Stimulus Intensity Level.

**Note:** A, B, C, D, are fixed effects, subjects random.

The error term is the next entry with no associated F.

<table>
<thead>
<tr>
<th>No.</th>
<th>Source</th>
<th>S.S.</th>
<th>df.</th>
<th>M.S.</th>
<th>F.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Between Subjects</td>
<td>21.724</td>
<td>15</td>
<td>1.448</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>4.719</td>
<td>3</td>
<td>1.573</td>
<td>1.158</td>
<td>N.S.</td>
</tr>
<tr>
<td>3</td>
<td>C</td>
<td>1.439</td>
<td>1</td>
<td>1.439</td>
<td>1.059</td>
<td>N.S.</td>
</tr>
<tr>
<td>4</td>
<td>AC</td>
<td>4.695</td>
<td>3</td>
<td>1.565</td>
<td>1.152</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Subjects within Groups</td>
<td>10.870</td>
<td>8</td>
<td>1.359</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Within Subjects</td>
<td>178.478</td>
<td>368</td>
<td>0.485</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>B</td>
<td>21.517</td>
<td>3</td>
<td>7.172</td>
<td>7.551</td>
<td>0.001</td>
</tr>
<tr>
<td>8</td>
<td>AB</td>
<td>6.550</td>
<td>9</td>
<td>0.728</td>
<td>0.766</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>BC</td>
<td>1.309</td>
<td>3</td>
<td>0.436</td>
<td>0.459</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>ABC</td>
<td>9.236</td>
<td>9</td>
<td>1.026</td>
<td>1.080</td>
<td>N.S.</td>
</tr>
<tr>
<td>11</td>
<td>BxSubjects within Groups</td>
<td>22.796</td>
<td>24</td>
<td>0.950</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>D</td>
<td>13.204</td>
<td>5</td>
<td>2.641</td>
<td>9.129</td>
<td>0.000</td>
</tr>
<tr>
<td>13</td>
<td>AD</td>
<td>5.274</td>
<td>15</td>
<td>0.352</td>
<td>1.215</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>CD</td>
<td>6.142</td>
<td>5</td>
<td>1.228</td>
<td>4.247</td>
<td>0.003</td>
</tr>
<tr>
<td>15</td>
<td>ACD</td>
<td>3.833</td>
<td>15</td>
<td>0.256</td>
<td>0.883</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>DxSubjects within Groups</td>
<td>11.571</td>
<td>40</td>
<td>0.289</td>
<td></td>
<td>N.S.</td>
</tr>
<tr>
<td>17</td>
<td>BD</td>
<td>11.278</td>
<td>15</td>
<td>0.752</td>
<td>2.646</td>
<td>0.001</td>
</tr>
<tr>
<td>18</td>
<td>ABD</td>
<td>13.245</td>
<td>45</td>
<td>0.294</td>
<td>1.036</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>BCD</td>
<td>2.426</td>
<td>15</td>
<td>0.162</td>
<td>0.569</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>ABCD</td>
<td>15.994</td>
<td>45</td>
<td>0.355</td>
<td>1.251</td>
<td>N.S.</td>
</tr>
<tr>
<td>21</td>
<td>BDxSubjects within Groups</td>
<td>34.103</td>
<td>120</td>
<td>0.284</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Total</td>
<td>200.202</td>
<td>383</td>
<td>0.523</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
D - The different stimulus intensity levels are significantly different in terms of the shifts in median response ratings occurring during sessions, disregarding, for the present, the relative proportions of this effect contributed by the different experimental treatment conditions (see BD below). This is not of particular interest or relevance.

CD - Males react differently to females in response to the different stimulus intensities, although there is no sex difference (C) overall. This is not of particular interest since the male/female difference was not affected by experimental treatment conditions (BC) i.e. there was no sex difference in the effectiveness of Acupuncture, Naloxone, suggestion, or no treatment.

BD - The difference between experimental treatment conditions was not the same at all stimulus intensity levels.

Clearly the most important components are B and BD, particularly the latter since the main effect can only be meaningfully interpreted in terms of the interaction.

Before proceeding to further stages of analysis, some of the more relevant, non-significant, results available from Table 20 on page 352 are summarised below. Thus for shifts in median response ratings:

- there are no treatment order effects overall (A)
- there are no sex differences overall (C)
- there are no differences between experimental treatment conditions due to their order of presentation (AB)
- there are no sex differences in the responses to different experimental treatment conditions (BC).
It should also be noted that:

\[ F = B \times \text{Subjects within Groups} = 3.35 \quad \text{df} = 24,120 \]

\[ BD \times \text{Subjects within Groups} = 2P = 0.000 \ 013 \ 00 \]

This is important in terms of some further analysis \( t \) - values below which use the pooled value as an error term. As a consequence the significance of these tests must be evaluated differently from a normal \( t \) - value.

(vii) Further analysis of the data was directed at illuminating the source components of the significant B factor (experimental treatment condition) above.

Group mean shifts in median response ratings from the first stimulus series compared to the second stimulus series were computed for each experimental treatment condition, and appear in Table 21 (a) Page 355, and as histograms in Fig. 33 Page 356. Each cell mean is derived from 96 observations, since all subjects (16), and all stimulus levels (6), were combined.

It can be observed that for both the 'Control' and 'Pseudo-Acupuncture' conditions subjects reported more intense sensory experiences overall, to the fixed stimuli, during the second stimulus series. This tendency towards use of higher rating scale categories was, however, rather small, the shift being well below one full category step. The effect was attenuated slightly during the 'Pseudo-Acupuncture' sessions.

Conversely, 'Genuine Acupuncture' produced a general reduction in intensity of reported sensory experiences, whilst the addition of Naloxone reversed this effect, almost returning the response pattern to that of 'Pseudo-Acupuncture'. Again the effects are small.
TABLE 21: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS:

(a) Mean (all subjects (16), all stimulus intensities (6))
SHIFT in Median Response Ratings, During Different
Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>t - Value</td>
<td>0.941</td>
<td>4.482</td>
<td>1.355</td>
</tr>
<tr>
<td>2P.</td>
<td>N.S.</td>
<td>0.000</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

(b) t - Test for Probability of Observed Differences
Between Each Pair of Experimental Treatment
Conditions (df = 96, error S.D. = 0.141).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>t - Value</td>
<td>3.542</td>
<td>0.414</td>
<td>-3.127</td>
</tr>
<tr>
<td>2P.</td>
<td>0.000 615</td>
<td>N.S.</td>
<td>0.002 34</td>
</tr>
</tbody>
</table>
FIG. 33: ACUPUNCTURE EXPERIMENT NO. 2:

CONVENTIONAL ANALYSIS:
Mean (all subjects (16), all stimulus intensities (6)) SHIFT in
Median Response Ratings, During Different Experimental
Treatment Conditions.

(t-test for probability of observed differences between
conditions).
For what it is worth, it can also be noted that the attenuation of responses as a result of the suggestion component ('Control' versus 'Pseudo-Acupuncture') is only approximately 21% of the total reduction induced by Acupuncture ('Control' versus 'Genuine Acupuncture'). One may further observe that Naloxone appears to antagonise approximately 88% of the additional effect of 'Genuine Acupuncture' compared to that induced by suggestion ('Pseudo-Acupuncture' versus 'Genuine Acupuncture').

(viii) Next t-tests were applied for the significance of the observed differences in mean median shift when each of the six possible pairs of experimental treatment conditions were compared. The resultant t-values and associated significant two-tailed probabilities* appear in Table 21 (b) Page 355, and the latter are also included visually in Fig. 33 Page 356.

It is clearly evident that, whilst the differences between the 'Control', 'Pseudo-Acupuncture', and 'Genuine Acupuncture plus Naloxone' conditions are not significant, 'Genuine Acupuncture' produces highly significant shifts in rating responses in the opposite direction compared to all these treatments.

(ix) Analysis next proceeded to further investigation of the BD interaction (Experimental Treatment Condition X Stimulus Intensity Level) reported above (section (vi)). Simple main effects analysis of variance procedures were applied to mean (n = 16) shifts in median response ratings at EACH stimulus intensity level (A-F), during each experimental treatment condition, and the output summary appears as Table 22 Page 358. There are highly significant differences between the effects of the four experimental

* Not corrected for multiplicity of analyses. It is preferred simply to test at a more stringent level. This applies to all similar t-tests in later sections.
TABLE 22: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS

Analysis of Variance, Output Summary Table for Within-Session Mean (n = 16) SHIFT in Median Response Rating at EACH Stimulus Intensity Level (A - F), All Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Stimulus Level</th>
<th>S.S.</th>
<th>df</th>
<th>M.S.</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>12.876</td>
<td>3</td>
<td>4.292</td>
<td>10.862</td>
<td>0.000 001 77</td>
</tr>
<tr>
<td>E</td>
<td>9.918</td>
<td>3</td>
<td>3.306</td>
<td>8.367</td>
<td>0.000 036 3</td>
</tr>
<tr>
<td>D</td>
<td>7.689</td>
<td>3</td>
<td>2.563</td>
<td>6.486</td>
<td>0.000 378</td>
</tr>
<tr>
<td>C</td>
<td>0.602</td>
<td>3</td>
<td>0.201</td>
<td>0.503</td>
<td>N.S.</td>
</tr>
<tr>
<td>B</td>
<td>1.495</td>
<td>3</td>
<td>0.498</td>
<td>1.261</td>
<td>N.S.</td>
</tr>
<tr>
<td>A</td>
<td>0.215</td>
<td>3</td>
<td>0.072</td>
<td>0.181</td>
<td>N.S.</td>
</tr>
<tr>
<td>Total</td>
<td>32.795</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Error Term</td>
<td>56.899</td>
<td>144</td>
<td>0.395</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Note: A < B
treatment condition at the three most intense stimulus intensity levels (D, E, F), the effect being most marked at the most intense level (F). These differences appear minimal at the three lowest stimulus intensities.

(x) Further examination of the sources of these significant effects continued with pairwise comparison of each possible combination of experimental treatment conditions by t-test.

The computed group mean shifts in median response rating at each stimulus intensity level are presented for each experimental treatment condition in Table 23 (a) Page 360. They are also graphed in Fig.34 Page 361. The three most intense stimulus levels have been separated from the lower three, both for purposes of visual clarity, and since there is a definite division into the two groups in terms of all shift magnitudes. The general pattern of positive shifts in intensity of rating responses during the 'Control' condition, with slight attenuation during 'Pseudo-Acupuncture', complete reversal during 'Genuine Acupuncture', and partial antagonism of the latter effect in the 'Genuine Acupuncture plus Naloxone' condition, is quite evident.

The mean shifts are also graphed against the six stimulus intensity levels in Fig.35 Page 362 and several interesting features are evident.

First, even at the lowest (non pain-inducing) stimulus intensities (A - C) there are marginal reductions in response ratings during all needle sessions compared to the 'Control' condition. At level B, however, there is a noticeable distinction between the curve shape common to both of the 'Genuine Acupuncture' treatments, and the 'Pseudo-Acupuncture' and
TABLE 23: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS:

(a) Mean (n = 16 subjects) SHIFT in Median Response Rating at EACH Stimulus Intensity Level (A – F), During Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus F</td>
<td>0.608</td>
<td>0.304</td>
<td>-0.594</td>
<td>0.282</td>
</tr>
<tr>
<td>level* E</td>
<td>0.685</td>
<td>0.365</td>
<td>-0.290</td>
<td>0.664</td>
</tr>
<tr>
<td>D</td>
<td>0.578</td>
<td>0.375</td>
<td>-0.209</td>
<td>0.228</td>
</tr>
<tr>
<td>C</td>
<td>0.148</td>
<td>0.069</td>
<td>-0.118</td>
<td>0.050</td>
</tr>
<tr>
<td>B</td>
<td>0.055</td>
<td>-0.044</td>
<td>-0.336</td>
<td>-0.228</td>
</tr>
<tr>
<td>A</td>
<td>0.005</td>
<td>-0.084</td>
<td>-0.158</td>
<td>-0.061</td>
</tr>
</tbody>
</table>

* Note: A < B

(b) t - Test for Probability of Observed Differences Between Each Pair of Experimental Treatment Conditions. (Error S.D. = 0.222, non-standard df. (see Kirk (1968) p.268(233)).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus level* ↓</td>
<td>t  2P</td>
<td>t  2P</td>
<td>t  2P</td>
<td>t  2P</td>
<td>t  2P</td>
<td>t  2P</td>
</tr>
<tr>
<td>F</td>
<td>1.368</td>
<td>N.S.</td>
<td>5.410</td>
<td>&lt;0.001</td>
<td>1.469</td>
<td>N.S.</td>
</tr>
<tr>
<td>E</td>
<td>1.558</td>
<td>N.S.</td>
<td>4.385</td>
<td>&lt;0.001</td>
<td>0.094</td>
<td>N.S.</td>
</tr>
<tr>
<td>D</td>
<td>-0.436</td>
<td>N.S.</td>
<td>3.560</td>
<td>&lt;0.001</td>
<td>1.574</td>
<td>N.S.</td>
</tr>
<tr>
<td>C</td>
<td>0.356</td>
<td>N.S.</td>
<td>1.198</td>
<td>N.S.</td>
<td>0.438</td>
<td>N.S.</td>
</tr>
<tr>
<td>B</td>
<td>0.447</td>
<td>N.S.</td>
<td>1.170</td>
<td>N.S.</td>
<td>1.275</td>
<td>N.S.</td>
</tr>
<tr>
<td>A</td>
<td>0.399</td>
<td>N.S.</td>
<td>0.730</td>
<td>N.S.</td>
<td>0.297</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* A < B
FIG. 34: ACUPUNCTURE EXPERIMENT NO. 2:
CONVENTIONAL ANALYSIS:
Mean (n = 16 subjects) SHIFT in Median Response Ratings at Each Stimulus Intensity (A-F), During Different Experimental Conditions.

Stimulus range: F = most intense; A = least intense.
FIG. 35: ACUPUNCTURE EXPERIMENT NO. 2:
CONVENTIONAL ANALYSIS:
Mean (n = 16) SHIFT in Median Response Rating
Category to Each Stimulus Intensity Level
(A-F), During Different Experimental Treatment
Conditions.
Stimulus range:
F = most intense
A = least intense
Stimulus Intensity Level
'Control' treatment curve shapes (which also have much in common).
This stimulus level D, to which the modal response for all subjects
was 'Warm*', displays the second largest decrement in response
magnitude of the 'Genuine Acupuncture' treatment condition.

The highest stimulus level (F) provided the largest response
decreases during the 'Genuine Acupuncture' sessions, but this level
is also associated with the most inhibited elevation of responses,
of the pain inducing stimulus levels (D-F), under the placebo or
'Pseudo-Acupuncture' treatment. At this level Naloxone returns
the Acupuncture induced response shift pattern to levels extremely
similar to those of the 'Pseudo' treatment.

Finally, the 36 t-tests were completed for each possible
combination of experimental treatment conditions using the above
data base for each individual stimulus intensity level. The t-values, together with their associated critical significance levels,
appear in Table 23 (b) Page 360. It should be noted that the t-tests
cannot be interpreted with the standard d.f. owing to the
non-homogeneity of variances mentioned at the end of section (vi)
above. The critical t-values are evaluated with the formula
below (23):

\[ t'_{\text{crit}} = \frac{t_{\text{crit}}(B \times SwG) \times MS(B \times SwG) + t_{\text{crit}}(B \times SwG) \times (U-1)}{MS(B \times SwG) + MS(BD \times SwG) \times (U-1)} \]

where U = number of stimulus intensity levels. Thus

\[ t'_{0.05} = 2.014, \quad t'_{0.01} = 2.689, \quad t'_{0.001} = 3.522. \]

Table 23 (b) Page 360 indicates that, apart from one maverick (Gen.Ac.
v Gen.Ac.+ Nal., stimulus level D) 'Genuine Acupuncture' signifi-
cantly differs from all other conditions at the three most intense,

* Also no individual subject produced a modal response indicative of
pain to this stimulus level.
or pain-inducing, levels. None of the other trends described above are significant.

(d) Rating Scale Responses (Personality Variables):

E.P.I. (Form B) scales were scored for all subjects and appear in Table 24 Page 365. As expected, apart from one aberrant male subject with an extraversion score of two, the subject group volunteering for pain experimentation was quite highly extraverted (grand mean score is 16.4, and males equal females if the abnormal male subject is excluded). This is unfortunate in that the restricted range severely limited the likelihood of observing any possible personality interactions.

A rather more useful range of scores was available on the neuroticism scale, and no subject was invalidated by an excessively high lie score, although females had slightly higher scores.

A possible relationship between personality variables and the pattern of rating scale responses was sought in two ways. First, the mean median response value (averaged over all stimulus levels, and all experimental treatment conditions), for the first (baseline) thermal stimulus series was computed for each subject. This was then examined for correlation with E and N scores by the Spearman rank correlation test (391). The results appear in Table 25 Page 366, from which it will be seen that no significant relationship emerged. For what it is worth, it is interesting to note that the subject with the largest N score also displayed the highest baseline responses, or in other words reported the most intense sensations resulting from the stimuli.

* Response scores, or score S.D.'s, were ranked largest to smallest against EPI scores largest to smallest.
### TABLE 24: ACUPUNCTURE EXPERIMENT NO 2:
**Eysenck Personality Inventory (form D)**
Scores:
(n = 16 subjects)

<table>
<thead>
<tr>
<th>Subject Code</th>
<th>Extraversion</th>
<th>Neuroticism</th>
<th>Lie</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>14.2</strong></td>
<td><strong>10.9</strong></td>
<td><strong>0.9</strong></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>21</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>14</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>13</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>16.7</strong></td>
<td><strong>11</strong></td>
<td><strong>1.6</strong></td>
</tr>
<tr>
<td><strong>Grand Mean</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>15.5</strong></td>
<td><strong>10.9</strong></td>
<td><strong>1.25</strong></td>
<td></td>
</tr>
<tr>
<td><strong>S.D.</strong></td>
<td><strong>4.4</strong></td>
<td><strong>4.2</strong></td>
<td>/</td>
</tr>
</tbody>
</table>
TABLE 25: ACUPUNCTURE EXPERIMENT NO 2: CONVENTIONAL ANALYSIS:
Eysenck Personality Inventory (Form B) Scores:

(a) Rank Correlation* with Baseline
Mean (all stimulus levels (6), all experimental
treatment conditions (4)) Median Rating Scale
Responses.
\(n = 16\) subjects.

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(r_s)</td>
<td>0.117</td>
<td>N.S.</td>
<td>-0.244</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

(b) Rank Correlation* with Variability (S.D.) of
Baseline Mean (all stimulus levels (6)) Median
Rating Scale Responses Across Different Test Days.

