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Investigating the specificity of neuropsychological performance in bulimic outpatients: a comparison with anxious and depressed outpatients.

Kate O’Sullivan

Doctorate in Clinical Psychology
University of Edinburgh
August 2012
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Thesis Abstract

Background

Eating Disorder research has highlighted the role of neuropsychological functioning, informing the treatment of Anorexia Nervosa. There is ambiguity in the data relating to cognitive impairment in Bulimia Nervosa, with the latest review providing inconclusive results. Executive function impairments in the area of set shifting and inhibition reported in BN are proposed to relate to traits of compulsivity and impulsivity. Other psychological disorders have also demonstrated executive function impairments. Among anxiety disorders, only PTSD and OCD have strong evidence of executive function deficits while a number of studies point towards executive function deficits in depression. This thesis aims to investigate the specificity of cognitive impairments seen in a group of female outpatients with bulimia nervosa, using a clinical comparison group of anxious and/or depressed female outpatients.

Methods

A systematic review was conducted to address a gap in the anxiety disorder literature and assess the neuropsychological profile of panic disorder. In order to address the main study aims, a comparison between a group of patients with BN and an anxious depressed group was conducted on neuropsychological measures of the Trail Making Test, Wisconsin Card Sorting Test, Hayling and Brixton tasks, Stroop and Verbal Fluency. In addition, psychological symptoms were assessed using SCL-90-R, Yale-Brown Obsessive Compulsive Scale and the Self-liking Self Competence scale. Social problems solving skills were assessed as a potential real world effect of executive function difficulties associated with eating disorders. The relationships between psychological and neuropsychological variables were investigated.

Results

The systematic review concluded that there was limited evidence of specific impairment in short term memory in panic disorder. The empirical study indicated no group differences on the above neuropsychological measures. Groups also did not differ on NART estimated IQ or self reported psychological symptoms. No
relationships were found between psychological symptoms and neuropsychological measures. Few individual participants were found to be impaired on neuropsychological measures in either group. However, those impaired in the BN group were exclusively impaired on the non-perseverative errors and categories completed variables of the WCST, which is thought to be related to impulsivity.

**Conclusion**

These findings suggest that the neuropsychological profile of bulimia is broadly similar to that of an anxious and/or depressed clinical group on measures of set shifting and inhibition. Although there was evidence of a deficit in inhibition among patients with bulimia further investigation is required.
Chapter 1: Introduction

1.2 Introduction to Thesis
This thesis focuses on the neuropsychological profile of Bulimia Nervosa (BN). Neuropsychological impairment in psychological disorders is a popular field of research as links between cognitive impairments central to a disorder and its symptoms can serve to identify predictors of the course of the illness (Keefe, 1995) and treatment outcomes (Porter et al., 2007). Knowledge about the specific cognitive profile of a disorder can also contribute to the development of disorder specific cognitive models and therapies (Dudley et al., 2011).

The aim of this thesis is to contribute to the body of research investigating the neuropsychological profile of BN by considering the specificity of the cognitive impairments reported in the literature. It is hoped that research into neuropsychological deficits in BN could increase our understanding of the disorder and inform treatment as it has in anorexia nervosa (AN) and schizophrenia (Kurtz et al., 2001; Tchanturia et al., 2008). The potentially confounding influences of comorbid anxiety disorders and depression in BN have been highlighted in recent reviews as a neglected area of research (Van den Eynde et al., 2011; Zakzanis et al., 2010). Therefore the current study incorporates a comparison group of anxious and/or depressed outpatients.

This chapter will provide an overview of the structure of this thesis submission.

1.3 Overview of Chapters
1.3.1 Chapter 2 – Systematic Review
Chapter 2 is a systematic review of the neuropsychological profile of panic disorder. This disorder has been selected, as a very recent review had comprehensively covered the neuropsychological profile of BN (Van den Eynde et al., 2011). Common comorbidities of BN such as OCD (Martinez-Gonzalez & Piqueras-Rodriguez, 2008), PTSD (Polak et al., 2012), social anxiety (O’Toole & Pedersen, 2011) and depression (Castaneda et al., 2008) have also been recently reviewed. No specific review was available on GAD, specific phobia or panic disorder when the literature was examined, which are also frequently comorbid with BN. The panic
disorder review provided the opportunity to make a useful contribution to the literature and it allowed for a review of the appropriate size for thesis requirements.

1.3.2 Chapter 3 – Bridging Chapter
Chapter 3 provides a brief summary of the research and the aims of the thesis. It contains bridging information, which will introduce themes and literature that could not be included in the journal article introduction.

Information relating to Aims 1 and 2 are presented and discussed in the journal article (Chapter 4) and information relating to Aim 3 will be introduced in Chapter 3 and analysed and discussed as ‘additional’ data in Chapters 6 and 7.

1.3.3 Chapter 4 – Journal Article
Chapter 4 is a journal article reporting on the comparison between a group of females in psychological treatment for bulimia and a group of females in psychological treatment for anxiety and/or depression on neuropsychological measures of set shifting and inhibition.

This article explores whether the neuropsychological profile of BN involves patterns of performance that are specific to BN or shared by other psychiatric disorders. Similarly to BN, conflicting results have been published in the literature relating to possible neuropsychological deficits in people with anxiety disorders and depression, as described further in Chapter 4.

1.3.4 Chapter 5 – Methods
The journal article is followed by a comprehensive Methods Chapter including extended description of the measures used in the study and details relating to recruitment of participants.

1.3.5 Chapter 6 – Additional Results
The data presented in Chapter 4 are further analysed and data related to two additional neuropsychological measures (D-KEFS Verbal Fluency and the Brixton task) and two additional psychological measures (Self-liking/Self competence scale (SLSC) and the Social Problem Solving Inventory (SPSI)) are presented. Further introductory information related to the SLSC and SPSI is provided within the bridging information in Chapter 3.
1.3.6 Chapter 7 – Additional Discussion
Discussion related to all additional results is contained in this chapter.
Chapter 2: Systematic Review
(Written for the Journal of Affective Disorders, see author guidelines in Appendix 1. 7,319 words including tables)

Abstract

Background: There is a growing body of literature investigating the neuropsychological profile of Panic Disorder (PD), some of which suggests potential cognitive dysfunction. This paper systematically reviews the existing literature on neuropsychological performance in PD.

Method: PsychINFO, Embase, Medline and PsychArticles databases were searched to identify articles reporting on neuropsychological function in PD published in English during the time period 1980 to March 2012. 14 studies were identified.

Results: There was limited support for impairment in short term memory among individuals with PD, although this was not found across all studies. Overall, the reviewed studies did not support the presence of impairment in other areas of cognitive functioning, including executive function, long term memory, visuospatial or perceptual abilities and working memory.

Limitations: Studies containing samples of less than 15 participants per group were excluded from this review. A limited amount of research has been published on this topic and small sample sizes (under 25 per group) have been used by many studies. Therefore, the current review is based on a small number of studies with limited statistical power.

Conclusions: There is limited evidence of specific neuropsychological impairments in participants with PD. Impairments in short term memory have been noted in some of the literature, which warrants further investigation to establish its relevance to clinical practice. Larger sample sizes and appropriate statistical adjustment for multiple comparisons in future studies is highly recommended.
2.1 Introduction

Panic disorder (PD) is a disabling mental health problem characterised by unexpected, recurrent panic attacks, fear about the implications of attacks and modifications of behaviour as a result of the attacks (American Psychiatric Association, 2000). PD can occur with or without agoraphobia and is associated with high levels of psychiatric comorbidity and severe role impairment (Baillie & Rapee, 2005; Kessler et al., 2006).

A growing interest in the neurobiology of anxiety disorders in recent years has led to increasing research into neuropsychological deficits associated with them (Millan et al., 2012). Neuropsychological deficits are of interest, as they may be the basis for some key symptoms of PD and have implications for treatment, as has been seen in schizophrenia and anorexia (Cavedini et al., 2006; Tabarés-Seisdedos et al., 2008). The cognitive (Clark, 1986; Beck and Clark, 1997) and learning (Bouton et al., 2001) theoretical models of panic, support a role for biased information-processing of threat-related stimuli in the formation and maintenance of the disorder. This suggests that neuropsychological deficits in areas of information processing may underlie some symptoms of panic disorder. A large body of evidence suggests that patients with PD tend to selectively and automatically direct their attention towards threat-related stimuli (Ehlers et al., 1988; Clark et al., 1997; Lundh et al., 1999; Teachman et al., 2007). A difficulty shifting focus away from perceived threats could be related to difficulty with cognitive set shifting. Such difficulties have been reported in some neuropsychological studies of individuals with Panic Disorder (e.g. Airaksinen et al., 2005). Memory difficulties may also contribute to the biased appraisal of threat if examples of overcoming potentially threatening situations are not available in memory. Recent research suggests that memories of panic attacks may have the same qualities as traumatic memories, being poorly processed and involving re-experiencing which may keep them predominant in memory (Hagenaars et al., 2009). If underlying neuropsychological difficulties were found consistently in patients with PD, this would support the modification of common therapeutic interventions, such as CBT, or the incorporation of specific interventions to improve memory or set shifting ability, such as those that have been used successfully with individuals with anorexia (Tchanturia et al., 2008).
Neuropsychological deficits may also act as measurable symptoms of underlying neurobiological dysfunction. Several studies have found structural brain abnormalities in patients with anxiety disorders, including patients with PD (Mataix-Cols & van den Heuvel, 2006; Phan et al., 2009; Szeszko et al., 2005; van den Heuvel et al., 2005). Patterns of impairments in executive function have been reported in a number of recent reviews of neuropsychological performance in OCD (Martinez-Gonzalez & Piquerias-Rodriguez, 2008; Menzies et al., 2008; Olley et al., 2007). Executive function deficits have also been implicated in Post Traumatic Stress Disorder (PTSD). Anxiety disorders such as social anxiety disorder (SAD) and PD have been less well researched.

In PD, some imaging studies have indicated abnormalities in specific brain regions compared to controls, including different metabolic activity in the hippocampal and parahippocampal areas (Bisaga et al., 1998) and abnormalities in the temporal lobe structures (Vythilingam et al., 2000). However, Reiman and colleagues have noted similar regional blood flow patterns in panic disordered patients as in healthy controls with anticipatory anxiety, which calls into question whether abnormalities seen relate to structural differences or transient effects of anxiety (Reiman, Fusselman, et al., 1989; Reiman, Raichle, et al., 1989). Brain abnormalities such as these may lead to learning and memory deficits, if present in panic disordered individuals.

Individual studies have found associations between PD and a number of neuropsychological deficits, including executive function and episodic memory deficits (Airaksinen et al., 2005). However, many conflicting results have been produced, with some studies supporting memory deficits in PD (Asmundson et al., 1994; Lucas et al., 1991) and others reporting no memory problems of any kind (Gladsjo et al., 1998). No review was found of neuropsychological performance in PD. This paper aims to provide a systematic review of neuropsychological performance in PD compared to healthy control (HC) participants.
2.2 Methods

2.2.1 Search Strategy
Relevant studies published between January 1980 and March 2012 were identified by systematic searches of the PsycInfo, Embase, PsycArticles and Medline databases. Articles reporting neuropsychological performance of all anxiety disorder groups were initially identified, as a preliminary search of the literature indicated that PD groups were often used as comparison groups in studies that focused on other anxiety disorders, such as OCD (e.g. Purcell et al., 1998). Keywords for the search were “neurocognition”, “attention”, “executive function”, “leaning”, “memory”, “inhibition” AND “neuropsychological tests” AND “anxiety”, “OCD”, “PTSD”. Terms were adapted and ‘exploded’ in keeping with subject headings for each database (see Appendix 2 for full search term list for each database). The reference lists of ten papers identified as appropriate after inclusion and exclusion criteria were applied, were checked for relevant studies, resulting in 3 additional papers. A ‘cited by’ search was conducted using Web of Science (1899-present) resulting in 2 additional papers. This resulted in 15 papers meeting study criteria. Subsequently two studies were discovered to be reporting on the same data (Lautenbacher et al., 2002; Spernal et al., 2003). The paper containing the most data was retained in the review, resulting in a total of 14 papers (Lautenbacher et al., 2002).

2.2.2 Inclusion and exclusion criteria
Studies were included if they reported on: (1) adults (18-65 years) (2) diagnosed with current PD according to DSM or ICD criteria (3) a comparison group of healthy controls (HC) (4) had ≥ 15 participants in each group and (5) were published in English. A relevant Spanish paper was found during the search but could not be included as it was only available in the Spanish language (Castillo et al., 2010). Studies on the effect of psychotropic medication or a treatment intervention were excluded. Investigations of cognitive performance in the presence of anxiety provoking words or stimuli were excluded. Studies of neuropsychological performance during brain imaging or brain activity recording were also excluded. The paper selection procedure is described in Figure 2.1, with a more detailed map in Appendix 3.
Figure 2.1 Flowchart showing search results, and the number of included and excluded studies.

2.2.3 Data Extraction

Data were extracted from each paper by the first author, according to a structured pro-forma covering key study characteristics. Data were extracted and compiled into Table 2.1.
2.2.4 Assessment of methodological quality

To rate the methodological quality of included studies, criteria were developed by the first author, drawing from the Cochrane Handbook for Systematic Review’s guidance on assessing risk of bias (Higgins & Altman, 2008) and the Centre for Reviews and Dissemination (CRD) guidance on conducting quality assessment (CRD, 2008). A checklist of 8 quality criteria were identified a priori (Appendix 4). The ratings for the included studies are listed in Table 2.2. For each criterion, included studies were assigned one of four outcome ratings: ‘well covered’ (2 points); ‘adequately addressed’ (1 point); ‘poorly addressed’ or ‘not addressed’ (both 0 points). Two additional raters independently reviewed four studies each. Exact agreement was reached on 88% and 84% of the ratings respectively. A difference of one point occurred on 12.5% of the items and by 2 points on 1.5% items. Differences in rating of criteria were discussed and amended.
Table 2.1 Key Study Characteristics

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample size</th>
<th>Groups matched on</th>
<th>Key exclusion criteria</th>
<th>Levels of anxiety compared between groups</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airaksinen et al. (2005)</td>
<td>33 PD (30 PD only and 3 Ag only) 175 HC</td>
<td>age, education</td>
<td>No exclusions</td>
<td>No comparisons</td>
<td>No medications excluded</td>
</tr>
<tr>
<td>Asmundson et al. (1994)</td>
<td>18 PD 16 HC</td>
<td>gender, age, education</td>
<td>Current major depression and Social phobia excluded</td>
<td>BDI: PD &gt; HC BAI: PD &gt; HC</td>
<td>1 PD taking p.r.n. benzodiazepines</td>
</tr>
<tr>
<td>Boldrini et al. (2005)</td>
<td>15 PD with Ag 15 HC</td>
<td>gender, age, education, handedness, intelligence</td>
<td>All Axis I or II excluded</td>
<td>No comparisons</td>
<td>Free from benzodiazepines (no time period) but SSRIs not excluded</td>
</tr>
<tr>
<td>Cavedini et al. (2002)</td>
<td>16 PD 34 HC</td>
<td>gender, age, education</td>
<td>All Axis I or II excluded</td>
<td>No comparisons</td>
<td>All medication free for at least 2 weeks</td>
</tr>
<tr>
<td>Deckersbach et al. (2011)</td>
<td>20 PD 20 HC</td>
<td>gender, age, education</td>
<td>Depression, psychosis and bipolar disorder excluded</td>
<td>STAI: PD &gt; HC BDI: PD &gt; HC</td>
<td>All free from benzodiazepines for at least 4 weeks. One PD taking Sertraline</td>
</tr>
<tr>
<td>Galderisi et al. (2008)</td>
<td>28 PD (26 with Ag) 32 HC</td>
<td>gender, age, education, handedness</td>
<td>MDD and other anxiety disorders excluded</td>
<td>No comparisons</td>
<td>Medication free for 4 weeks or drug naive</td>
</tr>
<tr>
<td>Gladsjo et al. (1998)</td>
<td>69 PD 19 HC</td>
<td>gender, age, education, ethnicity, handedness</td>
<td>All Axis I or II excluded</td>
<td>No comparisons</td>
<td>Medication free for at least 2 weeks</td>
</tr>
<tr>
<td>Gordeev (2008)</td>
<td>93 PA 36 HC</td>
<td>education</td>
<td>No information</td>
<td>BDI: PD &gt; HC STAI: PD &gt; HC</td>
<td>Medication free for 2 weeks</td>
</tr>
<tr>
<td>Gorini et al. (2010)</td>
<td>31 PD with Ag, 31 HC</td>
<td>gender, age, education</td>
<td>Other primary diagnoses excluded</td>
<td>No comparisons</td>
<td>Medication free for 1-2 weeks</td>
</tr>
<tr>
<td>Authors</td>
<td>Sample size</td>
<td>Groups matched on</td>
<td>Key exclusion criteria</td>
<td>Levels of anxiety compared between groups</td>
<td>Medication</td>
</tr>
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<td>-------------</td>
<td>--------------------------------</td>
<td>-------------------------------------------------------</td>
<td>-------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Kaplan et al. (2006)</td>
<td>22 PD (11 PD only, 11 PD + MDD) + 22 HC</td>
<td>gender, age, education</td>
<td>Other anxiety or depressive disorder excluded</td>
<td>MADRS: PD &gt; HC</td>
<td>All medication free (no time</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ham A: PD &gt; HC</td>
<td>period given)</td>
</tr>
<tr>
<td>Lautenbacher et al.</td>
<td>21 PD, (16 with Ag, 5 without Ag) + 20 HC</td>
<td>gender</td>
<td>Lifetime comorbidity of Axis 1 excluded</td>
<td>No comparison</td>
<td>Medication free for 6 days</td>
</tr>
<tr>
<td>(2001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lucas et al. (1991)</td>
<td>25 PD + 25 HC</td>
<td>gender, age, education,</td>
<td>Current mood disorder, or other anxiety disorder</td>
<td>BDI: PD &gt; HC</td>
<td>Patients remained on</td>
</tr>
<tr>
<td></td>
<td></td>
<td>handedness</td>
<td>excluded</td>
<td>STAI: PD &gt; HC</td>
<td>medication</td>
</tr>
<tr>
<td>Ludewig et al. (2003)</td>
<td>18 PD + 35 HC</td>
<td>gender</td>
<td>No information</td>
<td>No comparisons</td>
<td>14 of 18 PDs on medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>including SSRI and TCA</td>
</tr>
<tr>
<td>Purcell et al. (1998)</td>
<td>30 PD + 30 HC</td>
<td>gender, age, education,</td>
<td>Comorbid disorder excluded but anxiety or depression</td>
<td>Ham D: PD = HC</td>
<td>19 PD on medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>handedness, IQ</td>
<td>symptoms accepted</td>
<td>Ham A: PD &gt; HC</td>
<td></td>
</tr>
</tbody>
</table>

*a* PD group is mixed with and without agoraphobia with details unavailable unless otherwise specified, *b* Additional groups were included in the study which did not form part of this review, *c* MDD is episode secondary to PD, STAI= State Trait Anxiety Inventory, TCA = tricyclic antidepressant, SSRI = selective serotonin reuptake inhibitor

Ag = agoraphobia, HamA = Hamilton Anxiety rating scales, HamD = Hamilton Depression rating scale, BDI= Beck Depression Inventory, BAI= Beck Anxiety Inventory, MADRS = Montgomery Asberg Depression Rating Scale
Table 2.2 Quality Criteria applied to Reviewed studies

<table>
<thead>
<tr>
<th>Name of study</th>
<th>i exclusion criteria</th>
<th>ii group matching</th>
<th>iii diagnosis</th>
<th>iv neuropsychological measures</th>
<th>v sample size</th>
<th>vi uptake levels</th>
<th>vii outputs reported</th>
<th>viii stats used</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airaksinen et al. (2005)</td>
<td>WC</td>
<td>AA</td>
<td>WC</td>
<td>AA</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>AA</td>
<td>11</td>
</tr>
<tr>
<td>Asmundson et al. (1994)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>10</td>
</tr>
<tr>
<td>Boldrini et al. (2005)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>11</td>
</tr>
<tr>
<td>Cavedini et al. (2002)</td>
<td>AA</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>WC</td>
<td>11</td>
</tr>
<tr>
<td>Deckersbach et al. (2011)</td>
<td>AA</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>10</td>
</tr>
<tr>
<td>Galderisi et al. (2008)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>WC</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>11</td>
</tr>
<tr>
<td>Gladsjo et al. (1998)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>AA</td>
<td>AA</td>
<td>12</td>
</tr>
<tr>
<td>Gordeev (2008)</td>
<td>PA</td>
<td>PA</td>
<td>AA</td>
<td>AA</td>
<td>WC</td>
<td>NA</td>
<td>AA</td>
<td>WC</td>
<td>7</td>
</tr>
<tr>
<td>Gorini et al. (2010)</td>
<td>PA</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>WC</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>8</td>
</tr>
<tr>
<td>Kaplan et al. (2006)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>WC</td>
<td>12</td>
</tr>
<tr>
<td>Lautenbacher et al. (2001)</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>AA</td>
<td>AA</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>8</td>
</tr>
<tr>
<td>Lucas et al. (1991)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>NA</td>
<td>AA</td>
<td>AA</td>
<td>12</td>
</tr>
<tr>
<td>Ludewig et al. (2003)</td>
<td>PA</td>
<td>AA</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>NA</td>
<td>PA</td>
<td>AA</td>
<td>6</td>
</tr>
<tr>
<td>Purcell et al. (1998)</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>WC</td>
<td>AA</td>
<td>AA</td>
<td>WC</td>
<td>14</td>
</tr>
</tbody>
</table>

i. Eligibility criteria are specified, ii. Comparison group is matched, iii. Diagnosis using appropriate criteria and measure, iv. Neuropsychological Measures are robust, v. Sample size adequate for all groups, vi. Levels of uptake are reported, vii. Results – appropriate outputs provided, viii. Appropriate Statistical techniques, WC=well covered, AA=adequately addressed, PA=poorly addressed, NA=not addressed
2.3 Results

2.3.1 Search results and characteristics of studies
From the search, 14 papers were identified comparing a PD group with a HC group. The 14 studies involved 439 patients with PD in total and 510 HCs (see Table 2.1 for details). The median sample size was 23.5 for PD patients (range 15 - 93) and 27.5 for HCs (range 15 - 175).

Three studies reported on the presence or absence of agoraphobia in their PD sample, but 11 did not. Both Boldrini et al. (2005) and Gorini et al. (2010) reported all PD participants to have PD with agoraphobia. Twenty six of the 28 PD participants in Galderisi et al.’s (2008) study had PD with agoraphobia.

2.3.2 Findings of the review
As many neuropsychological measures can be said to assess a number of cognitive functions, Lezak et al.’s (2004) categorisation of neuropsychological assessments has been broadly followed when tabulating and discussing the measures used in the reviewed studies. However, the category of executive functioning was expanded from that of Lezak et al. (2004) in line with Burgess (2003) to incorporate tests of inhibition, coordinated dual tasks (e.g. the Trail Making Task) and verbal fluency. In the context of the reviewed studies, such measures were used with the purpose of assessing executive functioning. Measures used in the reviewed studies and their reported results are detailed in Tables 2.3 to 2.6.

2.3.3 Memory

2.3.3.1 Verbal Memory
Short and long term verbal memory were investigated in eight studies using ten measures. Of these, four found poor performance in a PD group compared to HC and four did not find group differences.

Short term verbal memory was measured by five studies and impairment of PD patients compared to HC was reported in three studies. Two studies indicating a relative impairment of PD participants used non-standardised short term recall tasks
(Airaksinen et al., 2005; Gordeev, 2008) and the other used the California Verbal Learning Test (CVLT; Asmundson et al., 1994; Delis et al., 1987). The CVLT was used in two other studies, which did not report on performance of people with PD on short term memory scales (Deckersbach et al., 2011; Gladsjo et al., 1998). No differences between PD and HC groups were reported by Lucas et al. (1991) or Deckersbach et al. (2011) in measures of immediate recall of stories or paired words, taken from the Wechsler Memory Scale (WMS; Wechsler, 1987). Mixed results were reported in relation to cued short term memory, with deficits seen on a non-standardised task (Airaksinen et al., 2005) but not on the cued recall subscale of the CVLT (Asmundson et al., 1994). Overall, there was some support for impairment in short term memory when assessed by non-standardised measures but little support from standardised assessment.

Delayed verbal memory was investigated by seven studies. No differences were found between PD and HC groups on delayed verbal memory using the CVLT (Asmundson et al., 1994; Deckersbach et al., 2011; Gladsjo et al., 1998), the Auditory Verbal Learning Test (AVLT) (Galderisi et al., 2008), or the paired associates and logical memory subscales of the Wechsler Memory Scale (WMS) (Lucas et al., 1991). Using a selective reminding procedure (J. M. Fletcher, 1985), conflicting results were produced by two studies with Lucas et al. (1991) observing a deficit in long term verbal memory in a PD sample compared to HC while Boldrini et al. (2005) did not.
<table>
<thead>
<tr>
<th>Verbal Memory Test</th>
<th>study/authors</th>
<th>PD v HC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CVLT</strong>&lt;br&gt; immediate free recall trial 5</td>
<td>Asmundson et al. (1994)</td>
<td>↓</td>
</tr>
<tr>
<td>immediate free recall trial 1</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>short delay free recall</td>
<td>Asmundson et al. (1994)</td>
<td>↓</td>
</tr>
<tr>
<td>total free recall</td>
<td>Asmundson et al. (1994)</td>
<td>↓</td>
</tr>
<tr>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Gladso et al. (1998)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>short delay cued recall</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>retention</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>response inhibition</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>response discrimination</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>Gladsjo et al. (1998)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><strong>Word Lists</strong>&lt;br&gt; AVLT delayed recall</td>
<td>Galderisi et al. (2008)</td>
<td>-</td>
</tr>
<tr>
<td>Warrington RMT</td>
<td>Gladso et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td>words remembered short term</td>
<td>Gordeev et al. (2008)</td>
<td>↓</td>
</tr>
<tr>
<td>words remembered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free recall</td>
<td>Airakssnen et al. (2005)</td>
<td>↓</td>
</tr>
<tr>
<td>Cued recall</td>
<td>Airakssnen et al. (2005)</td>
<td>↓</td>
</tr>
<tr>
<td>Hebb Digit Recurring test - accuracy index</td>
<td>Galderisi et al. (2008)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Buschke-Fuld Selective Reminding Test (SRT)</strong>&lt;br&gt; long term recall</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td>long term storage</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td>intrusions</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td>delayed recall</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Verbal Selective Reminding Test (SRT)</strong>&lt;br&gt; Long term storage</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>trials to criterion</td>
<td>Lucas et al. (1991)</td>
<td>-</td>
</tr>
<tr>
<td>delayed recall</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>long term retrieval</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td><strong>Logical Memory (WMS)</strong>&lt;br&gt; Delayed recall</td>
<td>Lucas et al. (1991)</td>
<td>-</td>
</tr>
<tr>
<td>immediate recall</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Paired associate learning (WMS)</strong>&lt;br&gt; Immediate recall</td>
<td>Lucas et al. (1991)</td>
<td>-</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>Lucas et al. (1991)</td>
<td>-</td>
</tr>
</tbody>
</table>

↓ Indicates significantly worse performance than HC  
↑ Indicates significantly better performance than HC  
- indicates no significant difference compared to HC
2.3.3.2 Visual Memory

Both short and long term visual memory in people with PD was investigated by eight studies using ten measures. Three studies reported deficits in people with PD compared to HC, while five reported no significant differences between these groups.

