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An Investigation of Set Shifting in Anorexia Nervosa
and
Clinical Research Portfolio

Ellie Wheeler MA (Hons)
Doctorate in Clinical Psychology

University of Glasgow
Section of Psychological Medicine

July 2009

Volume I

(Volume II bound separately)

Submitted in partial fulfilment of the requirements for the degree of doctorate in clinical psychology (D.Clin.Psy)

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Faculty of Medicine Graduate School

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Declaration of Interest

None

Chapter 1

Major Research Project
Systematic Review

What is the evidence for a cognitive impairment in adults with anorexia nervosa?

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Written according to guidelines for submission to Psychological Medicine
(Appendix 5.0 Instructions to contributors)

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Submitted in partial fulfilment of the requirements for the degree of doctorate in clinical psychology (D.Clin.Psy)

Abstract

Background

This systematic review explored the evidence for a specific cognitive impairment in adults with anorexia nervosa. It examined studies in which adults diagnosed with ongoing anorexia nervosa were compared to matched controls using standardised neuropsychological tests.

Method

A systematic search strategy was used to identify potential papers, which were then subject to specific inclusion criteria. Identified papers were rated using methodological scoring criteria.

Results

In total 15 suitable papers were included in the review, demographic and clinical information were extracted, and they were scored on their methodology. The papers were examined according to the neuropsychological tests that they had used and the cognitive domains they claimed to have examined.

Conclusion

From the papers that were reviewed cognitive impairments were found across language, memory, attention, executive function, perceptual and motor domains. The papers, however, were contradictory in their results. When the methodological quality of the papers was critically reviewed and taken into account, the strongest evidence was for impairments in aspects of attention and executive functioning. Methodological criticisms of all the papers were discussed, as were the limitations of this review. Finally, the implications of the review for clinical practice and future research were considered.

Introduction

This systematic review examined the evidence to support the existence of cognitive impairments in Anorexia Nervosa (AN) (see Appendix 1.0 for DSM-IV (APA, 1994) definition). It has been suggested that if specific impairments are identified, then this may have direct implications for a greater understanding of how the disorder develops and is maintained. Currently, there is no evidence-based treatment for adults with AN, and it has been proposed that interventions focusing on improving cognitive deficits may aid recovery (Tchanturia, Anderluh et al., 2004) and thus be a potential source of treatment.

Research into the neuropsychology of AN

Recent research has begun to focus on cognitive processes to better understand the causes, consequences and maintenance of AN. There has been investigation of the neurobiology and neuropsychology of AN (Key et al., 2006; Steinglass and Walsh, 2006). There is evidence supporting the existence of neurobiological dysfunction in AN; neurotransmitter abnormalities have been found and neuroimaging studies have shown brain irregularities (Southgate et al., 2005). A variety of cognitive impairments have been found (Kingston et al., 1996; Roberts et al., 2007), the most common findings being deficits in attention and executive functions (Tchanturia, Morris et al., 2004).

Duchesne et al. (2004) conducted a systematic review of the neuropsychology of AN. They summarised the research as suggesting that there were vigilance and selective attention deficits, memory bias for food/shape/weight related words, general visuospatial and visuoconstructive deficits and some executive functioning impairments. They acknowledged that the research was often contradictory and

suggested that slower processing speed often underlies attentional deficits and discussed the role this might have played in the research into attention in AN. Tchanturia et al. (2005) stated that there was no gross cognitive impairment in AN but that there might be more subtle deficits in attention and flexibility/inhibition responses. They concluded that the broad range of neuropsychological deficits found might reflect the heterogeneous and small clinical samples these studies have used. These systematic reviews were conducted four to five years ago and since then there has been considerable research investigating cognitive impairments in AN. Therefore, there is a need for a new systematic review to be conducted.

The possible impairments in attention and processing speed in AN have caused debate in the literature and there is apparently contradictory research evidence. Pieters et al. (2003) examined this and concluded that there was no evidence for impaired psychomotor speed or motor slowing, but that there was evidence for impaired attention with potentially many underlying explanations for this. They suggested that, whatever the cause, the attentional impairment could result in an apparent reduction in processing speed (cognitive reduction). This impaired processing speed could then result in impaired performance on many neuropsychological tests and thus result in contradictory research findings.