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(r_s)</td>
<td>-0.003</td>
<td>N.S.</td>
<td>0.590</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

(c) Rank Correlation* with SHIFTS in Mean (all
stimulus levels (6)) Median Rating Scale Responses
during each Experimental Treatment Condition.

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(r_s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>-0.486</td>
<td>N.S.</td>
<td>-0.093</td>
<td>N.S.</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>0.395</td>
<td>N.S.</td>
<td>0.260</td>
<td>N.S.</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>0.005</td>
<td>N.S.</td>
<td>-0.169</td>
<td>N.S.</td>
</tr>
<tr>
<td>Gen.Ac.+ Nal.</td>
<td>-0.073</td>
<td>N.S.</td>
<td>0.076</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Spearman Rank Correlation Coefficient.
Next, the test was repeated for correlation of E and N scores against the variability (S.D.) of the mean baseline values each subject produced on the four different test occasions he attended the laboratory. The results appear in Table 25 (b) Page366, from which it may be observed that, although extraversion is not related, neuroticism is significantly correlated \( p < 0.05 \) for a two-tailed test, with day to day variability. Despite this one positive result, the general paucity of the findings did not seem to merit further investigation upon those lines. Again, for what it is worth, it is interesting to note that the two subjects with the highest and lowest E scores occupied positions one and two respectively in terms of magnitude of baseline response variability.

The next focus of interest was upon the possibility of a relationship between personality measures and the response of the subject to the various experimental treatments. Accordingly, the Spearman test was applied to E and N scores in relation to the shift in mean median responses displayed by subjects as a result of each of the four experimental treatment conditions. The results appear in Table 25 (c) Page366. Apart from a negative correlation of \(-0.4^86\) between E and response shifts in the 'Control' condition (which just fails to reach \( p < 0.05 \) (two-tailed test)), the result is uniformly devoid of significance.

At a descriptive level, it was noted that in the 'Pseudo-Acupuncture' condition the subject with the largest upward shift in response ratings (or in other words probably the least response to the suggestive effects of the treatment) also produced the lowest E and N scores of the group. This was also partly true for 'Genuine

---

* Shifts were ranked largest (in terms of dominant shift polarity) to smallest against E.P.I. scores largest to smallest.
Acupuncture. The lowest E scoring subject displayed the largest positive shifts in responses (i.e., the least analgesia). In the case of N scores, the highest scoring subject produced the most analgesia, whilst the second most unstable subject displayed the least analgesia. Again, however, the general picture did not merit further enquiry.

(2) Signal Detection Theory Analysis:

The analysis next proceeded to a complete re-examination of the data by S.D.T. measures.

(a) Sensitivity Measures:

Differential discriminability between each adjacent pair of stimulus intensity levels (A-B, B-C, C-D, D-E, E-F) was estimated using the non-parametric measure P(A), which is fully described elsewhere. By calculating the proportion of the total area which lies beneath the R.O.C. curve, a value of P(A) normally between 0.5 and 1.0 is obtained, which is a direct index of the observer's ability to distinguish signal from noise events. Although proper curve fitting procedures, as evolved by various authors, require at least four plotting points, it has been shown that a single pair of hit and false alarm rates provide enough information to determine approximately the path of the entire R.O.C. curve. The tolerance of P(A) for this type of data impoverishment rendered it the only feasible measure, in addition to its non-parametric advantages.

* The requirements of the experiment (as discussed elsewhere in this work) inevitably limited the number of stimuli presented at each intensity level below optimal figures for parametric S.D.T. measures. However, since precise parametric data to fit psychophysical functions were not required, the measure is quite adequate to indicate differences in sensitivity from one experimental condition to another.
Fortunately the overlap in the data between response distributions was usually sufficient to provide several points, and thus improved measure robustness, and reduced implicit curve form assumptions.

The steps in the analysis procedures are outlined below:

(i) \( P(A) \) was computed using the trapezoidal rule method of estimation\(^{351} \). Although the method slightly underestimates the area (for a generally concave-downwards curve), depending upon the number of data points used, the error will rarely be marked\(^{393} \).

(ii) \( P(A) \) measures were then directly converted to \( \sqrt{2} \times z(A) \). This is equivalent to the \( d_a \) (or \( d \) related to area) measure proposed by Simpson and Fitter (1973)\(^{393} \) as the best index of discriminability (for unequal variance normal distributions of signal and noise). It has been shown that \( d_a = z(A) \), the normal transform of the area under the R.O.C. curve\(^{393} \). This transformation corrects \( P(A) \) for skew and also provides numerical value proportions which may be roughly equated with the parametric \( d' \) measure less cautiously employed by other authors for pain experimentation studies.

(iii) Next, for each of the five possible adjacent pairs of stimulus intensity levels (A-B, B-C, C-D, D-E, E-F), the shift in discriminability (\( d_a \)), occurring when the first (baseline) stimulus series was compared with the second (post-treatment) stimulus series, was computed for each subject, during each experimental treatment condition. This measure was to serve as the dependent variable for all subsequent analysis.
(iv) A split-plot factorial - pr.qu ANOVA\(^{(23)}\) was again applied to the data, using the file organisation described previously (see section (1)(c)(v)), and the output summary appears as Table 26 Page 37. Only the main effect of experimental treatment condition (B) emerges as significant, and this time there is no evidence of a BD interaction (condition (B) x stimulus intensity level pair (D)).

Again it may be useful to summarise the more relevant negative findings from Table 26 Page 37. Thus, for shifts in sensitivity (dₐ):-

- there are no treatment order effect - overall (A).
- there are no sex differences overall (C).
- there are no differences between experimental treatment conditions due to their order of presentation (AB).
- there are no sex differences in the responses to different treatment conditions (BC).
- there are no differences in the shifts at the five pairs of adjacent stimulus intensity levels overall (D).
- there are no sex differences in the shifts at the five pairs of adjacent stimulus intensity levels (CD).
- there are no differences in the shifts at the five pairs of adjacent stimulus intensity levels during the different experimental treatment conditions (BD).

It should be noted that again the variances of BD x Subjects within Groups and B x Subjects within Groups are non-homogeneous, although this is only slight (F = 2.181 with 96,24 d.f., 2P = 0.031 4).
TABLE 26: ACUPUNCTURE EXPERIMENT NO 2: S.D.T. ANALYSIS:

Analysis of Variance (type S.P.F. -42.45 (233)),
Output Summary Table for Within-Session SHIFT in
Sensitivity (d_a), All Experimental Treatment Conditions.

Key: A is Treatment Order Group.
B is Experimental Treatment Condition.
C is Sex of Subject.
D is Stimulus Intensity Level Pair.

Note: A, B, C, D, are fixed effects, subjects random.
The error term is the next entry with no associated F.

<table>
<thead>
<tr>
<th>No.</th>
<th>Source</th>
<th>S.S.</th>
<th>df.</th>
<th>M.S.</th>
<th>F.</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Between Subjects</td>
<td>6.169</td>
<td>15</td>
<td>0.411</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>0.328</td>
<td>3</td>
<td>0.109</td>
<td>0.185</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>C</td>
<td>0.100</td>
<td>1</td>
<td>0.100</td>
<td>0.170</td>
<td>N.S.</td>
</tr>
<tr>
<td>4</td>
<td>AC</td>
<td>1.011</td>
<td>3</td>
<td>0.337</td>
<td>0.570</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Subjects within Groups</td>
<td>4.730</td>
<td>8</td>
<td>0.591</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Within Subjects</td>
<td>68.709</td>
<td>304</td>
<td>0.226</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>B</td>
<td>2.535</td>
<td>3</td>
<td>0.845</td>
<td>8.569</td>
<td>0.000</td>
</tr>
<tr>
<td>8</td>
<td>AB</td>
<td>0.889</td>
<td>9</td>
<td>0.099</td>
<td>1.002</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>BC</td>
<td>0.100</td>
<td>3</td>
<td>0.033</td>
<td>0.337</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>ABC</td>
<td>1.252</td>
<td>9</td>
<td>0.150</td>
<td>1.523</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Subjects within Groups</td>
<td>2.367</td>
<td>24</td>
<td>0.099</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>D</td>
<td>1.653</td>
<td>4</td>
<td>0.413</td>
<td>1.326</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>AD</td>
<td>2.246</td>
<td>12</td>
<td>0.187</td>
<td>0.601</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>CD</td>
<td>1.749</td>
<td>4</td>
<td>0.437</td>
<td>1.403</td>
<td>N.S.</td>
</tr>
<tr>
<td>15</td>
<td>ACD</td>
<td>2.558</td>
<td>12</td>
<td>0.213</td>
<td>0.684</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Subjects within Groups</td>
<td>9.974</td>
<td>32</td>
<td>0.312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>BD</td>
<td>3.375</td>
<td>12</td>
<td>0.281</td>
<td>1.301</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>ABD</td>
<td>7.427</td>
<td>36</td>
<td>0.206</td>
<td>0.954</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>BCD</td>
<td>2.164</td>
<td>12</td>
<td>0.180</td>
<td>0.834</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>ABCD</td>
<td>9.568</td>
<td>36</td>
<td>0.266</td>
<td>1.229</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Subjects within Groups</td>
<td>20.752</td>
<td>96</td>
<td>0.216</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Total</td>
<td>74.878</td>
<td>319</td>
<td>0.235</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(v) Further analysis was directed at illuminating the source components of the significant B factor (experimental treatment condition) above.

Group mean shifts in $d_a$ from the first stimulus series compared to the second stimulus series were computed for each experimental treatment condition, and appear in Table 27 (Page 373) and as histograms in Fig. 36 (Page 374). Each cell mean is derived from 80 observations, since all subjects (16), and all adjacent stimulus pairs (5), were combined.

It can be observed that the situation is essentially consistent with the findings of the conventional analysis. The 'Control', 'Pseudo-Acupuncture', and 'Genuine Acupuncture plus Naloxone' conditions, all exhibit actual increases in sensitivity ($d_a$) after treatment, compatible with the increased intensity of sensory experience suggested by the elevated median response categories observed in the conventional analysis. Conversely, 'Genuine Acupuncture' appears to produce decrements in sensitivity ($d_a$). Upon closer examination, however, interesting differences appear. Despite the reduced intensity of median responses evident with the conventional analysis (see Fig. 33 (Page 356)), the 'Pseudo-Acupuncture' treatment appears actually to improve sensitivity compared to the 'Control' condition. Similarly, the antagonistic action of Naloxone not only reverses the sensitivity decrement caused by Acupuncture, but also increases it beyond levels prevailing in the 'Control' condition. The small size of even the most extreme difference between conditions ('Pseudo-Acupuncture' versus 'Genuine Acupuncture' = 0.242) should, however, be noted.
TABLE 27: ACUPUNCTURE EXPERIMENT NO 2: S.D.T. ANALYSIS:

(a) Mean (all subjects (16), all adjacent stimulus intensity pairs (5)) SHIFT in Sensitivity ($d_a$), During Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean $d_a$ Shift</td>
<td>0.050</td>
<td>0.137</td>
<td>-0.105</td>
<td>0.075</td>
</tr>
</tbody>
</table>

(b) $t$-Test for Probability of Observed Differences Between Each Pair of Experimental Treatment Conditions (df. = 80, error S.D. = 0.050)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$t$ - Value</td>
<td>-1.740 (N.S.)</td>
<td>3.129</td>
<td>0.002 (N.S.)</td>
</tr>
<tr>
<td>2P.</td>
<td>N.S.</td>
<td>0.002 45</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$t$ - Value</td>
<td>4.869</td>
<td>1.252</td>
<td>-3.617</td>
</tr>
<tr>
<td>2P.</td>
<td>0.000 005.55</td>
<td>N.S.</td>
<td>0.000 520</td>
</tr>
</tbody>
</table>
FIG. 36: ACUPUNCTURE EXPERIMENT NO. 2:

S.D.T. ANALYSIS:

Group (n = 16) Mean SHIFT in Discriminability ($d_a$) Between Adjacent Stimulus Intensities, During Different Experimental Conditions.

(t-test for probability of observed differences between conditions)
For what it is worth, one may observe that 'Pseudo-Acupuncture' increases sensitivity shift by 174% compared to the 'Control' condition. In addition, Naloxone antagonises approximately 74% of the analgesic effect of 'Genuine Acupuncture' compared to 'Pseudo-Acupuncture'.

(vi) Next *t*-tests were applied for the significance of the observed differences in mean sensitivity ($d_a$) shift when each of the six possible pairs of experimental treatment conditions were compared. The resultant *t*-values and associated significant two-tailed probabilities appear in Table 27 (b) Page 373 and the latter are also included visually in Fig. 36 Page 374. It is clear that, whilst the differences between the 'Control', 'Pseudo-Acupuncture', and 'Genuine Acupuncture plus Naloxone' conditions are not significant, 'Genuine Acupuncture' produces highly significant shifts in sensitivity in the opposite direction to all these treatments.

(vii) Although there was no evidence in the overall analysis of variance of a significant BD interaction (Experimental Treatment Condition (B) x Stimulus Intensity Pair (D)), it was nonetheless of interest to further explore the pattern of effects of the different experimental treatments on the discriminability ($d_a$) of the five different pairs of stimulus intensity levels. The results must, of course, remain suggestive only.

Accordingly, simple main effects analysis of variance testing was applied to the mean shifts in discriminability for each stimulus pair (A-B, B-C, C-D, D-E, E-F), and the output summary appears as Table 28 Page 376. Only the most intense (E-F), and the third most intense (C-D) stimulus pairs, display significant differences
TABLE 28: ACUPUNCTURE EXPERIMENT NO 2: S.D.T. ANALYSIS:

Analysis of Variance, Output Summary Table for Within-Session Mean (n = 16) SHIFT in Discriminability (da) for EACH Pair of Adjacent Stimulus Intensity Levels, All Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Stimulus* Pair</th>
<th>S.S.</th>
<th>df.</th>
<th>M.S.</th>
<th>F.</th>
<th>P.</th>
<th>Pooled F.†</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-F</td>
<td>1.652</td>
<td>3</td>
<td>0.551</td>
<td>2.858</td>
<td>.0399</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-E</td>
<td>1.297</td>
<td>3</td>
<td>0.432</td>
<td>2.245</td>
<td>N.S.</td>
<td>(0.0866)</td>
<td>2.847</td>
</tr>
<tr>
<td>C-D</td>
<td>1.987</td>
<td>3</td>
<td>0.662</td>
<td>3.438</td>
<td>.0191</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B-C</td>
<td>0.474</td>
<td>3</td>
<td>0.158</td>
<td>0.819</td>
<td>N.S.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A-B</td>
<td>0.501</td>
<td>3</td>
<td>0.167</td>
<td>0.866</td>
<td>N.S.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5.910</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Error Term</strong></td>
<td><strong>23.118</strong></td>
<td><strong>120</strong></td>
<td><strong>0.193</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Note: A < B

† d.f. 9,120
between the experimental treatment conditions. However, the pooled value of the top three pairs is significant. Comparing the F values of the three most intense stimulus pairs with the remaining two pairs suggests that the main effect of experimental treatment condition is contributed by the former.

(viii) Further examination of the sources of the above effects continued, as before, with pairwise comparison of each possible combination of experimental treatment conditions by t-test.

The computed group mean shifts in discriminability ($d_a$) at each of the five pairs of stimulus intensity levels are presented, for each experimental treatment condition, in Table 29 (a), Page 378. They are also graphed in Fig. 37. The three most intense stimulus pairs, 1(E-F), 2(D-E), 3(C-D), have been separated from the two lowest pairs, 4(B-C), 5(A-B), both for visual clarity, and since there is an arguable distinction between them in terms of magnitude of shifts displayed. There is, however, less distinction in terms of curve shape than was the case with the conventional analysis data.

Generally the 'Control' condition exhibits positive, or relatively neutral shifts in discriminability, apart from the lowest stimulus pair which is negative going for some reason. Apart from a slight decrement at stimulus pair No. 2 (D-E), 'Pseudo-Acupuncture' appears to leave sensitivity relatively unaffected at the higher intensities, but produces marked increases at the two lowest intensity pairs. It is important to note that these are not intensity pairs with which responses indicative of pain sensations are associated.

* The mean $d_a$ shifts are not also graphed against intensity, as was done with the conventional data, since there are too many overlaps of the curves to render an easily intelligible presentation.

** As the S.D.'s for S.D.T. data (Fig. 36 Page 374) and conventional data (Fig. 33 Page 356) indicate greater noise in the former, the meaningfulness of comparison is somewhat reduced.
TABLE 29: ACUPUNCTURE EXPERIMENT NO 2: S.D.T. ANALYSIS:

(a) Mean (n = 16) SHIFT in Discriminability (d) for EACH Pair of Adjacent Stimulus Intensity Levels, During Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus Pair</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-F</td>
<td>0.169</td>
<td>0.168</td>
<td>-0.192</td>
<td>-0.099</td>
</tr>
<tr>
<td>E-D</td>
<td>-0.010</td>
<td>0.065</td>
<td>-0.076</td>
<td>0.301</td>
</tr>
<tr>
<td>D-C</td>
<td>0.166</td>
<td>0.210</td>
<td>-0.242</td>
<td>0.026</td>
</tr>
<tr>
<td>C-B</td>
<td>0.004</td>
<td>0.179</td>
<td>0.172</td>
<td>0.233</td>
</tr>
<tr>
<td>A-B</td>
<td>-0.077</td>
<td>0.062</td>
<td>-0.187</td>
<td>-0.088</td>
</tr>
</tbody>
</table>

* Note: A < B

(b) t - Test for Probability of Observed Differences Between Each Pair of Experimental Treatment Conditions. (Error S.D. = 0.155, non-standard df. (see Kirk(1968) p268 (233)).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus Pair</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-F</td>
<td>0.005 N.S.</td>
<td>2.329 (5%)</td>
<td>1.729 N.S.</td>
<td>2.324 (5%)</td>
<td>1.724 N.S.</td>
<td>-0.600 N.S.</td>
</tr>
<tr>
<td>E-D</td>
<td>-0.484 N.S.</td>
<td>0.429 N.S.</td>
<td>-2.001 (5%)</td>
<td>0.913 N.S.</td>
<td>-1.518 N.S.</td>
<td>-2.431 (5%)</td>
</tr>
<tr>
<td>D-C</td>
<td>-0.283 N.S.</td>
<td>2.626 (5%)</td>
<td>0.900 N.S.</td>
<td>2.909 (5%)</td>
<td>1.831 N.S.</td>
<td>-1.726 (5%)</td>
</tr>
<tr>
<td>C-B</td>
<td>-1.130 N.S.</td>
<td>-1.087 N.S.</td>
<td>-1.478 N.S.</td>
<td>0.043 N.S.</td>
<td>-0.348 N.S.</td>
<td>-0.391 N.S.</td>
</tr>
<tr>
<td>A-B</td>
<td>-0.892 N.S.</td>
<td>0.709 N.S.</td>
<td>0.070 N.S.</td>
<td>1.601 N.S.</td>
<td>0.962 N.S.</td>
<td>-0.639 N.S.</td>
</tr>
</tbody>
</table>

* Note: A < B

(t' 0.05 = 1.988, t' 0.01 = 2.634)
FIG. 37: ACUPUNCTURE EXPERIMENT NO. 2:
S.D.T. ANALYSIS:
Group (n = 16) Mean SHIFT in Discriminability (d_a)
Between Each Pair (1-5) of Adjacent Stimulus Intensities,
During Different Experimental Conditions.
1 = Most Intense Stimulus Pair (E-F) 5 = Least Intense
Stimulus Pair (A-B)
'Genuine Acupuncture' produces marked discriminability decrements for all stimulus pairs, except at the second lowest intensity, 4(B-C). This pair does, however, display a very slightly lesser elevation of discriminability during 'Genuine Acupuncture' than during the other two conditions involving needle insertion. Naloxone appears to partially reverse the effect of 'Genuine Acupuncture' for three of the pairs, including the most intense pair (1(E-F)), generally associated with very painful sensations. However for the pair (2(D-E)) below this, in other words for stimuli typically inducing milder levels of pain, the drug not only reverses the effect of Acupuncture, but also produces an unparalleled elevation of the sensitivity measure, suggestive of hyperalgesia. Since a rather similar pattern is evident for pair 4(B-C), or in other words for sensations around the warmth range, there may even be a trend towards hyperaesthesia.