Short term visual memory was investigated in two studies, one using the Rey-Osterrieth Complex Figure test (RCFT; Rey, 1941) immediate recall scale (Deckersbach et al., 2011) and one using a non-standardised task, in which an array of numbers was visually presented followed by immediate recall (Gordeev, 2008). Both these tasks were associated with an impaired performance in people with PD compared to HC.

Seven studies reported on measures of long term visual memory, including measures of retention and recognition. Three studies used the Benton Visual Retention test (BVRT) (BVRT; Benton, 1945) with two of these reporting significantly worse long term visual memory in people with PD relative to HC (Asmundson et al., 1994; Deckersbach et al., 2011; Lucas et al., 1991). A selective reminding procedure (J. M. Fletcher, 1985) was used in two studies producing mixed results, as Lucas et al. (1991) reported poor performance in people with PD but this was not replicated by Gladsjo et al. (1998). Visual recognition memory was investigated using 3 subtests of the computerised Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, Cambridge, UK) and the Warrington Recognition Memory test (Faces) (Warrington, 1984). No differences were reported between PD and HC groups on these visual recognition tasks (Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998). People with PD also performed similarly to HC on the RCFT percent recall (Boldrini et al., 2005; Deckersbach et al., 2011), the Continuous Visual Memory test (Gladsjo et al., 1998; Trahan & Larrabee, 1989) and delayed recall of the Visual Reproduction subscale of the WMS (Lucas et al., 1991). These studies do not support a finding of difficulties in long term visual memory for people with PD.

In summary there is some support for a short term memory deficit in people with PD in both verbal and visual memory but the reliability and validity of a number of the
tasks providing this support is unclear. There is little support for impairment in either verbal or visual long term memory.

### Table 2.4 Visual memory in panic disorder compared to healthy controls

<table>
<thead>
<tr>
<th>Visual Memory Test</th>
<th>study/authors</th>
<th>HC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benton Visual Retention Test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Form F (BVRT-F)</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
</tr>
<tr>
<td>Errors</td>
<td>Deckersbach et al. (2011)</td>
<td>↓</td>
</tr>
<tr>
<td>Errors</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td><strong>RCFT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>immediate recall</td>
<td>Deckersbach et al. (2011)</td>
<td>↓</td>
</tr>
<tr>
<td>percent recall</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td>percent recall</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Visual Selective Reminding test (VSRT)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>long term storage</td>
<td>Gladsjo et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td>long term storage</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>total recalled</td>
<td>Gladsjo et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td>long term retrieval</td>
<td>Gladsjo et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td>long term retrieval</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>Trials to criterion</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
</tr>
<tr>
<td>Warrington RMT Faces</td>
<td>Gladsjo et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Continuous Visual Memory test (CVMT)</strong></td>
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<td></td>
</tr>
<tr>
<td>total recalled</td>
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<td>-</td>
</tr>
<tr>
<td>d-Prime</td>
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<td>-</td>
</tr>
<tr>
<td>Numbers remembered, short term</td>
<td>Gordeev et al. (2008)</td>
<td>↓</td>
</tr>
<tr>
<td>Visual Reproduction (WMS) - delayed recall</td>
<td>Lucas et al. (1991)</td>
<td>↓</td>
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<tr>
<td><strong>CANTAB</strong></td>
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<tr>
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</tr>
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<td>Spatial Recognition Memory</td>
<td>Purcell et al. (1998)</td>
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</tr>
<tr>
<td>pattern recognition memory</td>
<td>Kaplan et al. (2006)</td>
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</tr>
<tr>
<td>pattern recognition memory</td>
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<td>-</td>
</tr>
<tr>
<td>Delayed match to sample</td>
<td>Kaplan et al. (2006)</td>
<td>-</td>
</tr>
<tr>
<td>Delayed match to sample</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
</tr>
</tbody>
</table>

↓ Indicates significantly worse performance than HC
↑ Indicates significantly better performance than HC
- Indicates no significant difference compared to HC
2.3.4 Attention, perception and working memory

2.3.4.1 Working Memory

Working memory in people with PD was explored by seven studies using working memory span tasks. No difference between the performance of people with PD and HC were reported by four studies using the Digit Span (Wechsler, 1981) task. Two studies using the CANTAB computerised Spatial Span and Spatial Working Memory tasks also found no differences. Boldrini et al. (2005) and Galderisi et al. (2008) employed the Corsi Block Tapping Task (CBTT; Berch, 1998) to investigate working memory span, while Deckersbach et al. (2011) used the similar Spatial span task from the WMS (Wechsler, 1987). Performance was reported as no different to HC on measures of span (Boldrini et al., 2005; Deckersbach et al., 2011), however on the supraspan subscale, Boldrini et al. (2005) reported a poor learning process in spatial working memory in people with PD compared to HC. Galderisi and colleagues (2008) also administered the CBTT but only reported on the accuracy index, on which people with PD performed better than the HCs in their sample. In summary, there is very little support for working memory impairment in PD.

2.3.4.2 Attention

Attention was investigated in seven studies using six different tests. No impairments of people with PD were found compared to HC in any study (Airaksinen et al., 2005; Asmundson et al., 1994; Deckersbach et al., 2011; Galderisi et al., 2008; Gladsjo et al., 1998; Kaplan et al., 2006; Lucas et al., 1991).

2.3.4.3 Perception

Tests included in this section were classed primarily as tests of perception by Lezak et al. (2004) as they measure visual field perception, visual searching and facial recognition but also include selected and divided attention.

Four studies investigated these abilities in PD using six tasks. Poor performance was noted on three of these tasks. Individuals with PD performed poorly compared to HC on the Munsterberg Test, described as a test of selective attention and on a Schulte tables task of sustained attention (Gordeev, 2008). The Munsterberg test requires participants to find words in a random set of letters within a limited time. Psychometric properties for the Munsterberg task and Schulte tables were not found.
Some literature was found indicating that Schulte tables do not have well established psychometric properties (Ennok, 2010). In contrast to Gordeev’s (2008) finding of poor selective attention, Lautenbacher et al. (2002) did not find overall group differences on selective attention using a computerised signal detection task. Divided attention was also explored by Lautenbacher et al. (2002) using a visual field neglect task in which individuals with PD demonstrated impaired performance relative to HC. Information on psychometric properties could not be found for Lautenbacher et al.’s (2002) measures. Facial recognition in the absence of a memory condition was assessed using the Benton Facial Recognition test (short form) (Benton, 1983), where the participant must identify photographs of the target person taken from different angles. Individuals with PD were as good at identifying faces as HCs (Boldrini et al., 2005). No difference in ability was seen between the two groups on a digit cancellation test (Asmundson et al., 1994). Overall, some support was found for impaired perceptual/attention abilities in people with PD but the reliability of the measures used was uncertain.

2.3.5 Visuospatial Ability

Visuospatial ability was investigated in PD by five studies using four measures. Three of these measures were standardised tasks - the Block Design task from the Wechsler Adult Intelligence Scale-Revised (WAIS-R), the copy task of the RCFT and the mental rotation task (Vandenberg & Kuse, 1978) and one a novel computer-based task (Jacobs et al., 1997). Two studies found no group differences in visuospatial ability using the RCFT copy score (Boldrini et al., 2005; Deckersbach et al., 2011). Poor visuospatial ability of people with PD was seen on the Block Design task by Asmundson et al. (1994) but was not replicated (Gladsjo et al., 1998). The ability to perform spatial rotations mentally was investigated by Deckersbach et al. (2011) using the mental rotation test. The PD group performed as well as HCs on this test. A virtual environment was used by Gorini et al. (2010) to investigate spatial orientation and learning in people with PD. Their study used a virtual water maze analogue where participants had to find the hidden platform in a virtual environment, starting from a different position at each trial. Learning the position of the platform over trials was impaired in the PD group compared to HCs, however this was a novel task which has not been standardised and high variability of
performance was noted in both groups. In summary, only one study provided support for visuospatial impairment in people with PD, using a novel non-standardised measure.
Table 2.5 Working memory in panic disorder compared to healthy controls

<table>
<thead>
<tr>
<th>Cognitive function</th>
<th>Test</th>
<th>study/authors</th>
<th>PD v HC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Working Memory</strong></td>
<td>Digit span</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Deckersbach et al. (2011)</td>
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<td>Gladso et al. (1998)</td>
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<td></td>
<td>Lucas et al. (1991)</td>
<td>-</td>
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<tr>
<td>Corsi Block Tapping Task (CBT)</td>
<td>span</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Deckersbach et al. (2011)</td>
<td>↓</td>
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<tr>
<td></td>
<td>supraspan</td>
<td>Boldrini et al. (2005)</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>accuracy index</td>
<td>Galderisi et al. (2008)</td>
<td>↑</td>
</tr>
<tr>
<td>WMS-R</td>
<td>spatial span forward</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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<tr>
<td></td>
<td>spatial span backward</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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<tr>
<td>CANTAB</td>
<td>Spatial Span</td>
<td>Kaplan et al. (2006)</td>
<td>-</td>
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<tr>
<td></td>
<td>Spatial Span</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>Mental control task (WMS-R)</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Lucas et al. (1991)</td>
<td>-</td>
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<tr>
<td></td>
<td>Continuous performance test</td>
<td>Galderisi et al. (2008)</td>
<td>-</td>
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<tr>
<td></td>
<td>TMT A</td>
<td>Airaksinen et al. (2005)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Gladso et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Digit symbol (WAIS-R)</td>
<td>Galderisi et al. (2008)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Gladso et al. (1998)</td>
<td>-</td>
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<tr>
<td></td>
<td>Digit vigilance - time</td>
<td>Gladso et al. (1998)</td>
<td>-</td>
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<tr>
<td></td>
<td>Digit vigilance - errors</td>
<td>Gladso et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td>CANTAB</td>
<td>Rapid Visual Information Processing</td>
<td>Kaplan et al. (2006)</td>
<td>-</td>
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<tr>
<td><strong>Perception</strong></td>
<td>Digit Cancellation Test (DCT)</td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
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<td></td>
<td>Signal Detection (from Weiner-Test-System)</td>
<td>Lautenbacher et al. (2001)</td>
<td>-</td>
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<td></td>
<td>Munsterberg test</td>
<td>Gordeev (2008)</td>
<td>↓</td>
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<td>Gordeev (2008)</td>
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<td></td>
<td>Schulte tables</td>
<td>Lautenbacher et al. (2001)</td>
<td>↓</td>
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<td></td>
<td>Visual Field Neglect task (from TAP)</td>
<td>Lautenbacher et al. (2001)</td>
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<tr>
<td></td>
<td>Facial Recognition test (BFRT) short form</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td><strong>Visuospatial</strong></td>
<td>Block design (WAIS-R)</td>
<td>Asmundson et al. (1994)</td>
<td>↓</td>
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<tr>
<td>ability</td>
<td></td>
<td>Gladso et al. (1998)</td>
<td>-</td>
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<tr>
<td></td>
<td>Mental rotation test</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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<tr>
<td></td>
<td>Spatial orientation and learning – virtual water maze analogue</td>
<td>Gorini et al. (2010)</td>
<td>↓</td>
</tr>
<tr>
<td>RCFT</td>
<td>Copy</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Copy</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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</tbody>
</table>

- Indicates significantly worse performance than HC
↑ indicates significantly better performance than HC
- indicates no significant difference compared to HC
2.3.6 Executive function
Executive function was assessed by nine studies using nine measures. Results were considered under the headings of set shifting, verbal fluency, decision making and planning and organising. Significant group differences were reported only on two measures.

2.3.6.1 Planning and Organising
People with PD demonstrated impaired performance relative to HC on the organisation score of the RCFT (Deckersbach et al., 2011). Purcell et al. (1998) administered the Tower of London task (CANTAB; Cambridge Cognition, Cambridge, UK) and found comparable performance between the two groups.

2.3.6.2 Set shifting
The set shifting performance of people with PD in comparison to HC was examined by six studies using five tasks. Individuals with PD performed as well as HC on the Wisconsin Card Sorting Task (WCST; Boldrini et al., 2005; Heaton et al., 1993). There were also no group differences found in both studies using the CANTAB intradimensional and extradimensional shifting task (Kaplan et al., 2006; Purcell et al., 1998). Three studies reported on the Trail Making Task B (TMT B; R. M. Reitan & Davidson, 1974), with only one (Airaksinen et al., 2005) reporting slower times in people with PD compared to HC.

2.3.6.3 Verbal Fluency
Five studies investigated letter fluency abilities, finding individuals with PD produced as many words as HCs. One of these also investigated category fluency (Benton, 1989; Gladsjo et al., 1998) and again found no group differences in number of words produced.

2.3.6.4 Decision Making
Decision Making ability was examined by Cavedini et al. (2002) using the Iowa Gambling Task (IGT; Bechara et al., 1994), by Kaplan et al. (2006) using the Cambridge Gambling task (Rogers et al., 1999) and by Ludewig et al. (2003) using a two-choice prediction task (Paulus, 1997). Performance of the PD group was not significantly different to the control group for any task, although PD participants showed increased sensitivity to error, being more likely to search for a better
responding strategy even at low error rates in Ludewig et al.’s (2003) study. Kaplan et al. (2006) reported that within their sample comorbid major depressive disorder (MDD) was associated with slow decision making.

In summary, the evidence reviewed does not support an executive function deficit in PD.

**Table 2.6 Executive function in panic disorder compared to healthy controls**

<table>
<thead>
<tr>
<th>Cognitive function</th>
<th>Test</th>
<th>study/authors</th>
<th>PD v HC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Set shifting</strong></td>
<td>TMT B</td>
<td>Airaksinen et al. (2005)</td>
<td>↓</td>
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<tr>
<td></td>
<td></td>
<td>Asmundson et al. (1994)</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td>Gladsoj et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td><strong>WCST</strong></td>
<td>categories</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>total errors</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>perseverative errors</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>non-p errors</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>perseverative responses</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>null sorts</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td><strong>CANTAB</strong></td>
<td>Intradimensional-Extradimensional Shift</td>
<td></td>
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<tr>
<td></td>
<td>Total score</td>
<td>Kaplan et al. (2006)</td>
<td>-</td>
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<td></td>
<td>IDS trial score</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
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<td></td>
<td>EDS trial score</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
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<tr>
<td></td>
<td>Spatial working memory</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Planning and organising</strong></td>
<td>Tower of London</td>
<td>Purcell et al. (1998)</td>
<td>-</td>
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<tr>
<td></td>
<td>RCFT organisation</td>
<td>Deckersbach et al. (2011)</td>
<td>↓</td>
</tr>
<tr>
<td><strong>verbal fluency</strong></td>
<td>FAS in 60 sec</td>
<td>Airaksinen et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>FAS in 60 sec</td>
<td>Boldrini et al. (2005)</td>
<td>-</td>
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<tr>
<td></td>
<td>letter fluency</td>
<td>Gladsoj et al. (1998)</td>
<td>-</td>
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<td></td>
<td>COWAT</td>
<td>Deckersbach et al. (2011)</td>
<td>-</td>
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<tr>
<td></td>
<td>category fluency</td>
<td>Gladsoj et al. (1998)</td>
<td>-</td>
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<tr>
<td><strong>Decision making</strong></td>
<td>Iowa Gambling Task</td>
<td>Cavedini et al. (2002)</td>
<td>-</td>
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<td></td>
<td>Cambridge Gambling Task</td>
<td>Kaplan et al. (2006)</td>
<td>-</td>
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<td></td>
<td>Two-Choice Prediction Task</td>
<td>(Paulus et al., 1997)</td>
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<td>Ludewig et al. (2003)</td>
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*↓* Indicates significantly worse performance than HC, *↑* indicates significantly better performance than HC, - indicates no significant difference compared to HC
2.3.7 Summary of Neuropsychological findings

The findings of the reviewed studies suggest limited support for a short term memory deficit in people with PD in both verbal and visual memory, with five out of seven studies indicating a difference in performance. There is little support for impairment in perceptual ability, as although three out of four studies found differences, the reliability and validity of the measures used was unclear. Only three of fourteen studies found differences in long term memory compared to HC, which did not support long term memory impairment in PD. The findings reviewed did not indicate deficits in executive function, as only two of nine studies found group differences. Similarly, working memory was impaired only in one of seven studies and attention was not impaired in any of the seven studies incorporating tests of attention. Visuospatial abilities were impaired in two out of five studies, which does not suggest consistent impairment.

2.3.8 Assessment of Methodological Quality

Table 2.2 contains study ratings on the eight quality criteria selected. This rating system provides an indication of the relative methodological strengths of the studies reviewed, although it does not allow for detailed comparison.

Based on the chosen criteria, Purcell et al. (1998) was methodologically the strongest study, although the majority of studies were of average to high quality. Studies that reported significant results for more than half of the measures they utilised, tended to be of lower quality, as defined by the quality criteria. Four such studies (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002; Lucas et al., 1991) failed to describe adjustment for the multiple comparisons they used. In addition, three of these studies (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002) reported significant results on a measure for which no reliability or validity information was available. Gordeev (2008) used corrections for multiple comparisons and reported significant results for all the measures used, examining areas of perception and short term memory, however no reliability or validity data were available for any of these measures. These studies provided some of the support in favour of short term memory and perception difficulties in people with PD.
Studies which reported few significant differences associated with diagnosis of PD, tended to be of high quality as defined by the quality criteria. These studies (Asmundson et al., 1994; Boldrini et al., 2005; Deckersbach et al., 2011; Galderisi et al., 2008) reported significant differences between PD and HC participants for fewer than half of the measures they investigated. Although two (Asmundson et al., 1994; Galderisi et al., 2008) used one measure in their study that did not have reliability and validity data available, significant results were only reported on validated measures. These studies contributed findings supporting difficulties in short term memory, working memory span and learning, visuospatial abilities and executive function.

Four studies of high quality, as defined by the quality criteria, reported no significant differences between PD samples and HC (Cavedini et al., 2002; Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998). Three described no differences in relation to long term memory and set shifting (Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998); two in relation to decision making (Cavedini et al., 2002; Kaplan et al., 2006) and two relating to other aspects of executive functioning (Gladsjo et al., 1998; Purcell et al., 1998). One lower quality study also reported no significant findings on a decision making task for which no psychometric information was found (Ludewig et al., 2003). Studies with high methodological quality tended towards findings of little or no differences between PD and HC groups. However, three of the four high quality studies with negative findings had small sample sizes, reducing their power to detect differences.

Overall, within the studies reviewed, group matching, method of diagnosis and description of exclusion criteria were addressed adequately. Presentation of results was generally adequate, but all studies failed to provide confidence intervals or effect sizes with their results. Eight of the 14 studies reviewed reported sample sizes less than 25, indicating that they would have lacked the power to detect a large effect size with an alpha level of .05 in a 2-tailed comparison of two means (see Table 2.1). No studies described statistical power. Uptake levels were poorly reported or not addressed in all but three studies (Airaksinen et al., 2005; Gladsjo et al., 1998; Purcell et al., 1998). Eight studies reported corrections for multiple comparisons.
(Asmundson et al., 1994; Boldrini et al., 2005; Cavedini et al., 2002; Deckersbach et al., 2011; Galderisi et al., 2008; Gordeev, 2008; Kaplan et al., 2006; Purcell et al., 1998). As most studies included a number of measures and various post hoc tests, the absence of correction for multiple comparisons is a potential confound. The lack of these corrections may have led to Type I errors in the four studies that did not address these corrections and reported significant results (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002; Lucas et al., 1991).

No studies reported on the reliability and validity of the measures used, therefore these properties were further investigated. Most measures were described with psychometric properties in Lezak and colleagues’ (2004) detailed description of neuropsychological assessment and were described as valid and reliable for the groups in question. However, six studies used a measure or measures not described in Lezak et al. (2004) and did not provide a reference to an appropriate source of reliability and validity data (Airaksinen et al., 2005; Asmundson et al., 1994; Galderisi et al., 2008; Gordeev, 2008; Gorini et al., 2010; Ludewig et al., 2003). One study used a measure from a German test battery, which had no reliability or validity data in English (Lautenbacher et al., 2002). An appropriate search for these data could not be performed in German due to translation difficulties.

2.4 Discussion
This systematic review examined the neuropsychological profile of individuals with panic disorder using the available literature. With only 14 studies included in the review, it demonstrates the scarcity of research in the area. The results obtained in these studies have mostly indicated an absence of difficulties in PD participants relative to HC, with no deficits being consistently reported across studies.

There was some support in the reviewed studies for potential deficits in short term verbal and visual memory in people with PD compared to HC. Results provided little support for impairment in any other area of neuropsychological function.

A number of factors may have influenced the obtained results, including methodological quality and characteristics of the sample used by each study, such as
quality criteria were applied to the studies reviewed, in order to further evaluate the reported findings. Methodological strengths and weaknesses were highlighted. Key issues arising from the assessment of methodological quality were risk of Type I error by failing to correct for multiple comparisons and use of measures without evident reliability or validity data for this population. Considering only studies that did not suffer from these methodological weaknesses the overall profile changes very little: limited support remained for visual and verbal short term memory difficulties in people with PD (Asmundson et al., 1994; Deckersbach et al., 2011) but the lack of consistency of results does not support a conclusion of impairment in this area. No remaining studies supported verbal long term memory or perception deficits in people with PD, and only one of the five remaining studies reporting on visual long term memory provided support for deficits in that area (Deckersbach et al., 2011). This removal of the less methodologically robust studies did not change the overall findings of no group differences on tasks of working memory, attention, visuospatial ability and executive functioning.

As a number of Axis I and Axis II disorders have been associated with cognitive impairment (Trivedi, 2006), criteria allowing the inclusion of PD participants with comorbid disorders, may have impacted on the specificity of the findings. Eight studies reported having no comorbid disorders, two allowed all comorbidities, two excluded only depression and two did not clearly state their exclusions. Four out of five of those reporting no findings, excluded all comorbidities. The exclusion of comorbidities helps to isolate difficulties that are due to PD alone, without the influence of other psychological disorders. However, this also limits the generalisability of results, as in a typical clinical group, comorbidities are common. Within the reviewed studies, patients without comorbidity tended to perform similarly to HCs (Cavedini et al., 2002; Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998).

Half of the studies reviewed reported including participants on medication, although two of these excluded benzodiazepines. There were no trends in findings relating to
medication status of participants. This is somewhat surprising as benzodiazepines (Deckersbach et al., 2011) and tricyclic antidepressants (Stein & Strickland, 1998) have been associated with additional cognitive impairment while SSRIs have not been consistently associated with impairment (Mataix-Cols et al., 2002).

Ten of the fourteen studies matched groups on age, gender and education. Of the four poorly matched groups, three of these were among those who produced a high number of significant findings. Poor group matching at the outset may have influenced results, as differences in age, gender and education have been shown to impact on neuropsychological test performance (Corral et al., 2006; Lowe et al., 2003; Reitan & Wolfson, 1995).

State anxiety at the time of testing was measured in eleven of fourteen studies. Eight of these made comparisons between PD and HC groups. In these studies, statistical tests suggested that PD groups were more anxious than HC at the time of testing. There was no pattern in the data relating to participant groups identified as being more anxious subsequently performing worse on tasks. However, as higher levels of anxiety were consistent among PD patients where it was reported, it is likely that this was also the case in studies where comparisons were not made between PD and HC groups. Literature suggests that state anxiety is unlikely to impact on test performance but it has suggested that those with lower IQ tend to be more anxious in advance of testing (Gass & Curiel, 2011).

2.4.1 Limitations

Only papers written in English were included in this review, limiting its scope. At least one potentially relevant study, not published in English, was excluded (Castillo et al., 2010). Studies containing PD samples of less than 15 were excluded from the review. This also reduced the number of studies reviewed, however the statistical power of such studies would have been low and findings, particularly negative findings, would have been difficult to interpret (Bezeau & Graves, 2001). This review is based on a relatively small number of studies, however this is primarily due to the scarcity of literature rather than the exclusion of potentially relevant studies. The consistency of the findings across these studies allows for greater confidence in conclusions drawn from this small number of studies.
2.4.2 Recommendation/implication for future research

These studies seem to suggest no consistent cognitive deficits in individuals with PD, which is in keeping with similar findings in populations with Social Phobia and Generalised Anxiety Disorder (Airaksinen et al., 2005; O'Toole & Pedersen, 2011). As such, neuropsychological functioning is unlikely to impact significantly on clinical practice in the treatment of PD. An impairment in short term memory, if it were present in some PD patients, may impact on the psychoeducation phase of CBT treatment, as recommended by the National Institute of Health and Clinical Excellence (NICE, 2011). The provision of written materials and other memory aids could potentially be helpful.

Future research should consider using sample sizes appropriate to detecting medium to large effect sizes and reporting on the effect sizes obtained, in order to further illustrate the potential magnitude of any differences detected (Bezeau & Graves, 2001). Specific hypotheses focussing on the highlighted areas of potential impairment, particularly short term memory, with an effort to use the same or directly comparable measures to other studies, would contribute to the clarification of findings. In addition, the specificity of any potential impairment requires further examination. While PD has been compared to OCD on a number of occasions (Bannon et al., 2006), comparisons with disorders such as Social Phobia and GAD, which have demonstrated similar patterns of neuropsychological performance, may help to illustrate if there are any specific impairments related to PD.

2.4.3 Conclusion

This systematic review of the neuropsychological profile of Panic Disorder (PD) demonstrates that within the current literature there is little support for any neuropsychological impairment in PD. Some support was found for an impairment in short term memory, which requires further investigation using larger sample sizes (25 or more) in order to detect large effect sizes (d=0.8) using the parameters of a power of 80% and a 0.05 two tailed significance level. The use of appropriate clinical comparison groups to determine the specificity of any impairment found is also recommended.
2.5 References


NICE, 2011. Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113.


Tabarés-Seisdedos, R., Balanzá-Martínez, V., Sánchez-Moreno, J., Martínez-Aran, A., Salazar-Fraile, J., Selva-Vera, G., Rubio, C., Mata, I., Gómez-Beneyto, M., Vieta, E.,


Chapter 3: Bridging Chapter

As the introduction of the journal article is necessarily brief and focused on only the thesis aims covered in the article, additional introductory information is necessary to describe the areas covered by the additional data analysis conducted outside the scope of the journal article.

3.1 The Cognitive Model of Bulimia Nervosa

Fairburn et al.’s (2003) cognitive behavioural model of BN implicates a dysfunctional system for evaluating self worth as a central maintaining mechanism. They propose that sufferers evaluate themselves based on eating, shape and weight and on their ability to control them. They further suggest that, in certain patients, one or more of four additional maintaining mechanisms operate. These additional mechanisms are severe perfectionism, core low self esteem, mood intolerance and interpersonal difficulties. Fairburn et al. (2003) broadened this model of BN into a transdiagnostic theory of eating disorders, emphasising the similarities between eating disorders. They highlighted the fact that individuals will often move between diagnostic categories over time and suggested that the maintaining mechanisms proposed for BN are common to all eating disorders. As key maintaining factors relate to maladaptive cognitive processes, neuropsychological research has investigated whether there are similar patterns of neuropsychological impairment in BN as have been observed in AN.

Beyond the neuropsychological focus of the current study, additional data were collected relating to maintaining factors proposed for BN. The primary maintaining mechanism of dysfunctional evaluation of eating, weight and shape, was measured by the Eating Disorder Examination, a semi structured interview described further in the Methods chapter. Obsessive compulsive symptoms in BN, and their relation to neuropsychological performance were also addressed in the study. Obsessive compulsive symptoms are common in BN and are linked to the construct of perfectionism (Egan et al., 2011; Tchanturia, Morris, et al., 2004). Obsessive compulsive symptoms were measured using both the Yale-Brown Obsessive Compulsive Scale (YBOCS) and the Obsessive Compulsive scale of the Symptom
Checklist 90-Revised (SCL-90-R). Core low self esteem was addressed using the Self Liking/Self Competence scale and aspects of interpersonal difficulties were addressed using the Social Problem Solving Inventory (SPSI) and the interpersonal sensitivity scale of the SCL-90-R. The Self Liking/Self Competence scale and the Social Problem Solving Inventory are not included in the journal article and are introduced below.