There is a well documented attentional bias in AN which needs to be distinguished from an attentional deficit. Research using an emotional Stroop has shown a clear attentional bias to eating disorder related words (Southgate et al., 2005). It has been suggested that this bias is not representative of a fundamental neuropsychological deficit (Tchanturia et al., 2005). Finally, previous research studies examining the neuropsychology of AN

have often used samples consisting of both adolescents and adults. The diagnosis of AN is thought to be less stable in adolescence; many cases recover or evolve into bulimia nervosa (BN) (Roberts et al., 2007). Consequently, this systematic review only focused on research that has used adult populations.

In summary, the literature suggests that there may be attentional and executive functioning deficits in AN but has acknowledged that an attentional bias and impaired processing speed may have confounded the research, along with the methodological issues many of the papers have encountered. There is also evidence of differences between the adolescent and adult AN populations. To account for these issues all selected papers were rated for their methodological quality, with studies that only examine the attentional bias in AN excluded and only papers looking at adults included. The role of impaired processing speed was considered in the discussion.

Objectives

There is no clear picture of the possible cognitive impairments in adults with AN, therefore this systematic review was conducted to establish what the impairments may be. The aim was to critically summarise the research to help answer the question, what is the evidence for a cognitive impairment in adults with AN?

Method

A systematic literature review was conducted, all papers that had examined any aspect of the neuropsychology of AN were potentially eligible for inclusion.

Search strategy

A two-stage search process was used (see Fig.1 for a flow chart description of the search process). Initially, a search of the following databases was conducted to identify papers: EMBASE, Ovid MEDLINE, PsychINFO, and CINAHL; they were searched from their onset till October 2008 week 4. The databases were searched using the terms EATING DISORDER, ANOREXIA NERVOSA, NEUROPSYCHOLOGICAL, COGNITION, and PSYCHOLOGICAL TEST, along with the associated Ovid exploded terms for these definitions. The second stage of the search was to hand search the references of the included articles, to search Google scholar using the above terms, and to hand search leading eating disorder journals from the date of the most recent previous systematic review examining neuropsychology in AN: consequently, the International Journal of Eating Disorders and the European Eating Disorder Review were searched from the beginning of 2004 till October 2008.

********** INSERT FIGURE ONE HERE **********

Inclusion Criteria

All studies investigating any aspect of the neuropsychology of anorexia nervosa were eligible for inclusion; they then had to meet the following criteria:

1. Age group of 18 or over;
2. Standardised diagnostic criteria specified (DSM-IV/III or ICD-10) – including a body mass index (BMI) 17.5 or below;
3. Healthy weight normal controls;
4. Journal articles only (reviews, book chapters, dissertations excluded); and
5. Neuropsychological impairments examined and not just attentional bias

Data extraction

The methodological quality of each paper was assessed using quality criteria ratings based on Cook and Campbell's 33 threats to validity (1979) (taken from Ellis et al., 1996). These were then checked against the SIGN Methodology Checklist for Case-control Studies to ensure that all relevant potential threats were covered; the SIGN checklist did not include any additional threats. Threats to validity were removed from the criteria if they were either inapplicable to the papers or all papers scored the same (see Appendix 3.0 for a full list of excluded validity criteria). The threats 'selection' and 'history' were expanded on to ensure that they accurately reflected the relevant aspects of the research field. The threat 'history' became six separate threats relating to specific prior events; the threat 'selection' looked separately at the selection of AN group and the control group. This resulted in a pro forma being created which allowed the papers to be scored out of 21 on their methodological quality (see Appendix 2.0 for the scoring pro forma used). A second rated scored a third of the papers using the same pro forma to give them a numerical score; there was 100% agreement between raters. The second rater was a trainee clinical psychologist. In addition to the methodological rating, demographic and clinical information were extracted from all papers. Once the papers were scored they were split into three; the top third were labelled as higher quality papers and the bottom third were labelled as lower quality, this allowed for discussion and comparison between the different quality papers. As there had been strict inclusion criteria applied to the papers to ensure that overall higher quality papers were being reviewed it was not felt to be appropriate to completely discount the lower quality papers by excluding them from the review.