Finally, the 30 t-tests were completed for each possible combination of experimental treatment conditions using the above data base for each individual stimulus intensity pair. The t-values, together with their associated probabilities, appear in Table 29 (b) Page 378. Since the variances pooled for the error term are only slightly non-homogeneous (see section (2)(a)(iv) above) both the conservative (5% and 1%) critical indication**, and the P that arises with error d.f. = 120, are given. Table 29(b) Page 378 indicates that all the significant differences between experimental treatment conditions are found in the top three stimulus pairs, and the selective effect of Naloxone upon stimulus pair 2(D-E) is also significant.

* Particularly Pair 1(E-F) and Pair 3(C-D).
** \( t'_{0.05} = 1.988, \quad t'_{0.01} = 2.634 \).
(b) Sensitivity Measures (Personality Variables):

Extraversion and Neuroticism (E.P.I.) measures were tested for correlation (Spearman test) with baseline (ie. first stimulus series) mean (all stimulus pairs (5), all experimental treatment conditions) sensitivity ($d_a$). As Table 30 (a) Page 382 indicates, neither displayed a significant relationship.

E.P.I. measures were next tested for relationship with the variability (S.D.) of baseline sensitivity ($d_a$) across the different test days of the four experimental treatment conditions. Although Table 30 (b) Page 382 fails to indicate any significant relationship, it is of interest to note that the group contains one very aberrant subject displaying the highest E score and the lowest variability. This generates a ranking difference double that of any other subject. Exclusion of the subject renders extraversion and baseline $d_a$ variability positively correlated at 0.501 ($p<0.05$ one-tailed). Unlike the conventional data analysis, neuroticism does not this time correlate with variability.

Table 30 (c) Page 382 presents the results of tests for relationship between personality and shifts in sensitivity ($d_a$) during the different experimental treatment conditions. The picture is uniformly devoid of any apparent significant correlation.

Apart from a similar tendency towards a relationship between variability of baseline measures with personality dimensions, albeit different ones, the conventional and S.D.T. analyses appear to display no common pattern whatsoever.

(c) Response Criterion Measures:

An analysis of response criteria measures was not undertaken for several reasons. Principally, as discussed fully in chapter 4,
TABLE 30: ACUPUNCTURE EXPERIMENT NO 2: S.D.T. ANALYSIS:
Eysenck Personality Inventory (Form B) Scores:

(a) Rank Correlation* with Baseline
Mean (all stimulus pairs (5), all experimental
treatment conditions (4)) Sensitivity (d<sub>a</sub>)
(n = 16 subjects).

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>r&lt;sub&gt;s&lt;/sub&gt;</td>
<td>0.313</td>
<td>N.S.</td>
<td>0.056</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

(b) Rank Correlation* with Variability (S.D.) of
Baseline Mean (all stimulus pairs (5))
Sensitivity (d<sub>a</sub>) Across Different Test Days.

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>r&lt;sub&gt;s&lt;/sub&gt;</td>
<td>0.264</td>
<td>N.S.</td>
<td>0.206</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

(c) Rank Correlation* with SHỊJS in Mean (all
stimulus pairs (5)) Sensitivity (d<sub>a</sub>) during
Each Experimental Treatment Condition.

<table>
<thead>
<tr>
<th></th>
<th>Extraversion</th>
<th>2P.</th>
<th>Neuroticism</th>
<th>2P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>r&lt;sub&gt;s&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.201</td>
<td>N.S.</td>
<td>0.013</td>
<td>N.S.</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>0.221</td>
<td>N.S.</td>
<td>0.225</td>
<td>N.S.</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>-0.212</td>
<td>N.S.</td>
<td>0.049</td>
<td>N.S.</td>
</tr>
<tr>
<td>Gen.Ac. + Nal.</td>
<td>0.257</td>
<td>N.S.</td>
<td>-0.042</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Spearman Rank Correlation Coefficient.

† See text for comment.
in the presence of clear shifts in sensitivity, there is little value in applying tests to, or probably even estimating, bias measures, since they have been shown to shift as a function of the sensitivity changes themselves.

Bias measures are, of course, an invaluable source of second-line information if sensitivity is unaffected by the experimental treatments; but otherwise the lack of orthogonality, and the impracticability of separating out dependent and independent components of bias shifts, prohibits interpretation of any results which might be produced.

As a further consideration, data, such as obtained here, which is insufficiently good to calculate parametric sensitivity measures, permits even less confidence in its provision of reliable parametric $\beta$ values for the criteria. At least sensitivity measures are based on a line fitted to all points, whereas in determining $\beta$, each point on the R.O.C. curve must stand on its own merits. Should a criterion be placed well into the tails of the signal and noise distributions, small errors in hit or false alarm estimation may cause large errors in estimation of the heights of the distributions at the criterion. Furthermore, there is no fully satisfactory non-parametric alternative to $\beta$ analogous to $P(A)$. A crude alternative single bias score for each session would be available in the $B$ measure \(^{(327)}\). However, not only does this fail to provide a bias score for each point*, but it is also, of course, subject to the same contamination from sensitivity shifts discussed above. It is hoped, in the future, to find methods of 'cleaning-up' the bias data to obtain useful information, but this remains outside the scope of the present report.

* If an experimental treatment results in the observer spacing all his criteria more widely apart or closer together (as reported in some work\(^{(53)}\)), rather than moving all criteria up or down the axis, $B$ will not detect the changes.
Body Temperature Monitoring Analysis:

As described in the methods section above, abdominal and thoracic cutaneous temperatures, and oral temperature, were monitored prior to, and following, each stimulus series in every session. The summary results appear as group means in Table 31 (a)(b)(c) Page 385.

(a) First Stimulus Series (Baseline) - Pre and Post Temperatures:

Several observations may be made from Table 31. First, the initial baseline values ('Pre' First Stimulus Series) are well matched across the different experimental treatment conditions, and for all three body sites. The 'Genuine Acupuncture plus Naloxone' condition displays a slight tendency towards a higher abdominal and thoracic baseline value, for presumably random reasons. It is also interesting to note that initial baseline thoracic temperatures are slightly higher than their abdominal counterparts, whilst the oral temperatures are consistently higher than might be expected in a normal population, suggestive of a slight instrumentation miscalibration.

Most important is the consistent, and considerable, increase (mean 1.84°C) in abdominal surface temperatures (see Table 31 (a) Page 385) by the end of the first stimulus series in each experimental treatment condition. The increase is fairly uniform across conditions, with the slightly lower increase during the 'Genuine Acupuncture plus Naloxone' condition probably being attributable to the higher initial baseline referred to above. The significance of these temperature elevations in the generation of the observed increases in intensity of

* All results reported in this section must be viewed with a certain caution in view of mechanical problems associated with constancy of thermistor/skin contact for the abdominal and thoracic measures, and variability of positioning for the oral transducer. These led to increased error of significant proportions given the magnitude of the effects reported. These may, however, be assumed as probably randomly distributed across conditions.
TABLE 31: ACUPUNCTURE EXPERIMENT NO 2: Body Temperatures (°C):

Group Mean (n = 16) Baseline Values and SHIFTS (Δ) During Different Experimental Treatment Conditions.

(a) Abdominal:

<table>
<thead>
<tr>
<th>Condition</th>
<th>First Stimulus Series</th>
<th>Treatment</th>
<th>Second Stimulus Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Δ</td>
</tr>
<tr>
<td>Control</td>
<td>33.29</td>
<td>35.19</td>
<td>+1.90</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>33.21</td>
<td>35.05</td>
<td>+1.84</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>33.23</td>
<td>35.08</td>
<td>+1.85</td>
</tr>
<tr>
<td>Gen.Ac. + Nal.</td>
<td>33.37</td>
<td>35.14</td>
<td>+1.77</td>
</tr>
<tr>
<td>Grand Mean</td>
<td>33.27</td>
<td>35.11</td>
<td>+1.84</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.07</td>
<td>0.06</td>
<td>0.05</td>
</tr>
</tbody>
</table>

(b) Thoracic:

<table>
<thead>
<tr>
<th>Condition</th>
<th>First Stimulus Series</th>
<th>Treatment</th>
<th>Second Stimulus Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Δ</td>
</tr>
<tr>
<td>Control</td>
<td>33.34</td>
<td>33.88</td>
<td>+0.54</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>33.50</td>
<td>34.19</td>
<td>+0.69</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>33.36</td>
<td>33.86</td>
<td>+0.50</td>
</tr>
<tr>
<td>Gen.Ac. + Nal.</td>
<td>33.59</td>
<td>34.25</td>
<td>+0.66</td>
</tr>
<tr>
<td>Grand Mean</td>
<td>33.45</td>
<td>34.04</td>
<td>+0.59</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.12</td>
<td>0.20</td>
<td>0.09</td>
</tr>
</tbody>
</table>

(c) Oral:

<table>
<thead>
<tr>
<th>Condition</th>
<th>First Stimulus Series</th>
<th>Treatment</th>
<th>Second Stimulus Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Δ</td>
</tr>
<tr>
<td>Control</td>
<td>37.03</td>
<td>37.01</td>
<td>-0.02</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>37.03</td>
<td>37.00</td>
<td>-0.03</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>37.01</td>
<td>37.01</td>
<td>0.00</td>
</tr>
<tr>
<td>Gen.Ac. + Nal.</td>
<td>37.03</td>
<td>36.99</td>
<td>-0.04</td>
</tr>
<tr>
<td>Grand Mean</td>
<td>37.02</td>
<td>37.00</td>
<td>-0.02</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.01</td>
<td>0.01</td>
<td>0.02</td>
</tr>
</tbody>
</table>
response ratings, both during the course of the baseline stimulus series, and during the second stimulus series compared to the first, is discussed later.* It is interesting to note that the thoracic (Table 31 (b) Page 385) cutaneous surface also displays consistent temperature increases, although much more attenuated, despite the fact that radiant heat stimuli were not applied to the region.

This pattern is not evident for oral temperature (Table 31 (c) Page 385), which generally displays a very slight decrease during the first stimulus series only. The 'Genuine Acupuncture' condition does not appear to exhibit such decreases, probably due to its initially slightly lower baseline value. These differences are quite trivial; and otherwise oral temperature shows excellent uniformity and stability across all experimental treatment conditions.

Generally the uniformity of temperatures at the end of the first stimulus series (especially oral) may increase confidence in the validity of observed treatment effects reported in the next section.

(b) Temperature Shifts** During Different Experimental Treatments:

(i) Abdominal:

From Table 31 (c) Page 385, reductions in abdominal temperature are evident during all experimental treatments. Interestingly the 'Control' and 'Pseudo-Acupuncture' treatments are both associated with similar decrements, which are larger than those occurring during the other two treatments involving 'Genuine Acupuncture'. The latter pair also appear related.

The significance of these differences was tested by t-tests applied to each possible pair of experimental treatment conditions,

* and in chapter 5, p174-178
** ie. Second Stimulus Series 'Pre' minus First Stimulus Series 'Post'
Temperature = Treatment Δ.
the results appearing in Table 32 Page 262. It can be seen that both the 'Genuine Acupuncture' and 'Genuine Acupuncture plus Naloxone' treatments differ significantly from the 'Control' treatment, although not from each other. They both just fail to differ significantly from the 'Pseudo-Acupuncture' for a two-tailed test. However, the 'Pseudo-Acupuncture' versus 'Genuine Acupuncture' result may be interpreted at p<0.05 (one-tailed), in view of the peripheral temperature increase* hypothesised as accompanying 'Genuine Acupuncture' analgesia as a morphine-like process with its known naloxone-reversible peripheral vasodilatory effects.

Although 'Genuine Acupuncture plus Naloxone' would also display significantly less negative abdominal temperature shifts than 'Pseudo-Acupuncture' for a one-tailed test (p<0.05), this is contrary to the hypothesised antagonistic effect of Naloxone, and the result should therefore be accepted as non-significant. This does not imply any support for the hypothesised Naloxone action, since 'Genuine Acupuncture' and 'Genuine Acupuncture plus Naloxone' treatments do not differ**.

It would appear unlikely that these findings are significantly attributable to baseline differences between the conditions, since, even taking a mean (35.11°C) across all conditions for the 'Post' measures of the first stimulus series, the shifts during treatment maintain a very similar pattern, as shown below:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Temperature Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>Genuine Acupuncture</td>
<td></td>
</tr>
<tr>
<td>Genuine Acupuncture plus Naloxone</td>
<td></td>
</tr>
<tr>
<td>Pseudo-Acupuncture</td>
<td></td>
</tr>
</tbody>
</table>

* Or attenuated reduction.

** For what it is worth, however, it may be noted that differences between the treatments are in the hypothesised direction of reduced peripheral surface temperatures associated with Naloxone, although this may result simply from the higher baseline of the Gen.Ac.+ Nal. condition.
TABLE 32: ACUPUNCTURE EXPERIMENT NO 2: Body Temperatures (°C):

Temperature Shift (D = Stimulus series 1 (post) - Stimulus series 2 (baseline))
During Different Experimental Treatment Conditions:

\[ t \text{- test for Probability of Observed Differences Between Experimental Treatment Conditions} \ (d.f. = 15). \]

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Location</td>
<td>( t ) 2P</td>
<td>( t ) 2P</td>
<td>( t ) 2P</td>
<td>( t ) 2P</td>
<td>( t ) 2P</td>
<td>( t ) 2P</td>
</tr>
<tr>
<td>Abdominal</td>
<td>0.346 N.S.</td>
<td>2.417 &lt;0.05</td>
<td>2.956 &lt;0.01</td>
<td>1.861 &lt;0.10*</td>
<td>2.112 &lt;0.10*</td>
<td>-0.316 N.S.</td>
</tr>
<tr>
<td>Thoracic</td>
<td>-0.390 N.S.</td>
<td>1.221 N.S.</td>
<td>0.317 N.S.</td>
<td>1.789 &lt;0.10*</td>
<td>0.660 N.S.</td>
<td>-1.347 N.S.</td>
</tr>
<tr>
<td>Oral</td>
<td>1.518 N.S.</td>
<td>3.578 &lt;0.01</td>
<td>1.255 N.S.</td>
<td>2.748 &lt;0.02</td>
<td>0.707 N.S.</td>
<td>-0.636 N.S.</td>
</tr>
</tbody>
</table>

\* \( p < 0.05 \) (see text)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-1.02°C</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>-1.12°C</td>
</tr>
<tr>
<td>Gen. Ac.</td>
<td>-0.85°C</td>
</tr>
<tr>
<td>Gen. Ac. + Nal.</td>
<td>-0.82°C</td>
</tr>
</tbody>
</table>

It is also important to note that 'Pseudo-Acupuncture' and the 'Control' conditions do not differ significantly.

The importance of observed differences in strength of fasciculation accompanying 'Genuine' and 'Pseudo' Acupuncture are discussed later as factors contributing to the results reported here. In any event, all differences observed between conditions are extremely small, particularly in view of the error limits of the temperature recording techniques.

(ii) Thoracic:

All treatments except 'Genuine Acupuncture' display small decrements in thoracic temperature (Table 31 (b) Page 38). t-tests (Table 32 Page 38) again applied to all condition pairs as before, fail to indicate any significant differences apart from the 'Pseudo-Acupuncture' versus 'Genuine Acupuncture' comparison, which just achieves $p < 0.05$ for a one-tailed test (applicable for reasons outlined above).

There is a stronger suggestion of a Naloxone antagonistic effect in this case.

Even these indications must, however, be viewed with some caution since differences in condition baselines ('Post', First Stimulus Series) are substantial in terms of the size of observed shift effects. Calculation of temperature shifts during treatments from a mean (34.0°C) baseline (all conditions), as before, clearly alters the picture, as can be seen below:
<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-0.26°C</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>-0.05°C</td>
</tr>
<tr>
<td>Gen. Ac.</td>
<td>-0.01°C</td>
</tr>
<tr>
<td>Gen. Ac. + Nal.</td>
<td>+0.01°C</td>
</tr>
</tbody>
</table>

Differences between all needle conditions are virtually abolished, although the 'Control' condition remains distinct.

(iii) Oral:

Very small oral temperature shifts were recorded during all experimental treatment conditions (Table 31 (c) Page 385). In this case, however, increments occurred during all three treatments involving needle insertion, whilst the 'Control' condition produced a small decrement. The t-tests applied to differences between the treatments indicate very significant differences in the predicted direction between 'Genuine Acupuncture' and both the 'Control' (p < 0.005 one-tailed) and 'Pseudo-Acupuncture' (p < 0.01 one-tailed) treatments.

Again Naloxone produced no significant antagonism, although clearly effects were in the predicted direction. 'Control' and 'Pseudo-Acupuncture' treatment differences did not reach significance.

Although highly significant these effects are very small. However, the excellent stability of the baseline oral measures must strengthen confidence in the validity of the results.