3.1.1 The Self liking/Self Competence scale (Tafarodi & Swann, 2001)
The Self liking/Self Competence scale was developed by Tafarodi and colleagues (Tafarodi & Milne, 2002; Tafarodi & Swann, 2001) based on theoretical research using factor analysis of Rosenberg’s (1965) self esteem scale. The concept of self esteem used in Rosenberg’s scale, is a one-dimensional construct that taps into the ‘self worth’ element of self esteem. Tafarodi and Milne (2002) identified two separate dimensions of self-esteem, namely self liking and self competence. Self liking taps into the ‘self worth’ element of self esteem, while self competence relates to an individual’s perception of their ability to deal with challenges.

Low self esteem is considered to be a core element in eating disorder theory and treatment (Fairburn et al., 2003). It has also been associated with anxiety and depression in community and eating disordered samples (Ackard et al., 2011; Rosenberg, 1962; Takagishi et al., 2011). Self esteem, as measured by the Self Liking/Self Competence scale (Tafarodi & Swann, 2001) has been noted in the literature to be significantly lower in anorexic patient groups than in healthy controls (Paterson et al., 2007). Self competence has been significantly associated with increased perfectionism and interpersonal distrust in anorexia nervosa (AN), and changes in self liking and self competence have been associated with changes in eating disordered behaviours in both AN and BN (Gordon et al., 2005; Surgenor et al., 2007). This research suggests that self liking and self competence may be important factors in the development or maintenance of eating disorders.

3.1.2 Social Problem Solving Inventory (SPSI) (D’Zurilla et al., 2002)
Social problem solving has been proposed by D’Zurilla and Maydeu-Olivares (1995) to result from maladaptive cognitive processes and to be a risk factor for psychological disorder. They describe social problem solving as a multidimensional
construct relating to adaptive orientation towards problems and the use of effective problem solving strategies. The dimensions identified by the Social Problem Solving Inventory are Positive Problem Orientation, Negative Problem Orientation, Rational Problem Solving, Impulsivity/Carelessness style and Avoidance style.

Although interpersonal difficulties are considered to be important in BN (Fairburn et al., 2003), and interpersonal therapy has been found to be as effective for BN as Cognitive-Behavioural Therapy in the long term (Agras et al., 2000), no research is available investigating social problem solving in BN. However, the existing literature indicates that social problem solving is impaired in individuals with eating disorders (Paterson et al., 2011; Swanson et al., 2010). McFillin (2009) found that adolescents with an eating disorder demonstrated more hostile attributional biases and experienced a significantly greater intensity of negative emotions when presented with vignettes of social dilemmas than did healthy controls. Svaldi et al. (2011) found that women with binge eating disorder produced less effective social problem solving strategies than healthy controls. Using the SPSI, anorexic individuals have been found to show a significantly higher negative problem orientation than controls and to demonstrate impulsive and avoidant problem solving styles (Paterson et al., 2011; Swanson et al., 2010).

Anxiety and depression symptoms have also been associated with poor problem solving in non-clinical populations (Haaga et al., 1995; Haugh, 2006) and in clinical populations, such as the anxiety disorder group reported on by Abbass and Mohammad (2008). This clinical group consisted of OCD, PTSD and panic disorder patients, who demonstrated higher negative problem orientation, impulsivity/carelessness style and avoidance style than healthy controls. In a mixed clinical group with at least one Axis I disorder, patients were also found to use poor social problem solving relative to healthy controls (Bray et al., 2007). Poor social problem solving has been found to correlate with both impulsivity (McMurran et al., 2002) and perfectionism (Chang, 2002), and has been suggested to be associated with the orbitofrontal regions of the brain (Hanten et al., 2011).
3.1.3 Impulsivity

Impulsivity is another feature of BN that has been investigated in the literature (Waxman, 2009). This characteristic most commonly takes the form of binging behaviours, but bulimia is also associated with higher rates of shoplifting, substance abuse and self harm (Goldner et al., 2000; Hudson et al., 2007; Ruuska et al., 2005). Impulsive behaviours in BN may be a reflection of underlying cognitive deficits in inhibition (Engel et al., 2005; Kemps & Wilsdon, 2010; Kirisci et al., 2004; Rosval et al., 2006; Verdejo-García et al., 2006). In relation to this, Robinson et al. (2009) have proposed a model of impulsivity in bulimia where the effect of trait impulsivity is moderated by cognitive inhibition skills. They suggest that temperamental impulsivity is a risk factor for impulsive behaviour, but that temperamental impulsivity can be overcome by good cognitive inhibition. They propose that training in cognitive control could be helpful to eating disordered individuals high in impulsive behaviours. Levels of impulsivity may also have implications for recovery, with lower levels of impulsivity associated with better treatment outcomes in BN (Castellini et al., 2012).

3.2 Composition of the Patient groups used in this study

Selection criteria for the groups included in this study were chosen to allow a clinically representative sample of each disorder group. The comparison group was selected on the basis of being in treatment for anxiety and/or depression in the Adult Psychological Therapies Service in Tayside, and scoring in the moderate to severe range on either of the anxiety or depression subscales of the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983).

The BN group included any patients in treatment for bulimia nervosa - both patients diagnosed with Bulimia Nervosa and also those diagnosed with Eating Disorder Not Otherwise Specified - Bulimic type (EDNOS-BN). National Institute for Health and Clinical Excellence (NICE, 2004a) guidelines for the treatment of eating disorders recommend that treatment of EDNOS be conducted using the same model as the disorder it most closely resembles. Therefore, patients with EDNOS-BN are routinely treated in the same way as those with BN. This is similar to the inclusion
criteria for bulimic groups used in other studies (Bara-Carril et al., 2004; Schmidt et al., 2006). Different diagnostic systems were in use in the Tayside and Grampian Eating Disorder Services, therefore the ICD 10 diagnostic categories of BN and Atypical BN (excluding Binge Eating disorder) were applied (WHO, 2010). These are comparable to the DSM-IV-TR diagnoses of BN and EDNOS-BN.

The category of EDNOS exists in DSM-IV-TR to describe patients who do not meet all the criteria for BN or AN diagnoses, while ICD 10 includes categories of ‘Atypical Anorexia’, ‘Atypical Bulimia’ and ‘Eating Disorder Unspecified’ for this purpose. Recent studies have reported forty to sixty percent of those seeking treatment for eating disorders falling within the EDNOS category when using DSM-IV-TR criteria, making them an important patient group in eating disorder research (Button et al., 2005; Fairburn et al., 2007; Ricca et al., 2001; Rockert et al., 2007).

Differences between patients with BN and EDNOS-BN on measures of eating pathology and general psychopathology have been found to be non-significant (Garfinkel et al., 1995; Martin et al., 2000; Ricca et al., 2001; Tobin et al., 1997).

### 3.2.1 Gender of Participants

Both groups contained only female participants. This was decided in order to be comparable to the majority of the current literature relating to BN (Alvarez-Moya et al., 2009; Brand et al., 2007; Kemps & Wilsdon, 2010; Rosval et al., 2006; Van den Eynde et al., 2012). Male patients have been excluded from many recent eating disorder studies, due to the low numbers that present for treatment and the gender differences that have been found in the literature on eating disorders. The literature suggests that significantly fewer males suffer from eating disorders than females (Hudson et al., 2007; Treasure et al., 2010). In a large population study in the United States, a 0.5% lifetime prevalence of BN was reported among males compared to 1.5% among females and a 12 month prevalence of 0.1% in males compared to 0.5% in females (Hudson et al., 2007). In addition, proportions of males attending for treatment of bulimia, as represented in current literature, are of the order of 5-10% of consecutive referrals (Fairburn et al., 2007; Mehler et al., 2008; Zeeck et al., 2007). Differences between males and females with bulimia in relation to age of onset, premorbid obesity, homosexuality and concern with weight control have been reported in the literature although very few studies have reported on gender
differences (Carlat & Camargo Jr, 1991). As the literature suggests that there may be differences between male and female patients with bulimia, and that few male patients are likely to be available for participation, it was decided to include only female patients. This also allows the study sample to be directly comparable to existing key papers that have used only female participants.

3.3 Research Links of the current study
Beyond the investigation of the specificity of cognitive impairment in BN, the data gathered in this study will be incorporated into the Tayside Eating Disorder Research Group’s ongoing research into the neuropsychological profile of eating disorders. Data from a group of healthy control participants was collected by the research group, administering the same neuropsychological measures used in the current study. Therefore, data from an additional healthy control group was not collected as part of the current study. The neuropsychological measures administered to participants, which were not a priori key measures of set shifting and inhibition, were included in the current study in order to facilitate comparison of this data with Research Group data already collected from AN groups and healthy controls.

3.4 Summary
As stated in the introduction, the aim of this thesis is to contribute to the body of research investigating the neuropsychological profile of bulimia by considering the specificity of the cognitive impairments reported in the literature. The potentially confounding influences of comorbid anxiety disorders and depression in BN have been highlighted in recent reviews as a neglected area of research (Van den Eynde et al., 2011; Zakzanis et al., 2010). Therefore, this study incorporates a comparison group of anxious and/or depressed outpatients.

Current eating disorder theory emphasises the similarity between eating disorders and supports research investigating the presence of similar properties in BN as have been seen in AN. It also proposes potential shared maintaining factors of severe perfectionism, low self esteem, mood intolerance and interpersonal difficulties. These potential maintaining factors of BN will also be explored by this thesis, particularly in the areas of self esteem and social problem solving.
3.4.1 Study Aims

1. To investigate what differences are evident, if any, between the a BN group and a comparison group of anxious and/or depressed adult females on measures of general psychopathology, eating pathology, set shifting and cognitive inhibition.

2. To investigate the relationships between general psychopathology, eating pathology, set shifting and inhibition within the groups.

3. To investigate social problem solving and self esteem in BN, and any relationship they may have to set shifting and cognitive inhibition.
Chapter 4: Investigating the specificity of neuropsychological impairment in bulimic outpatients: a comparison with anxious and depressed outpatients.

Following guidelines of Journal of the International Neuropsychological Society (Appendix 5)

Abstract

Background: Bulimia Nervosa (BN) has been associated with deficits in set shifting and inhibition but reported results are inconsistent. Systematic reviews have highlighted the potentially confounding effects of comorbid disorders, and the specificity of deficits in BN has not been explicitly investigated.

Method: Twenty one female participants with BN were compared to 23 females, in treatment for anxiety and/or depression, on neuropsychological measures of set shifting and inhibition, including the Wisconsin Card Sorting Test, the Trail Making Test and the Stroop task. Psychological symptoms were measured using the Symptom Checklist 90-R, the Yale Brown Obsessive Compulsive Scale and the Eating Disorder Examination.

Results: No group differences were found on a priori selected neuropsychological measures or measures of anxiety, depression or obsessive-compulsive symptoms. The BN group reported significantly more eating disorder symptoms than the comparison group.

Conclusions: These findings suggest that, in this sample, there is no evidence of a specific neuropsychological deficit in BN and suggest that deficits seen are shared with other disorders.

4.1 Introduction

Bulimia nervosa (BN) is characterised by binge eating accompanied by a sense of lack of control, the use of compensatory behaviours such as vomiting or excessive exercise, and self-evaluation unduly influenced by shape and weight (American Psychiatric Association, 2000). Both anorexia and bulimia involve rigid beliefs...
about eating and purging, and strict adherence to personal rules, which have been associated with compulsive behaviour (Naylor et al., 2011). Compulsive behaviours are defined by Robbins et al. (2012) as “actions inappropriate to the situation which persist”, or as “a maladaptive perseveration of behaviour” (p83). Compulsive behaviour and the related construct of perfectionism are common in BN, and are associated with impaired neuropsychological task performance on measures of set-shifting (Egan et al., 2011; Tchanturia, Morris, et al., 2004). Impulsivity is also a feature of BN. This characteristic most commonly takes the form of binging behaviours, but BN is also associated with higher rates of shoplifting, substance abuse and self harm (Goldner et al., 2000; Hudson et al., 2007; Ruuska et al., 2005). A number of studies have linked impulsivity to cognitive disinhibition in BN patient groups and other disorders, suggesting a relationship between these variables (Kemps & Wilsdon, 2010; Kirisci et al., 2004; Rosval et al., 2006; Verdejo-García et al., 2006). Impulsive-compulsive behaviours often co-occur in BN and may be a reflection of underlying cognitive deficits in the areas of set-shifting and cognitive inhibition (Engel et al., 2005).

These neuropsychological deficits have become an area of interest for research as they are hypothesised to be the basis for some key symptoms of BN. Fairburn et al. (2003) theorise that clinical perfectionism, which is associated with compulsive behaviour and poor set shifting, is a key maintaining factor for some individuals with BN (Tchanturia et al., 2004). Where patients have a difficulty with set shifting, there can also be a difficulty engaging with CBT and using flexible thinking during the course of therapy. Current research in AN suggests that intervention directed at set shifting, where it is a difficulty, improves CBT treatment outcomes (Tchanturia et al., 2007). Observed impulsive binging and purging behaviour is theorised by Robinson et al. (2009) to relate to poor cognitive regulation of an underlying trait impulsivity. They propose that specific training in cognitive control to reduce impulsivity could be helpful to BN patients as part of therapy. Research demonstrating that lower impulsivity is associated with better treatment outcome supports this (Castellini et al., 2012).
The majority of neuropsychological research in eating disorders has focused on set-shifting ability in anorexia nervosa (AN), finding specific cognitive deficits as compared to healthy controls (HC) (Roberts et al., 2007). Comparisons have also been made between AN and other psychiatric groups such as obsessive compulsive disorder (OCD) (Murphy et al., 2004) and depression (Giel et al., In Press) to further clarify the specificity of these deficits. An increasing amount of research is now focussing on the neuropsychological profile of BN (Van den Eynde et al., 2011). As AN and BN are closely linked (Fairburn et al., 2003), set-shifting has also been a focus of research when investigating the neuropsychological profile of BN. While cognitive impairments have been reported in BN, there is little agreement between studies. Three recent systematic reviews on the topic have reached conflicting conclusions. Zakzanis et al. (2010) concluded that the core impairment in BN was an impairment in inhibition without impairments in set shifting, while the opposite trend was reported by Roberts et al. (2007). These reviews were limited in the number of studies they included, reviewing 14 and 4, respectively. The most recent comprehensive review examined 34 studies, reporting that the area was under-researched and that findings to date were inconclusive (Van den Eynde et al., 2011).

In Van den Eynde et al.’s (2011) review, impairment in inhibition was seen in BN in only one of five studies that used the classic Stroop task (Kemps & Wilsdon, 2010). Similarly, no clear pattern of impairment of inhibition was seen in studies using the Go/NoGo task or Matching Familiar Figures Test (Claes et al., 2006; Kemps & Wilsdon, 2010; Rosval et al., 2006; Southgate et al., 2008). One reviewed study used the Hayling sentence completion task as a measure of inhibition and found impairment in individuals with BN relative to controls (Kemps & Wilsdon, 2010). The Wisconsin Card Sorting Test (WCST) subscale of ‘number of non-perseverative errors’ has also been considered as a measure of inhibition. Alvarez-Moya et al. (2009) noted that individuals with BN had difficulty maintaining the correct set on the WCST, scoring significantly worse than controls on ‘non-perseverative errors’. The WCST is usually used as a measure of set shifting ability, with ‘number of perseverative errors’ used as a key measure of compulsive responding behaviour. Bulimic patients have demonstrated impairment relative to HCs using this variable in
some studies, although an equal number of studies have found no significant differences (Alvarez-Moya et al., 2009; Brand et al., 2007). Similarly, set shifting as measured by the Trail Making Task (TMT) has produced mixed results (Roberts et al., 2010; Tchanturia, Anderluh, et al., 2004).

Cognitive impairment in inhibition and set shifting has been seen across a range of other disorders. Studies on neuropsychological deficits in anxiety disorders have reported set shifting and inhibition impairment in Post Traumatic Stress Disorder (PTSD) and Obsessive Compulsive disorder (OCD) (Kuelz et al., 2004; Polak et al., 2012), but not in social anxiety, simple phobia, panic disorder or generalised anxiety disorder (Airaksinen et al., 2005; O'Toole & Pedersen, 2011; Chapter 2 of this thesis). (Ferreri, et al., 2011)Depression has also been associated with neuropsychological impairments in inhibition and set shifting (Gohier et al., 2009; Porter et al., 2007; Xu et al., 2012). However, much of the literature on depression has focused on the elderly, with deficits not consistently seen in young adult samples with mild to moderate depression (McClintock et al., 2010). When anxiety and depression co-occur, some research has reported increased impairments (Basso et al., 2007; Lyche et al., 2011), while others have reported that such clinical groups perform no differently to those with depression alone (Herrera-Guzman et al., 2009) or healthy controls (Graver & White, 2007). In anxiety and depression, as in BN, reviews indicate potential deficits in areas of set shifting and inhibition but conclude that further research and clarification of neuropsychological findings is required (Castaneda et al., 2008; Ferreri et al., 2011).

One possible confounder in assessments of neuropsychological performance is diagnostic comorbidity. Bulimia nervosa is frequently comorbid with both depression and anxiety disorders; up to 80% comorbidity is found with anxiety disorders and 60% comorbidity with Major Depressive Disorder (MDD) or dysthymia (Hudson et al., 2007). Overall, the neuropsychological literature in relation to BN is somewhat equivocal and the large clinical overlap with other disorder groups that also display similar cognitive impairments calls into question the specificity of the impairments seen in BN.
The reviews by both Van den Eynde et al. (2011) and Zakzanis et al. (2010) recommend that future research consider this overlap of diagnoses and symptoms when investigating the neuropsychological profile of BN. It is currently unclear if reported cognitive impairments are specific to BN or whether they are shared across other psychiatric diagnoses, representing a transdiagnostic, rather than disorder-specific feature. Knowledge about the specificity of cognitive impairments is important, in order to facilitate the development of disorder specific cognitive models and therapies (Dudley et al., 2011).

While one study has compared BN patients to OCD patients on neuropsychological measures (Murphy et al., 2004), no study to date has focused on further clarifying the specificity of reported cognitive impairments in BN through the use of a clinical group reflecting diagnoses that often co-occur with BN. The current study compared a group of females in psychological treatment for anxiety and/or depression (AD group), who were free from comorbid eating disorder, to a BN group. This study sought to investigate what differences, if any, exist between the two groups on measures of set shifting and inhibition. Further exploratory analyses were conducted on the relationships between reported anxiety, depression, obsessive compulsive and eating disorder symptoms and performance on the neuropsychological measures.
4.2 Methods

4.2.1 Participants
The BN group consisted of 21 outpatients, 14 with BN and 7 with Eating Disorder Not Otherwise Specified-Bulimic Type (EDNOS-BN), recruited from eating disorder services of NHS Grampian (n=5) and NHS Tayside (n=16). All patients meeting inclusion criteria and in treatment for BN with the NHS Tayside (29) were provided with study information by their clinicians. Patients in Grampian meeting the inclusion criteria were posted study information by their clinician. The number of patients contacted in Grampian was not available at the time of writing. Patients with EDNOS were included if they had subthreshold bulimic symptoms and were therefore being treated as a bulimic patient as per National Institute for Health and Clinical Excellence (NICE) guidelines for the treatment of EDNOS (NICE, 2004a). EDNOS patients with primarily anorexic features and patients with Binge Eating Disorder were excluded. Participants in the AD group were 23 outpatients in treatment for major depressive disorder (MDD) and/or an anxiety disorder in the Tayside Adult Psychological Therapies Service. A breakdown of their diagnoses appears in Table 4.1. AD group participants were required to score 11 or more on either scale of the Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983). All participants were adult females recruited between November 2011 and June 2012. All diagnoses met Diagnostic and Statistical Manual, 4th edition (DSM-IV; American Psychiatric Association, 2000) criteria, as determined by the treating clinician.
Patients were excluded if they were medically unstable, had a history of learning disability, substance abuse, developmental or neurological disorder, an uncorrected visual or motor impairment, or previous head injury involving loss of consciousness. In addition, AD group participants were excluded if they demonstrated significantly disordered eating (Eating Disorder Examination score ≥ 4). The study was approved by NHS Tayside Research Ethics Committee and all participants gave written informed consent.

The groups were matched on years of education, estimated premorbid IQ and Body Mass Index (BMI) (see Table 4.2). However, bulimic patients were significantly younger than AD group patients (t(42)= 2.918; p <.008). Mean age of disorder onset was also significantly lower in the BN group than in the AD group (U= 129, Z= -2.65, p <.008). Ninety percent of the BN group were right-handed compared to 74% of the AD group. This difference was not found to be significant using Fisher’s exact test (p=.432). Two BN participants reported having a previous diagnosis of anorexia. Forty eight percent of the BN participants and 65% of the AD participants were taking psychiatric medication, primarily antidepressants (5 SSRI, 3 serotonin-norepinephrine uptake inhibitors (SNRI) and 1 tetracyclic antidepressant in the BN group, 9 SSRI and 3 tetracyclic antidepressants in the AD group). Two BN participants were taking Quetiapine, while in the AD group one person was taking

Table 4.1 Diagnoses of AD group

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>11</td>
</tr>
<tr>
<td>GAD</td>
<td>3</td>
</tr>
<tr>
<td>PD (with agoraphobia)</td>
<td>3</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>1</td>
</tr>
<tr>
<td>Specific Phobia</td>
<td>1</td>
</tr>
<tr>
<td>OCD</td>
<td>2</td>
</tr>
<tr>
<td>Health Anxiety</td>
<td>1</td>
</tr>
<tr>
<td>MDD</td>
<td>3</td>
</tr>
<tr>
<td>Mixed anxiety and depression</td>
<td>9</td>
</tr>
</tbody>
</table>

MDD = Major Depressive Disorder, GAD = Generalised Anxiety Disorder, PD = Panic Disorder
Diazepam and one was taking Tramadol. No medications had been changed within the previous month.
Table 4.2: Characteristics of groups

<table>
<thead>
<tr>
<th></th>
<th>BN group n=21</th>
<th>AD group n=23</th>
<th>Cohen’s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean  SD</td>
<td>Median (range)</td>
<td>Mean  SD</td>
</tr>
<tr>
<td>Clinical Characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>29.29 10.49</td>
<td>39.52 12.75</td>
<td>2.918 .006**</td>
</tr>
<tr>
<td>Education (yrs)</td>
<td>14.60 2.41</td>
<td>15.17 2.91</td>
<td>0.721 .475</td>
</tr>
<tr>
<td>BMI (Kg/m²)a</td>
<td>24.07 4.15 (17.4-32.4)</td>
<td>26.96 6.90 (18.5-45.6)</td>
<td>178.5 .319</td>
</tr>
<tr>
<td>Age of disorder onset</td>
<td>18.19 7.28 16 (7-38)</td>
<td>29.43 14.87 27 (11-62)</td>
<td>129 .007**</td>
</tr>
<tr>
<td>Duration of disorder</td>
<td>10.17 7.45 9 (1-32)</td>
<td>9.19 11.85 3 (0.04-38)</td>
<td>170 .047*</td>
</tr>
<tr>
<td>NART estimated FSIQ</td>
<td>110.61 5.97</td>
<td>111.39 5.40</td>
<td>0.451 .665</td>
</tr>
</tbody>
</table>

Note. BMI= Body Mass Index, BN=Bulimia Nervosa, AD= Anxiety and/or Depression
* p < 0.05
**Bonferroni correction for 6 comparisons α=.008
a: data available for only 42 patients (data missing for 2 BN participants)
4.2.2 Measures
Participants were administered a battery of standardised assessment measures relating to psychopathology and neuropsychological performance in the areas of set shifting and cognitive inhibition.

4.2.2.1 Psychopathology Measures
Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)
The HADS is a self-report measure containing two scales relating to anxiety and depression symptoms. The HADS depression subscale has 90% sensitivity and 86% specificity for depression compared to the gold standard of a structured diagnostic interview (Zigmond & Snaith, 1983). Good reliability for both scales has been well documented in adults. A recent review by Bjelland et al. (2002) reported the reliability of the Anxiety subscale to vary from 0.68 to 0.93 (mean 0.83) and for the Depression subscale from 0.67 to 0.90 (mean 0.82). The HADS was administered to AD group patients as part of routine clinical practice. A score of 11 or more on either scale indicated moderate to severe symptoms.

Eating Disorders Examination (EDE) Version 12 (Fairburn & Cooper, 1993)
The EDE is a semi-structured clinical interview, which measures eating disordered attitudes and behaviours. It contains four subscales (Dietary Restraint, Eating Concern, Weight Concern and Shape Concern), and a global score. All subscale mean scores and the global score range from 0-6. Good internal consistency, (Beumont et al., 1993; Cooper et al., 1989) concurrent (Rosen et al., 1990) and discriminant (Cooper et al., 1989; Rosen et al., 1990; Wilson & Smith, 1989) validity, and inter-rater reliability (Black & Wilson, 1996; Cooper & Fairburn, 1987; Rosen et al., 1990; Wilson & Smith, 1989) have been demonstrated for the EDE in adults.

The YBOCS consists of a 58 item symptom checklist and a 10 item severity scale. The symptom checklist covers a range of obsessions and compulsions, clustered by behavioural expression and thematic content. Obsessions and compulsions are assessed over the 5 dimensions of time spent, interference in functioning, distress, efforts to resist and perceived control, creating a 10 item severity measure relating to the past 7 days. The YBOCS can be administered in the form of interview or self-report. Good agreement has been found between these for both the symptom checklist and severity ratings (Steketee et al., 1995). The current study used a self-report version (Baer, 1991).

*Symptom Check List–90 Revised (SCL–90-R) (Derogatis, 1994; Derogatis et al., 1973)*

The SCL–90-R is a 90–item self–report instrument for measuring general psychopathology for use with community, medical and psychiatric respondents. It comprises nine primary symptom dimensions; - Somatisation, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism - and three global indices; the Global Severity Index (GSI), the Positive Syndrome Distress Index (PSDI) and the Positive Symptom Total (PST). Good internal consistency of the primary symptom dimensions and global indices has been demonstrated across a number of populations. The SCL–90-R has been found to have good test-retest reliability across a range of patient groups and test-retest intervals (Derogatis, 2000). The Depression and Anxiety subscales have the most evidence of convergent and discriminant validity (Bech et al., 1992; Derogatis, 2000; Koeter, 1992). The Obsession-Compulsion subscale has been shown to be internally consistent (Woody et al., 1995) but also demonstrates poor discriminant validity, therefore the YBOCS was taken as the primary measure of obsessive compulsive symptoms in this study (Kim et al., 1992; Woody et al., 1995).

4.2.2.2 Neuropsychological Measures

*National Adult Reading Test (NART) (Nelson, 1982; Nelson & Willison, 1991)*
The NART is a measure of premorbid intellectual ability. The participant is asked to read aloud 50 irregularly spelled words (e.g. cough). The number of pronunciation errors is used to estimate the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981) full scale IQ from standardised norms. The NART’s validity as a measure of premorbid intelligence has been well documented (e.g. Crawford et al., 2001).