Results

The individual database searches identified 2449 papers, title searches of these papers identified 273 potential papers, 128 of these were duplicates, 49 did not meet the inclusion criteria and a further 40 were excluded at abstract stage. Forty-six papers were excluded at the full text stage due to having no control group, using a child/adolescent population, not using DSM/ICD criteria, not being a journal article, only measuring attentional bias or not providing enough information to ascertain suitability (see Appendix 4.0 for a list of excluded full text papers). Thus, the electronic search identified ten papers that were suitable for inclusion and hand searching revealed a further five papers.

The included studies are described below; only the relevant neuropsychological aspects of the papers have been discussed. The demographic information from the studies is summarised in Table one, along with the paper's exclusion criteria and how the groups were matched.

********** INSERT TABLE ONE HERE **********

Summary of the neuropsychological findings from the included papers

Bosanac et al. (2007) compared executive functioning, memory and visuospatial functioning in patients with AN, patients recovered from AN, and healthy controls. The study used the Cognitive Drug Research Battery (Wesnes et al., 1998) and the Iowa Gambling Task (Bechara et al., 1994). They found an attentional deficit in the AN group that was not present in the weight restored group. This included measures of sustained and selective attention, though the authors did not examine these separately.

They also found impaired motor performance compared to the controls. There was a significant difference in the anxiety and depression measures between the groups and the authors acknowledged that they did not account for this or for the confounding effect of medication in their results.

Cavedini et al. (2004) hypothesised that AN is a type of Obsessive Compulsive Disorder (OCD). The aim of the paper was to investigate tasks looking at decision making that patients with OCD have been shown to perform poorly on, to try and help identify common neurofunctional correlates. They compared patients with AN with healthy weight controls on the Iowa Gambling Task, Weigl's Sorting Test (Weigl, 1941) Object Alternation Test (Freedman, 1990) and the Wisconsin Card Sort Test (WCST) (Bergh, 1948). They found a significant difference on the Gambling Task between the controls and the AN group. They reported no other significant differences on the other tests. The authors concluded that poor nutrition, severity of symptoms, and general cognitive impairment, did not appear to be responsible for the decision-making impairment.

Cavedini et al. (2006) followed on from their previous research using the same measures to assess decision making as a predictor of outcome, comparing patients with AN before and after a CBT and medication programme, with healthy weight controls. The paper found an impairment in decision making in patients with AN; good decision making performance was reflective of better treatment outcome.

Lawrence et al. (2003) argued that impaired appetitive function in AN extends to deficits in visual discrimination learning, stating:

> "Dopamine is critical for error driven learning, AN is associated with impaired dopamine signaling, therefore AN should show an impairment in such learning"

The study used the Visual Discrimination Learning Suite (Roberts et al., 1998) and Pattern Recognition Memory (Sahakian et al., 1988) to measure visual learning. No difference was found between the groups on Pattern Recognition Memory and the only significant difference on the Visual Discrimination Learning Suite was in the initial stage, where the AN group made more errors. The authors argued that this is the expected result with a dopamine neurotransmitter impairment and suggested that this was not related to just food restriction as they did not find a correlation between BMI and performance.

Lopez et al. (2008) examined central coherence in AN and healthy weight controls. They proposed that there may be a link between obsessive-compulsive traits, autistic spectrum disorder (ASD) and AN, stating that a fifth of patients with AN meet criteria for ASD. The authors argued that ASD is associated with weak central coherence. Central coherence consists of local and global processing, weak central coherence refers to a bias towards local or detailed focus processing. Specifically, research has shown strong local processing, with there being less evidence to support the idea of a deficit in global processing. The study used a variety of neuropsychological tasks designed to assess central coherence in ASD. The authors argued that the results suggested that patients with AN showed strength in local processing and deficits in central coherence. They proposed that a fear of making mistakes or poor set shifting may have impacted on the results along with possible ceiling effects on some of the tasks.

Ohrmann et al. (2004) compared cognitive impairment and cerebral metabolites in AN and controls using a variety of cognitive tests. Overall, the AN group showed significantly lower verbal intelligence, worse verbal short term memory and reduced divided attention. They found that the AN group was significantly more depressed than the control group, and when this was co-varied for there was no longer a significant difference suggesting that depression can play a role in cognitive performance. The authors suggested that the verbal deficits could be considered to be representative of a working memory problem, whilst the divided attention deficit could reflect an increased susceptibility to interference.