(c) Second Stimulus Series – Pre and Post Temperatures:

Very little firm comment may be made concerning measures at this stage in view of the likely interactions with treatment effects. However, a few points are evident.
(i) Abdominal:

Marked temperature increases again occurred during the second stimulus series, not only counteracting the fall during the treatment phase, but also finally, in all experimental treatment conditions, elevating levels to their highest values of the entire session. Differences between conditions in temperature elevation during the second stimulus series would appear very largely attributable to the different initial starting values.

(ii) Thoracic:

Thoracic temperatures again increased during the second stimulus series although, like the abdominal elevations, these increases were less marked than during the first stimulus series. The thoracic area was not, of course, subjected to radiant heat stimuli, yet the pattern of temperature shifts is again very similar to that of the abdomen, although on a reduced scale.

The pattern of thoracic temperature shifts also appears related to pre-stimulus series levels. However, an interesting departure from the pattern occurs with the 'Genuine Acupuncture plus Naloxone' condition which, although recording the highest pre-stimulus series temperature, still displayed the greatest positive temperature shift.

(iii) Oral:

Like the abdominal and thoracic results, oral temperature shifts also represented a swing in the opposite direction to the changes occurring during the treatment phase of the sessions. It will be recalled, however, that unlike the general cooling effects
evident at the abdominal and thoracic sites during the treatment period, oral temperatures predominantly increased. Likewise, oral shifts generally move in the opposite direction to the other two test areas during this second stimulus series phase of the sessions.

Whilst pre-stimulus series initial values appear, as usual, to contribute to differences between the experimental conditions in temperature shifts during the second stimulus series, it is extremely interesting to note that the 'Genuine Acupuncture plus Naloxone' condition displays almost twice as much oral temperature reduction compared to 'Genuine Acupuncture', despite an initially lower pre-stimulus series level.

All shifts are once more exceedingly small, and must again be suggestive only.

(4) Blood Sample/Beta-Endorphin Radioimmunoassay*:

(i) Method:

All blood samples obtained during the experiment were assayed blind for levels of the C-Fragment of lipotropin (residues 61-91, also known as $\beta$-Endorphin) by the following radioimmunoassay procedures.

0.5ml. and 2ml. volumes of neat serum were evaporated to dryness in vacuo, and the residue was taken up in 200$\mu$l. of 0.05N sodium phosphate of pH 7.6 containing 0.25% human serum albumin. $^{125}$I/C-Fragment (20,000 c.p.m., approximately 10pg.) in 50$\mu$l. of the phosphate buffer was added, followed by 50$\mu$l. of the phosphate buffer, and then 50$\mu$l. of C-Fragment antiserum at a dilution of 1:16,000, giving 60-70% binding of the radioactive peptide.

* Performed by Dr S Zacarian, National Institute for Medical Research, Mill Hill, London NW7 1AA.
The mixture was incubated overnight at 4°C, and then the bound peptide was separated from unbound material by the addition of 200μl of a suspension of activated charcoal (3g. activated charcoal, 0.73g. dextran MW 73,000, 10ml. of 0.5M Sodium phosphate pH 7.6, and 60ml. of horse serum, the total being diluted with H₂O to 100ml.).

The mixture was centrifuged at 3,000 r.p.m. for 30 minutes at 4°C and the supernatant, which contained the bound peptide, was transferred and counted in a Wallach γ-counter.

Antibody Specificity: Radioimmunoassay of the antibody to C-Fragment showed that the antisera reacted with porcine lipotropin and with C'-Fragment, in addition to the C-Fragment; the molar potencies of these peptides were respectively six and four times less than the potency exhibited by the C-Fragment. The antiserum did not react with the nonadecapeptide (LPH 61-79), γ-endorphin (LPH 61-77), Methionine enkephalin (LPH 61-65), or corticotropin.

(ii) Results:

It is difficult to derive completely certain indications from the results of the immunoassay, owing to its insufficient sensitivity in relation to C-Fragment (β-endorphin) circulation levels. None of the samples contained more than 0.002pmole of C-Fragment in 500μl. of serum. This means that the resting level of C-Fragment in the circulation is not more than 0.004pmole per ml., and that none of the Acupuncture samples or control samples exceeded this value. It is evident that the resting C-Fragment levels are
very low and that any change in systemic C-Fragment concentration related to Acupuncture would have to be very small indeed. The results would seem completely clear that Acupuncture does not lead to a significant rise in circulating C-Fragment (\(\beta\)-endorphin). It has been demonstrated that the amount of C-Fragment necessary to cause analgesia by intravenous injection in man is of the order of 2-3mg., which would provide a circulating concentration very much higher than that found in any samples from the study (495).

It would appear certain that neither lipotropin nor C-Fragment (\(\beta\)-endorphin) in the bloodstream account for observed analgesic effects associated with Acupuncture stimulation.

For what it is worth at a purely descriptive level, it is interesting to note that there was some very crude indication of a distinction, in terms of shifts in C-Fragment concentration, between the different treatments. Table 3 on page 395 indicates that very similar shifts occurred during the two 'Genuine Acupuncture' treatments*. Paradoxically, however, the direction

* It will be noted from the methods section that the second blood sample was taken prior to injection of Naloxone during the 'Genuine Acupuncture plus Naloxone' sessions. This observation is, therefore, entirely appropriate to the expected unity of conditions.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Group ≤ Shift</th>
<th>Group Mean Shift</th>
<th>(%Δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>- 1,242</td>
<td>- 78</td>
<td>-0.4</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>+12,478</td>
<td>+780</td>
<td>+3.4</td>
</tr>
<tr>
<td>Gen.Ac.</td>
<td>+ 6,901</td>
<td>+431</td>
<td>+1.9</td>
</tr>
<tr>
<td>Gen.Ac. + Nal.</td>
<td>+ 7,516</td>
<td>+469</td>
<td>+2.1</td>
</tr>
</tbody>
</table>
of shift is actually suggestive of a decrease in the circulating endogenous opiate levels following treatment. 'Pseudo-Acupuncture' displays an even more marked (almost double) reduction, whilst conversely, the 'Control' condition produces very slightly increased levels.

These observations are suggestive of some type of distinction between the experimental treatments, but the picture is paradoxical and exceedingly difficult to interpret in any meaningful way*.

(5) Questionnaires and Subjective Rating Scales:

The 10cm. line visual analogue rating scales (Appendix 5 Page 474) were scored, 0-10 for unipolar scales, 0-5 for bipolar scales, and results appear below.

(i) Mood Rating Scale:

Mood dimensions (a) to (c) from rating scale forms (ii), (iv) and (v)(d) Appendix 5 Page 474 were scored, and results are presented as 'P<sub>1</sub>-Score', 'Δ Score 1', and 'Δ Score 2' respectively in Table 34 Page 397. It will be recalled that the scales were all of a comparative type, requiring subjects to indicate changes or shifts in mood within each session. Δ Score 1 thus represents the group mean

* It is possible from the pattern of mood shifts reported in section (5)(i) that circulating endogenous opiate levels are affected by the slight tension and anxiety associated with insertion of needles, but this would require specific experimental examination.
<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Mood Dimension</th>
<th>(a) Depressed - Elated</th>
<th>(b) Calm - Anxious</th>
<th>(c) Inactive - Restless</th>
<th>(d) Relaxed - Tense</th>
<th>(e) Clear-headed - Dreamy</th>
<th>(f) Unable to concentrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Pre-Sc.</td>
<td>+0.31</td>
<td>+0.16</td>
<td>+0.22</td>
<td>-0.47</td>
<td>-0.38</td>
<td>-0.53</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>Pre-Sc.</td>
<td>-0.09</td>
<td>+0.31</td>
<td>+0.28</td>
<td>0.00</td>
<td>-0.81</td>
<td>-0.25</td>
</tr>
<tr>
<td>Gen. Ac.</td>
<td>Pre-Sc.</td>
<td>-0.13</td>
<td>-0.03</td>
<td>+0.03</td>
<td>+0.50</td>
<td>-1.00</td>
<td>-0.50</td>
</tr>
<tr>
<td>Gen. Ac. +Nal.</td>
<td>Pre-Sc.</td>
<td>+0.03</td>
<td>+0.41</td>
<td>+0.19</td>
<td>-0.03</td>
<td>-1.19</td>
<td>-0.66</td>
</tr>
</tbody>
</table>
shift in mood immediately following the experimental treatment compared to the pre-treatment baseline (Pre-score). The baseline (Pre-score) itself served to indicate mood compared to the subjects' normal day to day state. Finally, \( \Delta \)Score 2 indicates group mean shifts in mood by the end of the experimental session, i.e. approximately 30 minutes after cessation of the experimental treatment.

As is usual with data of this imprecise type, a considerable proportion of random variability appears to be present. Observations must therefore be treated as merely suggestive.

(a) Pre-Scores:

There is some indication on dimensions (a) and (d) respectively that subjects may have felt slightly less cheerful and more tense just prior to the insertion of needles in all Acupuncture sessions compared to the 'Control' condition. Subjects may also have been slightly more anxious (dimension (b)) at this point in the 'Genuine Acupuncture' condition compared to the other three conditions, a point important in the interpretation of later changes on this dimension discussed below. Subjects may also have been a little more restless (c) at this point in the 'Genuine Acupuncture plus Naloxone' condition.

Little further comment may be made.

(b) \( \Delta \)Score 1:

There is suggestion of a slightly depressive (dimension (a)) effect of 'Genuine Acupuncture' not found with the other three conditions. This could be considered marked since subjects were already reporting rather lower spirits at the 'Pre-Score' point in the condition anyway. However, the observation must be discounted since a swing in the opposite direction is evident in the 'Genuine Acupuncture plus Naloxone' sessions. As the mood scales were completed prior to
injection of Naloxone there should be no marked difference between the two 'Genuine Acupuncture' conditions.

There is a trend towards greater calm (b) after all experimental treatments, but occurrence of the largest shifts in the two 'Genuine Acupuncture' conditions may indicate that this is an associated side effect. It is impossible to determine the effect of the higher anxiety baseline in the 'Genuine Acupuncture' condition. It might be argued as artificially aggrandising the later apparent calming effect of Acupuncture, or of inhibiting potentially larger shifts towards calm. The fact that similar, if somewhat attenuated, shifts occurred with 'Pseudo-Acupuncture' probably indicates that rhythmic electrical stimulation itself is passifying.

The same mechanism may perhaps be implicated in the relatively uniform movement towards relaxation (d) in all needle sessions, although equally this may simply be the result of the initially higher anxiety levels.

All conditions, presumably simply by virtue of requiring the subject to remain passively supine during treatment, produce similar tendencies towards feeling inactive (c).

There is a general trend in all conditions towards less alertness and a more dreamy, distant mood (e), doubtless again an offshoot from lying inert for over 40 minutes, although there is perhaps some indication that this may be more marked in the two 'Genuine Acupuncture' conditions. The 'Genuine Acupuncture' condition, although already displaying below average clarity and awareness at the baseline point, still produces the largest additional shift towards 'dreamy', 'distant', moods. Unfortunately the 'Genuine Acupuncture plus Naloxone' condition only just produces the second largest shift in the same direction, although it may be noted that this is against a background baseline of
above average clear-headedness. However, since 'Pseudo-Acupuncture' again provides similar, if slightly attenuated, changes, it is difficult to interpret these observations as meaningful.

Shifts in concentration (f), whilst decreasing over all conditions, appear otherwise without distinct characteristics.

(c) Δ Score 2:

Very few notable features appear here. Although all conditions display shifts toward elevated spirits (a), it is interesting to observe that 'Genuine Acupuncture' lags behind slightly. The addition of Naloxone provides a pattern consistent with the hypothetical partial antagonism model, by providing greater elevations of mood whilst remaining slightly below the 'Control' and 'Pseudo-Acupuncture' sessions.

Depending upon the observer's implicit assumptions about congruent mood states, the results for dimension (b) may, however, contradict or support the above interpretation, since 'Genuine Acupuncture plus Naloxone' produces the largest shifts towards calm amidst a uniform trend in that direction. This is consistent with dimension (d) which clearly indicates a disproportionate trend towards relaxation in the presence of Naloxone.

Otherwise only expected general shifts across all conditions towards alertness (e) and improved concentration (f) are worth mention, although it is interesting to note that the greatest improvements in concentration also occur with the Naloxone treatment.

In summary it may be said that the results for mood rating scales provide little clearcut information. Perhaps the strongest observation is the tendency for more tension, anxiety, and depressed mood just prior to the insertion of Acupuncture needles, compared to the
'Control' condition. This concern has already been mentioned in section (1)(a)(vi) and chapter 3 and will be discussed further later.

There may be indications of slight calming and relaxing side effects from 'Genuine Acupuncture', but this may simply result from any rhythmic stimulation as it is associated to a lesser extent with 'Pseudo-Acupuncture'.

'Genuine Acupuncture' may also induce rather 'dreamy', 'distant' subjective states, whilst Naloxone, if it has any effect at all, produces shifts indicative of relaxation and calm, contrary to the expected outcome. It may, however, be associated with improved concentration as expected.

(ii) Pain Sensitivity Rating Scales, Stimulation Intensity Rating Scales, and Injection Identification Scores:

Again, given the generally small magnitude of results reported below, and the imprecise nature of the rating procedures, all subsequent observations must be treated as suggestive only.

(a) Intensity of Stimulation Rating Scales:

Scale (a) in section (iii) Appendix 5 Page 476 was scored from 0-10 for intensity of sensations arising from the Acupuncture needles and electrical stimulation for all conditions, except, of course, the 'Control' sessions in which needles were not inserted. The group mean values for each condition appear in the first column of Table 35 Page 402 and the scores indicate both that the stimulation procedures were experienced as relatively intense under all experimental treatment conditions, and that there was close matching of conditions. There is slight evidence of lesser intensity of sensation during 'Pseudo-Acupuncture' compared to the two 'Genuine Acupuncture' treatments, but, as this is no greater than the difference
### TABLE 35: ACUPUNCTURE EXPERIMENT NO 2: Subjective Rating Scales:

Group Mean (n = 16) Pre-Treatment Predictions of Sensitivity Change (Δ), Post-Treatment Estimates of Sensitivity Change (Δ), Stimulation Intensity Ratings, and Injection Identification Success Rate (%), During Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Intensity of Stimulation Score</th>
<th>Pre-Treatment Δ Prediction Score</th>
<th>Post-Treatment Estimate Δ Scores Attributed to Treatment</th>
<th>Attributed to Injection</th>
<th>Injection Identification % Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>N/A</td>
<td>+0.13</td>
<td>+0.22</td>
<td>+0.47</td>
<td>62%*</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>6.16</td>
<td>-0.13</td>
<td>-0.16</td>
<td>+0.41</td>
<td>69%*</td>
</tr>
<tr>
<td>Gen. Ac.</td>
<td>6.63</td>
<td>-0.25</td>
<td>-1.06</td>
<td>+0.03</td>
<td>81%*</td>
</tr>
<tr>
<td>Gen. Ac. + Nal.</td>
<td>7.16</td>
<td>-0.13</td>
<td>-0.13</td>
<td>+0.31</td>
<td>44%</td>
</tr>
</tbody>
</table>

* Correct
between the latter treatments themselves, it may be safely discounted
as a significant source of bias in the pattern of responses to thermal
stimuli during the different experimental treatment conditions.

As a final check, reported intensity of stimulation was tested
for correlation with both the conventional response data (shifts in
median response ratings to the thermal stimuli) and the S.D.T. data
(shifts in discriminability), during each experimental condition.
No significant relationship was found in any case, and indeed all
correlations were extremely low.

(b) Pre-Treatment Prediction of Sensitivity Change Rating Scales:

Scale (b) in section (iii) Appendix \( \leq \) Page \( \geq 76 \) was scored
from +5 to -5 for the subject's prediction of the likely effect of
the stimulation he was currently experiencing upon his pain sensiti-
ity. During the 'Control' condition subjects were asked similarly to
ratethe likely effects of the simple passage of time.

Group mean scores appear in the second column of Table 35
Page \( \leq 02 \) from which several observations may be derived.

First there are slight indications that subjects predicted an
increase in sensitivity as a result of the passage of time without
treatment, in contrast to slight decreases (i.e. predicted analgesia)
associated with all forms of Acupuncture stimulation. The 'Genuine
Acupuncture' condition displays slightly greater prediction of
analgesia than the 'Pseudo-Acupuncture' treatment. This might be
cause for minor concern as a possible non random variable were it not
for the fact that the 'Genuine Acupuncture plus Naloxone' condition
(which was identical in all respects at this point) does not display
a similar pattern. Since, in fact, of the two 'Genuine Acupuncture'

* 5% of maximum possible score.
treatments, it is the 'Genuine Acupuncture plus Naloxone' condition which is associated with the more intense reported stimulation sensations (see first column), the difference in analgesic predictions would appear essentially random and unimportant.

(c) Post-Treatment Estimates of Sensitivity Change Rating Scales, and Injection Identification Success Rates:

Scales (a) and (c) of section (v) Appendix 5 Page 478 were scored +5 to -5 as appropriate for the degree, if any, of observed change in sensitivity which the subject attributed to the needle treatment (or passage of time in the 'Control' condition), and to the injection respectively at the end of the session. Results appear as group mean change values in the third column of Table 35 Page 402. Part (b) of section (v) Appendix 5 Page 478 was simply scored correct or incorrect for identification of the active or inactive injection, and the results appear in column four of Table 35 Page 402, from which the percentage of correct identifications occurring in each experimental condition may be derived.

Under the 'Control' condition subjects reported increased pain sensations attributed partially to the passage of time alone. However, over one third of the subjects incorrectly identified the inert injection as active, and attributed moderate increases to it. In fact, across all conditions, subjects who believed the injection to be active reported its effects as enhancing sensitivity, whilst conversely the effects of all needle treatments were believed to diminish pain sensations.

Within this general pattern, however, some important distinctions between experimental treatment conditions are evident. First, it would appear from column four of Table 35 Page 402 that subjects were at least to some extent able to detect the presence of Naloxone.
Alternatively, in the absence of the sensations* leading to identification of Naloxone, there was a clear bias towards reporting the injection as inert**.