*Delis–Kaplan Executive Function System (D-KEFS) (Delis et al., 2001)*

Two tests from the D-KEFS were used:

**Colour Word Inference Test (CWIT)** – This is a measure of response inhibition and cognitive flexibility based on the Stroop procedure. The CWIT has four conditions: colour naming (condition 1), word reading (condition 2), inhibition (colour word interference, condition 3) and set shifting (Inhibition Switch, condition 4). In each condition, the outcome is the time taken to read 50 items and the number of errors made.

**Trail Making Test (TMT)** – This is a measure of planning and cognitive flexibility based on the traditional TMT A and B. The TMT has 5 conditions: visual scanning (condition 1), number sequencing (condition 2), letter sequencing (condition 3), number-letter switching (condition 4), and motor speed (condition 5). The procedure for the first condition involves a timed visual search. The remaining conditions involve drawing a line connecting the target items (numbers, letters or empty circles) as quickly as possible. The switching task involves switching back and forth between connecting numbers and letters, completing the task as quickly as possible. In each condition, the outcome measures are time to complete task and number of errors. Good to moderate test retest reliability and internal consistency are described in the technical manual for CWIT and TMT (Delis et al., 2001).

*The Hayling task (Burgess & Shallice, 1997)*
The Hayling task evaluates initiation speed, by requiring participants to complete 15 sentences as quickly as possible. Part one requires sensible completion of the sentence while part two requires an unrelated word. This is a measure of response suppression. Outcome measures are the time taken to respond and total number of errors. Adequate inter-rater reliability and test-retest reliabilities have been reported for this task (Andres & Van der Linden, 2000; Burgess & Shallice, 1997).

**Wisconsin Card Sort Test (WCST) (Heaton et al., 1993)**

The WCST measures concept formation, set-shifting, and set maintenance. Four stimulus ‘key cards’ with symbols differing in colour, shape and number are placed in front of the participant, who is given a pack of 128 response cards and instructed to match each response card to one of the key cards. The researcher only provides feedback of ‘correct’ or ‘incorrect’ for each trial. After coupling 10 cards with the first criterion (colour), the subject is required to shift to the second criterion (shape) and then to the third (number). The procedure is repeated twice or until all 128 cards have been used. Good test-retest and inter-rater reliabilities have been reported in adults (Axelrod et al., 1992; Bowden et al., 1998; Heaton et al., 1993). The official computer package was used to score this task.

**4.2.3 Measures selected as a priori key variables for set shifting and inhibition**

Seven specific variables were selected from the neuropsychological battery as a priori key measures. The key variables chosen were those on which neuropsychological deficits have been previously reported in BN patients compared to HCs. The 4 key variables selected to reflect set shifting performance were ‘number of perseverative errors’ and ‘categories completed’ from the WCST (Roberts et al., 2010) and the completion time and number of errors in TMT condition 4 (Brand et al., 2007; Konstantakopoulos et al., 2011; Roberts et al., 2010; Tchanturia, Morris, et al., 2004). The 3 key variables selected to reflect cognitive inhibition were the WCST ‘number of non-perseverative errors’ (Alvarez-Moya et al., 2009), condition 3 from the CWIT and the number of errors made on the Hayling
task part two (Kemps & Wilsdon, 2010). Information on the additional outcome variables included in the above measures was provided in the form of secondary variables, as recommended by Van den Eynde et al.’s (2011) review.

4.2.4 Procedure/Protocol
Suitable patients were identified by their clinician and invited to participate. They were provided with study information and contacted by the first author no sooner than 24 hours after expressing interest in the study. Demographic and historical information relating to participant characteristics was collected first using a questionnaire designed for the study, followed by administration of the EDE, the neuropsychological battery (in the order listed above) and the self report measures (in the order listed above). Testing lasted approximately 1.5 to 2 hours.

4.2.5 Data Analysis
Data were analyzed using SPSS (version 15). Means were calculated for all continuous variables and frequencies for categorical variables. Means of the two groups were compared on assessment measures and demographic characteristics using t-tests, where data were normally distributed. The non-parametric Mann Whitney U statistic was used to compare non-normal variables between groups. Appropriate effect sizes, Cohen’s d or r, were calculated for these comparisons. Associations between a priori key measures and psychopathological variables within groups were investigated using the non-parametric Kendall’s tau.

4.2.5.1 Power for comparison of means
The literature indicated expected effect sizes ranging from 0.78 to 1.2 for differences between BN and AD groups. This suggested optimal samples sizes of 26 in order to detect large effect sizes (d=0.8, r=0.5) using the parameters of a power of 80% and a 0.05 two tailed significance level. Due to difficulties with recruiting this number of participants, the resulting sample sizes had the power to detect an effect size of d=0.88 with a power of 80% and a 0.05 two tailed significance level (calculated using GPower 3.1.2).
4.3 Results

4.3.1 Group comparisons on psychological and neuropsychological measures

Participants on medication did not perform significantly differently on key measures to those not taking medication using Mann Whitney U tests (all p>.05). Descriptives and statistical group comparisons for psychological and neuropsychological variables are presented in Table 4.3 and Table 4.4 respectively.

The BN group was not significantly different to the AD group in self reported obsessive compulsive symptoms as measured by the YBOCS, or on any of the symptom clusters measured by the SCL-90-R including anxiety and depression. The BN group scored significantly higher than the AD group on all scales of the EDE.

On the a priori measures of set shifting and inhibition, the BN group did not perform significantly differently from the AD group (See Table 4.4). As groups differed significantly on age, differences between the groups on age normed scaled scores were investigated on neuropsychological measures where such scaled scores were available. There were also no significant differences using age normed scores (all p > .05).
Table 4.3: Comparison of groups on psychological variables

<table>
<thead>
<tr>
<th>Psychological Measures</th>
<th>Bulimic group n=21</th>
<th>Anx/Depressed group n=23</th>
<th>Cohen's</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median (range)</td>
</tr>
<tr>
<td>SCL-90 (GSI)</td>
<td>1.37</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>O-C</td>
<td>18.00</td>
<td>8.80</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>25.33</td>
<td>10.95</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>11.33</td>
<td>8.41</td>
<td>9 (1-35)</td>
</tr>
<tr>
<td>Phobia</td>
<td>5.38</td>
<td>6.47</td>
<td>2.5 (0-21)</td>
</tr>
<tr>
<td>Somatisation</td>
<td>14.91</td>
<td>10.87</td>
<td>12.5 (1-41)</td>
</tr>
<tr>
<td>Hostility</td>
<td>5.19</td>
<td>3.37</td>
<td></td>
</tr>
<tr>
<td>I-S</td>
<td>16.62</td>
<td>6.45</td>
<td></td>
</tr>
<tr>
<td>YBOCS *</td>
<td>13.75</td>
<td>7.35</td>
<td>14.5 (0-27)</td>
</tr>
<tr>
<td>EDE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restraint</td>
<td>3.60</td>
<td>1.38</td>
<td>3.8 (0.3-6)</td>
</tr>
<tr>
<td>Eating concern</td>
<td>3.21</td>
<td>1.36</td>
<td>3.3 (0.6-5.2)</td>
</tr>
<tr>
<td>Shape concern</td>
<td>4.59</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td>Weight concern</td>
<td>4.10</td>
<td>1.22</td>
<td>4.1 (1.4-6)</td>
</tr>
<tr>
<td>Global Score</td>
<td>3.87</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

Note. SCL-90= Symptom Checklist-90-Revised, GSI= Global Severity Index, O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12), Anx=Anxious. all analysis are two tailed, \( r = Z/\sqrt{N} \)
\( a: n=20 \) in BN group

* indicates significance at Bonferroni corrected alpha level of 0.05/17=.002

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Table 4.4: Comparison of groups on key Set Shifting and inhibition variables

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>Bulimic group n=21</th>
<th>Anxious/Depressed group n=23</th>
<th>Cohen’s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median (range)</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>10.71</td>
<td>6.37</td>
<td>10 (4-28)</td>
</tr>
<tr>
<td>Categories completed</td>
<td>5.19</td>
<td>1.66</td>
<td>6 (0-6)</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number/letter switch</td>
<td>69.21</td>
<td>22.41</td>
<td>120.9</td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of errors</td>
<td>0.91</td>
<td>1.95</td>
<td>0 (0-8)</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>16.62</td>
<td>20.46</td>
<td>7 (2-74)</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Word Inhibition</td>
<td>47.06</td>
<td>10.67</td>
<td>46.1 (30.8-67.5)</td>
</tr>
<tr>
<td>Hayling Errors</td>
<td>1.05</td>
<td>1.99</td>
<td>1 (0-7)</td>
</tr>
<tr>
<td>Secondary Measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of trials to complete first</td>
<td>16.76</td>
<td>25.73</td>
<td>11 (10-129)</td>
</tr>
<tr>
<td>% Conceptual level responses</td>
<td>68.05</td>
<td>23.54</td>
<td>76 (9-91)</td>
</tr>
<tr>
<td>Failure to maintain set</td>
<td>0.43</td>
<td>0.60</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>Learning to learn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-3.68</td>
<td>8.54</td>
<td></td>
</tr>
<tr>
<td>Trials administered</td>
<td>95.57</td>
<td>22.17</td>
<td>92 (70-128)</td>
</tr>
<tr>
<td>Colour Word</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition Shift</td>
<td>52.82</td>
<td>12.94</td>
<td>64.56</td>
</tr>
</tbody>
</table>

*p < .01, **indicates significance at Bonferroni corrected alpha level of 0.05/7=.007 for à priori key variables,
† indicates significance at Bonferroni corrected alpha level of 0.05/10=.005 for secondary variables, all analysis are two tailed, r =Z/√N
4.3.2 Relationship of Psychopathological Symptoms to Set Shifting and inhibition

Relationships between neuropsychological performance and anxiety or depression symptoms, as measured by the SCL-90-R or obsessive compulsive symptoms as measured by the YBOCS were investigated using Kendall’s tau correlations within each group. Correlations were performed between the seven a priori key variables, the three psychopathological measures and the subscales of the EDE (Table 4.5).

A significance level of $p < .01$ was chosen, as a Bonferroni correction was considered too conservative for this analysis. There was a significant relationship between the number of Hayling task errors and EDE Eating Concern in the BN group. Within the AD group, the YBOCS correlated with WCST categories completed (0.46) and anxiety was correlated with TMT errors (-0.48) (Table 4.6). However, there were strong floor effects on the Hayling task and TMT errors and a ceiling effect in the WCST categories completed. On visual inspection of the variables, within the AD group, the YBOCS correlation did not appear to be a true relationship (graphs in Appendix 6).
Table 4.5: Correlation of Set shifting and inhibition key measures with psychopathology measures in bulimic group

<table>
<thead>
<tr>
<th></th>
<th>SCL-90</th>
<th>YBOCS</th>
<th>EDE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anx</td>
<td>Dep</td>
<td>Restraint</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>.045</td>
<td>.130</td>
<td>.126</td>
</tr>
<tr>
<td>Categories completed</td>
<td>.164</td>
<td>-.104</td>
<td>-.040</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number/letter switch</td>
<td>-.087</td>
<td>-.044</td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number of errors</td>
<td>-.007</td>
<td>-.070</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>.044</td>
<td>.118</td>
<td>.141</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Word Inhibition</td>
<td>Number/letter switch</td>
<td>.189</td>
<td>-.058</td>
</tr>
<tr>
<td>Hayling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Errors</td>
<td>-.247</td>
<td>-.400*</td>
<td>-.006</td>
</tr>
</tbody>
</table>

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12). Anx = Anxiety subscale, Dep = Depression subscale, *p<.05, **p<.01

Table 4.6 Correlation of key set shifting and inhibition measures with psychopathology in the AD group

<table>
<thead>
<tr>
<th></th>
<th>SCL-90</th>
<th>YBOCS</th>
<th>EDE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anx</td>
<td>Dep</td>
<td>Restraint</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>-.016</td>
<td>.045</td>
<td>-.230</td>
</tr>
<tr>
<td>Categories completed</td>
<td>.127</td>
<td>.058</td>
<td>.462**</td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>-.012</td>
<td>.127</td>
<td>-.382*</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number/letter switch</td>
<td>-.177</td>
<td>-.044</td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number of errors</td>
<td>-.484**</td>
<td>-.345*</td>
</tr>
<tr>
<td>Colour Word Inhibition</td>
<td>Number/letter switch</td>
<td>-.121</td>
<td>-.171</td>
</tr>
<tr>
<td>Hayling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Errors</td>
<td>-.072</td>
<td>-.080</td>
<td>.082</td>
</tr>
</tbody>
</table>

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12). Anx = Anxiety subscale, Dep = Depression subscale *p<.05, **p<.01
4.3.3 Post hoc exploratory analysis

4.3.3.1 Association between psychopathological variables and neuropsychological performance using data from combined groups

As no significant differences were found between groups on the a priori neuropsychological measures, the two groups were combined and Kendall’s tau correlations were used to investigate associations between psychopathological variables and neuropsychological performance in the entire sample (Table 4.7). Using the whole sample, significant correlations (p < .05) were seen between the YBOCS and WCST categories completed (0.25), and between SCL-90-R Anxiety and TMT errors (-.25). For the same reasons as above, these relationships must be interpreted with caution due to the noted floor and ceiling effects. Again, the YBOCS correlation did not appear to be a true relationship. Graphs are provided in Appendix 6.

Table 4.7: Correlation of key set shifting and inhibition measures with psychopathology in both groups combined

<table>
<thead>
<tr>
<th></th>
<th>SCL-90</th>
<th>YBOCS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anx</td>
<td>Dep</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>.030</td>
<td>.075</td>
</tr>
<tr>
<td>Categories completed</td>
<td>.100</td>
<td>.002</td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>.020</td>
<td>.126</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number/letter switch</td>
<td>-.176</td>
<td>-.103</td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors</td>
<td>-.247*</td>
<td>-.170</td>
</tr>
<tr>
<td>Colour Word</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>.001</td>
<td>-.132</td>
</tr>
<tr>
<td>Hayling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Errors</td>
<td>-.134</td>
<td>-.211</td>
</tr>
</tbody>
</table>

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, Anx = Anxiety subscale, Dep = Depression subscale *p<.05, **p<.001.
4.3.3.2 Regression

Further analysis explored any possible predictive relationship between anxiety, depression and obsessive symptoms and neuropsychological performance, using multiple linear regression analysis. A priori key variables were used as the dependent variables and the YBOCS and the SCL-90-R subscales of anxiety and depression were independent variables (Table 4.8). Seven separate linear regression analyses were performed.

Using 43 participants (one participant did not complete the YBOCS) this sample had the power to detect a large effect size using 3 predictors (power 0.8, $\alpha = .5$) according to the calculations of Miles and Shevlin (2001). Due to the non-normality of the data, some outliers were removed for regression analysis (detailed in Table 4.8). In order to control for interaction effects between predictors, all variables entered the regression analysis simultaneously. Relationships between variables were investigated using Kendall’s tau correlations and examination of eigenvalues. The anxiety and depression subscales of the SCL-90-R were noted to correlate and to load primarily on the same small eigenvalue, indicating some collinearity. No bivariate correlations exceeded 0.70 so no variables were excluded (Tabachnick & Fidell, 2001). The assumption of normally distributed errors of the regression was violated for a number of the models, as determined from examination of graphs and a Kolmogorov-Smirnov test on the standardised residuals. This violation of assumptions suggests that the results of the regression analysis will generalise poorly.

None of the models were significant (for all F values, $p > .05$), suggesting that in this sample, anxiety, depression and obsessive compulsive symptoms did not predict neuropsychological performance.
Table 4.8: Adjusted Beta values for predictor variables in the regression analyses

<table>
<thead>
<tr>
<th></th>
<th>WCST</th>
<th>TMT</th>
<th>CWIT</th>
<th>Hayling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Perseverative errors(^a)</td>
<td>Categories completed(^bh)</td>
<td>Non perseverative errors(^c)</td>
<td>Number/letter switch(^d)</td>
</tr>
<tr>
<td>Beta</td>
<td>Beta</td>
<td>Beta</td>
<td>Beta</td>
<td>Beta</td>
</tr>
<tr>
<td>SCL-90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>-0.06</td>
<td>-0.154</td>
<td>-0.09</td>
<td>-0.311</td>
</tr>
<tr>
<td>Depression</td>
<td>0.32</td>
<td>-0.091</td>
<td>0.197</td>
<td>-0.07</td>
</tr>
<tr>
<td>YBOCS</td>
<td>-0.317</td>
<td>0.283</td>
<td>-0.343*</td>
<td>-0.018</td>
</tr>
<tr>
<td>AdjR(^2)</td>
<td>0.086</td>
<td>0.021</td>
<td>-0.024</td>
<td>0.070</td>
</tr>
<tr>
<td>F</td>
<td>2.283</td>
<td>1.295</td>
<td>0.666</td>
<td>2.046</td>
</tr>
</tbody>
</table>

\(*p < .05, **p < .01, ***p < .001\)

\(^a\) n=42, 1 outlier removed, 4 standard deviations from the mean
\(^b\) n=43 because data is missing for one BN participant on YBOCS
\(^c\) n=41, 2 outliers removed, each 3.2 standard deviations from the mean
\(^d\) n=43,
\(^e\) n=42, 1 outlier removed, 4.62 standard deviations from the mean
\(^f\) n=42, 1 outlier removed, 3.2 standard deviations from the mean
\(^g\) n=42, 1 outlier removed, 4.76 standard deviations from the mean
\(^h\) assumption of normality of errors violated

4.3.4 Exploratory analysis of performance on secondary set shifting and inhibition variables

4.3.4.1 Analysis of Secondary Variables

The BN group were significantly slower on the CWIT condition 4 than the AD group with a large effect size of 0.84. However, this was no longer significant after Bonferroni correction (Table 4.4).
4.4 Discussion

The present study was the first to use a clinical comparison group of people with anxiety and/or depression to investigate the specificity of neuropsychological impairments among patients with BN. The a priori set shifting and inhibition variables were selected because they have been highlighted in the literature as demonstrating potential deficits in individuals with BN as compared to healthy controls (Alvarez-Moya et al., 2009; Brand et al., 2007; Roberts et al., 2010). No statistically significant differences were found between the BN group and the AD group on these measures, indicating similar levels of neuropsychological ability in both groups. While there was a significant relationship between anxiety and one neuropsychological measure, a regression analysis demonstrated that anxiety, depression and obsessive compulsive symptoms were not predictive of neuropsychological performance.

Although no studies were found that conducted neuropsychological comparisons between a BN and AD group, over half of the AD group were diagnosed with depression and literature would suggest that a depressed group may perform worse on tasks of inhibition and set shifting than an eating disordered group. Giel et al. (In Press) found that individuals with unipolar depression performed significantly worse than those with AN on set shifting, using the TMT and WCST perseverative errors, and on cognitive inhibition using the Parametric Go/NoGo task (PGNG; Langenecker et al., 2007). As the performance of BN patients in the literature is reported as the same or better than AN patients (Lauer et al., 1999; Roberts et al., 2010), it may have been expected that the BN group would also perform better than a depressed group. However, in Giel et al.’s (In Press) study, only AN patients without comorbid depression were included, and as a result, the AN group reported significantly fewer depression symptoms than the unipolar depression group. This was not the case in the current study where comorbid depression was not excluded in the BN group and similar levels of depression were reported in both groups. It is possible that an AN group with no comorbid depression is a particular subgroup of AN, which is not comparable to the BN sample of mixed comorbidity used in the current study. Subgroups of AN have been demonstrated to show significantly
different levels of ability on neuropsychological tasks (Lauer et al., 1999; Roberts et al., 2010).

The literature provides some indications that particular anxiety disorders, such as OCD and PTSD, may demonstrate greater impairment on inhibition and set shifting tasks than BN. Murphy et al. (2004) reported that BN participants performed significantly better on the TMT than an OCD group. However, while OCD is an anxiety disorder with replicated neuropsychological impairments (Martinez-Gonzalez & Piqueras-Rodriguez, 2008) most participants in the AD group were diagnosed with GAD, specific phobia or panic disorder with or without comorbid depression. The literature would suggest that these anxiety disorders are less likely to have specific deficits in set shifting or inhibition than a group of OCD patients, and are therefore less likely to differ from a BN group (Airaksinen et al., 2005; Chapter 2 of this thesis; McClintock et al., 2010; O'Toole & Pedersen, 2011).

In the BN group, higher scores on the EDE eating concern scale were significantly associated with fewer errors on the Hayling task, suggesting that those higher in Eating Concern were better able to inhibit incorrect responses on this task. However, this correlation was influenced by a floor effect and needs to be interpreted with caution. Within the literature for BN, eating disordered symptoms have not been found to be associated with neuropsychological performance, on set shifting measures such as the TMT (Murphy et al., 2004) on a task of conditional associative learning (Murphy et al., 2004) or on a gambling task (Guillaume et al., 2010). The finding, in this study, that most other neuropsychological measures were not correlated with ED symptoms is consistent with this literature.

No associations were found between anxiety, depression and obsessive-compulsive symptoms and neuropsychological performance in the BN group, consistent with the existing literature in BN, which has found no such associations using a cognitive flexibility test battery (Tchanturia, Anderluh, et al., 2004), the TMT (Murphy et al., 2004), and a decision making task (Brand et al., 2007). In the AD group and the combined groups, correlational analyses suggested some relationships between anxiety and TMT errors, and obsessive-compulsive symptoms and the WCST ‘categories completed’ variable. However, these relationships need to be interpreted
with caution due to the noted floor and ceiling effects. These correlations are not consistent with reports in the literature that psychological distress and trait anxiety are unrelated to TMT performance in young adults suffering from anxiety disorders (Castaneda et al., 2011). However, it should be noted that no significant associations were found on measures with more normally distributed data.

A regression model using anxiety, depression and obsessive-compulsive symptoms, did not predict performance on any a priori measure when data from the two groups were combined. This is consistent with the literature mentioned above, which has found no relationships between psychological symptoms and neuropsychological test performance in BN and anxiety groups. In relation to patients with depression, McClintock et al.’s (2010) review reported that associations between neuropsychological performance and depression symptoms have been found but are not consistent across studies.

4.4.1 Limitations

There are limitations to the present study, which may restrict the generalisability of the findings. The BN and AD groups in the current study were chosen on the basis of their primary diagnosis with no exclusion of comorbid major depression or anxiety disorder. The BN group were a general clinical group, with participants who potentially had comorbid anxiety disorders and/or major depression, as is common in BN (Hudson et al., 2007). However, there was no assessment of the BN participants for comorbid disorder. Such assessment could have further contributed to the understanding of the data.

The power achieved within the study due to sample size, meant that only effect sizes above $d=0.88$ were detectable as significant in group comparisons. A number of trends were observed in the data, which may have been found to be significant if the study had the statistical power to detect smaller effect sizes. However, Bezeau and Graves (2001) concluded that clinical neuropsychology research commonly deals with large effect sizes, suggesting that power to detect large effect sizes ($d=0.8$) is adequate.
4.4.2 Implications and future directions

The pattern of findings suggests that neuropsychological performance in BN is broadly the same as a clinical comparison group of anxious and/or depressed outpatients. This implies that deficits seen in studies comparing BN to HC may reflect impairments that are shared with other disorders, rather than impairments that are specific to BN. Future research may wish to document the comorbidities present in the BN sample or if possible include a BN group without comorbidities. The inclusion of comparison groups for anxiety disorders and major depression separately, might help to further clarify how cognitive impairments may be shared among common psychological disorders, whether there are causal effects of particular comorbid disorders or if the neuropsychological performance patterns are epiphenomena of pathology. The inclusion of a healthy control group would also be useful to examine how performance of clinical groups deviates from healthy performance. At present, these findings suggest that the development of therapies based on a specific neuropsychological profile of BN is unnecessary.

4.4.3 Conclusion

This study examined set-shifting and cognitive inhibition performance in 21 bulimic patients and 23 matched clinical comparison patients in treatment for anxiety and/or depression. The results indicated no significant differences between the two groups on a battery of neuropsychological tests focused on measures of set shifting and inhibition. Further analysis indicated that shared anxiety, depression and obsessive-compulsive symptoms were not predictive of neuropsychological test performance. These findings do not support the specificity of impairments in set shifting and inhibition in BN.
4.5 References


planning, or attention? *The International Journal Of Eating Disorders, 39*(7), 590-593.


Chapter 5: Methodology

The methodology outlined in this chapter is based on clinical guidelines and best research practice for eating disorder populations, self harm and those with diagnoses of anxiety or depression (NHS QIS, 2006; NICE, 2004a, 2004b, 2010, 2011).

5.1 Design

The current study incorporated a quantitative framework with a between groups cross sectional design. Data were collected using formal neuropsychological testing, questionnaires and interview. The study was designed to address methodological limitations recently highlighted by a systematic review of the current literature relating to neuropsychological correlates of bulimia nervosa (Van den Eynde et al., 2011). Design features addressing these limitations include use of a comparison group to address the issue of specificity and potentially confounding comorbidities, reporting of effect sizes within results and using measures already reported on within the literature in order to facilitate comparisons between studies.

In addition, this project was designed within the context of the Tayside Eating Disorder Research Group to complement recent research relating to neuropsychological correlates of inpatients and outpatients with anorexia.

5.2 Participants

5.2.1 Inclusion/exclusion criteria

The inclusion/exclusion criteria for each group; outpatients with Bulimia Nervosa or Eating Disorder Not Otherwise Specified with bulimic features (EDNOS-BN), and outpatients with anxiety and/or depression, are listed below.

Group 1: Outpatients with Bulimia Nervosa or EDNOS-BN

Inclusion Criteria:

- Female
- English speaking
- Age 18-65
- Meet DSM-IV criteria for a diagnosis of Bulimia Nervosa or EDNOS-BN (or ICD 10 criteria for Bulimia Nervosa or Atypical Bulimia, excluding Binge Eating Disorder1)
- Receiving treatment for Bulimia Nervosa or EDNOS-BN on an outpatient basis as part of NHS Tayside or NHS Grampian Eating Disorder Services

Exclusion Criteria:
- Medically unstable
- Current diagnosis of Anorexia Nervosa
- Psychosis
- Previous inpatient treatment for their eating disorder
- History of Learning Disability/Developmental Disorder
- History of head injury involving loss of consciousness
- History/current Neurological Disorder
- Uncorrected significant visual or motor impairment
- Past substance abuse/related disorder
- Knowledge of Neuropsychological tests

**Group 2: Outpatients with Anxiety and/or Depression**

Inclusion Criteria:
- Female
- English speaking
- Age 18-65
- Meet DSM-IV criteria for Anxiety or Major Depression (any Anxiety disorder was acceptable as long as HADS scores were in the clinical range)
- Score 11 or above on either the anxiety or depression scale of the HADS
- Receiving treatment for anxiety and/or depression at primary care in Tayside

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1 ICD 10 criteria were used by recruiting clinicians in Grampian, further explained in Chapter 3
Exclusion Criteria:

- History of Learning Disability/Developmental Disorder
- Significant current Medical/Psychiatric Disorder. Significant psychiatric disorder is identified if the individual is receiving treatment from specialist mental health services for a disorder.
- Any significant suicidal ideation or intent
- History of head injury involving loss of consciousness
- History/current Neurological Disorder
- Uncorrected significant visual or motor impairment
- Past substance abuse/related disorder
- EDE score above 4
- Knowledge of Neuropsychological tests
5.2.2 The BN Group: Outpatients with Bulimia Nervosa or EDNOS-BN

The BN group consisted of 21 female outpatients meeting the inclusion and exclusion criteria, as defined in Section 5.2.1, who were recruited from NHS Tayside and NHS Grampian Eating Disorder Services. Demographic characteristics of the sample are primarily described in the journal article in Chapter 4 (Table 4.2). Additional information on descriptive categorical variables is provided in Table 5.1.