Pendleton Jones et al. (1991) compared participants with AN, participants recovered from AN and healthy controls. A large battery of tests was used to assess: attention–vigilance, attention–focusing/execution, verbal, memory/comprehension and visuospatial domains. The AN group was significantly worse in all of the domains compared to the controls except vigilance. Levels of depression and anxiety were found to be significantly higher in the AN group. When the results were co-varied to account for this, anxiety was found to impact on performance whilst depression did not. The authors noted that the differences found were subtle rather than large and that the results had to be viewed with caution due to the impact of anxiety.

Seed et al. (2000) investigated the association between hypercortisolism and cognitive impairment in AN. The study specifically investigated attention, learning and memory, and their relationship with cortisol levels. Participants with AN were compared with healthy controls on a number of neuropsychological tests and measures of depression, anxiety, irritability, eating attitudes and intelligence. The AN group was significantly

more depressed, anxious and irritable but the results were not analysed to account for this. The AN group showed significant differences on the tasks that looked at vigilance and long term recall of auditory verbal learning. The authors suggested that these results may provide evidence of an increased vulnerability to distraction in AN.

Seed et al. (2002) continued the research into the role of hypercortisolism in AN and its relationship with cognitive impairment; high cortisol levels have been linked with learning and memory impairments. The study used the Cognitive Drug Research computerised assessment system, comparing AN participants with healthy weight controls. The AN group was found to be significantly impaired on measures of attention, long term memory and working memory, but there was no cortisol abnormality. Depression and anxiety scores were significantly higher in the AN group; however, the results were not co-varied to account for this. The authors concluded that the deficits found were all related to an increased distractibility within the AN group. They argued that a "heightened sensitivity to distraction" was present and that they had an attentional deficit rather than a memory problem. Previous research has shown impaired distracter inhibition in depression and the authors stated that this may partially account for their results due to the high depression levels in the AN group.

Tchanturia et al. (2001) investigated differences in 'perceptual processing style' in AN and BN using the Fixed Set paradigm (Uznadze, 1966). It has been suggested that this paradigm can be used to distinguish different personality characteristics. The authors proposed that the AN group would show a more rigid perceptual style. The study showed that the AN group took longer to recognize change and made more perseverative errors suggestive of a more rigid perceptual style. The paper proposed that

this perceptual style could account for the rigid and persistent behaviours seen clinically in AN.

In a follow up to the Tchanturia et al. (2001) study, Tchanturia et al. (2002) proposed that the rigid perceptual style found in the previous research was evidence of a deficit in the executive function set shifting. The paper examined set shifting across the perceptual and cognitive domains in participants with AN, participants who had recovered from AN, and healthy weight controls. As before, the perceptual set shifting was examined using the Fixed Set paradigm and cognitive set shifting was examined by using a modified version of a paradigm by Eliava (1964) called CatBat. The paper found that the AN and recovered AN group were significantly worse than the controls at both the perceptual and cognitive tasks; however, when the anxiety scores were controlled for in the analysis there was no longer any difference between the groups.

Tchanturia, Anderluh et al. (2004) investigated cognitive flexibility in AN and BN. They suggested that impaired mental flexibility could be measured using tasks that looked at set shifting. They used tests that examined verbal, haptic perceptual, contextual, and attentional set shifting. The paper used factor analysis to separate set shifting into different components: simple alteration, mental flexibility, perseveration and perceptual shift. The study found that AN participants showed difficulties in the first and last components even after the results had been co-varied to account for depression, anxiety and obsessive-compulsive scores. The authors recognized the impact that speed of processing and malnutrition might have placed on their results.

Tchanturia, Morris et al. (2004) examined set shifting across different stages of AN and explored whether there was a link between set shifting difficulties and behavioural characteristics of obsessive-compulsive personality disorder. The authors stated that they wanted to cover all aspects of set shifting and used a variety of tests to measure: rapid simple alteration between sets; problem solving and set shifting; perceptual set shifting; and cognitive retrieval and flexibility in cognitive search operations. The study found that the AN group was significantly worse on all tests except for the verbal fluency 'FAS' task (Lezak et al., 2004). The recovered AN group was significantly worse than the controls on the Fixed Set paradigm and the Set Flexibility Picture Set Test (Surguladze, 1995). The AN group had significantly higher anxiety, depression and obsessive-compulsive score, however these were not co-varied for within the analysis and may have impacted the results. The authors also acknowledged that speed of processing and/or attentional deficits could have influenced their results.