From column three of Table 35 it is clear that 'Genuine Acupuncture' was associated with subjective impressions of reduced pain sensation to a much larger extent than either the 'Pseudo-Acupuncture' or 'Genuine Acupuncture plus Naloxone' conditions. This may reasonably be interpreted as follows. Following the 'Genuine Acupuncture' treatment, subjects detected clear pain reduction without noticeable injection sensations, hence the high treatment attribution score, low injection attribution score, and elevated confidence that the injection was inert. During the 'Genuine Acupuncture plus Naloxone' condition, however, the antagonistic effect of Naloxone upon the Acupuncture treatment would remove or reduce the subjective impression of analgesia, hence the low treatment attribution score. On the other hand, if not completely antagonised by Naloxone, the competing effect of Acupuncture would restrain the subjective impression of increased pain sensation which would otherwise normally occur (see 'Control' condition), hence the slightly lower injection attribution effect compared to the 'Control' and 'Pseudo-Acupuncture' conditions. Thus subjects would fail to detect either analgesic or marked hyperalgesic shifts (despite evidence of ability to identify Naloxone by some other means). This interpretation is entirely consistent with the results of the conventional analysis of response ratings to the thermal stimuli (see Fig. 33 Page 356), where Naloxone is shown

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* See next section (d).

** This is perfectly reasonable as subjects were aware of the 0.75 probability of receiving saline, and were also instructed to carefully evaluate their experiences for possible origin simply from the ambient conditions of the experimental cubicle, lying supine for long periods etc.etc.
largely to reverse analgesia associated with 'Genuine Acupuncture',
but still to provide slightly lesser increases in intensity of
response ratings than the 'Control' or 'Pseudo-Acupuncture' treatments.
The interpretation is also largely consistent with the S.D.T. analysis
of the response data (see Fig. 36 Page 374).

Finally it must, of course, be noted that all the effects
discussed above are extremely small, and hence must remain suggestive
only.

(d) Physical Side-Effect Reports:

Physical side-effect reports during the different experimental
treatment conditions are presented in Table 36 Page 407.

Only one observation is salient, in that Naloxone may be associated
with increased reports of sleepiness. This symptom would appear to be
a major component in the identification of the Naloxone injection as
active by subjects. During the 'Genuine Acupuncture plus Naloxone'
condition, five of the 13 subjects reporting sleepiness directly
associated this with the injection, rated the effect as marked, and
correctly identified the drug as active. The remaining 8 subjects
observed their sleepiness during the Acupuncture stimulation phase of
the session. In contrast, during the 'Genuine Acupuncture' condition,
only one subject reported sleepiness in association with the injection
(which, of course, was inert), whilst the remaining five reported it
as an adjunct of Acupuncture.

* If valid, this apparent effect upon arousal might both directly
influence sensory sensitivity, and affect bias variance leading
to indirect apparent alteration of sensitivity measures.
Furthermore, it must somewhat question the exact matching of the
psychological environment during the second stimulus test series
of the two 'Genuine Acupuncture' conditions.
### TABLE 36: ACUPUNCTURE EXPERIMENT NO 2: Subjective Reports:
Group (n = 16) Total Physical Side-Effects Reported During Different Experimental Treatment Conditions.

<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>Dizzy</th>
<th>Sleepy etc</th>
<th>Nausea etc</th>
<th>Headache etc</th>
<th>Vision + / -</th>
<th>Shaky</th>
<th>Itchy</th>
<th>Dry Salivating</th>
<th>Tingling</th>
<th>Numb</th>
<th>Warm</th>
<th>Cold</th>
<th>Heart Activity</th>
<th>Other Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>8</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>Intoxicated after injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tension in legs</td>
</tr>
<tr>
<td>Pseudo-Ac.</td>
<td>-</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Gen. Ac.</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>-</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&quot;Perspiration&quot;</td>
</tr>
<tr>
<td>Gen. Ac. + Nal.</td>
<td>-</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>
Although the apparent effect of Naloxone reported above was not observed during testing of the drug alone, prior to the start of the study, and is contrary to its anticipated action, the observation may be compatible with some of the other apparently paradoxical indications reported earlier for mood shifts, such as possible relaxing (scale (d) Table 3\, Page 397), calming (scale (b)), and inactivating (scale (c)) effects.

The only other possible physical effects were some dryness of the mouth, and dizziness, associated with 'Genuine Acupuncture'. These effects were all reported during the Acupuncture treatment phase of the sessions, apart from one subject who reported dizziness in conjunction with the injection.

(e) Free Response Section (Structured Interview) (see section (vi) Appendix 5 Page 482):

As might be anticipated, a wide range of different, often contradictory and bizarre, statements were obtained in this section at the end of each session. Therefore only the salient summary trends and impressions will be outlined.

Concentration, motivation, and response consistency and accuracy were all reported as generally well maintained throughout all sessions, although some slight fall off in performance was reported by approximately one third of subjects during the second thermal stimulus series of all needle conditions.

The effect of time passing (treatment interval) during the 'Control' condition was reported as generally stimulating by four subjects and sedating by one, otherwise no effects were observed. Acupuncture was reported as sedating in its overall effect by twice the

* Pseudo-Ac. 10 Sedating 4 Stimulating
Gen. Ac. 10 " 5 "
Gen.Ac.+Nal. 9 " 5 "
number of subjects describing its effects as stimulating, in all three needle conditions. Three subjects in the 'Genuine Acupuncture' condition, and two subjects in the 'Genuine Acupuncture plus Naloxone' condition, described Acupuncture as both stimulating and sedating. Three said a sedatory phase (more predominant) followed an initial stimulatory period, whilst the other two distinguished mental and physical aspects of the effect, one reporting mental stimulation and bodily sedation, and the other the converse. Little, other than the probable sedating effect of rhythmic electrical stimulation, irrelevant of site of application, may be deduced from this data.

The injection was reported as generally sedating by three subjects in the 'Control' condition, and four subjects in the 'Genuine Acupuncture plus Naloxone' condition. It was described as sedating by two subjects, and stimulating by one subject, in the 'Pseudo-Acupuncture' condition, with two subjects opting for each direction of effect in the 'Genuine Acupuncture' condition. Insofar as any comment may be made here, the process of injection alone may induce sedation, although the four sedation versus no stimulation reports in response to the Naloxone injection may indicate some discrimination in view of its association with sleepiness discussed earlier.

Some initial mild anxiety and stress was associated with all Acupuncture procedures, although this was quickly dissolved. Some discomfort, rather than anxiety, was reported several times in connection with obtaining the blood samples, but no problems were associated with the thermal stimuli.

When questioned closely at the end of their final experimental session, only four subjects were able to retrospectively discern qualitative, although not quantitative, differences between the
stimulation sensations resulting from the 'Pseudo-Acupuncture' treatment and the two 'Genuine Acupuncture' treatments. The 'Pseudo-Acupuncture' stimulation was described as sharper, more stinging, and superficial, when compared to the duller, deeper, aching sensations associated with 'Genuine Acupuncture'. These observations were not offered spontaneously, and all four subjects reported that they had not considered these differences until questioned by the experimenter, and were not aware of assuming any different analgesic effectiveness for the treatments during the experimental sessions.

Finally, and most important of all, when advised of the full details of the experimental design, no subject reported any previous awareness, or even suspicion, as to the experimental strategy, employed in the provision of a placebo or 'Pseudo-Acupuncture' treatment as a control condition.

Summary and Conclusions:

Results of this major study of 'Acupuncture analgesia' appear to have confirmed in a most clear-cut manner the majority of the principal hypotheses of the experiment, in addition to confirming the findings of the first experiment, and validating the practicality and applicability of Signal Detection Theory analysis to pain experimentation of this type.

To a very large extent the results speak for themselves. However, some further discussion and summary is appropriate.

* Generally subjects predicted no effect whatsoever, or a mild analgesia, as a result of Acupuncture treatment in all conditions.
The conventional analysis of rating scale response data indicates highly significant reductions in perceived sensory intensities after 'Genuine Acupuncture' compared to all three other experimental treatment conditions*. This strongly confirms both the analgesic effects of Acupuncture beyond those of suggestion or placebo, and their antagonism by Naloxone.

The t-tests for individual stimulus levels show that, although 'Genuine Acupuncture' reduced median response ratings to ALL stimulus levels, this is more likely to represent some form of internal scaling accommodation by subjects than evidence for anaesthetic effects of Acupuncture, since only the three most intense stimulus levels** (associated almost entirely with pain response categories) differed significantly from the 'Control' and 'Pseudo-Acupuncture' conditions.

Having said this, the intriguing, and marked, reduction*** in ratings for stimulus level B (modal response warmth) after 'Genuine Acupuncture' may be complementary to other work (74,77) which has suggested sensory effects of Acupuncture at low intensity stimulus levels. It is also interesting to note that Naloxone did not appear to antagonise this effect of Acupuncture***. Although speculative, it is just possible that Acupuncture has non-Endorphin mediated anaesthetic effects.

* These conditions, in fact, all exhibited increases in intensity of rating responses in the second stimulus series (even including the 'Control' (no-treatment) condition). This may be partly attributable to practice effects (330), local tissue irritation (186), and to the slight elevation of baseline abdominal cutaneous temperature observed in the second stimulus series (38,166,178,250, 472). The latter, fortunately, were well equated across all experimental treatment conditions and, therefore, did not generate artifactual differences.

** In particular the most intense stimulus level.

*** See Fig. 35 Page 362.
Overall the analgesic effects of Acupuncture were significantly antagonised by Naloxone, thus strongly supporting the Endorphin hypothesis. The reversal was almost entirely complete, returning responses to within 12% of 'Pseudo-Acupuncture' levels. This slight residual attenuation, although non-significant, may represent some remaining Endorphin receptor competition. As responses were not returned to 'Control' condition levels there is some confirmation that the modest (non-significant) attenuation of responses achieved by 'Pseudo-Acupuncture' compared to the 'Control' condition may represent a residual psychological response to the stimulation procedures which is unrelated to Endorphin mechanisms.

Results from the S.D.T. analysis suggest that, despite the measure reliability problems encountered with individual subjects during pilot work the method is viable with group data.

The analysis, in all crucial points, confirms the findings of the conventional analysis. 'Genuine Acupuncture' produced highly significant sensory sensitivity decrements compared to all other conditions. The latter three conditions, which did not differ significantly, in fact displayed increased sensitivity after treatment, a finding in line with the increased intensity of sensory-experience suggested by the elevated mean median responses observed for these conditions in the conventional analysis. Such increased sensitivity is by no means peculiar to this study as it has been reported elsewhere and may be attributed to practice effects, or to local inflammatory responses to the radiant-heat stimulation (100,186,330)*.

An important distinction between the S.D.T. and conventional analyses results is, however, evident in the fact that 'Pseudo-

* See discussion in chapter 4.
Acupuncture is actually associated with greater increase in sensory sensitivity than is the 'Control' condition, whereas, in terms of rating scale category responses, attenuated intensity of sensory experience was suggested. It appears that paradoxically subjects responded to the suggestive and placebo qualities of 'Pseudo-Acupuncture' with slightly reduced pain reports when, in fact, their sensory sensitivity may have been elevated (although not significantly) above 'Control' conditions.

It is rather difficult to account for the increase in sensitivity following 'Pseudo-Acupuncture'. One possibility, however, lies in the increased discomfort, arousal, and anxiety, associated with needle insertion and stimulation procedures as indicated by subjective reports from the volunteers in both this experiment and the previous study. Similar effects might well have been observed with 'Genuine Acupuncture' treatments were it not for the sensory decrement resulting directly from the treatment. Indeed, when this effect was successfully antagonised by Naloxone (see Fig. 36), an increment in sensory sensitivity beyond 'Control' condition levels was evident.

This outcome also represents another interesting difference between the S.D.T. and conventional analyses since, although the latter also demonstrated Naloxone antagonism of 'Acupuncture analgesia', pain report patterns still remained lower than those in the 'Control' and 'Pseudo-Acupuncture' conditions. The equally interesting possibility of a hyperalgesic effect of Naloxone must, therefore, be raised.

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* There was evidence for this in Table 29(b) and Fig. 37. See S.D.T. Results section (a)(viii) Page 377.
Either way these comments must remain speculative as the Naloxone induced increment failed to achieve significance for all stimulus level pairs overall, and its antagonism of Acupuncture effects was again incomplete (26% of the difference between 'Pseudo-Acupuncture' and 'Genuine Acupuncture' conditions remaining).

The S.D.T. examination of the effects of Acupuncture at different levels of stimulus intensity provides further information in this connection. It will be recalled from Tables 28 and 29(b) Pages 376 and 378, that the significant differences between 'Genuine Acupuncture' and the other treatments resided in the three most intense stimulus pairs (i.e. predominantly painful stimuli), again suggestive of analgesic rather than anaesthetic mechanisms of Acupuncture.

Naloxone did not completely reverse these effects for the most intense and third most intense stimulus pairs. However, for the second most intense stimulus pair (i.e. for stimuli typically producing milder levels of pain) the drug not only reversed the effects of Acupuncture, but also produced an unparalleled significant elevation of sensitivity, suggesting hyperalgesia.

Since a rather similar pattern was evident for the stimulus pair associated with sensations around the warmth range, there may even have been a trend towards hyperaesthesia. This is, however, contradicted by the lack of Naloxone effect in this sensory range as indicated by the conventional analysis. Although the question is open to debate, the most parsimonious interpretation must firmly place the principal effects of Acupuncture within the nociceptive sensory ranges.

The significant results of this study clearly completely contradict the negative findings of the most directly comparable study by
Clark and Yang 1974(100) despite the many similarities of methodology. It would appear that compensation for the criticisms levelled against their study in chapter 4 and their work may entirely alter the experimental outcome. The results are generally in agreement with the other S.D.T. studies reviewed in chapter 4, although effects here appear more dominant in the higher nociceptive ranges than in some work(74,77).

In common, however, with virtually all experimental studies of Acupuncture (including the first study in this laboratory) the effects upon pain sensitivity are very small in practical terms. Again mild hypalgesia is clearly the most apt description for the phenomenon which, for the subject group as a whole, failed to even decrease mean-median response category ratings for any stimulus level by one complete response category. Clearly this degree of pain relief would be clinically useless, but again the limitations upon the likely magnitude of results to be expected with experimentally-induced pain (as discussed in chapter 3) must be recalled before making such assessments.

The study has provided most important validation of the involvement of endogenous opiates for Acupuncture analgesia in man as suggested by evidence from less well controlled conditions elsewhere (304,305). Antagonism of direct sensory effects of Acupuncture by Naloxone has been confirmed by S.D.T. analysis for the first time, and the finding was supported by evidence for significant increase in oral temperature during 'Genuine Acupuncture' (with partial antagonism by Naloxone) and decline after termination of treatment*. This is

* Similar trends were evident with abdominal (excluding direct stimulus heating effects) and thoracic cutaneous temperatures, although some conflicting elements were present.
entirely consistent with the known peripheral vasodilatory effects of opiates, particularly flushing of the head and neck areas (214)*. The effects of the endogenous agent (β-Endorphin) specifically hypothesised as involved in 'Acupuncture analgesia' (for reasons discussed in chapter 6) on oral, or cutaneous, temperature do not appear to have been reported yet, but, as with morphine, rectal temperature is said to decrease in rats. This again is consistent with the known brain/core compensatory opposition of temperature change (494). Clearly temperature regulation during induction of 'Acupuncture analgesia' in man may be an informative area for further enquiry.

The results of the radioimmunoassay for β-Endorphin levels in the circulation before and after each treatment unfortunately proved entirely inconclusive owing to insufficient sensitivity of the assay in relation to basal peptide levels. The results do, however, at least make it clear that large increases in circulating β-Endorphin were not associated with the observed analgesic effects of Acupuncture in this experiment. There were certain interesting trends which defy proper interpretation within the present state of knowledge. However, in general, either systemic Endorphin release, when endogenously stimulated, is considerably more analgetically potent than is currently assumed, or future Acupuncture research should concentrate on monitoring C.S.F. which has already provided encouraging results (395)**.

* Characteristic dry mouth was also present to some extent during 'Genuine Acupuncture'.

** This is unfortunate since, as in this study, practical and ethical considerations may often preclude such investigation.
It does appear, however, that endogenous opioid peptides other than \( \beta \)-endorphin may be the active agents in the analgesic effects of Acupuncture. In particular, as discussed earlier in Chapter 6, the relative functions of the pentapeptide Met-enkephalin and the larger Endorphins remain unclear, but an extremely recent publication from Clement-Jones et al 1979(497) has demonstrated significant increase in C.S.F. Met-enkephalin following "Electro-Acupuncture". The authors failed to observe similar increase in plasma levels, and, in addition, report unchanged \( \beta \)-endorphin levels, in plasma (thereby replicating the result in this laboratory) and C.S.F.

This implication of Met-enkephalin is surprising in view of the evidence(27,160,443) for its comparative lack of analgesic power, and duration, even when administered intraventricularly. This led to the perhaps incorrect, but reasonable, choice of \( \beta \)-endorphin as the target, and the use of a radioimmunoassay with antibody specificity excluding Met-enkephalin. Clearly the comment made earlier that "this does not, of course, necessarily exclude enkephalins from an important role when endogenously stimulated "may have been more correct than anticipated.
The subjective mood scales were also rather inconclusive in result. In summary, it can only be said that there were consistent indications of anxiety and tension associated with impending Acupuncture needle insertion, and some slight predominance of calming and relaxing effects, and dreamy, distant mood states in association with 'Genuine Acupuncture'. All these observations accord well with the serendipitous findings of the first experiment, and with anticipated sedative effects of opiates and Endorphins as discussed in chapter 6. Naloxone, if it had any effects at all on mood, produced relaxation and calm (quite contrary to expectation), although its association with improved concentration appears logical.

As with the first experiment, subjective rating scales indicated the successful, and vital, matching of Acupuncture stimulation intensity under the different experimental conditions. In addition, stimulation intensity reported by subjects was tested for correlation with analgesic response (conventional and S.D.T.) to treatment in each condition without significant result.

There were no significant differences between pre-treatment predictions of effectiveness for the different conditions, again suggesting equal suggestive potency for the stimulation sensations.

Post-treatment estimates of sensitivity change indicated some ability of subjects to discern analgesic effects associated with 'Genuine Acupuncture'. More important, however, was the tentative indication of some ability to identify the active injection Naloxone, when administered. The likely derivation of this ability has already

* It should be noted that these predictions were obtained after commencement of Acupuncture stimulation.
been fully discussed in sections (5)(ii)(c) and (d) above, but it appears likely that, in addition to possible detection of anti-
analgesic action directly, the drug may also have been associated with the completely unexpected, and previously unreported, side-effect of slight sleepiness. Although when given alone during pilot work, no discernible side-effects were noted (in line with evidence in the literature\(^{214}\)), it is possible that sleepiness may result from its administration in the presence of abnormally elevated Endorphin levels. However contradictory this may be to normal clinical observations with opiates, or to logically predicted arousing effects, it could also explain some of the other rather paradoxical mood shifts towards relaxation, calm, and inactivity, possibly noted in association with the drug earlier (see Table 34 Page 347).