5.2.2.1 Identification of Participants

Potential participants were identified by their treating clinicians within the Eating Disorders Services, as those they felt were medically and psychiatrically fit to participate in the study. Treating clinicians were Clinical Psychologists, Clinical Associates in Applied Psychology or Senior Nurse Specialists. Clinicians offered these patients the Participant Information Sheet and briefly discussed the study with them. For most participants, this information was provided during a therapy appointment. A number of potentially suitable participants in Grampian were informed of the study by letter by their clinician, as there was a long time lapse between appointments within the service. The letter text is reproduced in Appendix 7. The Participant Information Sheet was enclosed (Appendix 8), along with a short description of the procedure. Contact information was provided in the event that the patient wished to participate or to seek further information.

Participation was voluntary and patients were informed that their choice to participate or not would have no affect on their treatment. 29 patients were offered study information by clinicians in Dundee and approximately the same number in Grampian, although exact numbers could not be obtained at the time of writing. Twenty nine patients agreed to be contacted by the researcher. Of these, 2 dropped out before testing, 4 were unavailable, 1 was excluded for dyslexia and 1 for previous electroconvulsive therapy
As described in the Introduction Chapter (Chapter 1), male patients were not included in this study, which allows the sample to be directly comparable to existing key papers that have used only female participants.

5.2.3 The AD Group: Outpatients with Anxiety and/or Depression

The AD group consisted of 23 female outpatients being treated for anxiety disorders and/or Major Depressive Disorder (MDD) within NHS Tayside Adult Psychological Therapies Services. All participants met inclusion and exclusion criteria as set out in Section 5.2.1. Demographic characteristics of the sample are primarily described in the journal article in Chapter 4 (Table 4.2). Additional information on descriptive categorical variables is provided in Table 5.1.

Although difficulties with set shifting and cognitive inhibition ability have been found in patient groups with symptoms of anxiety and depression, results have been mixed, as described in Chapter 4. This group was included as a clinical comparison group to investigate if deficits which have been reported in BN are shared with other common psychological disorders.

5.2.3.1 Identification of Participants

Potential participants were identified by clinicians in the same way as patients with BN. All Clinical Psychologists, Counselling Psychologists, CBT therapists and Clinical Associates in Applied Psychology working with the Angus, Dundee and Perth Adult psychological therapies services were informed of the study and asked to consider if patients on their caseload may be suitable. As a large number of participants were sought and the time commitment was expected to discourage some potential participants, a large number of patients were invited to participate.

Approximately 100 patients were offered study information by clinicians. The Dundee Adult Psychological Therapies team reported 50 patients invited to participate, the Angus Adult Psychological Therapies team reported 29 patients invited to participate and the Perth Adult Psychological Therapies team were unable
to report an accurate number. If an approximate number of 30 patients invited to participate is estimated for the Perth team, the total number of patients invited to participate in the AD group was approximately 109. In total, 37 patients agreed to be contacted by the researcher. Of these, 9 were ultimately unavailable to participate, 2 were excluded for dyslexia, 1 for having poor quality spoken English, 1 did not meet inclusion criteria related to the HADS and 1 was unavailable for 2 consecutive hours.

### 5.3 Additional Descriptive data for BN and AD groups

The main participant characteristics are described in Chapter 4, Table 4.2. Table 5.1 below provides further information on descriptive data for both groups. No significant differences were found between the groups on handedness, the amount of time since they had last eaten or the report of any birth related complications. Similar proportions of each group were current alcohol and medication users. No one in either group was a current illegal drug user.

<table>
<thead>
<tr>
<th></th>
<th>Bulimic Group n=21</th>
<th>Anxious/Depressed Group n=23</th>
<th>Fisher’s exact test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Handedness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>19 90</td>
<td>17 74</td>
<td>.432</td>
</tr>
<tr>
<td>Left</td>
<td>1 5</td>
<td>4 17</td>
<td></td>
</tr>
<tr>
<td>Ambidextrous</td>
<td>1 5</td>
<td>2 9</td>
<td></td>
</tr>
<tr>
<td><strong>Time Last Eaten</strong></td>
<td></td>
<td></td>
<td>.369</td>
</tr>
<tr>
<td>Within 3 hours</td>
<td>13 62</td>
<td>16 70</td>
<td></td>
</tr>
<tr>
<td>3-6 hours ago</td>
<td>1 5</td>
<td>3 13</td>
<td></td>
</tr>
<tr>
<td>6-24 hours</td>
<td>7 33</td>
<td>4 17</td>
<td></td>
</tr>
<tr>
<td><strong>Current Alcohol User</strong></td>
<td>18 86</td>
<td>17 74</td>
<td>.462</td>
</tr>
<tr>
<td><strong>Current Drug User</strong></td>
<td>0 0</td>
<td>0 0</td>
<td>.999</td>
</tr>
<tr>
<td><strong>Currently Taking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>11 52</td>
<td>15 65</td>
<td>.541</td>
</tr>
<tr>
<td><strong>Pre/Post Natal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>8 38</td>
<td>8 35</td>
<td>.999</td>
</tr>
</tbody>
</table>
5.4 Measures

5.4.1 Psychological Measures

Psychological Measures used are listed in Table 5.2.

Table 5.2 Psychological Measures

<table>
<thead>
<tr>
<th>Psychological Measure</th>
<th>Areas Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>Current anxiety and depressive</td>
</tr>
<tr>
<td></td>
<td>symptoms</td>
</tr>
<tr>
<td>Eating Disorders Examination (EDE)</td>
<td>Eating psychopathology</td>
</tr>
<tr>
<td>Symptom Check List–90 Revised (SCL–90R)</td>
<td>General psychopathology</td>
</tr>
<tr>
<td>Self Liking/Self Competence Scale</td>
<td>Self esteem</td>
</tr>
<tr>
<td>Yale–Brown Obsessive-compulsive Scale (Y–BOCS)</td>
<td>Obsessive and compulsive symptoms</td>
</tr>
<tr>
<td>Social Problem Solving Inventory Revised (SPSI–R)</td>
<td>Social problem solving ability</td>
</tr>
</tbody>
</table>

5.4.1.1 Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)

The HADS is a self-report measure of experienced anxiety and depression, which has been used extensively in clinical studies (Bjelland et al., 2002). It contains an anxiety and a depression scale, each consisting of 7 questions with 4 possible responses relating to the severity of the symptom in question. The response is translated into a score from 0 to 3 for each question. The anxiety and depression scores are categorised individually as normal (0-7), mild (8-10), moderate (11-14) and severe (15-21). The HADS was administered to adult outpatients as part of routine clinical practice and ongoing review.

The HADS depression subscale has 90% sensitivity and 86% specificity for depression compared to the gold standard of a structured diagnostic interview (Zigmond & Snaith, 1983). Crawford, Henry et al. (2001) reported the reliability of the HADS as acceptable and the subscales moderately correlated (0.53). A recent
review by Bjelland et al. (2002) reported the reliability of the Anxiety subscale to vary from 0.68 to 0.93 (mean 0.83) and for the Depression subscale from 0.67 to 0.90 (mean 0.82).

5.4.1.2 Eating Disorders Examination (EDE) Version 12 (Fairburn & Cooper, 1993)

The EDE is a semi-structured, investigator based clinical interview that is generally regarded as the ‘gold standard’ instrument for measuring eating disordered attitudes and behaviours. It contains 23 items rated in regards to the past 28 days on a 7-point Likert scale, ranging from ‘0’ (‘not at all’) to ‘6’ (‘markedly’ or ‘every day’), with higher scores indicating more severe eating pathology. Responses are used to calculate four subscales (Dietary Restraint, Eating Concern and Weight Concern, each ranging from 0-30, and Shape Concern, ranging from 0-48), and a global score (mean of the 4 subscales). All subscale mean scores and the global score range from 0-6. The EDE can also be used as a diagnostic tool for DSM-IV, containing frequency measures of binge eating and compensatory behaviours.

Good internal consistency, (Beumont et al., 1993; Cooper et al., 1989) concurrent (Rosen et al., 1990) and discriminant (Cooper et al., 1989; Rosen et al., 1990; Wilson & Smith, 1989) validity, and inter-rater reliability (Black & Wilson, 1996; Cooper & Fairburn, 1987; Rosen et al., 1990; Wilson & Smith, 1989) have been demonstrated for the EDE in adults. It also discriminates well between different types of eating disorder (Beumont et al., 1995; Fairburn & Cooper, 1993).

5.4.1.3 Symptom Check List–90 Revised (SCL–90R) (Derogatis, 1994; Derogatis et al., 1973)

The SCL–90R is a 90-item self-report instrument for measuring general psychopathology for use with community, medical and psychiatric respondents. It contains 90 problem items rated in regards to the past 7 days on a 5-point Likert scale of distress from 0 ‘Not at All’ to 4 ‘Extremely’. It comprises nine primary symptom dimensions - Somatisation, Obsession-Compulsion, Interpersonal...
Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism – for which mean scores (range 0-4) are calculated. An ‘Additional’ scale is also included in the measure which contains a collection of symptom items relating to disturbed sleep, feelings of guilt, overeating, thoughts of death and poor appetite.

Responses to these subscales are used to calculate three global indices: the Global Severity Index (GSI), the Positive Syndrome Distress Index (PSDI) and the Positive Symptom Total (PST). The GSI is the mean value of all the items (total divided by 90). GSI thus ranges from 0-4. The PST is the number of items which have been scored higher than zero. PST thus ranges from 0-90. The PSDI is the total sum of all ratings divided by the PST, and ranges from 0-4.

Good internal consistency of the primary symptom dimensions and global indices has been demonstrated across a number of populations including control groups (Derogatis, 1983), psychiatric inpatients (Rauter et al., 1996), and substance abuse inpatients (Zack et al., 1998) as well as cancer patients (Fitch et al., 1995). Alpha coefficients have ranged from 0.77 to 0.90 in one study of 209 symptomatic volunteers (Derogatis et al., 1976) and from 0.79 to 0.90 with a sample of psychiatric outpatients (Horowitz et al., 1988). More recently, similar results have been found with Cronbach’s alpha coefficient ranging from 0.77 for the Hostility subscale to 0.90 for the Somatisation and Depression subscales among psychiatric outpatients in Finland (Holi, 2003; Holi et al., 2003). The SCL-90-R has been found to have good test-retest reliabilities across a range of patient groups and test-retest intervals (Derogatis, 2000). Therefore, previous completion of the SCL-90-R was acceptable among participants. Good convergent-discriminant validity for the SCL-90R has also been demonstrated in patients and healthy controls (Boleloucky & Horvath, 1974; Derogatis et al., 1976; Peveler & Fairburn, 1990); however examination of the convergent and discriminant validity of the subscales has produced mixed results. The Depression and Anxiety subscales have the most evidence of convergent and discriminant validity (Bech et al., 1992; Derogatis, 2000; Koeter, 1992). The Obsession-Compulsion subscale has been shown to be internally consistent (Woody et al., 1995) but has also been found to have poor discriminant validity (Kim et al.,
The SCL-90 has been used in BN patient groups to assess general psychopathology (Brand et al., 2007; Fairburn et al., 2007; Krug et al., 2008), and found to have good concurrent validity within a BN patient group using comparison with an investigator based interview, the Present State Examination (Peveler & Fairburn, 1990).

Scores for all scales were recorded for the purpose of comparison between the two groups on psychological distress. The symptoms dimensions of Depression, Obsession-Compulsion and Anxiety were used in the investigation of the relationship between psychopathology and performance on neuropsychological tasks of set shifting and inhibition.

5.4.1.4 **Self-Liking/Competence Scale (Revised) (SLCS–R) (Tafarodi & Swann, 2001)**

The SLSC–R is a 16 item measure of two-dimensional self-esteem composed of two interdependent subscales of self liking and self competence. It contains 8 items relating to self worth and self competence and 8 items relating to sense of self-efficacy. Participants rate the items on a 5-point Likert scale ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). The item scores are then summed and combined into an overall subscale score. These can range from 8 to 40, with higher scores indicating higher self-competence or higher self-liking. It has been tested for discriminant and convergent validity and found to constitute best fit on all indices, when compared to other self esteem measures. Reliability and validity of a translated version of the questionnaire were found to be appropriate in a Dutch sample (Vandromme et al., 2007). Internal consistency was found to be good in an American sample, with alpha coefficients of 0.90 for Self-Liking and 0.82 for Self-Competence (Mar et al., 2006). Self competence has also been found to correlate with eating pathology in a recent study (Paterson et al., 2007).
5.4.1.5 *Yale–Brown Obsessive Compulsive Scale–Symptom Check List (Y−BOCS−SC)* (Goodman, Price, Rasmussen, & Mazure, 1989).

Regarded as the 'gold standard' for the assessment of obsessive compulsive symptoms, (Deacon & Abramowitz, 2005; Frost *et al*., 1995; Moritz *et al*., 2002), the YBOCS consists of a 58 item symptom checklist and a 10 item severity scale. The symptom checklist covers a range of obsessions and compulsions, clustered by behavioural expression (e.g. checking compulsions) and thematic content (e.g. contamination obsessions). Obsessions and compulsions are assessed over the 5 dimensions of time spent, interference in functioning, distress, efforts to resist and perceived control, creating a 10-item severity measure.

Respondents used the symptom checklist to identify their main symptoms and then completed the YBOCS severity scale with these in mind, in relation to the past 7 days. Items are rated on a 5-point scale from 0 (no symptoms) to 4 (extreme symptoms.) The symptom checklist is not scored. Scores on the YBOCS thus range from 0-40 with higher scores indicating more severe OCD symptoms.

The YBOCS can be administered in the form of interview or self-report. There are small differences between the two versions, such as the inclusion of plain-language explanations of the concepts and the removal of an ‘other’ option in the symptom checklist. A number of studies have demonstrated the validity and reliability of the interview version (Goodman, Price, Rasmussen, & Mazure, 1989; Goodman, Price, Rasmussen, Mazure, *et al*., 1989; Kim *et al*., 1990; Woody *et al*., 1995). Comparison of interview and self-report administration showed moderate to good agreement between both the symptom checklist and severity ratings, with Federici *et al*., (2010) noting that the compulsions scales were more highly correlated between versions than were the obsessions scales (Steketee *et al*., 1995). The current study uses a self-report version of the YBOCS (Baer, 1991) which was also used by Federici *et al*., (2010). The YBOCS has been used to measure obsessive and compulsive symptoms in bulimic patients in a number of studies (Kaye, 2005; Matsunaga *et al*., 1999; Murphy *et al*., 2004; Roberts *et al*., 2010).
5.4.1.6 Social Problem Solving Inventory Revised (SPSI−R) (D'Zurilla et al., 1998)
(D'Zurilla & Maydeu-Oliveres, 1995)

The SPSI−R is a 52−item, multidimensional, self-report measure of social problem solving ability. Each item is rated on a five-point scale from 0 ‘not at all true of me’ to 4 ‘extremely true of me’. The SPSI-R comprises two problem orientation measures (positive problem orientation, negative problem orientation) and three actual problem-solving measures (rational problem-solving, impulsivity/carelessness style, avoidance style), as described in Table 5.3.

Table 5.3 Subscales of the SPSI-R

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Attitudes and Behaviours Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Problem Orientation</strong></td>
<td></td>
</tr>
<tr>
<td>Positive Problem Orientation (PPO)</td>
<td>Positive appraisal, self-efficacy and outcome expectancies.</td>
</tr>
<tr>
<td>Negative Problem Orientation (NPO)</td>
<td>Dysfunctional cognitive processes, threat perception and frustration tolerance.</td>
</tr>
<tr>
<td><strong>Problem Solving</strong></td>
<td></td>
</tr>
<tr>
<td>Rational Problem Solving (RPS)</td>
<td>Systematic problem solving, realistic goal setting and evaluating outcomes</td>
</tr>
<tr>
<td>Impulsivity/Carelessness Style (ICS)</td>
<td>Impulsive, incomplete or careless problem solving strategies</td>
</tr>
<tr>
<td>Avoidance Style (AS)</td>
<td>Procrastination, passivity and inaction</td>
</tr>
</tbody>
</table>

The problem solving subscales of the SPSI-R have been shown to accurately predict academic success after controlling for aptitude, indicating ecological validity of the subscales (D'Zurilla & Sheedy, 1992). Acceptable convergent, construct and discriminant validity have been reported among psychiatric inpatients and healthy adults (Chang & D'Zurilla, 1996; D'Zurilla et al., 1998; D'Zurilla & Maydeu-Oliveres, 1995). Test-retest reliabilities range from 0.72 for positive problem orientation to 0.88 for negative problem orientation (D'Zurilla et al., 1998).
The negative problem orientation and avoidance subscales have been linked to eating pathology in anorexia (Paterson et al., 2007). These scales have also been linked to depressive symptoms (Klein et al., 2011; Londahl et al., 2005). Negative problem orientation has also been found to be a significant predictor of worry after controlling for trait anxiety (Belzer et al., 2002).

5.4.2 Neuropsychological Measures

As executive function describes a broad spectrum of cognitive abilities, and tests of executive function have been shown to require the use of a number of cognitive functions simultaneously, it is difficult to isolate an ability such as set shifting or inhibition in any one task (Burgess, 2003). Many studies have consistently reported varying performance among their subjects on neuropsychological tests which measure similar constructs (for example in BN samples; Alvarez-Moya et al., 2009; Brand et al., 2007; Tchanturia, Morris, et al., 2004). For these reasons the test battery contained a number of measures designed to access set shifting and cognitive inhibition ability but which necessarily also overlap with other executive functions.

Table 5.4 Neuropsychological Measures and Primary Areas Assessed

<table>
<thead>
<tr>
<th>Neuropsychological Measures</th>
<th>Primary Areas Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Adult Reading Test (NART)</td>
<td>Pre-morbid intellectual ability</td>
</tr>
<tr>
<td>Delis–Kaplan Executive Function System (DKEFS) Trail Making Task</td>
<td>Attention, Set shifting, cognitive flexibility</td>
</tr>
<tr>
<td>Delis–Kaplan Executive Function System (DKEFS) Verbal Fluency</td>
<td>verbal fluency Cognitive flexibility, set shifting (condition 3),</td>
</tr>
<tr>
<td>Delis–Kaplan Executive Function System (DKEFS) Colour-Word Interference</td>
<td>Response inhibition, (also set shifting in condition 4)</td>
</tr>
<tr>
<td>Hayling Test</td>
<td>Response inhibition</td>
</tr>
<tr>
<td>Brixton Test</td>
<td>Set shifting</td>
</tr>
<tr>
<td>Wisconsin Card Sort Test (WCST)</td>
<td>Set shifting, category formation and set maintenance</td>
</tr>
</tbody>
</table>
5.4.2.1 National Adult Reading Test (NART) (Nelson, 1982; Nelson & Willison, 1991)

The NART is a measure of premorbid intellectual ability. The participant is asked to read aloud 50 irregularly spelt words (e.g. cough). The number of pronunciation errors is recorded and used to estimate the Wechsler Adult Intelligence Scale (WAIS-R; Wechsler, 1981) score from standardised norms. The NART’s validity as a measure of premorbid intelligence has been well documented (e.g. Crawford, Deary, et al., 2001). Recently Bright et al. (2002) demonstrated that neither the use of demographic variables or a combination of NART score and demographic variables was significantly better than NART scores at estimating premorbid IQ. NART performance remains preserved despite a number of cognitive impairments, however its preservation in some disorders, such as Alzheimer’s and Huntington’s disease has been questioned. The NART has demonstrated good internal consistency (Crawford et al., 1988; Nelson & Willison, 1991), test-retest reliability, and inter-rater reliability (Crawford et al., 1989). The NART has been used as a measure of premorbid IQ in eating disordered patients in a number of neuropsychological studies (Guillaume et al., 2010; Lopez et al., 2008; Tchanturia, Morris, et al., 2004; Van den Eynde et al., 2012).

5.4.2.2 Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2001)

Three tests from the D-KEFS were used:

Verbal Fluency Test – This is a measure of spontaneous production of words in conditions of letter fluency (FAS, condition 1), category fluency (Animals and Boys names, condition 2) and a category switching condition where a participant must switch between naming items from each of 2 categories (Fruits and Furniture, condition 3). In each condition, the score is the total number of correct responses generated in 60 seconds.

FAS test-retest reliability and inter-rater reliability were found to be good by Vlaar and Wade (2003). Test-retest reliability for D-KEFS category fluency is 0.79 (Delis
et al., 2001). The inter-rater reliability for general category fluency tasks is very good (Spreen & Strauss, 1998). Good internal consistency has been reported for the verbal fluency component and category switching component in the D-KEFS manual (Delis et al., 2001). Performance of BN patients on the FAS task is not different to controls according to the current literature (Brand et al., 2007; Tchanturia, Anderluh, et al., 2004). However, the switching element of condition 3 in the D-KEFS is not a component of the standard verbal fluency task, which usually only includes a letter and category fluency task (Lezak et al., 2004). This switching task may highlight difficulties in set shifting in individuals with BN.

**Colour Word Inference Test** – This is a measure of selective attention and response inhibition. The Stroop test, which is a longstanding test of cognitive flexibility and inhibition, has been modified in the D-KEFS battery to include a baseline colour naming condition (condition 1) and a set shifting condition (Colour Word Inhibition Switch, condition 4) in addition to the traditional colour word reading (condition 2) and colour word interference tasks (condition 3). In each condition, the outcome measures are the time taken to read 50 items and the number of errors made. Good internal consistency and test-retest reliability has been reported (Delis et al., 2001). Colour word interference 3 has been identified as an a priori key variable as significant differences have been found on this measure between samples of people with BN and healthy controls (Kemps & Wilsdon, 2010).

**Trail Making Test (TMT)** – This test assesses planning and cognitive flexibility. There are 5 conditions in the D-KEFS TMT in contrast to the 2 conditions in the traditional TMT. The five conditions are visual scanning (condition 1), number sequencing (condition 2), letter sequencing (condition 3), number-letter switching (condition 4), and motor speed (condition 5). The procedure for the first condition involves a timed visual search. The remaining conditions involve drawing a line connecting the target items (numbers, letters or empty circles) as quickly as possible while ignoring distracter items. The switching task involves switching back and forth between connecting numbers and letters, completing the task as quickly as possible. In each condition, the outcome measures are time to complete task and
number of errors. Good internal consistency and moderate test-retest reliability are described in the technical manual (Delis et al., 2001). TMT4 completion time and TMT4 number of errors were identified as key variables, due to significant differences between BN patients and healthy controls found on these subscales in recent studies (Brand et al., 2007; Konstantakopoulos et al., 2011; Roberts et al., 2010; Tchanturia, Morris, et al., 2004).

5.4.2.3 Hayling & Brixton (Burgess & Shallice, 1997)

The Hayling and Brixton tests measure behavioural regulation, including response inhibition and set shifting.

The Hayling test evaluates initiation speed, by first requiring participants to logically complete 15 sentences as quickly as possible. The second part of the task requires them to complete 15 sentences with unrelated words as quickly as possible, which is a measure of response suppression. The sum of time to respond and total number of errors are the outcome measures. The number of errors in the Hayling test part 2 was chosen as an a priori key measure as a composite value using this measure described significant differences between people with BN and healthy controls (Kemps & Wilsdon, 2010).

The Brixton test is a concept formation and set shifting task. The test consists of 56 pages, each consisting of the same array of ten circles numbered 1–10 (one circle coloured blue). Participants are asked to predict the movement of the blue circle from page to page by detecting a logical pattern from previous pages. The pattern changes 8 times during the task and the participant has to determine the new pattern. The outcome measure is the total number of incorrect predictions made. No differences have been found to date between patients with BN and healthy controls on this task (Roberts et al., 2010; Tchanturia, Anderluh, et al., 2004; Van den Eynede et al., 2011).
The technical manual reports the test-retest reliabilities for both tasks as adequate (Burgess & Shallice, 1997). Adequate inter-rater reliability was reported for the Hayling test by Andres and Van der Linden (2000).

5.4.2.4 Wisconsin Card Sort Test (WCST) (Heaton et al., 1993)

The WCST is one of the most widely used tasks in the assessment of cognitive function. It measures the aspects of executive function thought to be related to the frontal lobes, such as concept formation, set-shifting, and set maintenance. The WCST was administered in the standardized format (Heaton et al., 1993). Four stimulus ‘key cards’ with symbols differing in colour, shape and number are placed in front of the participant, who is given a pack of 128 response cards and instructed to match each response card to one of the key cards by placing it on the table under that key card. The researcher informs the participant whether each pairing is correct or incorrect. The participant’s aim is to match cards according to the current criterion. After coupling 10 cards with the first criterion (colour), the subject is required to shift to the second one (shape) and then to the third one (number). The procedure is repeated twice or until all 128 cards have been used. The official computerised scoring package was used to compute scores.

Test-retest reliabilities for the WCST have been examined by Heaton et al. (1993) and reported as ranging from 0.39 to 0.72. Bowden et al. (1998) reviewed these data and investigated reliability in an alcoholic and student population leading them to report a lower test-retest reliability of 0.22 to 0.55. Although previous literature had expected large practice effects to be seen in the WCST, these were not present in Bowden et al.’s (1998) data (Franzen, 1989). Ingram et al. (1999) also reported similar test-retest reliability 0.34 to 0.83 (mean=0.64) among sleep apnoea patients. Participants in the current study are unlikely to have encountered the WCST before and re-testing is not part of the procedure. Variable values for inter-rater reliability have been reported, ranging from excellent (Axelrod et al., 1992) to quite low correlations (Flashman et al., 1991).
Number of Perseverative errors, categories completed and non-perseverative errors were identified as a priori key measures based on significant findings related to these variables found in BN patient groups in studies by Roberts et al. (2010) and Alvarez-Moya et al. (2009). A perseverative error is one where the participant continues to sort the cards in the same way, after the examiner says the card is wrong or changes criteria. Number of categories completed is the number of runs of 10 correct responses in a row (max. 6). A non-perseverative error is any error not categorised as a Perseverative error. Non-perseverative errors have been hypothesised to contain both efficient errors, which are used to test out and establish the new criterion, and inefficient errors, which have been linked to disinhibition and distraction in responding (Alvarez-Moya et al., 2009; Barceló & Knight, 2002).

5.5 Procedure

A diagram representing the participant journey from being approached by clinical staff to completion of participation is shown in Figure 5.1.
Figure 5.1 Participant Journey

5.5.1 The BN Group: Patients with Bulimia/EDNOS-BN

*Study Sites: NHS Tayside Eating Disorder Service and Grampian Eating Disorder Service*

Any outpatients attending NHS Tayside Eating Disorders Service, NHS Grampian Eating Disorders Service or NHS Tayside Adult Psychological Therapies Services
for treatment of an Eating Disorder and meeting inclusion criteria for the BN group were considered for participation in the study. The Adult Psychological Therapies pathway was ultimately not used for the BN group as the department was transitioning to a model where all eating disordered patients were transferred to the Eating Disorder Service.

Participants were recruited to the study through their treating clinician, as described in section 5.2.2.1. Patients with a possible interest in participation were given verbal and written information about the study by their clinician (Appendix 8). This information included details of the researcher’s clinical supervisor within NHS Tayside Department of Clinical Neuropsychology, who could be contacted for further information. Patients who expressed a wish to participate and gave consent for their contact details to be passed on to the researcher, were given 24 hours to consider the information provided. When contacted by the researcher, participants were asked if they still had an interest in taking part. Most participants chose to give telephone contact details but email contact details were also used. Previous research has used similar methodology to contact potential participants and has demonstrated a high response rate (Crombie et al., 2008; Kiezebrink et al., 2009).