Finally, however, it must be said that all these indications are extremely tentative, and very probably overemphasized given the present complete absence of similar findings from any studies using Naloxone in conjunction with Acupuncture. Nonetheless, it does seem important to mention this potential control problem since, although it would obviously be more critical in a conventional study of 'Acupuncture analgesia', it is also possible that such a general effect on arousal might both directly influence sensory sensitivity, and affect bias variance (leading to indirect apparent alteration of sensitivity measures) in the S.D.T. experiment. However, within the present minimal state of knowledge concerning Naloxone in relation to Acupuncture, it would seem quite unreasonable to dismiss the antagonistic action of the drug as observed in this experiment on such flimsy grounds. As far as attitudinal factors are concerned, even if subjects
were able to detect the active injection, they were not in possession of any information which should suggest an enhancing rather than inhibiting effect upon pain sensitivity. In addition, there was no indication whatsoever of such speculation from interview reports obtained from subjects at the end of the sessions.

Finally, it should be noted that the post-experimental interviews also confirmed both the subjective equality of needle stimulation in the different experimental conditions, and the complete maintenance of the 'Pseudo-Acupuncture' blind control.

Two final negative findings from the study deserve mention. Neither EPI personality dimension of extraversion or neuroticism appeared to correlate in any significant manner with baseline pain report patterns (conventional analysis) or sensory sensitivity (S.D.T. analysis), or with the response to Acupuncture, 'Pseudo-Acupuncture', or Naloxone. This is disappointing in view of evidence reviewed in Chapter 5, but may simply reflect the limitations of the subject sample.

Finally, although consistent baseline trends towards reports of more intense sensory experience were evident for females, (consistent with their lower thresholds and tolerances in the first experiment) none of the variables examined exhibited significant sex-related differences.
Concluding Comments

The results of the two experimental investigations of "Acupuncture analgesia" reported here appear entirely consistent and complementary.

It is clear that, although Acupuncture procedures have suggestive and placebo effects upon pain responses, a significant and replicable additional attenuation of noxious sensation is produced. These effects extend across a wide range of painful sensation from the just perceptible to the just tolerable, and may extend well beyond the period of Acupuncture stimulation.

S.D.T. analysis of the data, and the observed localisation of sensitivity reduction, demonstrate that at least two Acupuncture "points" may have specific sensory effects, in addition to indications of more general effects on arousal and other components of the "response to pain".

The evidence presented suggests that Acupuncture may have effects at many levels in the nervous system. Particularly implicated, however, is the release of a humoral agent, or agents, with opiate-like characteristics; and the exciting possibility of regional specificity is raised.

Certain limitations must, however, be placed upon interpretation of the results presented here. First, both of the studies must be considered almost entirely behavioural in their level of observation, rather than anatomical, neurophysiological, or biochemical. Chapter
six has already provided a detailed review and discussion of studies conducted in other laboratories employing types of scientific investigation suitable to elucidate the likely structures and processes substantive to "Acupuncture analgesia". Although the results of the studies conducted here, and indeed the evolution of the experimental hypotheses and methodology, have been discussed in the context of these possible substrates, the conclusions drawn must inevitably be considered only inferential. The primary goal throughout this investigation has been the establishment, or refutation, of "Acupuncture analgesia" as a behavioural phenomenon.

Secondly, it did not prove possible to include a controlled clinical trial as part of this investigation. Cogent arguments were presented in earlier chapters for the necessity of employing the experimental pain paradigm, despite its discussed limitations, in order to apply sufficiently rigorous methodologies. With this, the perennial problem of questionable applicability to the clinical field has been incurred. Although review of clinical studies, and comparison of data with clinical observations, has appeared in many parts of the text, it is, of course, obvious that the stimulus and response instruments employed were abstractions generating findings which may have little validity for pathological pain.
It is clearly impossible, and pointless, to extrapolate upon what significant percentage changes in "Pain Thresholds" or "sensory sensitivity" might mean in the clinical situation.

For what it is worth, however, the feeling of this author, although admittedly without direct clinical experience, is that the analgesic potency of Acupuncture may be rather slight, and it is unlikely to supplant conventional western treatments in its present stage of development. Its true potential may be as a research tool for the investigation of pain mechanisms, particularly in the continual search for non-addictive analgesic agents, less prone to the development of tolerance and undesirable side effects during chronic administration.

In addition, however, given the present vast array of unsynthesised, and often paradoxical or conflicting, evidence from atomistic approaches to pain research, a more immediately practical concern may be the development of techniques inducing activation of complete endogenous antinociceptive systems, (particularly if discrete regional effects are possible) which may prove more effective than any products of the current emphasis upon identification of isolated antinociceptive agents or mechanisms.
The wide ranging effects of Acupuncture, and absence of associated problems or complications, noted in this report, suggest that it may provide (with further research) just such access to major complementary systems in a manner more congruent with normal functioning and homeostatic mechanisms.

To this end, this investigation of Acupuncture has concentrated to a fully equal extent upon the development, and presentation, of more optimal techniques of pain measurement and assessment, which may provide a model for subsequent work on this, or similar, analgesic techniques. It is thereby hoped that, by the provision of a complete and logically justified methodology of demonstrated efficacy (with provision of complete stimulus-response system and detailed calibration information) to promote some standardisation of experimentation techniques in this area, and thus permit a direct comparability of results which is currently lacking from the multifarious, and often ad hoc, methods reported in the literature to date.

It is suggested that important initial applications of the methodology might be directed towards examining the possibilities of development of dependence or tolerance with Acupuncture, or of Acupuncture cross-tolerance with Morphine or the Endorphins.

It is also hoped that applications of S.D.T. methods and analysis similar to those presented here may see increasing extension into many other areas of pain experimentation.
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**ADDENDUM**


GENERAL MEDICAL QUESTIONNAIRE

NAME: ........................................

AGE: ........................................

SEX: ........................................

OCCUPATION: ................................

DATE: ........................................

PLEASE COMPLETE THE FOLLOWING MEDICAL CHECKLIST AS CAREFULLY AS POSSIBLE. IT IS ESSENTIAL THAT YOU DO NOT OMIT TO MENTION ANY PHYSICAL WEAKNESS OR ILLNESS WHICH YOU HAVE NOW OR HAVE SUFFERED IN THE PAST. PLEASE PAY PARTICULAR ATTENTION TO QUESTIONS 16 to 19.

PLEASE INCLUDE ANYTHING YOU THINK RELEVANT IN QUESTION 20 AND DO NOT HESITATE TO ASK QUESTIONS.
GENERAL MEDICAL QUESTIONNAIRE

PLEASE MARK YOUR ANSWER BY PLACING AN 'X' IN THE APPROPRIATE BOX:

1. (a) Have you at any time suffered from pain or tightness in your general chest area? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.

2. (a) Have you at any time suffered from a chronic cough? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.

3. (a) Have you at any time suffered from prolonged severe vomiting attacks? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.

4. (a) Have you at any time vomited blood? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.

5. (a) Have you at any time suffered severe prolonged abdominal pain? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.

6. (a) Have you at any time suffered from prolonged diarrhoea or constipation? YES [ ] NO [ ]
   (b) If yes! Please give details including recency, severity, and known cause, if any.
7. (a) Have you at any time suffered prolonged periods of bladder control problems?

(b) If yes: Please give details including recency, severity, and known cause, if any.

8. (a) Have you at any time suffered from prolonged severe headaches?

(b) If yes: Please give details including recency, severity, and known cause, if any.

9. (a) Have you at any time suffered from periods of fainting, blackouts or fits?

(b) If yes: Please give details including recency, severity, and known cause, if any.

10. (a) Have you at any time suffered from dizzy spells?

(b) If yes: Please give details including recency, severity, and known cause, if any.

11. (a) Have you at any time suffered from periods of blurred vision?

(b) If yes: Please give details including recency, severity, and known cause, if any.

12. (a) Have you at any time suffered from periods of numbness or of pins and needles in your arms or legs?

(b) If yes: Please give details including recency, severity, and known cause, if any.

13. (a) Have you suffered from any serious physical illness at any time in the past?

(b) If yes: Please give details including recency, severity, and known cause, if any.
14. (a) Have you at any time in the past undergone, or are you due to undergo, any operation?  
(b) If yes! Please give details of condition being treated, approximate date in past or future, and outcome of operation.

15. (a) Have you just finished, or are you currently taking any drugs, tablets, or medication of any kind?  
(b) If yes! Please give details including type of drug, source of supply and reason for taking them.

16. (a) Have you at any time suffered from any type of skin disease or other skin problem?  
(b) If yes! Please give details including disease or problem, recency, severity, and known cause, if any.

17. (a) Would you say that your skin is either unusually sensitive or unusually insensitive to PAIN, HEAT or TOUCH?  
(b) If yes! Please give details, stating your reasons for thinking this.

18. (a) Would you say that your sensitivity to PAIN, HEAT or TOUCH varies from day to day?  
(b) If greatly! Why do you think this and which of pain, heat or touch sensation is most affected?

19. (a) Have you at any time experienced physical problems or anxiety associated with injections?  
(b) If yes! What kind of problems or anxieties?
20. (a) Are there any other details of your medical history which you feel might be relevant? 

(b) If yes! Please give details including recency, severity, and known cause, if any.

21. Are you pregnant?

Experiment No 2 only

22. Can you confirm that you have not taken any narcotic drug (including cannabis or hashish) in the last 2 months?

23. Can you confirm that you are in no way physically dependent upon any narcotic drug?
I, the undersigned, voluntarily consent to take part in the experiment outlined below as a 'subject'. The meanings of any technical terms used below have been explained to me and they are clearly understood by me. In addition, the nature of all the procedures to which I will be subjected has been clearly demonstrated practically, and explained. No coercion whatsoever has been used to obtain my consent to participate in the experiment, and I understand that I may withdraw at any time during the experimental series, although, of course, this cancels my right to payment.

I understand that whilst every possible safeguard has been taken (these have been demonstrated to me) to ensure that I sustain no injury during the experiment, should such injury occur, neither Mr Duncan Stewart, the University of Edinburgh, nor the Royal Edinburgh Hospital may be held in any way responsible.

I certify that I am not currently a student at Edinburgh University.

The experiment will involve the placement of six 12 volt bulb units acting as heat stimuli on my skin surface at the following locations. The ventral surface of the left upper arm and dorsal surface of the right forearm. The anterior surface of the left lower leg and the anterior surface of the right thigh, a few inches above the knee. The upper abdominal region, and the central upper chest area.

The heat units will be activated at regular intervals during the experiment to provide the required painful stimulation, and will be
cancelled when my maximum tolerable pain level is reached, by means of a switch under my control. I understand that I am not required to endure great pain, but simply to tolerate a consistent intensity of pain before switching off the heat. I understand that safety cut-outs have been installed to prevent any accidental tissue damage. I also understand that sterilised Acupuncture needles will be inserted in any, or all, of the following antiseptically prepared body sites.

1. In the region of the skin web between the thumb and index finger. Needles will be inserted in both hands to a depth of up to 1.0 inch. **Technical description** - Midway between the junction of the first and second metacarpal and the fold, slightly towards the index finger.

2. In the region just below the bony protruberance beneath the knee cap and slightly towards the outer side of the leg. Needles will be inserted in both legs to a depth of up to 1½ inches. **T.D.** - Approximately 3 cm. (1 Body inch*) distal and lateral to the tibial tubercle (tuberosity).

3. In the region of the frontal upper thigh, well towards the side of the leg, and just over one third of the way towards the knee from the hip bone. Needles will be inserted in both legs to a depth up to 1.0 inch. **T.D.** - Approximately 8-9 cm. (3 Body inches*) distal from the Greater Trochanter, and slightly lateral of a line from the lateral extremity of the Greater Trochanter to the lateral border of the Patella.

4. In the region of the upper arm, a little below the tip of the shoulder and slightly towards the front. Needles will be inserted in both arms to a depth of up to 1.0 inch.

* All measurements refer to 'body inches', i.e. distance between joint creases of the interphalangeal joints of subject's middle finger when flexed.
T11E. - Approximately 7-8 cm. (2½ Body inches*) directly distal from the centre tip of the Acromion and 1.5 cm (0.5 Body inch*) anterior.

5. Any other similarly prepared body site to which I may agree as indicated by my continued participation in the experiment.

It is also understood that electrodes will be attached to the inserted needles and a small electrical pulse delivered from a 6 volt battery stimulator unit. Current will be passed for several periods of up to 10 minutes each during an experimental session. I understand that the intensity of stimulation will be adjusted under my instruction to ensure comfortable levels, but that mild involuntary muscular twitching may be present.

I also agree to the requirement that I should refrain from discussing any aspect of the experiment, with anyone, until the study is completed.

Signed ................................ Witness ..............................
Date  .................. Date  .....................
Address  .........................
.....................................
Introduction

The experiment for which you have volunteered is designed to test the Chinese claims, which you may have seen reported in the media, that the insertion of Acupuncture needles into the body can produce changes in sensitivity to pain. On a scientific basis, these claims are, as yet, entirely unsubstantiated. What evidence we have is ambiguous since some investigation has shown a reduction in sensitivity to pain, some no change at all, and some studies have even shown increased sensitivity to pain following Acupuncture. Pain sensitivity can also vary spontaneously from moment to moment, and day to day, without any treatment at all.

For these reasons, and since you have already indicated that you have no special knowledge of Acupuncture, we suggest that you keep an open mind as to whether there will be an effect or not. Do not especially try to predict or monitor your sensitivity to pain, just concentrate on reporting what you feel accurately and consistently, as instructed below.

Procedure

1. Pain Stimulation and Responses:

As you have already seen in the previous demonstration session, the procedure is really quite simple.

The six small heat units will be attached to various parts of your body as before. They are very quickly and easily removed, simply by pulling, as demonstrated earlier. You will be advised by the experimenter as to when a trial is about to begin and you should then concentrate on detecting the first feelings of warmth from one of the heat units.
You will not be able to predict which heat unit will be activated first, exactly when it has been activated, or in what order the other heat units will subsequently be activated, since this is all controlled by a random programmer. Do not, therefore, spend time trying to work things out, just concentrate on what you 'feel' and wait for the first detectable sensations.

Once you detect warmth at one of the test sites on your body, concentrate your attention there. The sensation will gradually increase in strength through hot, and very hot, until the heat suddenly focuses down to a small point accompanied by a sharp pricking sensation. IMMEDIATELY you 'feel' this sensation, push your LEFT HAND button (green) with your little finger as you were shown before. We define this point as your 'Pain Detection Threshold'.

After this point the sensations will be slightly painful, and will become increasingly painful as time passes. As soon as you reach a level of pain which you feel you could not continue to tolerate for any longer, then push your RIGHT HAND button (red) IMMEDIATELY. This will switch off the heat stimulation unit immediately; but do not be alarmed if you still experience some pain for a very brief moment longer after pressing the button, as it takes your skin and the device a moment to cool down adequately.

It is emphasised strongly that THIS IS NOT A TEST OF ENDURANCE - DO NOT TRY TO BE HEROIC. All that is required is that you decide upon an intensity of pain, beyond which you are not prepared to tolerate, and CONSISTENTLY stick to it each time a stimulus is presented, at any part of the body, and throughout the whole experiment. We define this point as your 'Pain Tolerance'. It does not matter what subjective method you use to decide upon this point, or how brave or cowardly you are. What is vital, is that you are CONSISTENT in the amount of pain you tolerate.
Do not worry if it seems to take a long time before you feel the need to press the 'Pain Tolerance' button: safety timer cut-outs will automatically deactivate the heat units, if necessary, to avoid skin damage.

Do not attempt to time yourself or count in any way to establish either your 'Pain Detection Threshold', or 'Pain Tolerance' points. Just rely entirely on what you feel!

Remember:

'Pain Detection Threshold' then 'Pain Tolerance'

(heat focuses to a point then pricking sensation) (maximum tolerable pain)

LEFT BUTTON RIGHT BUTTON

Note: A display on the ceiling above you in the experimental room will remind you of the button functions.

There will be a 15 second interval between termination of one heat unit and activation of the next. Just relax and rest during this period rather than worry about which unit will be next etc. Once all body sites have been tested, there will be a ten minute interval until the next trial during which relaxing music will be played. You will be advised, over the intercom, of the beginning of a new trial. There will be a minimum of four, and a maximum of eight, trials in the experimental session. You will not be advised of the number in advance of, or during, the experiment, and please do not spend time trying to guess the number, as again this is a random factor.

Please advise the experimenter immediately if any of your body test sites remain painful during the interval between heat trials.

2. Acupuncture:

In two of the three experimental sessions, 4 Acupuncture needles will be inserted in body sites, and stimulated electrically for approximately 35 minutes, as already demonstrated. All you are required to do is indicate sites of maximum sensitivity or tenderness during probing.
for Acupuncture 'points', and ensure that the level of electrical
stimulation is maintained as high as possible without undue discomfort
or any pain. A slight twitching of the muscles is quite normal, and
remember, the level of stimulation is entirely under your control at
all times. You should avoid sudden and extensive movement whilst
needles are in place, as this may cause discomfort and bend needles.

3. Subjective Rating Scales:

These simple rating scales are largely self-explanatory, and
have already been shown to you. They do, however, require some care
and thought, so remember a few points.

First, there are no right or wrong responses; it is entirely
what you 'feel' at the time which should be expressed. Do not tend to
mark in the middle to 'play safe', or feel frightened to express your
feelings strongly by marking well along the lines. Conversely, do not
feel obliged to say you anticipate, feel, or felt any effect from the
Acupuncture if this is not the case. Remember the whole phenomenon is
still wide open to question either way.

Do not attempt to remember where you mark the lines each time,
just to mark the same point later for consistency. It is quite possible
that your feelings and sensations may vary during the experiment, and
you should simply use your intuition to mark the lines at the point
which best reflects your state at that moment, without trying to
remember where you marked before.

Please note: It is vital for your continued participation in the
experiment that you do not discuss ANY aspect of the study with ANYONE
other than the experimenter until it is fully completed.

Thank you for your interest and participation in this experiment. Your
assistance is valuable and greatly appreciated. Your sustained care and
concentration when making responses throughout the study will contribute
very greatly towards making the work worthwhile.
ACUPUNCTURE
EXPERIMENT NO 2

EXPERIMENTAL CONSENT FORM

I, the undersigned, voluntarily consent to take part in the experiment outlined below as a 'subject'. The meanings of any technical terms used below have been explained to me and they are clearly understood by me. In addition, the nature of all the procedures to which I will be subjected has been clearly practically demonstrated and explained. No coercion whatsoever has been used to obtain my consent to participate in the experiment, and I understand that I may withdraw at any time during the experimental series, although, of course, this cancels my right to payment.

I understand that whilst every possible safeguard has been taken (these have been demonstrated to me) to ensure that I sustain no injury during the experiment, should such injury occur, neither Mr Duncan Stewart, the University of Edinburgh, nor the Royal Edinburgh Hospital may be held in any way responsible.

I certify that I am not currently a student at Edinburgh University.

---

I understand that the experiment will consist of 4 experimental sessions all on separate days. I will be required to attend at the University Department of Psychiatry, Royal Edinburgh Hospital, for a total of approximately 8 - 9 hours for which I will be paid £30.

During each session a series of 108 radiant heat stimuli will be administered to me during the first approximately twenty minutes, and again during the last approximately twenty minutes of the session.

I understand and accept the nature of the apparatus and stimuli, and I am satisfied that the levels of painful stimuli will be acceptable.
to me, and that the safety factors which allow me to withdraw from, or terminate the stimuli by means of a push-button under my control, are adequate.

I understand that, with regard to the most intense stimulus level, I am not required to endure great pain but simply to tolerate a consistent intensity of pain before terminating the heat stimulus.

I understand also that 12 small areas on my abdomen will be blacked with stage make-up. This should not prove irritative to my skin, but I accept that this cannot be guaranteed.

I understand that I will receive one intravenous injection during each experimental session. On three occasions the substance will be inert, on the other occasion I will receive a small amount, within normal clinical dosages, of a drug affecting the central nervous system. I understand, however, that I am very unlikely to discern any effect of this drug. Side-effects are also considered very unlikely although this cannot be guaranteed.

I confirm that I have not recently taken any narcotic drugs, and that I am in no way physically dependent upon such drugs.

I also understand that, on three of the experimental sessions, a total of four sterilised acupuncture needles will be inserted, by a physician trained in their use, at any of the following antiseptically prepared body sites.

1. Two different sites in the region of the skin web between the thumb and index finger. Needles will be inserted in both hands to a depth of up to 1.0 inch. Technical description – Midway between the junction of the first and second metacarpal and the fold, slightly towards the index finger.
2. Two different sites in the region just below the bony protruberance beneath the knee cap, and slightly towards the outer side of the leg. Needles will be inserted in both legs to a depth of up to 1½ inches. T.D. - Approximately 3 cm. (1 Body inch*) distal and lateral to the tibial tubercle (tuberosity).

3. Two different sites in the region of the frontal upper thigh, well towards the side of the leg, and just over one third of the way towards the knee from the hip bone. Needles will be inserted in both legs to a depth up to 1.0 inch. T.D. - Approximately 8-9 cm. (3 Body inches*) distal from the Greater Trochanter, and slightly lateral of a line from the lateral extremity of the Greater Trochanter to the lateral border of the Patella.

4. Two different sites in the region of the upper arm, a little below the tip of the shoulder and slightly towards the front. Needles will be inserted in both arms to a depth of up to 1.0 inch. T.D. - Approximately 7-8 cm. (2½ Body inches*) directly distal from the centre tip of the Acromion and 1.5 cm (0.5 Body inch*) anterior.

5. Any other similarly prepared body site to which I may agree as indicated by my continued participation in the experiment.

It is also understood that connections will be made to the inserted needles and small adjacent surface electrodes, and a small electrical pulse delivered from a 6 volt battery stimulator unit. Current will be

* All measurements refer to 'body inches', i.e. distance between joint creases of the interphalangeal joints of subject's middle finger when flexed.
passed for a period of just over 40 minutes during an experimental session. I understand that the intensity of stimulation will be adjusted under my control to ensure comfortable levels, but that I may experience involuntary muscular twitching.

I also understand that two small samples of venous blood will be taken during the course of every experimental session.

Finally, I agree to the requirement that I should refrain from discussing any aspect of the experiment, with anyone, until the study is completed.

Signed .......................... Witness ..........................

Date  ................. Date  .................

Address  .......................... ..........................

........................................

........................................
ACUPUNCTURE EXPERIMENT NO. 2:
QUESTIONNAIRES AND SUBJECTIVE RATING SCALES:

(i) Pre-Session Assessment Questionnaire:

NAME ........................................
SEX ............

Do not Write in this Box
Code No .......... Date ........
Group ........... Time ........
Session ........ Special
Conditions

IMPORTANT: Please give details of the following:

(a) Any medicines or drugs you have taken AT ALL since you last attended. Include everything whether prescribed by a doctor, purchased from a chemist, or obtained otherwise. In particular mention PAIN KILLERS, tranquillisers, sedatives, sleeping pills, stimulants, social drugs etc. (This information is entirely confidential.)

(Blood samples will be taken during the experiment)

(b) Any illness or physical problem you may have, or had, since your last visit.

(c) Any heavy drinking period since your last visit.

(d) Any unusually stressful events and periods, or anxieties which you have experienced since your last visit.

Women only:

(e) Any change in your oral contraception regimen.
(ii) Mood Rating Scales:

Instructions:

Please indicate your responses to the statements below by marking the appropriate point on the line with a cross (x). Remember, there are no right or wrong responses, simply indicate what you believe or feel. Do not put "normal" or "about the same as before" if you really think you feel different. Likewise do not feel that you should necessarily feel in the slightest bit different if you do not. Do not worry if some of your feelings seem inconsistent with others.

Compare to how I normally feel, most of the time, my mood and spirits are at present:

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(f) About Normal

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<td>than usual</td>
<td>than usual</td>
<td></td>
</tr>
</tbody>
</table>

Other comments, special circumstances etc. ..........................................................

..........................................................

..........................................................
(iii) Stimulation Potency Rating Scales:

(a) Sensations arising from the Acupuncture needles and electrical stimulation are:

Hardly Detectable | Very Powerful

Please describe the sensations briefly ..........................................
................................................................
................................................................
Other comments, special circumstances etc ..................................
................................................................

(b) As a result of Acupuncture stimulation/the passage of time* my stomach WILL become:

LESS sensitive to Pain | About Normal | MORE sensitive to Pain

Other comment on details of the effect (if any), special circumstances etc ..................................
................................................................

* Deleted in all sessions except 'control' session where alternative was deleted.
(iv) Mood Rating Scales:

Compared to how I felt when I rated my mood and spirits the last time I NOW feel:

(Do not worry if some of your feelings seem inconsistent with others)

(a)

About the same
as before

More

DEPRESSED
than before

More

ELATED
than before

(b)

About the same
as before

More

CALM
than before

More

ANXIOUS
than before

(c)

About the same
as before

More

INACTIVE
than before

More

RESTLESS
than before

(d)

About the same
as before

More

RELAXED
than before

More

TENSE
than before

(e)

About the same
as before

More

CLEARHEADED

SHARP, AWARE

OF THINGS
than before

More

DREAMY,

DISTANT

UNAFFECTED

BY THINGS
than before

(f)

About the same
as before

More

UNABLE TO

CONCENTRATE
than before

More

ABLE TO

CONCENTRATE
than before

Other comments, special circumstances etc........................

........................................................................

........................................................................
(v) Post-Treatment Rating Scales:

(a) As a result of Acupuncture stimulation/the passage of time*, my stomach became:

<table>
<thead>
<tr>
<th></th>
<th>About Normal</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Less</td>
<td></td>
<td>More</td>
</tr>
<tr>
<td>sensitive to Pain</td>
<td></td>
<td>sensitive to Pain</td>
</tr>
</tbody>
</table>

Other comment on details of the effect (if any), special circumstances etc

(b) I believe that the injection I received was of a substance which was

[ ] Inactive  [ ] Active

Put a cross (x) in the appropriate box.

State the reasons for your belief

Other comment, special circumstances etc

(c) As a result of the injection my stomach became:

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<thead>
<tr>
<th></th>
<th>About Normal</th>
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<tr>
<td>Less</td>
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<td>More</td>
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<tr>
<td>sensitive to Pain</td>
<td></td>
<td>sensitive to Pain</td>
</tr>
</tbody>
</table>

Other comment on details of the effect (if any), special circumstances etc

* Deleted in all sessions except 'control' session where alternative was deleted.
(v) continued ...

(d) Compared to how I felt when I rated my mood and spirits the last time I NOW feel:
(Do not worry if some of your feelings seem inconsistent with others)

<table>
<thead>
<tr>
<th>(a)</th>
<th>More</th>
<th>About the same</th>
<th>More</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DEPRESSED</td>
<td>as before</td>
<td>ELATED</td>
</tr>
<tr>
<td></td>
<td>than before</td>
<td>than before</td>
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<tr>
<th>(b)</th>
<th>More</th>
<th>About the same</th>
<th>More</th>
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<tbody>
<tr>
<td></td>
<td>CALM</td>
<td>as before</td>
<td>ANXIOUS</td>
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<tr>
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<td>than before</td>
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<th>More</th>
<th>About the same</th>
<th>More</th>
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<tbody>
<tr>
<td></td>
<td>INACTIVE</td>
<td>as before</td>
<td>RESTLESS</td>
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<td></td>
<td>than before</td>
<td>than before</td>
<td></td>
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<th>More</th>
<th>About the same</th>
<th>More</th>
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<tbody>
<tr>
<td></td>
<td>RELAXED</td>
<td>as before</td>
<td>TENSE</td>
</tr>
<tr>
<td></td>
<td>than before</td>
<td>than before</td>
<td></td>
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<th>(e)</th>
<th>More</th>
<th>About the same</th>
<th>More</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CLEAR-, HEADED, SHARP, AWARE OF THINGS</td>
<td>as before</td>
<td>DREAMY, DISTANT, UNAFFECTED BY THINGS</td>
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<tr>
<td></td>
<td>than before</td>
<td>than before</td>
<td></td>
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<tr>
<th>(f)</th>
<th>More</th>
<th>About the same</th>
<th>More</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>UNABLE TO CONCENTRATE</td>
<td>as before</td>
<td>ABLE TO CONCENTRATE</td>
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<td>than before</td>
<td>than before</td>
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If you have experienced any changes in mood or spirits during the session, would you attribute this to:

The Acupuncture  The Injection  A Combination of both

[ ] or [ ] or [ ]

or Other [ ]

Put a cross (x) in the appropriate box.

State the reasons for your belief ..........................................................

.................................

Other comments, special circumstances etc .................................

.................................
(vi) Post-Experimental Structured Interview:

Did you, at any time during the session, experience any of the physical effects listed below? If your answer is 'YES' put an X in the appropriate box and indicate below at what point during the session you first noticed the effect. Also, describe the sensations and indicate their duration (approximately) and their severity. Please consider whether any sensation you noticed is genuinely unusual, or might result simply from the physical environment of the experiment.

<table>
<thead>
<tr>
<th>Effect</th>
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<th>NO</th>
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<tr>
<td>Dizziness</td>
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<tr>
<td>First noticed (description)</td>
<td></td>
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<tr>
<td>Duration</td>
<td></td>
<td></td>
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<tr>
<td>Severity</td>
<td></td>
<td></td>
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<tr>
<td>Sleepiness, tiredness or drowsy feelings, heavy eyes, head or limbs</td>
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<tr>
<td>First noticed (description)</td>
<td></td>
<td></td>
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<tr>
<td>Duration</td>
<td></td>
<td></td>
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<tr>
<td>Severity</td>
<td></td>
<td></td>
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<tr>
<td>Nausea, or discomfort in the stomach</td>
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<tr>
<td>First noticed (description)</td>
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<tr>
<td>Duration</td>
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<td></td>
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<tr>
<td>Severity</td>
<td></td>
<td></td>
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<tr>
<td>Headache, or pressure and tightness in head or neck</td>
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<td></td>
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<tr>
<td>First noticed (description)</td>
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<tr>
<td>Duration</td>
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<td></td>
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<tr>
<td>Severity</td>
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<td></td>
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<tr>
<td>Difficulty in focusing and reading</td>
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<tr>
<td>Severity</td>
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<tr>
<td>Shakiness (other than as a result of electrical stimulation of needles)</td>
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<tr>
<td>First noticed (description)</td>
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<tr>
<td>Duration</td>
<td></td>
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<tr>
<td>Severity</td>
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<table>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<tr>
<td>Severity</td>
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<tr>
<td>Dry mouth or excessive salivation</td>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<td>Severity</td>
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<tr>
<td>Tingling and/or numbness</td>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<td>Severity</td>
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<tr>
<td>Feeling unusually Warm or Cold</td>
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<td>(other than on your abdomen)</td>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<tr>
<td>Severity</td>
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<tr>
<td>Increased heart activity or palpitation</td>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<tr>
<td>Severity</td>
<td></td>
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<tr>
<td>Any other effect not listed above</td>
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<td>First noticed (description)</td>
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<td>Duration</td>
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<tr>
<td>Severity</td>
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</tbody>
</table>
(vi) continued ...

FREE RESPONSE SECTION

Mentation (concentration, motivation, consistency and accuracy etc)

Stimulation/Sedation

Mood (elevated/depressed etc)

General Responses to and evaluation of elements of experiment
(Acupuncture sensations, electrical stimulation, needle placement, injections, blood samples, pain stimuli etc. Effectiveness, pleasantness, stress, confusion, accuracy, consistency, awareness of experimental strategy, extraneous factors of relevance to responses)
APPENDIX

ACUPUNCTURE

EXPERIMENT NO. 2

INSTRUCTIONS TO SUBJECTS

Please read these instructions very carefully - even if you feel you are already fully familiar with all the details of the experiment. Ask the experimenters any questions you wish until you fully understand and remember everything you will be required to do in the experiment.

Introduction

The experiment in which you are about to participate is concerned with some of the recent claims made that Acupuncture can alter your sensitivity to painful stimulation. Some points on the body, when needled, have been reported to make one less sensitive to pain, others to make one more sensitive to pain, whilst others may have no effect at all. You should not therefore predict that there will be changes in any particular direction, and would be safest to assume that no change at all will occur.

All the procedures described below will be exactly as demonstrated in your training session. Nonetheless, please study the instructions below with care.

Procedure

1. Pain Stimulation and Responses:

During the coming session a great variety of different intensities of heat will be applied to the spots marked on your abdomen. All you have to do is choose the description from the list above you which best describes the strongest sensation you feel as a result of the stimulus.

As you know, the shutter on the apparatus opens for three seconds each time (unless you push the cut-out button). The illuminated
indicator board above you will tell you the precise moments when the shutter opens and closes. As soon as the 'shutter open' light comes on, concentrate very hard on your abdominal area, and monitor the sensations there. You should describe the most intense sensation you feel by the time the shutter closes. For example, a strong stimulus might make the test site feel 'Warm' after one second of exposure, 'Very Hot' after two seconds, and finally reach 'Painful' just as the shutter closes. You should report 'Painful', and ignore the previous sensations.

Immediately the shutter closes, the illuminated indicator board will instruct you to 'Rate Sensation Now'. Whilst you will have plenty of time (7 sec.) to give your rating, and you should not feel rushed, do not delay your response too long as you will very quickly forget what the sensation was like.

Try to establish, and hold, in your mind, a particular consistent sensation which relates to each of the rating categories. In other words decide for yourself what type, and intensity, of sensation you will call 'Faint Pain' etc, and every time you feel a similar sensation give that report.

Although there are no right or wrong responses, and you should simply report what you feel, here is some guidance as to how to locate the response categories:

(a) Look for a sensation where the heat appears to build up, and then quickly focuses down to a small point, followed by a sharp pricking sensation just before the shutter closes. Take this sensation as the dividing line between no pain and pain. If you do not feel this sensation at all, and there is clearly no definite pain, you should be using one of the categories from 'Nothing' to 'Very Hot'. If you just feel the sensation and nothing stronger by the time the shutter closes,
use the 'Very Faint Pain' category. If the sensation comes more quickly, and/or you feel quite definite pain, you should use one of the more intense descriptions as appropriate.

(b) With regard to the most painful sensations, please remember the following points. First THIS IS NOT A TEST OF ENDURANCE - DO NOT TRY TO BE HEROIC. You have a stimulus 'cut-out' button under your right hand which you can use whenever the pain becomes too strong. It does not matter what subjective method you use to decide on this point, or how brave or cowardly you are. What is vital is that you are CONSISTENT in the amount of pain you tolerate. If you press the button you should also give the verbal response 'Withdraw' as indicated on the board above you.

Despite the comments above, you should also bear in mind that the maximum intensities of stimulation have been carefully limited to levels which are completely safe. They will not damage your skin in any way, other than possibly a slight redness for a short period after the experiment. This means that you can afford to ascertain just how painful a stimulus is, before pushing the button if it is too intense. There is no need to push the button in anticipation, just to be safe, when you are not really sure the stimulus will exceed the level you can tolerate. Remember the stimuli are very brief, and the apparatus will move to a new skin test site each time.

There are a number of other points you should also keep in mind:

All the many different intensities of heat stimulation will be applied in a random order. This means it will be pointless for you to try and predict what intensity will be presented next - just concentrate on what you feel and report accordingly.

Although it is not entirely certain, the great variety of different intensities of stimulation employed make it likely that you will
experience sensations approximating to all, or most of, the response categories available, at some point in the session. Try to be as sensitive as possible in your responding, by choosing the most appropriate category each time. Do not just use one or two categories to be safe, or to make life easier, if you can differentiate sensations more finely. On the other hand do not feel obliged to use any, or all the categories, just for the sake of using them, if you never experience the appropriate sensations. You should make sure that you are equally familiar with all the points on the rating scale by committing them to memory. You will be tested for this later.

Do not be surprised if some of the stimuli are so low that they do not seem to generate any sensation at all. Feel quite free to report 'Nothing', if that is what you feel. When making your assessments, particularly at the lower end of the intensity scale, you should take account of three factors:

(a) First, you should ignore any residual sensation of warmth which you may feel emanating from the apparatus in contact with your abdomen. This will be very slight, but you should not report warmth to a stimulus on the basis of this alone. Look for an increased sensation, which was not previously present, when the display above you advises that the shutter is open. If there is no increased sensation, report 'Nothing'.

(b) Second, ignore any residual feeling in your skin either at the site being tested, or elsewhere. For example, if one skin site has just received a high intensity stimulus, it may still feel very slightly warm. Ignore this, and use your sense of touch to concentrate on the new skin area now beneath the testing apparatus. Please advise the experimenter IMMEDIATELY if any skin area gives you particular difficulty this way, or remains painful when not under stimulation.
(c) Finally try to adapt to, and ignore, any variations in touch and pressure sensations associated with the contact of the apparatus.

Finally, please remember to speak clearly when giving your response ratings and try to avoid changing your mind too often.