Patients wishing to participate met with the researcher in a clinic room at NHS premises convenient to their location within Tayside or Grampian. At the meeting, patients were given the opportunity to ask any further questions, screened for inclusion/exclusion criteria and if these were met, completed consent forms. They were informed that their participation was confidential and that they could withdraw from the study at any time without giving a reason.

The research procedure consisted of a semi-structured interview, to collect demographic information, and administration of the Eating Disorder Examination (EDE), which took 20 to 30 minutes. This was followed by formal neuropsychological testing in the order indicated in Table 5.2. Following this, a break was offered and then the remaining questionnaires were completed.
Neuropsychological tests lasted on average 45 to 60 minutes and the 4 questionnaires took approximately 20-30 minutes to complete.

Following completion of the measures, the researcher discussed with the participant her feelings about the experience of participation and any concerns or questions she had. In addition, items of the YBOCS and SCL-90-R relating to thoughts of death and self harm were checked by the researcher. If such items were endorsed, the researcher discussed with the participant their current levels of risk and support. If the researcher identified an unmet need for support, a protocol was in place to contact a clinical supervisor for further advice (see section 5.6.4).

5.5.2 The AD Group: Patients being treated for anxiety or depressive disorders in the Adult Psychological Therapies Service

Any outpatients attending NHS Tayside Adult Psychological Therapies Services for treatment of anxiety or depressive symptoms and meeting inclusion criteria for the comparison group were considered for participation in the study. Participants were recruited and testing administered as described in section 5.5.1.

5.5.3 Recruitment activity at the level of clinicians

Recruitment procedure was designed using recommendations from current literature, involving close collaboration with recruiting colleagues, regular feedback to them and using these discussions to consider the impact of study design on recruitment (Patel et al., 2003). The researcher met with clinical teams before recruitment began, presenting information about the background, rationale and procedure for the study at team meetings. Meetings were attended periodically during the study and the researcher was in regular contact with the teams by email, including through reminder emails and recruitment updates to clinical leads. Clinical teams were also provided with updated feedback at intervals on the numbers of participants recruited. In addition, various methods were used to encourage recruitment within the teams, such as placement of reminder posters in team areas, placing study information in
Clinic rooms or placing study information in patient files with coloured reminders pinned to the exterior of files.

Clinician workload in recruiting was minimised to identification of suitable participants and provision of study information for the BN group and additionally, the use of the HADS questionnaire to establish inclusion criteria for the AD group. Low clinician workload related to a study has been found to be associated with increased referral to Randomised Controlled Trials (B. Fletcher et al., 2012). Clinicians were told that telephone numbers were the preferred method of contact, as previous experience and Cochrane reviews of literature on recruitment have indicated that telephone follow up can significantly increase recruitment levels (Treweek et al., 2010; Watson & Torgerson, 2006) as have individual studies (Zaslavsky et al., 2002).

5.6 Ethical Issues

5.6.1 Approval

Ethical approval was granted from the NHS Tayside Research Ethics Committee. Management approval was granted from NHS Tayside Research and Development Department and NHS Grampian Research and Development Department (see Appendix 9).

5.6.2 Confidentiality

The confidentiality of all information collected during the study was communicated to the participants in the Participant Information Sheet, the consent form and during discussion (Appendices 8 & 10). The limits to confidentiality in the event of a disclosed risk and the procedure to be followed were also highlighted in the Participant Information Sheet (see Appendix 8).

Personally identifiable data (name and date of birth) were recorded on consent forms and the data anonymising key only. All other data collected at assessment were
encoded with a unique identifier for each participant. Only the researcher and her clinical supervisor at the NHS Tayside Eating Disorder Service (EDS) had access to personally identifiable data.

5.6.3 Data Storage

Consent forms were stored in a locked filing cabinet in a locked office within a locked department on NHS Tayside property. Only the researcher and her clinical supervisor at NHS Tayside Eating Disorder Service had access to this cabinet. A key to anonymised data was stored on a password protected NHS secured memory stick which is designed to erase all data if an incorrect password is used or if it is damaged. Only the researcher had access to this password. No personally identifiable information was stored on a computer. Study related documents, such as consent forms, were transferred using personal transport.

Non identifiable data was stored in a locked filing cabinet in the same way as consent forms, but within a different NHS office. All data stored on computer was anonymised and all computers used were password protected, including a home laptop which also had anti-virus software. One NHS memory stick, as described above, was used to transfer data between sites. Data was stored in line with the Data Protection Act (Department of Health, 1998), NHS Tayside Information Governance Policy (2010) and NHS Code of Practice on Protecting Patient Confidentiality (Scottish Executive, 2003).

Following study completion, personally identifiable data will be stored for 6-12 months and then destroyed, as recommended by NHS Tayside Research and Development Office. Non-identifiable data will be stored for 5 years from the date of publication in accordance with NHS Tayside Research and Development guidance (Tayside Medical Science Centre, 2011).
5.6.4 Potential Distress to Participants/Disclosure of risk issues

There was a risk that participants may have found the questionnaires and neuropsychological testing upsetting. A number of measures were taken to address this possibility. Referring clinicians were asked to use their judgement as to the current emotional state of the patient and their ability to undergo neuropsychological testing. Then, at the beginning of the session, participants were reminded that they were free to withdraw at any time. In addition, following participation, the investigator had a general discussion with the participant about how they found the testing, providing general feedback on neuropsychological test performance and explanation of the normal range of test performance. Written feedback was available on request.

As self harm and suicidality can be a risk factor in BN, as well as a potential risk factor for patients with severe anxiety or depression, items 15 and 59 of the SCL-90-R, relating to distress caused by ‘thoughts of ending your life’ and ‘thoughts of death or dying’, were routinely checked after administration of the questionnaire and discussed with the participant if any issues of risk were highlighted. Similarly, the first two items on the YBOCS symptom checklist, ‘I fear I might harm myself’ and ‘I fear I might harm other people’ were also checked and discussed with the participant if endorsed.

In the event of the procedure causing distress or an issue of risk being disclosed, participants were able to speak to the researcher in the first instance and, if further assistance was needed, the researcher’s clinical supervisor, a Consultant Clinical Neuropsychologist, was contactable to advise on immediate and longer term care for the patient including discussing the issue with their treating clinician and/or referral to other appropriate areas of the service.

As participation in the study required approximately 1.5 to 2 hours, there was potential for the participant to become fatigued. For this reason, participants were offered a break between neuropsychological testing and questionnaire completion.
There were potential benefits for participants. Participants may have enjoyed the experience of participation in neuropsychological testing, as neuropsychological research indicates many participants do (Bennett-Levy et al., 1994). They may also have felt positive about contributing to research that will increase the understanding of their condition and potentially help future patients.

5.7 Data analysis

Data were analysed using SPSS version 15.

5.7.1 Investigating assumptions for parametric statistical testing

The data was first explored using graphing, tests of normality and homogeneity of variance to confirm that it met the assumptions for appropriate use of parametric statistics.

5.7.2 Main analysis

The main aim of the study was to explore potential differences between the two groups on measures of set shifting, inhibition, psychopathology and eating pathology. A priori key measures were identified in order to reduce the number of comparisons within the data. Key measures chosen were TMT4 completion time and TMT4 number of errors, WCST Perseverative errors, WCST categories completed, WCST non-perseverative errors, Stroop Interference 3 and Hayling number of errors.

Comparisons were made using independent samples t-tests and Mann-Whitney U tests with Bonferroni corrections for multiple comparisons. When a number of comparisons are being performed on a dataset, Bonferroni’s correction dictates that the alpha level should be divided by the number of comparisons. The alpha level used for this study was 0.05, however where Bonferroni’s correction is applied a smaller value will be required to reach significance.

The relationship of general psychopathology and eating pathology to set shifting and inhibition was explored within groups using correlational analysis. Kendall’s tau
correlations were conducted between the identified a priori set shifting and inhibition variables and the relevant psychological measures. Anxiety symptoms were described by the anxiety scale of SCL-90 and by the YBOCS score. Depressive symptoms were described by the SCL-90 depression subscale (as described in Chapter 4).

As differences between the groups on neuropsychological measures were non-significant, a post-hoc regression analysis was conducted to investigate the predictive ability of measures of anxiety, depression and obsessive-compulsive symptoms on neuropsychological performance (Chapter 4).

5.7.3 Additional Analysis

Further analysis of the data presented in Chapter 4, and analysis of measures not chosen as a priori key measures, but included in the research, are also described.

Following that, analysis related to the secondary aims of the thesis, and the measures of Social Problem Solving and Self Esteem are described.

5.7.3.1 Clinical significance of impaired performance

Clinically significant impairment in set shifting and inhibition was determined on a case by case basis by using standardised test norms.

In order to investigate clinically significant impairment, two comparisons were conducted. Each participant’s performance on key measures was compared to their estimated premorbid IQ and to normative data. Z scores were calculated for the NART estimated IQ and each a priori key measure using standard scores. Underperforming was defined as the Z score of neuropsychological test performance falling one standard deviation (SD) or more below the Z score of the individual’s estimated premorbid ability, indicated by NART IQ. Participants underperforming on 3 or more measures were highlighted as potentially impaired relative to past ability. Each participant’s performance was also compared to the normative data for each measure using 2 SDs below the mean as a cut off point for impairment.
5.7.3.2 Secondary Variables

Further exploratory analysis of set shifting and inhibition were conducted comparing the performance of the two groups on other variables not identified as key variables but commonly reported in the literature. Secondary variables were DKEFS Letter Fluency, DKEFS Category Fluency, DKEFS Category Shift and Brixton total errors.

Secondary variables were DKEFS Letter Fluency, DKEFS Category Fluency, DKEFS Category Shift and Brixton total errors. Self reported self esteem as measured by the SLSC and self reported social problem solving style as measured by the SPSI were also compared between groups. The relationship between social problem solving and self esteem, set shifting and inhibition was also investigated using correlational analysis in the Additional Results Chapter (Chapter 6).

5.7.4 Missing Data

Missing data were treated as follows:

Missing values were found in the items of both the SCL-90 and SPSI-R for two participants. These missing items were replaced by the participant’s average value for the existing items on that subscale assuming that no more than 2 items were missing from a subscale. Neither questionnaire had more than 1 missing value per participant in the collected data. One BN participant failed to complete the SPSI, YBOCS or SLSC. This participant was excluded from analyses of these variables.

5.8 Statistical Power and Sample Size

The issue of limited power due to small sample sizes has been highlighted in many recent reviews of neuropsychological impairment in BN, as a major limitation present in most of the current research (Roberts et al., 2007; Van den Eynde et al., 2011). Only 13 of 37 studies included in a recent systematic review of neuropsychological impairment in BN patients, had sample sizes of 26 or greater, which is a necessary sample size to detect large effect sizes between two groups using t-tests with 80% power and a 0.05 two-tailed significance level (Van den Eynde et al., 2011). Effect sizes found in comparisons between BN groups and healthy controls are reported to be large to medium (Van den Eynde et al., 2011).
No studies were found that compared bulimic and anxious or depressed groups on similar measures of cognitive abilities, from which to estimate an expected effect size for the comparisons in this study. An appropriate sample size was determined by first estimating an expected effect size from the literature. Means and standard deviations for samples of people diagnosed with bulimia, anxiety and depressive disorders were obtained from existing literature, relating to the a priori key subscales of the WCST. Effect sizes were estimated using these data and subsequently appropriate sample sizes were determined using the parameters of a power of 80% and a 0.05 two-tailed significance level (using GPower 3.1.2). Difficulties related to these comparisons are reported in section 5.8.1.

Effect sizes estimated for the variable ‘categories completed’ were calculated using data from Alvarez-Moya et al. (2009) and Roberts et al. (2010) in samples of patients with BN, and from Stordal et al. (2004) and Merriam et al. (1999) in samples of patients with depressive symptoms. Effect sizes estimated from this data ranged from 0.78 to 1.2 and group size determined ranged from 12 participants per group to 27 participants per group.

Effect sizes estimated for the variable ‘perseverative errors’ were calculated using data from Galderisi et al. (2011) for a BN sample, from Merriam et al. (1999) and Stordal et al. (2004) for samples of patients with depressive symptoms and from Boldrini et al. (2005) and Abbruzzese et al. (1995) for samples of patients with anxiety disorders. Effect sizes estimated from this data ranged from 0.14 to 0.76 comparing samples of patients with BN to those with anxiety disorders, and from 0.806 to 1.06 comparing samples of patients with BN and depression. These effect sizes lead to proposed sample sizes of 14, 15, 21, 28, 123 and 781 participants per group.

In light of the varied sample sizes determined from the data, a maximum sample size of 40 participants was chosen for each group. A sample size of 26 was determined to be adequate to detect the large to medium effect size estimated from the literature.
5.8.1 Difficulties identifying appropriate data for use in determining sample size

Unfortunately, as has been pointed out in many review papers (Van den Eynde et al., 2011; Zakzanis et al., 2010), it is a limitation of the available research that tests have been chosen and results reported in such a way that direct comparisons between papers are difficult. In reviewing recent studies, it was found that even when the same test measures are used, some studies may report medians, while some report means; some report a combined or composite scores such as TMT B-A, while others report B and A separately. As such, comparison of means and standard deviations across the areas of eating disorders, anxiety disorders and depression, was only possible for some of the a priori key measures and for some patient samples in order to estimate the effect sizes to be expected in this study.
Chapter 6: Additional Results

Analyses of data relating to Aims 1 and 2 of the Thesis project are described in Chapter 4. Further analysis of these data, including the assessment of normality, is described below. Analysis of measures not chosen as a priori key measures, but included in the research are also described here. Following this, analysis related to Aim 3 of the thesis, exploring social problem solving and self esteem in the BN and AD groups is reported.

6.1 Further analysis of data presented in Chapter 4

6.1.1 Assessing Normality of the Data

The a priori variables were assessed for the assumptions of normality by examining the Z scores of skewness and kurtosis, the Shapiro-Wilkes test of normality and Levene’s test of equal variance between the BN group and the AD group (see Table 6.1). Results indicated that only the variable Stroop interference, met the assumptions of normality in both groups. The variable TMT condition 4 also met the assumptions of normality but only in the BN group. All other variables analysed were assessed for normality in a similar way.
<table>
<thead>
<tr>
<th>Table 6.1 Test of Normality Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>WCST perseverative Errors</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>Categories completed</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>Non-perseverative errors</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>TMT4</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>TMT4 errors</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>Stroop interference</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td><strong>Hayling errors</strong></td>
</tr>
<tr>
<td>BN</td>
</tr>
<tr>
<td>AD</td>
</tr>
</tbody>
</table>

ns = non-significant, Z = value/SE, †= values not consistent with assumptions of normality
6.1.2 Further details on analysis of Age normed scaled scores for a priori variables
As described in Chapter 4, the BN group was significantly younger than the AD group. Therefore, differences between the groups on age normed scaled scores were investigated on neuropsychological measures, where such scaled scores were available. These data were non-normal for all but CWIT inhibition, therefore Mann Whitney U tests were used in the majority of comparisons. Further detail of these comparisons is provided here.

WCST perseverative errors scaled scores (SS) did not differ significantly between the BN group (Mdn=97) and the AD group (Mdn=96), U=202.5, Z=-.918, ns, r=-0.14. The BN group (Mdn=10) also did not differ significantly from the AD group (Mdn=11) on TMT condition 4 scaled scores, U=205.5, Z=-.857, ns, r=-.13. Differences between the BN group (M=11.24, SD=2.68) and the AD group (M=10.74, SD=3.25) were non-significant on CWIT inhibition, t(42)=0.552, p=.584, r=.007, and on CWIT inhibition switch (BN median =12, AD median = 11), U=173, Z=-1.62, ns, r=-.25. These results still indicate the non-significant effects seen when using non age corrected variables.

6.1.3 Relationship of general and eating psychopathology
A number of associations between general psychopathology and eating disorder psychopathology were seen in the BN group. A significance level of p < .01 was chosen, as a Bonferroni correction was considered too conservative for this analysis. Increased Eating Restraint was associated with increased depression among BN participants. Increased Restraint was also associated with increased distress on the ‘Additional’ subscale of the SCL-90-R, which contains items related to sleep and appetite disturbance. Increased Eating Concern was significantly associated with obsessive-compulsive symptoms as measured by the SCL-90-R but not by the YBOCS, and with higher distress on the ‘Additional’ scale. Weight concern was significantly associated with increased scores on the ‘Additional’ scale and the Positive Syndrome Distress Index. Only Shape Concern was not significantly associated with increased psychological symptoms, at the p < .01 level.
### Table 6.2 Correlation of general and eating psychopathology in BN group

<table>
<thead>
<tr>
<th>SCL-90</th>
<th>YBOCS</th>
<th>EDE</th>
<th>Restraint</th>
<th>Eating</th>
<th>Shape</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-C</td>
<td>.114</td>
<td>.272</td>
<td>.459**</td>
<td>.332*</td>
<td>.403*</td>
<td></td>
</tr>
<tr>
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<td>.426**</td>
<td>.390*</td>
<td>.254</td>
<td>.364*</td>
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<tr>
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<td>.355*</td>
<td>.365*</td>
<td>.294</td>
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<td>.230</td>
<td>.156</td>
<td>.212</td>
<td>.412*</td>
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</tr>
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<td>.297</td>
<td>.350*</td>
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<td>.139</td>
<td>.095</td>
<td>.075</td>
<td></td>
</tr>
<tr>
<td>I-S</td>
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<td>.103</td>
<td>.189</td>
<td>.005</td>
<td>.137</td>
<td></td>
</tr>
<tr>
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<td>-.025</td>
<td>.168</td>
<td>.069</td>
<td>-.030</td>
<td></td>
</tr>
<tr>
<td>Psychoticism</td>
<td>.361*</td>
<td>.139</td>
<td>.284</td>
<td>.275</td>
<td>.257</td>
<td></td>
</tr>
<tr>
<td>Additional</td>
<td>.102</td>
<td>.457**</td>
<td>.475**</td>
<td>.295</td>
<td>.537**</td>
<td></td>
</tr>
<tr>
<td>GSI</td>
<td>.208</td>
<td>.307</td>
<td>.388*</td>
<td>.360*</td>
<td>.377*</td>
<td></td>
</tr>
<tr>
<td>PSDI</td>
<td>.117</td>
<td>.272</td>
<td>.373*</td>
<td>.402*</td>
<td>.419**</td>
<td></td>
</tr>
</tbody>
</table>

| Y-BOCS       | 1.000 | .038 | .160      | .096   | -.043 |        |

O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity

* *p<.05, ** p<.01, PSDI=Positive Syndrome distress index, GSI = Global Severity Index

In the AD group, there was only one significant relationship between eating pathology and general pathology. Increased Eating Restraint was associated with lower Phobic anxiety as measured by the SCL-90-R, however this did not appear to be a true trend in the data after inspection of graphs (see Appendix 11).
Table 6.3 Correlation of general and eating psychopathology in AD group

<table>
<thead>
<tr>
<th></th>
<th>YBOCS</th>
<th>EDE</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Restraint</td>
<td>Eating</td>
<td>Shape</td>
<td>Weight</td>
</tr>
<tr>
<td>SCL-90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O-C</td>
<td>.213</td>
<td>-.089</td>
<td>.270</td>
<td>.242</td>
</tr>
<tr>
<td>Depression</td>
<td>.202</td>
<td>-.249</td>
<td>.168</td>
<td>.231</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.225</td>
<td>-.355*</td>
<td>.099</td>
<td>.065</td>
</tr>
<tr>
<td>Phobia</td>
<td>.118</td>
<td>-.538**</td>
<td>-.110</td>
<td>.095</td>
</tr>
<tr>
<td>Somatisation</td>
<td>-.021</td>
<td>-.265</td>
<td>-.113</td>
<td>.004</td>
</tr>
<tr>
<td>Hostility</td>
<td>.258</td>
<td>-.037</td>
<td>.156</td>
<td>.267</td>
</tr>
<tr>
<td>I-S</td>
<td>.212</td>
<td>-.222</td>
<td>.137</td>
<td>.270</td>
</tr>
<tr>
<td>Paranoia</td>
<td>.181</td>
<td>-.101</td>
<td>.142</td>
<td>.212</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>.358*</td>
<td>-.189</td>
<td>.311</td>
<td>.348*</td>
</tr>
<tr>
<td>Additional</td>
<td>.256</td>
<td>-.185</td>
<td>.197</td>
<td>.228</td>
</tr>
<tr>
<td>GSI</td>
<td>.290</td>
<td>-.288</td>
<td>.185</td>
<td>.237</td>
</tr>
<tr>
<td>PSDI</td>
<td>.274</td>
<td>-.244</td>
<td>.204</td>
<td>.261</td>
</tr>
<tr>
<td>Y-BOCS</td>
<td>1</td>
<td>.045</td>
<td>.125</td>
<td>.207</td>
</tr>
</tbody>
</table>

O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity
*p<.05, ** p<.01, PSDI=Positive Syndrome distress index, GSI = Global Severity Index

6.1.4 Clinically Significant Impairment

17 patients (81%) from the BN group and 18 (78%) from the AD group performed at least 1 standard deviation (SD) below their estimated premorbid ability on one or more a priori measure. Underperformance relative to estimated premorbid ability on 3 or more measures was defined as impaired, relative to estimated premorbid ability. Seven from the BN group and 12 from the AD group demonstrated underperformance on 3 or more measures (Table 6.4).

Impaired performance relative to normative data was defined as performance at 2 SDs or more below the normative mean on one or more measures. Five people from the AD group and 3 from the BN group were impaired relative to normative data. These participants were also impaired relative to past ability.

The measures on which the underperformance and impaired performance occurred are described in Table 6.4.
Table 6.4: Number of participants demonstrating underperformance and impairment

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>Underperformance on at least 1 measure (%)</th>
<th>Underperformance on 3 or more measures (%)</th>
<th>Impaired relative to normative group on 1 or more measure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BN</td>
<td>Anx/Dep</td>
<td>BN</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>9 (43)</td>
<td>14 (61)</td>
<td>7 (33)</td>
</tr>
<tr>
<td>Categories completed</td>
<td>10 (48)</td>
<td>13 (57)</td>
<td>7 (33)</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number/letter switch</td>
<td>6 (29)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Trail Making test</td>
<td>Number of errors</td>
<td>2 (10)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>11 (52)</td>
<td>14 (61)</td>
<td>7 (33)</td>
</tr>
<tr>
<td>Colour Word Inhibition</td>
<td>4 (19)</td>
<td>6 (26)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Hayling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Errors</td>
<td>1 (5)</td>
<td>2 (9)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Total Number of individuals</td>
<td>17 (81)</td>
<td>18 (78)</td>
<td>7 (33)</td>
</tr>
</tbody>
</table>

Those defined as impaired relative to past ability were significantly younger than unimpaired participants (U=119.5, Z=-2.799, p < .05), scored lower on EDE restraint (U= 126, Z = -2.657, p < .05), had higher estimated premorbid IQ (t(42) = 3.82, p <.05) and scored lower on the YBOCS (t(442) = 2.42, p < .05). There was no difference in BMI, years of education or SCL-90-R subscales anxiety, depression or obsessive compulsive symptoms.

Individuals from either group with a deficit relative to normative data were not significantly different to the rest of the participants (all p>.05) on age, BMI, premorbid IQ, years of education, EDE restraint, SCL-90-R subscales of anxiety, depression, obsessive compulsive symptoms or the YBOCS.

The proportions of each group who were impaired relative to normative data (p = .701; FET) or relative to previous ability (p =.239; FET) were not significantly different.
6.1.5 Relationships between performance on different neuropsychological measures

In the BN group, there were no significant correlations of set shifting measures with each other after a correction for multiple comparisons of $p < .01$ was applied, although increased perseverative errors were associated with fewer categories completed, at the level of $p < .05$. However, non-perseverative errors were significantly correlated with categories completed, indicating that increased non perseverative errors was strongly related to fewer categories being completed by BN participants. No significant correlations were found between the inhibition measures, suggesting that participants in the BN group did not perform in a similar way on all the inhibition measures (Table 6.5).

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>WCST</th>
<th>DKEFS TMT</th>
<th>WCST</th>
<th>CWIT</th>
<th>Hayling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PE</td>
<td>CC</td>
<td>N/L switch</td>
<td>Errors</td>
<td>PE</td>
</tr>
<tr>
<td>WCST</td>
<td>-467*</td>
<td>.138</td>
<td>.255</td>
<td>.632*</td>
<td>-.128</td>
</tr>
<tr>
<td>Perseverative errors (PE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Categories completed (CC)</td>
<td>-467*</td>
<td>.037</td>
<td>-.084</td>
<td>-.646**</td>
<td>.373*</td>
</tr>
<tr>
<td>DKEFS</td>
<td>.138</td>
<td>.037</td>
<td>.247</td>
<td>.170</td>
<td>.329*</td>
</tr>
<tr>
<td>Trail Making test Number/letter switch</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test No. of errors</td>
<td>.255</td>
<td>-.084</td>
<td>.247</td>
<td>.132</td>
<td>-.041</td>
</tr>
<tr>
<td>Inhibition</td>
<td>WCST</td>
<td>.632*</td>
<td>-.646**</td>
<td>.170</td>
<td>.132</td>
</tr>
<tr>
<td>Non-perseverative errors (NPE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DKEFS</td>
<td>-.128</td>
<td>.373*</td>
<td>.329*</td>
<td>-.041</td>
<td>-.077</td>
</tr>
<tr>
<td>Colour Word Inhibition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayling Errors</td>
<td>-.101</td>
<td>.195</td>
<td>.093</td>
<td>-.414*</td>
<td>-.076</td>
</tr>
</tbody>
</table>

*p<.05, **p<.01

In the AD group, there were no significant correlations between measures of inhibition. However, a trend was seen relating increased WCST non-perseverative errors with longer times to complete the CWIT inhibition condition. Measures of set shifting tended to be significantly correlated with each other in the AD group,
indicating that participants who performed poorly on one set shifting task also showed impairment across the others. However, the number of errors on TMT number/letter switch was not correlated with other set shifting measures, which suggests that it may not reflect the same difficulties as the other set shifting measures.

There were also significant correlations between inhibition and set shifting measures, as increased non-perseverative errors were associated with increased time to complete the TMT number/letter switch task and increased perseverative errors. This indicates that participants who performed poorly on set shifting tasks also committed more non-perseverative errors, suggesting that their cognitive inhibition was also impaired.

Unlike the BN group, correlations within the AD group indicate that both perseverative and non-perseverative errors contributed approximately the same amount to impaired category completion among AD participants (Table 6.6).

Table 6.6 Relationship between performance on set shifting and inhibition measures in the anxious and/or depressed group

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>WCST</th>
<th>DKEFS/TMT</th>
<th>WCST</th>
<th>CWIT</th>
<th>Hayling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PE</td>
<td>CC</td>
<td>N/L switch</td>
<td>Errors</td>
<td>NPE</td>
</tr>
<tr>
<td>WCST Perseverative errors (PE)</td>
<td>-.666**</td>
<td>.490**</td>
<td>.208</td>
<td>.717**</td>
<td>.288</td>
</tr>
<tr>
<td>Categories completed (CC)</td>
<td>-.666**</td>
<td>-.447**</td>
<td>-.147</td>
<td>-.691**</td>
<td>-.312</td>
</tr>
<tr>
<td>DKEFS Trail Making test Number/letter switch</td>
<td>.490**</td>
<td>-.447**</td>
<td>.286</td>
<td>.435**</td>
<td>.217</td>
</tr>
<tr>
<td>Trail Making test No. of errors</td>
<td>.208</td>
<td>-.147</td>
<td>.286</td>
<td>.151</td>
<td>.314</td>
</tr>
<tr>
<td>Inhibition WCST Non-perseverative errors (NPE)</td>
<td>.717**</td>
<td>-.691**</td>
<td>.435**</td>
<td>.151</td>
<td>.346*</td>
</tr>
<tr>
<td>DKEFS Colour Word Inhibition</td>
<td>.288</td>
<td>-.312</td>
<td>.217</td>
<td>.314</td>
<td>.346*</td>
</tr>
<tr>
<td>Hayling Errors</td>
<td>.163</td>
<td>-.215</td>
<td>.212</td>
<td>.149</td>
<td>.168</td>
</tr>
</tbody>
</table>

*p<.05, **p<.01
6.2 Non-key Executive function measures and additional subscales of the SCL-90-R
The groups were compared on the Brixton task and the three conditions of the DKEFS Verbal Fluency task, which formed part of the neuropsychological battery, but were not chosen as a priori measures. No significant differences were observed between the groups on the Brixton task or the three tasks of Verbal Fluency. Similar levels of psychopathology symptoms, on the paranoia, psychoticism and ‘additional’ subscales of the SCL-90-R were also seen in the two groups (Table 6.7).

6.3 Analysis Relating to Aim 3 - Social Problem Solving and Self Esteem
The self esteem and social problem solving styles of the BN and AD participants were investigated using the Self-Liking/Self Competence scale (SLSC) and the Social Problem Solving Inventory (SPSI).

6.3.1 Social Problem Solving Style
The dimensions identified by the Social Problem Solving Inventory are Positive Problem Orientation (PPO), Negative Problem Orientation (NPO), Rational Problem Solving (RPS), Impulsivity/Carelessness style (ICS) and Avoidance style (AS). Adaptive social problem solving is indicated by the subscales PPO and RPS. Maladaptive problem solving is indicated by subscales NPO, ICS, AS. The SPSI provides standard scores for each dimension of social problem solving with a mean of 100 and a standard deviation of 15.

Both groups obtained mean scores one standard deviation lower than the normative group on PPO and one standard deviation higher than the normative group in NPO, indicating maladaptive problem orientation in both groups (Figures 6.1 and 6.2).
6.3.2 Group comparisons of self esteem and social problem solving

As all the variables were found to be normally distributed, t-tests were used to compare groups. The age standardised scores for the SPSI were used for the comparison as the two groups had been found to differ significantly on age (Chapter 4).
The BN group indicated significantly lower self liking and sense of self competence than the anxious/depressed group, illustrated on the total score of the Self Liking/Self Competence scale (t(41)=2.824, \( p < .01 \)) and on its individual scales, Self liking (t(41)=2.674, \( p < .05 \)) and Self competence (t(41)=2.417, \( p < .05 \)). The two groups demonstrated no significant differences in social problems solving styles (Table 6.7).
Table 6.7: Comparison of groups on additional psychological variables and non key executive function measures

<table>
<thead>
<tr>
<th>Psychological Variables</th>
<th>Bulimic group n=21</th>
<th>Anxiety/Depression group n=23</th>
<th>Cohen’s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median (range)</td>
</tr>
<tr>
<td>SCL-90-R (PSDI)</td>
<td>2.35</td>
<td>0.71</td>
<td>2.12</td>
</tr>
<tr>
<td>Paranoia</td>
<td>6.81</td>
<td>6.87</td>
<td>5 (0-25)</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>6.52</td>
<td>5.87</td>
<td>5 (0-21)</td>
</tr>
<tr>
<td>Additional</td>
<td>12.52</td>
<td>6.97</td>
<td>9.48</td>
</tr>
<tr>
<td>SPSI-R a</td>
<td>79.35</td>
<td>18.93</td>
<td>75.96</td>
</tr>
<tr>
<td>PPO</td>
<td>115.95</td>
<td>18.20</td>
<td>119.09</td>
</tr>
<tr>
<td>NPO</td>
<td>85.3</td>
<td>12.17</td>
<td>85.74</td>
</tr>
<tr>
<td>RPS</td>
<td>101.65</td>
<td>14.21</td>
<td>100.30</td>
</tr>
<tr>
<td>I-CS</td>
<td>106.20</td>
<td>15.28</td>
<td>112.22</td>
</tr>
<tr>
<td>Avoidance style</td>
<td>87.55</td>
<td>17.62</td>
<td>81.74</td>
</tr>
<tr>
<td>Global Score</td>
<td>15.25</td>
<td>4.89</td>
<td>19.30</td>
</tr>
<tr>
<td>SLSC a</td>
<td>17.55</td>
<td>6.18</td>
<td>21.6</td>
</tr>
<tr>
<td>Total Score</td>
<td>32.8</td>
<td>9.75</td>
<td>40.9</td>
</tr>
<tr>
<td>Neuropsychological Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DKEFS Verbal Fluency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter Fluency</td>
<td>42.71</td>
<td>10.12</td>
<td>39.48</td>
</tr>
<tr>
<td>Category Fluency</td>
<td>45.19</td>
<td>7.96</td>
<td>41.65</td>
</tr>
<tr>
<td>Category Shift, total switching acc</td>
<td>14.33</td>
<td>3.69</td>
<td>13.78</td>
</tr>
<tr>
<td>Brixton errors</td>
<td>12.62</td>
<td>3.35</td>
<td>21.57</td>
</tr>
</tbody>
</table>

*a one participant failed to complete the SPSI-R and the SLSC, therefore n=20 in the BN group on these measures

*p<.05, ** p<.01, PSDI=Positive Syndrome distress index
6.3.3 Relationship between a priori variables and Social Problem Solving

A significance level of \( p < .01 \) was chosen, as a Bonferroni correction was considered too conservative for the analysis. Social problem solving was not significantly related to any of the neuropsychological measures in the BN group (Table 6.8).

**Table 6.8: Correlation of Social Problem Solving Patterns and a priori variables in the BN group**

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>Adaptive Problem Solving</th>
<th>Maladaptive Problem Solving</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPO</td>
<td>RPS</td>
</tr>
<tr>
<td>WCST</td>
<td>Perseverative errors</td>
<td>.134</td>
</tr>
<tr>
<td></td>
<td>Categories completed</td>
<td>.057</td>
</tr>
<tr>
<td>DKEFS</td>
<td>Trail Making test</td>
<td>Number/letter switch</td>
</tr>
<tr>
<td></td>
<td>Trail Making test</td>
<td>No. of errors</td>
</tr>
<tr>
<td>Inhibition</td>
<td>WCST</td>
<td>Non-perseverative errors</td>
</tr>
<tr>
<td>DKEFS</td>
<td>Colour Word Inhibition</td>
<td>.097</td>
</tr>
<tr>
<td></td>
<td>Hayling Errors</td>
<td>-.026</td>
</tr>
</tbody>
</table>

*\( p < .05 \), **\( p < .01 \) PPO = Positive Problem Orientation, RPS = Rational Problem Solving, NPO = Negative Problem Orientation, ICS = Impulsivity/Carelessness Style, AS = Avoidance Style

Within the AD group, trends of association were seen that were not significant at the chosen \( p < .01 \) level. There was a trend of association between NPO and WCST categories completed and between Impulsivity/Carelessness style and errors on the Hayling task. Endorsement of rational problem solving strategies showed a trend of association with fewer errors on the TMT. Upon visual inspection of graphs, there were no visible trends in the data (see graphs in Appendix 11).
Table 6.9 Correlation of Social Problem Solving Patterns and a priori variables in the AD group

<table>
<thead>
<tr>
<th></th>
<th>Adaptive Problem Solving</th>
<th>Maladaptive Problem Solving</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPO</td>
<td>RPS</td>
</tr>
<tr>
<td>Set Shifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>.137</td>
<td>-.176</td>
</tr>
<tr>
<td>Categories completed</td>
<td>-.134</td>
<td>.152</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number/letter switch</td>
<td>.238</td>
<td>-.171</td>
</tr>
<tr>
<td>Trail Making errors</td>
<td>.303</td>
<td>-.401*</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>.127</td>
<td>-.143</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Word</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>-.040</td>
<td>-.020</td>
</tr>
<tr>
<td>Hayling Errors</td>
<td>.222</td>
<td>-.062</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01 PPO = Positive Problem Orientation, RPS = Rational Problem Solving, NPO = Negative Problem Orientation, ICS = Impulsivity/Carelessness Style, AS = Avoidance Style

6.3.4 Relationship between a priori variables and Self-Liking and Self-Competence

No relationships were found between reported self liking or self competence and performance on the set shifting and inhibition measures in either group (Table 6.10).
Table 6.10: Association between a priori variables and self liking/self competence

<table>
<thead>
<tr>
<th>Set Shifting</th>
<th>BN Group</th>
<th>AD Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SL</td>
<td>SC</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perseverative errors</td>
<td>.184</td>
<td>.172</td>
</tr>
<tr>
<td>Categories completed</td>
<td>-.049</td>
<td>.049</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number/letter switch</td>
<td>.309</td>
<td>.292</td>
</tr>
<tr>
<td>Trail Making test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of errors</td>
<td>.114</td>
<td>.303</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-perseverative errors</td>
<td>.176</td>
<td>.038</td>
</tr>
<tr>
<td>DKEFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Word</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition Errors</td>
<td>.249</td>
<td>-.005</td>
</tr>
<tr>
<td>Hayling</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<.05, ** p<.01, SL = Self Liking, SC = Self Competence, Tot = Self Liking/Self Competence total score
Chapter 7: Additional Discussion

Further analysis was performed on the data presented in Chapter 4 and data relating to two additional measures of set shifting and measures of self esteem and social problem solving were analysed in Chapter 6. The findings of these analyses will now be discussed in the order they were presented in Chapter 6.

7.1 Age differences between groups

Participants in the BN group were significantly younger than patients in the AD group. This difference was most likely related to the fact that the average age of onset of bulimia (20yrs) is younger than average onset of depression (30yrs), GAD (31 yrs) or Panic Disorder (24yrs) although not of OCD (19yrs) (Hudson et al., 2007; Kessler et al., 2005). As such, these age differences are likely to represent inherent characteristics of the two groups. An analysis of key variables using age normed scaled scores revealed a similar pattern of results to those using raw scores, suggesting that age did not influence the pattern of results.

7.2 Relationships of general and eating pathology

In the BN group, there were a number of correlations indicating significant relationships between eating disorder symptoms and psychopathology. This is consistent with the literature reporting a high level of comorbidity between BN and other disorders (Hudson et al., 2007) and associations found in the literature such as Herpertz-Dahlmann and Remschmidt’s (1993) report of a high correlation between depression and eating disorder symptoms.

In the AD group, there was no significant relationship between eating pathology and general pathology. This is to be expected, as the AD group were chosen to be without problematic levels of eating disorder symptoms (EDE < 4).

7.3 Clinically significant impairment

Clinical significance calculations indicated that very few participants in each group were impaired on any neuropsychological test compared to normative data. Similar proportions of participants in each group underperformed and demonstrated impairments in relation to normative data. Overall, the performance of each group was relatively unimpaired compared to normative data, although a high proportion of
participants were underperforming relative to their own estimated premorbid ability. This is consistent with many findings of no impairments relative to controls in studies of BN, anxiety and depression on executive function tasks (Brand et al., 2007; Claes et al., 2006; McClintock et al., 2010). Most participants in the AD group used here were diagnosed with GAD, specific phobia or panic disorder with or without comorbid depression. The literature would suggest that a group of this composition would not have specific deficits in set shifting or inhibition (Airaksinen et al., 2005; Chapter 2 of this thesis; O'Toole & Pedersen, 2011). Findings of relatively few participants who were significantly impaired among a sample of eating disorder patients is consistent with the literature. Approximate proportions of 65% unimpaired and 35% impaired were reported by Lauer et al. (1999) in relation to their own study of BN and AN and in their discussion of other eating disorder studies (Kingston et al., 1996).

When considering performance among the impaired participants, different patterns were seen. Participants in the AD group were impaired across all a priori measures, while BN participants were exclusively impaired on WCST non-perseverative errors (NPE) and number of categories completed (CC). A pattern similar to this in BN participants was reported by Alvarez-Moya et al. (2009), where BN participants made significantly more non-perseverative errors than healthy controls. Barceló and Knight (2002) have suggested that WCST NPE can reflect random errors relating to impairments in maintaining set, due to distractibility or impulsivity. In their sample of patients with prefrontal lobe injuries, the CC score, which is often taken to relate to set shifting errors, was in fact more commonly lowered due to failure to continue with a correct responding pattern. This implies that where NPE is impaired, impaired CC may not indicate set shifting difficulties but is rather a consequence of the high number of NPEs. There is a ‘failure to maintain set’ scale in the WCST, which measures a similar construct, but this only counts errors after five or more correct matches. NPE may reflect shorter durations of set-consistent responding. Although these impairments suggest the presence of cognitive disinhibition, similar impairments relative to normative data were not seen on the other measures of inhibition, i.e. the Stroop inhibition task and the Hayling task.
7.4 Relationships between performance on neuropsychological measures

Set shifting measures correlated with each other in the AD group but not in the BN group. This analysis suggests (in addition to the clinical impairment analysis) that despite non-significant differences between groups, the style of performance was different in each group.

In the BN group, there were no significant correlations of set shifting measures with each other, after a correction for multiple comparisons, nor were inhibition measures correlated with each other. However, non-perseverative errors were significantly correlated with categories completed. This indicates that increased non perseverative errors were strongly related to fewer categories being completed by BN participants, and supports the idea that a low number of categories completed is related to loss of set, rather than perseverative set maintenance, in this group.

In the AD group, there were no significant correlations between measures of inhibition, suggesting that AD participants performed differently on each measure of inhibition. Measures of set shifting tended to be significantly correlated with each other, suggesting that participants who performed poorly on one set shifting task also displayed impairment across other set shifting tasks. However, the number of errors on TMT number/letter switch task was not correlated with the other set shifting measures, which suggests that participants in the AD group did not perform on it in the same way as they did on the other set shifting measures. Many neuropsychological measures can be said to assess a number of cognitive functions (Burgess, 2003). In this case, the number of errors on the TMT number/letter switch task may not have been primarily tapping into the same ability as the other set shifting tasks in the AD group.

There were significant correlations between inhibition and set shifting measures in the AD group, as increased non-perseverative errors were associated with increased time to complete the TMT number/letter switch task. This suggests that participants who performed poorly on set shifting tasks also committed more non-perseverative errors and indicates that patients with set shifting impairments in this group may also have been impaired in cognitive inhibition.
Unlike the BN group, where only NPE made a significant contribution to the categories completed variable in the WCST, in the AD group both perseverative and non-perseverative errors contributed approximately the same amount to impaired category completion.

7.5 Non-key Executive Function Measures

No group differences were found on the additional measures of verbal fluency and set shifting, which is consistent with the lack of group differences on set shifting measures reported in Chapter 4. It is also consistent with literature that indicates that the performance of BN patients on the FAS task is not different to controls (Brand et al., 2007; Tchanturia, Anderluh, et al., 2004).

7.6 Aim 3 – Social Problem Solving and Self Liking/Self Competence

Both groups were found to have social problem solving styles characterised by low positive problem orientation and high negative problem orientation. This similarity is consistent with the literature which suggests that BN participants would display high negative problem orientation (NPO) (Paterson et al., 2011), and that high NPO has also been associated with depression (Klein et al., 2011) and high levels of worry (Belzer et al., 2002). These findings suggest that maladaptive social problem solving is not specific to BN and may be related to other shared factors such as anxiety and depression symptoms.

No significant differences were found in social problem solving style between the two groups. Social problem solving style was also not related to neuropsychological task performance among BN participants or AD participants.

Self esteem, as measured by the Self Liking/Self Competence scale was significantly lower in the BN group than in the comparison group of females with anxiety and/or depressive disorders. This is consistent with reports in the literature of low self-liking and self competence in AN groups relative to healthy controls (Paterson et al., 2011; Paterson et al., 2007). It is not consistent with similar reports of low self esteem in anxiety and depression (Silverstone & Salsali, 2003). However, neither self-liking nor sense of self competence was significantly associated with
performance on set shifting or inhibition tasks in either group. At the time of writing, no literature could be found that explored this association. However, the literature on self liking and self competence suggests that self competence is associated with perfectionism in AN (Gordon et al., 2005; Surgenor et al., 2007), and as perfectionism is associated with impaired set shifting (Egan et al., 2011; Tchanturia, Morris, et al., 2004), some relationship may have been expected between self-competence and set shifting performance. However, as has been demonstrated in a number of studies, AN and BN do not perform in the same way on neuropsychological measures (Murphy et al., 2004; Roberts et al., 2010), so these findings for AN may not be applicable in a BN group.

Fairburn et al.'s (2003) cognitive behavioural model of BN includes severe perfectionism, core low self esteem, mood intolerance and interpersonal difficulties as maintenance mechanisms for the disorder. In relation to this model of BN, these data demonstrate evidence for three of these maintaining factors. Participants in the BN group demonstrated significantly lower self esteem than a comparison group suffering from psychological distress. Perfectionism, in the form of obsessive compulsive traits, may be present at a higher level in the BN group as trends were seen (Chapter 4), however they were not found to be significant. Interpersonal difficulties also showed a trend towards being increased in the BN group on the interpersonal sensitivity scale of the SCL-90-R and the BN group demonstrated higher negative problem orientation and lower positive problem orientation than the normative group on the SPSI.

7.7 Limitations
Limitations were described in the journal article in Chapter 4.

7.8 Implications and future directions
In AN, set shifting impairments have been found to impact on Cognitive Behavioural Therapy (CBT) treatment. Cognitive remediation therapy has been used to improve cognitive flexibility and facilitate the implementation of CBT strategies with patients with anorexia (Tchanturia et al., 2008). In light of the suggestion that BN participants’ impairment on WCST categories completed may not relate to set shifting and in view of the small numbers demonstrating impairment, these data do
not support a need for cognitive remediation in most cases of BN. The trends relating to deficits in WCST non-perseverative errors suggest cognitive impulsivity may be a significant problem for a proportion of people with BN and as such, this study supports the possible use of some form of cognitive control training in the treatment of BN, as proposed by Robinson et al. (2009).

The finding of small proportions of a BN group demonstrating neuropsychological impairments has been seen in other studies (Lauer et al., 1999) and suggests that future research may best utilise large sample sizes to investigate this small proportion of the BN population and any characteristics that may define them. Larger sample sizes would also facilitate investigation of small to medium differences that may exist between BN groups and groups representing disorders commonly comorbid with BN.

7.9 Conclusion

Eating pathology was be related to anxiety and depression symptoms in the BN group but not the AD group. Further analysis indicated that few participants in either group were impaired in relation to normative data on neuropsychological measures. This evidence suggests that cognitive performance difficulties are not widespread in BN or related to anxiety, depression or obsessive compulsive symptoms. There was some tentative indication of a deficit in inhibition but this requires further investigation.
Chapter 8: References


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Appendices
Appendix 1 Author Guidelines for Journal of Affective Disorders

Journal of Affective Disorders

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Papers should be divided into sections headed by a caption (e.g., Introduction, Methods, Results, Discussion). A structured abstract of no more than 250 words should appear on a separate page with the following headings and order: Background, Methods, Results, Limitations, Conclusions (which should contain a statement about the clinical relevance of the research). A list of three to six key words should appear under the abstract.

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*e.g.*, Author X designed the study and wrote the protocol. Author Y managed the literature searches and analyses. Authors X and Z undertook the statistical analysis, and author W wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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Appendix 2 Systematic Review Database Search Terms

Embase Search Terms

1. cognition/ or attention/ or executive function/ or learning/ or memory/ or mental capacity/ or mental performance/ or orientation/ or social cognition/ or "theory of mind"/ or thinking/

2. neurocognition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

3. exp task performance/ or exp attention/ or exp learning/ or exp cognition/

4. "inhibition (psychology)"/co [Complication]

5. inhibition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

6. central coherence.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

7. exp cognitive defect/

8. exp memory/ or exp short term memory/ or exp autobiographical memory/ or exp procedural memory/ or exp spatial memory/ or exp auditory memory/ or exp associative memory/ or exp tactile memory/ or exp working memory/ or exp visual memory/ or exp explicit memory/ or exp implicit memory/ or exp sensory memory/ or exp memory disorder/ or exp declarative memory/ or exp verbal memory/ or exp long term memory/ or exp semantic memory/ or exp episodic memory/

9. decision making.mp. or exp decision making/

10. exp motor control/

11. exp spatial discrimination/ or exp hemispheric dominance/ or exp task performance/

12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

13. Neuropsychological test.mp. or exp neuropsychological test/

14. 12 or 13

15. exp anxiety/ or exp anxiety neurosis/ or exp generalized anxiety disorder/ or exp anxiety disorder/ or exp "mixed anxiety and depression"/

16. exp panic/
17 exp agoraphobia/
18 exp social phobia/ or exp phobia/
19 exp posttraumatic stress disorder/
20 exp obsession/ or exp obsessive compulsive disorder/ or exp compulsion/
21 social anxiety.mp.
22 15 or 16 or 17 or 18 or 19 or 20 or 21
23 14 and 22
24 limit 23 to (english language and yr="1980 -Current")
25 13 and 24
26 limit 25 to adult <18 to 64 years>
**Medline Search Terms**

1. exp Cognition/ or exp Cognition Disorders/ or exp Neuropsychological Tests/ or neurocognition.mp.
2. attention.mp. or exp Attention/
3. exp Problem Solving/ or executive function.mp. or exp Executive Function/ or exp Mental Processes/
4. exp Association Learning/ or exp Learning/ or exp Paired-Associate Learning/ or learning.mp. or exp Discrimination Learning/ or exp Verbal Learning/
5. memory.mp. or exp Memory/ or exp Memory, Long-Term/ or exp Memory, Episodic/ or exp Memory Disorders/ or exp Memory, Short-Term/
6. exp Mental Competency/ or exp Decision Making/ or exp Mental Processes/ or mental capacity.mp. or exp Intelligence/
7. exp Psychomotor Performance/ or mental performance.mp.
8. orientation.mp. or exp Orientation/
9. exp Social Perception/ or social cognition.mp.
10. theory of mind.mp. or exp "Theory of Mind"/
11. thinking.mp. or exp Thinking/
12. task performance.mp. or exp "Task Performance and Analysis"/
13. inhibition.mp. or exp "Inhibition (Psychology)"/
14. central coherence.mp.
15. decision making.mp. or exp Decision Making/
16. exp Motor Skills/ or motor control.mp.
17. exp Visual Perception/ or exp Pattern Recognition, Visual/ or visuospatial processing.mp.
18. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. exp Anxiety/ or exp Anxiety Disorders/ or anxiety.mp.
20. generalised anxiety disorder.mp.
21. (mixed anxiety and depression).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
22. exp Panic Disorder/ or exp Panic/ or panic.mp.
23. agoraphobia.mp. or exp Agoraphobia/
24. phobia.mp. or exp Phobic Disorders/
25. social anxiety.mp.
26. post traumatic stress disorder.mp. or exp Stress Disorders, Post-Traumatic/
obsessive compulsive disorder.mp. or exp Obsessive-Compulsive Disorder/

ocd.mp.

obsession.mp. or exp Obsessive Behavior/

exp Compulsive Behavior/ or compulsion.mp.

19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30

Neuropsychological test.mp. or exp Neuropsychological Tests/

18 and 31 and 32

limit 33 to (english language and yr="1980 -Current" and "all adult (19 plus years)" and humans)

limit 34 to ("young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years")

PsycInfo Search terms

1. exp Cognition/ or exp Cognition Disorders/ or exp Neuropsychological Tests/ or neurocognition.mp.
2. attention.mp. or exp Attention/
3. exp Problem Solving/ or executive function.mp. or exp Executive Function/ or exp Mental Processes/
4. exp Association Learning/ or exp Learning/ or exp Paired-Associate Learning/ or learning.mp. or exp Discrimination Learning/ or exp Verbal Learning/
5. memory.mp. or exp Memory/ or exp Memory, Long-Term/ or exp Memory, Episodic/ or exp Memory Disorders/ or exp Memory, Short-Term/
6. exp Mental Competency/ or exp Decision Making/ or exp Mental Processes/ or mental capacity.mp. or exp Intelligence/
7. exp Psychomotor Performance/ or mental performance.mp.
8. orientation.mp. or exp Orientation/
9. exp Social Perception/ or social cognition.mp.
10. theory of mind.mp. or exp "Theory of Mind"/
11. thinking.mp. or exp Thinking/
12. task performance.mp. or exp "Task Performance and Analysis"/
13. inhibition.mp. or exp "Inhibition (Psychology)"/
14. central coherence.mp.
15. decision making.mp. or exp Decision Making/
16. exp Motor Skills/ or motor control.mp.
17. exp Visual Perception/ or exp Pattern Recognition, Visual/ or visuospatial processing.mp.
18. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. exp Anxiety/ or exp Anxiety Disorders/ or anxiety.mp.
20. generalised anxiety disorder.mp.
21. (mixed anxiety and depression).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
22. exp Panic Disorder/ or exp Panic/ or panic.mp.
23. agoraphobia.mp. or exp Agoraphobia/
24. phobia.mp. or exp Phobic Disorders/
25. social anxiety.mp.
26. post traumatic stress disorder.mp. or exp Stress Disorders, Post-Traumatic/
27. obsessive compulsive disorder.mp. or exp Obsessive-Compulsive Disorder/
28  ocd.mp.
29  obsession.mp. or exp Obsessive Behavior/
30  exp Compulsive Behavior/ or compulsion.mp.
31  19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32  Neuropsychological test.mp. or exp Neuropsychological Tests/
33  18 and 31 and 32
34  limit 33 to (human and english language and adulthood <18+ years> and yr="1980 -Current")
PsycArticles search terms

1 neurocognition.mp. [mp=title, abstract, full text, caption text]
2 cognition.mp. [mp=title, abstract, full text, caption text]
3 attention.mp. [mp=title, abstract, full text, caption text]
4 learning.mp. [mp=title, abstract, full text, caption text]
5 memory.mp. [mp=title, abstract, full text, caption text]
6 mental capacity.mp. [mp=title, abstract, full text, caption text]
7 executive function.mp. [mp=title, abstract, full text, caption text]
8 mental performance.mp. [mp=title, abstract, full text, caption text]
9 orientation.mp. [mp=title, abstract, full text, caption text]
10 social cognition.mp. [mp=title, abstract, full text, caption text]
11 thinking.mp. [mp=title, abstract, full text, caption text]
12 theory of mind.mp. [mp=title, abstract, full text, caption text]
13 task performance.mp. [mp=title, abstract, full text, caption text]
14 inhibition.mp. [mp=title, abstract, full text, caption text]
15 central coherence.mp. [mp=title, abstract, full text, caption text]
16 cognitive defect.mp. [mp=title, abstract, full text, caption text]
17 cognitive deficit.mp. [mp=title, abstract, full text, caption text]
18 decision making.mp. [mp=title, abstract, full text, caption text]
19 motor control.mp. [mp=title, abstract, full text, caption text]
20 visuospatial processing.mp. [mp=title, abstract, full text, caption text]
21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22 Neuropsychological test.mp. [mp=title, abstract, full text, caption text]
23 anxiety.mp. [mp=title, abstract, full text, caption text]
24 anxiety disorder.mp. [mp=title, abstract, full text, caption text]
25 GAD.mp. [mp=title, abstract, full text, caption text]
26 (mixed anxiety and depression).mp. [mp=title, abstract, full text, caption text]
27 panic.mp. [mp=title, abstract, full text, caption text]
28 agoraphobia.mp. [mp=title, abstract, full text, caption text]
29 phobia.mp. [mp=title, abstract, full text, caption text]
30 social anxiety.mp. [mp=title, abstract, full text, caption text]
31 post traumatic stress disorder.mp. [mp=title, abstract, full text, caption text]
32 ptsd.mp. [mp=title, abstract, full text, caption text]
33 ocd.mp. [mp=title, abstract, full text, caption text]
34 obsessive compulsive disorder.mp. [mp=title, abstract, full text, caption text]
35 obsession.mp. [mp=title, abstract, full text, caption text]
36 compulsion.mp. [mp=title, abstract, full text, caption text]
37 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38 21 and 22 and 37
39 limit 38 to yr="1980 -Current"
Appendix 3 Detailed Search Diagram for Systematic Review
Total Number of articles found in search over 4 databases
n=3431