2. Acupuncture:

In most of the experimental sessions, 4 Acupuncture needles will be inserted in some of the body sites which were shown to you in the demonstration session. The needles will be stimulated electrically for approximately 40 minutes. All you are required to do is indicate sites of maximum sensitivity, or tenderness, during probing for the locations, and to ensure that the level of electrical stimulation is as high as you can accommodate without undue discomfort or any pain. A slight twitching of the muscles is quite normal, and remember, the level of stimulation is entirely under your control at all times. You should avoid sudden and extensive movement whilst needles are in place, as this may cause discomfort and bend needles. Try to observe your subjective mood and feelings during the Acupuncture so that you can report changes, if any, later. Also please check your vision for sharpness by reading the rating scale above you at regular intervals.

3. Subjective Rating Scales and Questionnaire:

The simple rating scales are largely self-explanatory and have already been shown to you. They do, however, require some care and thought if they are to be completed properly, so please remember a few points.

First, there are no right or wrong responses, it is entirely what you 'feel' at the time which should be expressed. Do not tend to mark
in the middle of the line to 'play safe', or feel frightened to express your feelings strongly. Conversely, do not feel obliged to say you anticipate, feel, or felt, any effect from the Acupuncture, injections, passage of time etc if this is not the case. Remember, the evidence is all quite contradictory as to whether you should feel anything at all, in any direction.

Do not attempt to remember where you mark the lines each time, just to mark the same point later. This would be pointless, and on some scales would even generate a false impression of change. Take particular care with the 'Hood' rating scales since they are of a 'comparative' type. That is to say you are asked to rate how you are feeling at the time compared to how you felt previously. Try therefore to make a mental record of how you feel at each point so that you can compare back to it later. You will note that the scales allow for changes in either direction. Do not worry should you find yourself expressing feelings, or changes in feelings, which seem inconsistent with others, or paradoxical.

Similarly, with the questionnaire at the end of the session, please try to indicate any strong, or unexpected, feelings or sensations you may have had, the exact points in the experiment at which they began, and how long they lasted. This should not be restricted to the specific items to which the experimenter may refer, but should include your own spontaneous observations. Remember even the most apparently silly, or trivial, observation may be of importance. Again, however, you are warned against assuming that you should feel anything particular at all. You should assess whether any feelings you report are sufficiently strong, or unexpected, to be due to the Acupuncture or injections etc, or whether you might normally expect to experience them simply as a result of lying in a warm room for two hours, receiving the heat stimuli, and giving blood samples.
To summarise - remember:-

(a) Report only the most intense sensation experienced as a result of each heat stimulus.

(b) Be consistent as to your use of the rating categories, eg. decide what 'Very Painful' means to you in terms of sensation, and stick to it throughout the experiment.

(c) Use the sharp pricking sensation as the dividing line between 'Very Faint Pain' and merely 'Very Hot'.

(d) Do not be either heroic or overly timid in the levels of pain you tolerate before 'Withdrawing'.

(e) Feel free to use the whole range of rating scale categories provided as widely and sensitively as possible to indicate subtle differences in your sensations.

(f) Ignore residual warmth sensations from the apparatus or your skin.

(g) Keep adjusting the electrical stimulation of Acupuncture needles to remain as high as possible, without undue discomfort or any pain.

(h) Do not hesitate to report subjective changes if you experience them. However, realistically assess their most likely cause, and do not feel that changes should inevitably occur.

(i) Please note that it is vital for your continued participation in the experiment that you do not discuss any aspect of the study with anyone other than the experimenter until it is fully completed.

Thank you for your interest and participation in this experiment. Your assistance is valuable and greatly appreciated. Your sustained care and concentration when making responses throughout the study will contribute very greatly towards making the work worthwhile.
**TABLE INDEX**

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<thead>
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<th>No.</th>
<th>Page</th>
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<tbody>
<tr>
<td>1a</td>
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**FIGURE INDEX**

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Acupuncture analgesia: an experimental investigation

DUNCAN STEWART, JOAN THOMSON, IAN OSWALD

British Medical Journal, 1977, 1, 67-70

Summary

A study was designed to establish whether acupuncture has any analgesic properties beyond those of suggestion. In three one-hour experimental sessions the increases in detection thresholds and tolerances for thermal pain at six body locations on 12 subjects were compared. A control session (without needles) was followed by one session in which electrically stimulated needles were inserted in accord with Chinese practice, and another in which the needles were inserted to avoid all recognised acupuncture "points." Acupuncture was significantly more effective than suggestion in raising overall body pain thresholds but just below significance for tolerances. A significant disproportionate effect on the epigastrium, predicted by the choice of acupuncture points, was found for tolerances but not thresholds.

Introduction

Anecdotal reports and neurophysiological speculation about Chinese acupuncture analgesia are widespread, yet an explanation in terms of suggestion remains inadequately assessed despite supportive evidence. The traditional use of acupuncture in China, its support by Maoist doctrine, and the careful selection and psychological preparation of patients would tend to ensure maximum belief in the efficacy of the "analgesic" technique.
Furthermore, until recently, probably at most 2% of Chinese surgical operations were carried out under general anaesthesia, with regional anaesthesia, mainly epidural blockade, extended to perhaps another 18% of cases. Consequently consciousness during operations may elicit less anxiety in Chinese patients than in Western patients.

Narcotic analgesics, local anaesthetics, and sedatives are often given in conjunction with acupuncture needles, and acupuncture is little used when there is much traction of abdominal viscera, pleura, or peritoneum. Reports indicate that acupuncture analgesia is usually incomplete, with both physiological and behavioural evidence of discomfort. In about 10% of cases this is severe enough to require the operation to be finished under chemical anaesthesia.

It is, of course, well known that Western patients may become insensitive to pain after inactive drugs, suggestion with or without hypnotic induction, simple attentional manipulation, or counterirritation. The effect may indicate that patients are less prepared to label a sensation as painful (increased tolerance) rather than that they have a diminished sensory experience (increased threshold). One study suggests that a similar process may underlie acupuncture analgesia, while another found close correlation between the hypnotic suggestibility of patients and pain relief from acupuncture.

Acupuncturists certainly seem to use suggestion, if not hypnosis, while the discomfort from needling and electrical stimulation through the needles must produce distraction with counterirritation.

We therefore conducted an experiment to determine whether acupuncture, in the presence of controls for suggestion, could produce analgesia and whether Chinese claims of a specific relation between the position of the needle and the site of the effect would be supported.

Subjects and methods

Twelve paid volunteers (six men) aged 18-32 years, in normal health and knowing little about acupuncture, took part in a balanced experiment which compared both their detection thresholds and tolerances for pain induced by heat stimuli under three different conditions. All procedures were approved by the Royal Edinburgh Hospital ethics committee and were demonstrated to the written satisfaction of all volunteers in an initial adaptation session.

The first experimental treatment for all subjects was a control session without acupuncture. Two days later six subjects (three men) took part in a session during which needles were inserted according to
current Chinese practice (genuine acupuncture session) followed, two
days later, by one of simulated acupuncture (pseudoacupuncture
session). The order of the acupuncture sessions was reversed for the

![Diagram](image_url)

**Completion of rating scales**

- Attachment of heat stimuli to 6 body locations
- Baseline pain detection threshold and pain tolerance values established for each location
- Insertion of 4 acupuncture needles (genuine or pseudo locations)
- 10 min (electrical stimulation of needles)
- 1st experimental trial (threshold and tolerance values recorded, all locations)
- 10 min (electrical stimulation of needles)
- 2nd trial
- 10 min (electrical stimulation of needles)
- 3rd trial
- 10 min (Needles removed)
- 4th trial
- 6th trial
- Postexperimental interview (rating scales)

**FIG 1**—One-hour experimental procedure for all sessions. Items in italics were not included in control session.

other six subjects. The procedural sequence common to all sessions is
outlined in fig 1.

Thermal pain stimuli were produced by 12-V light units (6-mm
diameter), which delivered a heat output rising linearly over time to an
automatic safety cut-off point. One unit was attached to each of the
following sites on the supine subjects: the central epigastrium, the
mid-sternum, the lateral surface of the left upper arm, the antero-
medial surface of the left lower leg, the dorsal right forearm, and the
anterior right thigh.
BASELINE VALUES

A baseline pain-detection threshold and a pain-tolerance value were then established sequentially for each of the six stimulus sites. The measure used was the time (in seconds) from onset of a heat stimulus to the subject's indication, by pushing a button, that his pain detection threshold had been reached and shortly afterwards, by pushing another button (which also cancelled the stimulus), that his pain tolerance duration had been exceeded. A 15-second interval followed before the onset of the next stimulus at another body site.

The pain detection threshold was defined as "the moment when the experience of heat suddenly coalesces to a point accompanied by a sharp pricking sensation." Subjects identified this sensory point with ease. Instructions on pain tolerance countermanded heroics and emphasised consistency.

The length of stimulus taken as the baseline for each body location was the second of two readings obtained after a 3-minute interval, since a pilot study had indicated that this response would closely approximate to the mean of several such closely consecutive responses.

After these session baselines had been established the remainder of a session consisted of the sequential presentation, in random order, of one heat stimulus to each of the six cutaneous locations, with automated recording of threshold and tolerance values at those sites, once every 10 minutes for the next hour.

ACUPUNCTURE SESSIONS

_Genuine acupuncture_—Needles were inserted in both the genuine and pseudoacupuncture sessions immediately after the baseline values had been established. Two acupuncture points were selected, on the basis of current Chinese practice, for bilateral insertion. The point "Ho-Ku," is located in the skin web between the thumb and index finger about midway between the junction of the first and second metacarpals and the fold. It is said to induce diffuse analgesia. Insertion was perpendicular to the dorsal cutaneous surface to a depth of 2.0 to 2.5 cm. The second point, "Tsu-San-Li," is located about 3-cm distal and lateral to the tibial tuberosity and is specified for most abdominal operations since this is expected to be the principal locus of its effect. Insertion was perpendicular and to a depth of 3.0 to 3.5 cm. With the selection of these two points we expected (a) a general increase of all threshold or tolerance values, or both, with (b) a disproportionately greater increase in the epigastrium. The predicted local effect was unknown to the physician inserting the needles.

_Pseudoacupuncture_—Two needles were also inserted bilaterally in the pseudoacupuncture session. One was inserted about 9 cm distal from the acromioclavicular joint, insertion being perpendicular and to a depth of 2.0 to 2.5 cm. The second position was about 6 cm distal from the greater trochanter along a line from the greater trochanter to the lateral border of the patella. Insertion was at 45° to the skin surface, penetrating posteriorly to a depth of 2.0 to 2.5 cm. These locations were selected to avoid recognised acupuncture points, while
providing a source of suggestion and distraction comparable to genuine acupuncture.13

Electrical stimulation was applied to needle pairs in both sessions from a 6-V battery stimulator, of Chinese design, delivering an AC output at 2.5 Hz at a maximum comfortable intensity sufficient to induce local fasciculation. Current was passed only during the 10-minute intervals between the first three heat stimulus trials. Thereafter all needles were removed, since a period of about 35 minutes is said to be adequate for analgesia.14 The sessions ended with a structured interview in which subjects reported their experiences. They also made a 10-cm line rating of the degree, and sites, of any analgesic effects, ranging from "No effect at all" to "A very considerable effect." Before the session they had each indicated in a similar manner the degree of analgesia they expected as a result of acupuncture. This had followed a standardised description of the experiment as an investigation of the claimed, but still unproved analgesic properties of acupuncture.

Results

Owing to variation in the baseline time values that each subject recorded at the outset of his three sessions, a proportional arithmetic correction was applied to all data from the needle sessions. This standardised the baselines of the genuine and pseudoacupuncture sessions so that they equalled the corresponding baseline values for each body location in the control session, and thus allowed direct comparison of subsequent trial values at corresponding stages during the three sessions.

CHANGES WITHIN SESSIONS

A measure of change of threshold within each session was then obtained for each stimulus site in each subject by subtracting his session baseline value from the mean of his six subsequent trial values obtained at the same location later during the session. Measures of tolerance change within each session were similarly obtained. An increase of both thresholds and tolerances occurred during all three sessions.

A mean representing the magnitude of within-session change in threshold shown by the body as a whole was then obtained for each subject, for each session, from his six threshold "change values" (described above). Mean tolerance change values were similarly calculated.

Group means (table I) derived from these mean change values for all 12 subjects indicated that the largest increases in both thresholds and tolerances occurred in the genuine acupuncture session followed by the pseudoacupuncture session.
TABLE I—Group mean increases in pain thresholds and tolerances (pain stimulus duration in seconds) for whole body during each session. Standard errors are shown (n=12)

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<thead>
<tr>
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<th>Genuine acupuncture session</th>
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<td>Threshold increase</td>
<td>1.6±0.5</td>
<td>2.3±0.5</td>
<td>3.4±0.8</td>
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<td>Threshold increase (%)</td>
<td>16.4±6.6</td>
<td>23.2±4.4</td>
<td>35.3±7.6</td>
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<tr>
<td>Tolerance increase</td>
<td>2.5±0.6</td>
<td>3.7±0.9</td>
<td>4.6±0.9</td>
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<td>Tolerance increase (%)</td>
<td>19.3±3.2</td>
<td>28.3±5.5</td>
<td>36.6±5.3</td>
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CHANGES BETWEEN SESSIONS

A Friedman two-way analysis of variance by ranks applied to the same data indicated that there were significant differences among the three experimental conditions for thresholds ($\chi^2 = 6.43; P<0.05; DF=2; n=12$) and for tolerances ($\chi^2 = 8.73; P<0.02; DF=2; n=12$). A Wilcoxon matched-pairs, signed-ranks test was applied to determine the significance of these intersession differences (table II).

The results indicated that increases in tolerance during both the pseudoacupuncture and genuine acupuncture sessions were significantly greater than increases during the control session. Increases in thresholds were significantly better than control levels during only the genuine acupuncture session. Genuine acupuncture was significantly better than pseudoacupuncture for thresholds but not for tolerances.

TABLE II—Significance levels for observed intersession differences in increase of pain thresholds and tolerances. (Wilcoxon matched-pairs, signed-ranks test). Probability (P) of observed differences between sessions and mean of differences between two sessions are shown

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<td>Overall body data (all subjects)</td>
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<td>Control v pseudoacupuncture</td>
<td>+0.8 0.080*</td>
<td>+1.2 0.007</td>
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<tr>
<td>Control v genuine acupuncture</td>
<td>+2.0 0.012</td>
<td>+2.1 0.005</td>
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<td>Pseudoacupuncture v genuine acupuncture</td>
<td>+1.2 0.035</td>
<td>+0.9 0.065*</td>
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<td>Epigastrium data (all subjects)</td>
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<td>+1.8 0.726*</td>
<td>+1.0 0.025</td>
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<tr>
<td>Control v genuine acupuncture</td>
<td>+3.2 0.087*</td>
<td>+4.1 0.010</td>
</tr>
<tr>
<td>Pseudoacupuncture v genuine acupuncture</td>
<td>+1.5 0.119*</td>
<td>+3.1 0.019</td>
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*Not significant.

Epigastrium—Analysis of increases in tolerance at the different body sites confirmed that, as had been predicted, a disproportionate increase on the epigastrium had occurred during the genuine acupuncture session. The Friedman test applied to the data of table III indicated
significant differences across the three sessions at this location ($\chi^2 = 10.60; P < 0.01; DF = 2; n = 12$), in contrast to the failure to reach individual significance in the case of the other five locations. The Wilcoxon test indicated that the increases in tolerance on the epigastrium were significantly better during the genuine acupuncture session than during either the control or pseudoacupuncture sessions (table II and fig 2).

No significant intersession differences of threshold increase were found for any single body location.

**Subjects' ratings**—The subjects' 10-cm line presession predictions and postsession estimates of the analgesic effect of acupuncture were examined for correlation (Spearman rank correlation) with the actual percentage increases over baselines in thresholds and tolerances that they showed in the same session. Significant correlations with postsession estimates of analgesia were found for thresholds in both the pseudoacupuncture session ($r_s = 0.91; P < 0.01; n = 12$) and the genuine acupuncture session ($r_s = 0.65; P < 0.05; n = 12$) but this was not the case with presession predictions. No significant correlation was found between the subjective ratings and tolerance increases. Both the pseudoacupuncture and genuine acupuncture sessions showed similar declines in the degree of efficacy that subjects attributed to acupuncture analgesia at the end of the session compared with the beginning. This similarity occurred despite indications of more intense needle sensations in the genuine acupuncture session. Ratings showed no bias towards greater analgesia under either of the experimental conditions, nor at any particular body location.
FIG 2—Increase of tolerances on epigastrium (mean values from 12 subjects).

Discussion

We conclude from the overall body data that acupuncture is significantly more effective than suggestion in raising pain thresholds. A similar interpretation is indicated with regard to tolerance, although the superiority of genuine acupuncture over pseudoacupuncture just failed to reach significance (table II).

Substantial support for the superiority of acupuncture is provided by the disproportionate increases of tolerance on the epigastrium during the genuine acupuncture session, as had been predicted. Counterirritation or anything short of the most highly specific suggestion are difficult explanations to apply to such a localised effect. Furthermore, both the lack of reference to the epigastrium in subjects' rating scales and the ignorance of the experimental significance of the epigastrium on the part of the physician inserting the needles render specific cueing unlikely. Chinese claims of a highly localised analgesic effect remote from one acupuncture point are supported. Since this effect did not apply to thresholds, however, the mode of action may be similar to that of morphine, which, when applied to experimental pain, is really effective only at suprathreshold levels.¹⁴

The significantly greater increase in tolerances on the epigastrium during the pseudoacupuncture session compared with that which occurred in the control session could not have resulted from specific suggestion since this effect had not been predicted.
A possible explanation comes from the fact that, as we now realise, both genuine and pseudoacupuncture needle locations were situated in the same dermatomes.\(^{17}\) This might imply a similar segmental afferent input in both cases, although, perhaps, as acupuncturists would claim, there was a more intense stimulation from genuine acupuncture points.\(^{18}\)

Since the control session always came first, any significant differences between it and either the pseudoacupuncture or genuine acupuncture sessions may have been the result of an order effect. This explanation, however, cannot be used to explain any of the demonstrated superiority of genuine acupuncture over pseudoacupuncture since these sessions were in balanced order of presentation.

The conclusion must be that acupuncture may have analgesic effects. This is consistent with the results of other research on Western populations which has controlled for suggestion\(^{19}\) and with several recent studies on man and animals which implicate neurophysiological mechanisms.\(^{20} - {21}\) The practical value of acupuncture, however, still remains to be established.

The financial support of the Mental Health Trust and Research Fund and of the Edinburgh University Sleep Research Fund, and the help and advice of Dr Vlasta Březinová and Dr John Beloff are gratefully acknowledged.

References


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