<table>
<thead>
<tr>
<th>Database</th>
<th>Articles</th>
<th>Participants over 65</th>
<th>Participants under 18</th>
<th>Imaging studies</th>
<th>Drug trial/intervention study</th>
<th>Review</th>
<th>Study protocol only</th>
<th>Less than 15 per group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embase</td>
<td>945</td>
<td>9</td>
<td>6</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>22</td>
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<td>Psych</td>
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<td>41</td>
<td>24</td>
<td>3</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>Medline</td>
<td>2134</td>
<td>2</td>
<td>1</td>
<td>41</td>
<td>24</td>
<td>3</td>
<td>1</td>
<td>37</td>
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<td>PsychInfo</td>
<td>166</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

No anxiety disorder n=680
No test of cognitive function n=42
Participants over 65 n=9
Participants under 18 n=6
Imaging studies n=7
Drug trial/intervention study n=3
Review n=1
Study protocol only n=1
Less than 15 per group n=22

No anxiety disorder n=185
No test of cognitive function n=109
Participants over 65 n=8
Participants under 18 n=1
Imaging studies n=41
Drug trial/intervention study n=24
Review n=3
Less than 15 per group n=37

No anxiety disorder n=1663
Participants over 65 n=8
Participants under 18 n=1
Imaging studies n=41
Drug trial/intervention study n=24
Review n=3
Less than 15 per group n=37

No anxiety disorder n=123
Participants under 18 n=1
Less than 15 per group n=2

References combined as described in Figure 2.1
Appendix 4 Details of Quality Criteria

i. Eligibility criteria are specified
   - Well-covered (2)  Inclusion criteria clearly detailed and appropriate
   - Adequately addressed (1)  Inclusion criteria are not outlined clearly, though they can be ascertained from the details given.
   - Poorly addressed (0)  Some information is given about eligibility for the trial, though it could not be confidently replicated.
   - Not addressed (0)

ii. Comparison group is matched
   - Well-covered (2)  A suitable comparison group is matched on age, gender, education or IQ
   - Adequately addressed (1)  Group only matched on some of the above.
   - Poorly addressed (0)  Not matched/ no details given
   - Not addressed (0)

iii. Diagnosis using appropriate criteria and measure
   - Well-covered (2)  Diagnosis (or absence of diagnosis for HCs) ascertained by DSM/ICD criteria, structured interview by clinician
   - Adequately addressed (1)  Diagnosis by DSM/ICD criteria, using questionnaire based on DSM/ICD criteria
   - Poorly addressed (0)  Unspecified diagnosis procedure or questionnaire not specifically designed to reflect diagnostic criteria
   - Not addressed (0)

iv. Neuropsychological Measures are robust
   - Well-covered (2)  Outcome measures robust for this population (valid, reliable) reliability and validity specified in paper or easily obtainable using Lezak et al.’s (2004) reference text or reference provided in the paper.
   - Adequately addressed (1)  Tests well described but reliability and validity not found as described in under ‘well covered’.
   - Poorly addressed (0)  Outcome measures poorly described and less robust.
   - Not addressed (0)
### v. Sample size adequate for all groups

<table>
<thead>
<tr>
<th>Coverage Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-covered (2)</td>
<td>Sample size 25 or more in each group because of minimum number needed to detect large sample size</td>
</tr>
<tr>
<td>Adequately addressed (1)</td>
<td>Sample size 15-25 in each group</td>
</tr>
<tr>
<td>Poorly addressed (0)</td>
<td>Sample size not adequate (less than 15)</td>
</tr>
<tr>
<td>Not addressed (0)</td>
<td></td>
</tr>
</tbody>
</table>

### vi. Levels of uptake are reported

<table>
<thead>
<tr>
<th>Coverage Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-covered (2)</td>
<td>Levels of uptake are reported and affects of uptake levels considered</td>
</tr>
<tr>
<td>Adequately addressed (1)</td>
<td>Levels of uptake described in detail</td>
</tr>
<tr>
<td>Poorly addressed (0)</td>
<td>Levels of uptake not described</td>
</tr>
<tr>
<td>Not addressed (0)</td>
<td></td>
</tr>
</tbody>
</table>

### vii. Results – appropriate outputs provided

<table>
<thead>
<tr>
<th>Coverage Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-covered (2)</td>
<td>Means, standard deviations and confidence intervals reported</td>
</tr>
<tr>
<td>Adequately addressed (1)</td>
<td>Enough reported to facilitate comparison, not all of the above</td>
</tr>
<tr>
<td>Poorly addressed (0)</td>
<td>Some of above reported but not enough to make a complete comparison, or Selective reporting of initial measures mentioned in methods.</td>
</tr>
<tr>
<td>Not addressed (0)</td>
<td></td>
</tr>
</tbody>
</table>

### viii. Appropriate Statistical techniques

<table>
<thead>
<tr>
<th>Coverage Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-covered (2)</td>
<td>Appropriate statistics used, compensations for multiple comparisons, new alpha level clearly stated.</td>
</tr>
<tr>
<td>Adequately addressed (1)</td>
<td>No corrections for multiple comparisons but otherwise adequate statistics used.</td>
</tr>
<tr>
<td></td>
<td>Questionable statistics used - Post hoc tests used after a MANOVA or a variable used as a covariate where group differences exist on that variable</td>
</tr>
<tr>
<td>Poorly addressed (0)</td>
<td>Inappropriate statistics used</td>
</tr>
<tr>
<td>Not addressed (0)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 5 Author Guidelines for Journal of the International Neuropsychological Society

Manuscript Length

In order to increase the number of manuscripts that can be published in the JINS, please adhere to the following length requirements. Please provide a word count on the title page for abstract and for manuscript (not including abstract, tables, figures, or references).

Manuscripts will be returned if they exceed length requirements.

Regular Research Articles: Maximum of 5,000 words (not including tables, figures, or references) and a 200 word abstract.

Manuscript Preparation and Style

The entire manuscript should be typed double-spaced throughout using any word processing program. Unless otherwise specified, the guideline for preparation of manuscripts is the Publication Manual of the American Psychological Association (6th edition). This may be ordered from: APA Order Dept., 750 1st St. NE, Washington, DC 20002-4242, USA.

Pages should be numbered sequentially beginning with the Title Page. The Title Page should contain the full title of the manuscript, the full names and affiliations of all authors, a contact address with telephone and fax numbers and e-mail address, and the word count for abstract and for manuscript (excluding title page, abstract, references, tables, and figures). At the top right provide a short title of up to 45 characters preceded by the lead author’s last name. Example: Smith-Memory in Parkinson’s Disease. This running headline should be repeated at the top right of every following page.

The Abstract and Mesh terms (Keywords) on page 2 should include a brief statement of the problem, the method, the key findings, and the conclusions. Six mesh or key words should be provided (see http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=mesh for list), and they should not duplicate words in the title.

The full text of the manuscript should begin on page 3. For scientific articles, including Regular Research Articles, Brief Communications, Rapid Communications, and Symposia, the format should include an Abstract, Introduction,
Method, Results, and Discussion. This should be followed by References, Appendixes, Acknowledgments, Tables, Figures, and Figure Legends.

The use of abbreviations, except those that are widely used, is strongly discouraged. They should be used only if they contribute to better comprehension of the manuscript. Acronyms should be spelled out at first mention. Metric system (SI) units should be used.

**Special Note Regarding Figures**

Please upload your figure(s) in either a .doc or pdf. format. When uploading figures (colour or black and white), they need only be a high enough resolution for the reviewers and editors to identify the information you are trying to convey. However, if your manuscript is accepted for publication, your figures must meet the following criteria:

High quality digital images (600 dpi or higher) should be provided in PDF, EPS, or TIFF formats. If a digital image is not available, please scan in the image. Figures should be numbered consecutively as they appear in the text. Any indication of features of special interest should also be included. Figures should be twice their intended final size and authors should do their best to construct figures with notation and data points of sufficient size to permit legible photo reduction to one column of a two-column format.

Colour figures can be accepted. All colour graphics must be formatted in CMYK and not in RGB, because 4-color separations cannot be done in RGB. However, the extra cost of printing these figures must be paid by the author: $500 for the first colour page, $250 for each colour page thereafter.

Tables and figures should be numbered in Arabic numerals. The approximate position of each table and figure should be provided in the manuscript: [INSERT TABLE 1 HERE]. Tables and figures should be on separate pages. Tables should have short titles and all figure legends should be on separate pages.

If you plan to use figures or tables that have been redrawn or modified from other publications, and you are not the copyright holder, please obtain permission for this re-use. Authors should err on the side of caution and seek advice from the editorial office if they are uncertain whether to seek permission.
Financial Support

Please provide details of the sources of financial support for all authors, including grant numbers. For example, “This work was supported by the National Institutes of Health (grant number XXXXXXX).” Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with “and” before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors’ initials. For example, “This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH).” Where no specific funding has been provided for research, please provide the following statement “This research received no specific grant from any funding agency, commercial or not-for-profit sectors.”

References

References should be in American Psychological Association, 6th Edition, style (see the examples presented below).

Text references should be cited as follows: “. . . Given the critical role of the prefrontal cortex (PFC) in working memory (Cohen et al., 1997; Goldman-Rakic, 1987; Perlstein et al., 2003a, 2003b) . . .” with multiple references in alphabetical order. Another example is: “For example, Cohen et al. (1994,1997), Braver et al. (1997), and Jonides and Smith (1997) demonstrated . . .”

References cited in the text with two authors should list both names. References cited in the text with three, four, or five authors, list all authors at first mention; with subsequent citations, include only the first author’s last name followed by et al. References cited in the text with six or more authors should list the first author et al. throughout. In the reference section, list all authors up to seven. For eight or more, list the first six, then three ellipses, and end with the last author’s name. Examples of the APA reference style are as follows:

Online/Electronic Journal Article with DOI:

Scientific Article:


Book:


Book Chapter:


Report at a Scientific Meeting:


Manual, Diagnostic Scheme, etc.:


Proofs

The publisher reserves the right to copyedit manuscripts. The corresponding author will receive PDFs for final proofreading. These should be checked and corrections returned within 2 days of receipt. The publisher reserves the right to charge authors for excessive corrections.

Offprints and PDF Files

The corresponding author will receive a free pdf. This pdf can also be mounted on the authors’ web pages. Offprints must be ordered when page proofs are returned. The offprint order form with the price list will be sent with your PDF.
EDE Eating Concern and Hayling Errors in BN group

YBOCS and WCST categories completed in the AD group
Anxiety (SCL-90-R) and TMT errors in AD group
Relating to Section 4.3.3 – Both groups combined

YBOCS and WCST Categories Completed in Combined group

TMT errors and Anxiety (SCL-90-R) in Combined Groups
Appendix 7 Invitation letter to NHS Grampian Participants

Dear ,

I am writing to you as someone who is currently waiting for treatment for Bulimia with the NHS Grampian Eating Disorders Service. The service is currently supporting a research project investigating how people think and solve problems, as well as their flexibility when they are suffering from bulimia or atypical bulimia. This is being run in conjunction with colleagues from NHS Tayside.

Participation involves meeting with a researcher at the Eating Disorder Service at the Royal Cornhill Hospital and completing some brief neuropsychological pen-and-paper tasks which assess this flexibility. Some general feedback would be available on the outcome of these tasks. Participation would also involve gathering information about your current psychological symptoms through interview and questionnaires.

The project will run until the end of June. I have enclosed a leaflet with further information. If you have an interest in participating in the project or would like additional information please contact my colleagues Kate O’Sullivan or Jan Templeton whose details are listed below.

Yours sincerely,

Dr Phil Crockett

For further information contact:

Jan Templeton
Clinical Associate in Applied Psychology
Eating Disorder Service
Royal Cornhill Hospital
Tel: 01224 557 392 (main office)

Kate O’Sullivan
Trainee Clinical Psychologist
TSMS
Constitution House
Dundee
DD1 1LB
Tel: 0750 307 3108
Appendix 8 Participant Information Sheets

Eating disorder service Participant Information Sheet
Participant Information Sheet: NHS Grampian and NHS Tayside Eating Disorder Services
Neuropsychological Correlates of Eating Disorders in Adult Females
You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study
Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?
The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical group, as you are receiving treatment for an eating disorder in NHS Tayside or NHS Grampian. Everyone meeting certain criteria attending NHS Eating Disorder Services in Tayside or Grampian may be asked to consider taking part in the study.

Do I have to take part?
It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. Your decision to take part or not, and the answers that you give will not influence any treatment that you are currently being given or may receive in the future.

What does taking part involve?
If you decide you would like to take part in the study, you should let your clinician
know, and they will pass your details on to a member of the research team to
arrange a meeting. During the meeting you will be given the opportunity to ask
questions about the study and then if you wish to proceed to complete a consent
form. The investigator will interview you about your eating behaviour and collect
some basic information. The investigator will then administer a range of
neuropsychological tests. These are similar to tests seen on “brain training” games
and involve problem solving and pen and paper tasks. This will take approximately
45-60 minutes. You will then be given a short break before being asked to fill in 4
questionnaires. In total this will take about 1.5-2 hours. After participation in the
study you will have the opportunity for discussion with the investigator and get
general feedback about your neuropsychological test performance. The treatment
you will receive if you do take part in the study will be no different from the treatment
you would receive otherwise.

**What are the possible disadvantages and advantages of taking part?**
The study will take approximately 1.5-2 hours to complete, which you may find an
inconvenience. The questions and tests administered are the same for every
participant, and are not intended to reflect any personal causes of eating disorders
however some of the questions asked during interview or in the questionnaires may
give rise to difficult feelings. The investigator will be available to discuss any issues
that may arise during participation, and can direct you to internal and external
sources of support. After participation you will have a discussion with the
investigator and get general feedback about your neuropsychological test
performance, which may be of interest. It is hoped that the information gathered will
be of value in enhancing our understanding of eating disorders and in informing new
interventions.

**Will my taking part in the study be confidential?**
Participation in the study is completely confidential. Confidentiality may be limited if
there is an issue of risk to yourself or others, in which instance the investigator may
contact her supervisor Dr Alison Livingston and clinical staff within the relevant
Eating Disorder Service may be informed.

**Has this study been ethically reviewed?**
The study has been reviewed by The University of Edinburgh’s School of Health
ethics committee and The University of Stirling Psychology Department ethics
commitee. It has been approved through NHS Tayside Research Ethics Committee
and NHS Tayside Research and Development Department.

**How can I make a complaint about this study?**
If you believe that you have been harmed in any way by taking part in the study you
have the right to pursue a complaint and seek any resulting compensation through
the usual NHS process. To do so you can submit a written complaint to the Patient
Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027
5507). Note that the NHS has no legal liability for non-negligent harm. However if
you are harmed and this is due to someone's negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

**Contact Details**
If you would like more information on the study or have any questions, please contact:

Kate O'Sullivan, Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net; Tel: 01382 306150

Dr Alison Livingstone, Consultant Clinical Neuropsychologist & Lead Clinician,
Department of Clinical Neuropsychology, Level 6, Ninewells Hospital, Dundee, DD1 9SY.
Tel: 01382 740 406
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.
Participant Information Sheet: NHS Tayside Psychological Therapies Service
Neuropsychological Correlates of Eating Disorders in Adult Females

You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study
Anxiety and depression are often comorbid with eating disorders. Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Since anxiety and depression can also affect brain functioning, they need to be taken into account when we investigate brain function in eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

This study aims to investigate executive function in eating disorders and account for comorbidity by also studying a clinical comparison group of age and gender matched individuals with anxiety and/or depression. It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?
The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical comparison group, as you are receiving treatment in NHS Tayside Adult Psychological Therapies Service. Everyone meeting certain criteria attending NHS Tayside Adult Psychological Therapies Service may be asked to consider taking part in the study.
Do I have to take part?
It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. **Your decision to take part or not, and the answers that you give will not influence any treatment that you are currently being given or may receive in the future.**

What does taking part involve?
If you decide you would like to take part in the study, you should let your clinician know, and they will pass your details on to a member of the research team to arrange a meeting. During the meeting you will be given the opportunity to ask questions about the study and then if you wish to proceed to complete a consent form. The investigator will interview you about your eating behaviour and collect some basic information. The investigator will then administer a range of neuropsychological tests. These are similar to tests seen on “brain training” games and involve problem solving and pen and paper tasks. This will take approximately 45-60 minutes. You will then be given a short break before being asked to fill in 4 questionnaires. In total this will take about 1.5-2 hours. After participation in the study you will have the opportunity for discussion with the investigator and get general feedback about your neuropsychological test performance. The treatment you will receive if you do take part in the study will be no different from the treatment you would receive otherwise.

What are the possible disadvantages and advantages of taking part?
The study will take approximately 1.5-2 hours to complete, which you may find an inconvenience. The questions and tests administered are the same for every participant, and are not intended to reflect any personal causes of eating disorders however some of the questions asked during interview or in the questionnaires may give rise to difficult feelings. The investigator will be available to discuss any issues that may arise during participation, and can direct you to internal and external sources of support. After participation you will have a discussion with the investigator and get general feedback about your neuropsychological test performance, which may be of interest. It is hoped that the information gathered will be of value in enhancing our understanding of eating disorders and in informing new interventions.

Will my taking part in the study be confidential?
Participation in the study is completely confidential. Confidentiality may be limited if there is an issue of risk to yourself or others, in which instance the investigator may contact her supervisor Dr Alison Livingston and clinical staff within NHS Tayside Adult Psychological Therapies Services may be informed.
Has this study been ethically reviewed?
The study has been reviewed by The University of Edinburgh’s School of Health ethics committee and The University of Stirling Psychology Department ethics committee. It has been approved through NHS Tayside Research Ethics Committee and NHS Tayside Research and Development Department.

How can I make a complaint about this study?
If you believe that you have been harmed in any way by taking part in the study you have the right to pursue a complaint and seek any resulting compensation through the usual NHS process. To do so you can submit a written complaint to the Patient Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027 5507). Note that the NHS has no legal liability for non-negligent harm. However if you are harmed and this is due to someone’s negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

Contact Details
If you would like more information on the study or have any questions, please contact:
Kate O'Sullivan, Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net;
Tel: 01382 306150

Dr Alisón Livingstone, Consultant Clinical Neuropsychologist & Lead Clinician,
Department of Clinical Neuropsychology,
Level 6, Ninewells Hospital, Dundee, DD1 9SQ.
01382 740 406
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.
You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study
Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?
The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical group, as you are receiving treatment for an eating disorder in NHS Tayside. Everyone meeting certain criteria attending NHS Tayside Adult Psychological Therapies Service may be asked to consider taking part in the study.

Do I have to take part?
It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. Your decision to take part or not, and the
answers that you give will not influence any treatment that you are currently being given or may receive in the future.

What does taking part involve?
If you decide you would like to take part in the study, you should let your clinician know, and they will pass your details on to a member of the research team to arrange a meeting. During the meeting you will be given the opportunity to ask questions about the study and then if you wish to proceed to complete a consent form. The investigator will interview you about your eating behaviour and collect some basic information. The investigator will then administer a range of neuropsychological tests. These are similar to tests seen on “brain training” games and involve problem solving and pen and paper tasks. This will take approximately 45-60 minutes. You will then be given a short break before being asked to fill in 4 questionnaires. In total this will take about 1.5-2 hours. After participation in the study you will have the opportunity for discussion with the investigator and get general feedback about your neuropsychological test performance. The treatment you will receive if you do take part in the study will be no different from the treatment you would receive otherwise.

What are the possible disadvantages and advantages of taking part?
The study will take approximately 1.5-2 hours to complete, which you may find an inconvenience. The questions and tests administered are the same for every participant, and are not intended to reflect any personal causes of eating disorders however some of the questions asked during interview or in the questionnaires may give rise to difficult feelings. The investigator will be available to discuss any issues that may arise during participation, and can direct you to internal and external sources of support. After participation you will have a discussion with the investigator and get general feedback about your neuropsychological test performance, which may be of interest. It is hoped that the information gathered will be of value in enhancing our understanding of eating disorders and in informing new interventions.

Will my taking part in the study be confidential?
Participation in the study is completely confidential. Confidentiality may be limited if there is an issue of risk to yourself or others, in which instance the investigator may contact her supervisor Dr Alison Livingston and clinical staff within NHS Tayside Adult Psychological Therapies Services may be informed.

Has this study been ethically reviewed?
The study has been reviewed by The University of Edinburgh’s School of Health ethics committee and The University of Stirling Psychology Department ethics
committee. It has been approved through NHS Tayside Research Ethics Committee and NHS Tayside Research and Development Department.

How can I make a complaint about this study?
If you believe that you have been harmed in any way by taking part in the study you have the right to pursue a complaint and seek any resulting compensation through the usual NHS process. To do so you can submit a written complaint to the Patient Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027 5507). Note that the NHS has no legal liability for non-negligent harm. However if you are harmed and this is due to someone’s negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

Contact Details
If you would like more information on the study or have any questions, please contact:
Kate O'Sullivan, Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net; Tel: 01382 306150
Dr Alison Livingstone, Consultant Clinical Neuropsychologist & Lead Clinician,
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.
Appendix 9 Letters of Ethical Approval

Approval of Substantial amendment to Tayside Eating Disorder Research Group existing approval.
Dear Dr Livingstone

Study title: Neuropsychological Correlates of Eating Disorders in Adult Females
REC reference: 08/S1401/133
Amendment number: AM06 (For REC Reference Only)
Amendment date: 24 September 2011

The above amendment was reviewed at the meeting of the Sub-Committee held on 29 September 2011.

Ethical opinion

There were no ethical issues noted.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV - Professor Kevin G. Power</td>
<td></td>
<td>26 September 2011</td>
</tr>
<tr>
<td>CV - Ms Kate O’Sullivan</td>
<td></td>
<td>26 September 2011</td>
</tr>
<tr>
<td>CV - Mrs Alison Peaker</td>
<td></td>
<td>26 September 2011</td>
</tr>
<tr>
<td>Electronic Form: Patient Contact Details</td>
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</tr>
<tr>
<td>Description of new sites: Group 4 &amp; 5</td>
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<td>24 September 2011</td>
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<tr>
<td>Group 5 Inclusion/Exclusion Criteria</td>
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<tr>
<td>Questionnaire: Group 4 Bulimia</td>
<td>2</td>
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<tr>
<td>Participant Information Sheet: Group 5 Comparison Group</td>
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<td>24 September 2011</td>
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<tr>
<td>Participant Information Sheet: Group 4 Bulimic Group</td>
<td>2</td>
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<tr>
<td>Participant Information Sheet: Group 5 Anxious and/or</td>
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<td>24 September 2011</td>
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Depressed Patients

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<td>Participant Information Sheet: Group 4 Bulimic Patients for Adult Services</td>
<td>24 September 2011</td>
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<tr>
<td>Participant Information Sheet: Group 4 Bulimic Patients from Eating Disorder Services</td>
<td>24 September 2011</td>
</tr>
<tr>
<td>Protocol</td>
<td>24 September 2011</td>
</tr>
<tr>
<td>Notice of Substantial Amendment (non-CTIMPs)</td>
<td>AM08</td>
</tr>
<tr>
<td>Covering Letter</td>
<td>27 September 2011</td>
</tr>
<tr>
<td>Details of Local Collaborator</td>
<td></td>
</tr>
</tbody>
</table>

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

08/S1401/133: Please quote this number on all correspondence

Yours sincerely

Dr Fergus Daly
Alternate Vice-chair

Email: lorraine.reilly@nhs.net

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: Ms Elspeth Currie, Edinburgh Clinical Trials Unit
         NHS Tayside R&D Office
Tayside Committee on Medical Research Ethics A

Attendance at Sub-Committee of the REC meeting on 29 September 2011

Committee Members:

<table>
<thead>
<tr>
<th>Name</th>
<th>Profession</th>
<th>Present</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Fergus Daly</td>
<td>Clinical Trial Manager</td>
<td>Yes</td>
<td>Alternate Vice-chair</td>
</tr>
<tr>
<td>Mr John Macleod</td>
<td></td>
<td></td>
<td>Yes</td>
</tr>
</tbody>
</table>

Also in attendance:

<table>
<thead>
<tr>
<th>Name</th>
<th>Position (or reason for attending)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mrs Lorraine Reilly</td>
<td>Co-ordinator</td>
</tr>
</tbody>
</table>
Dear Dr Crockett

Project Title: Neuropsychological correlates of Anorexia Nervosa in Adult Females

Amendment no: AM06

Amendment date: 24/09/2011

Ethics ref: 08/S1401/133


This letter is confirmation that this amendment does not alter local NHS Grampian R & D management permission of the project.

Yours sincerely
Susan Ridge
Non Commercial Manager

Cc Dr Alison Livingstone, Consultant Clinical Neuropsychologist/ Lead Clinician, NHS Tayside
Kate O'Sullivan, Trainee Clinical Psychologist, NHS Tayside
Ethical Approval for Original Study submission not including the groups used in the current study.
Dear Ms Swanson

Full title of study: Neuropsychological Correlates of Anorexia Nervosa
REC reference number: 08/S1401/133

Thank you for your letter of 19 January 2009, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Sub-Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:
Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Progress and safety reports
- Notifying the end of the study
The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.nosa.nhs.uk.

| 08/S1401/133 | Please quote this number on all correspondence |

Yours sincerely

[Signature]

Dr. Carlos Wigderowitz
Chair

Email: ethicshelpline.tayside@nhs.net

Enclosures: “After ethical review – guidance for researchers”
Site approval form

Copy to: Ms Elspeth Currie, Edinburgh Clinical Trials Unit
NHS Tayside R&D office
Appendix 10 Consent form

Consent Form

Title of Project: Neuropsychological Correlates of Eating Disorders in Adult Females

This form must be completed and signed by the subject in the presence of someone with knowledge of the research designated by the Principal Investigator. This may be a doctor, nurse, clinical psychologist or other member of the research team who must countersign the form as witness to the subject’s signature.

1. I confirm that I have read and understood the subject information sheet for the above study.

2. I have had an opportunity to ask questions and further discuss the study; and have received satisfactory answers to all my questions. I feel I have now received enough information about the study.

3. I understand that my participation is entirely voluntary and that I have the right to withdraw from the study at any stage without giving a reason. I understand this will have no impact on my present or future medical care. If I decide to withdraw from the study the data already collected with consent will be retained and included in the study analysis.

4. I understand that all information collected during study participation will be confidential. Confidentiality may be limited if there is an issue of risk to myself or others, in which instance the Clinical/University staff will be informed.

5. I agree to participate in this study.

_______________________         ____________________
Name of Subject                            Signature                                  Date

_______________________         ____________________
Name of Witness                            Signature                                  Date
Appendix 11 Graphs of Correlations relating to Additional Results section

EDE Restraint and Phobia (SCL-90-R)

EDE Restraint

Phobia (SCL-90-R)

WCST Categories Completed

Negative Problem Orientation Standard Score