Tchanturia et al. (2007) explored decision making in AN and in controls using the Iowa Gambling Task (IGT). A significant difference was found between the AN and control group. The AN group, however, scored as being significantly more depressed than the controls and there was an association between depression scores and the IGT scores. The study failed to exclude participants with obsessive-compulsive disorder, borderline personality disorder or substance abuse, which have all been shown to impact on performance on the IGT.

Thompson (1993) used a battery of neuropsychological tests to explore the profile of participants with AN when compared to healthy weight controls, hypothesising that there would be a measurable cognitive deficit in the AN group. The study found that

symptoms of depression and obsessive-compulsive disorder could impact on the performance on some neuropsychological tests, but suggested that there was still evidence of an impairment in AN. The results showed that there were significant differences on 16 of the 40 tests used. When the scores were co-varied to account for depression and obsessive-compulsive symptoms there were significant differences on the Trail Making Test (Reitan, 1958), the Auditory Verbal Learning Test (Taylor, 1959) and the information sub test of the Wechsler Adult Intelligence Scale (Revised) (Wechsler, 1981).

Neuropsychological Tests used and Deficits Identified

The identified papers used a broad range of neuropsychological tests. Table two lists the specific tests used by the individual papers along with whether significance was found, they were categorised by the cognitive domains the papers state they have tested.

********** INSERT TABLE TWO HERE **********

Methodological Ratings

The papers were rated on their methodological quality across twenty-one potential threats to their validity. Table three shows the individual scores across all the criteria for the separate papers.

********** INSERT TABLE THREE HERE **********

Discussion

Summary of results

The papers reviewed showed a varied pattern of neuropsychological deficits in adults with AN. They reported deficits across language, memory, attention, executive function, perceptual, and motor domains.

Language

There was a mixed pattern of results regarding language deficits. A number of papers found deficits in verbal intelligence, with contradictory results found for the same cognitive tests. When the only paper of higher methodological quality[1] was considered (Pendleton Jones et al., 1991) the picture was less varied and suggested possible verbal intelligence problems. The paper acknowledged that this may have been due to other deficits such as attentional problems or confounded by other difficulties such as anxiety. This implied that, whilst verbal intelligence problems appear to be evident, they might be explained by other factors.

Memory

There were varied results for memory impairments. Some papers suggested general memory problems and working memory difficulties, whilst others found no problems. When the methodological quality of papers were considered, the only high scoring paper that examined memory found no working memory difficulties (Bosanac et al., 2007). Pendleton Jones et al. (1991) reported general memory problems, but stated that this result needed to be viewed with caution as it was not a gross deficit and there was

[1] 'Higher quality papers' refers to the top third of the papers when the overall methodological score was considered. Due to tied scores this was the following six papers: Lopez et al. (2008), Cavedini et al. (2006), Cavedini et al. (2006), Pendleton Jones et al. (1991), Bosanac et al. (2007), Tchanturia, Anderluh et al. (2004), Tchanturia et al. (2007).

an elevated level of anxiety, which had been shown to impact on memory (Lezak et al., 2004).

Some papers examined verbal memory specifically. Whilst Seed et al. (2000), Seed et al. (2002) and Thompson (1993) showed a varied pattern of results that often contradicted other papers, all three papers were rated as being of poor methodological quality. The higher methodological quality paper (Bosanac et al., 2007) suggested possible verbal memory problems, but acknowledged the influence of confounding factors, such as anxiety.

Lawrence et al. (2003), Ohrmann et al. (2004), Seed et al. (2000) and Seed et al. (2002) examined visual learning and memory and found contradictory results regarding visual learning and no deficits in visual memory. It would seem from the papers reviewed that there was no clear evidence of a specific deficit in memory.

Attention

There were mixed results from the papers that had examined attention. When the methodological quality of papers was considered, only one high rated paper had assessed attention and found a significant deficit (Bosanac et al., 2007). Two papers examined vigilance and found contradictory results; Seed et al. (2000) reported a vigilance deficit, but was the lowest rated paper on methodological quality. By contrast, Pendleton Jones et al. (1991) found no vigilance deficit. This may have been viewed as contradictory to the papers that found an attention deficit, as vigilance could be considered a component of attention. This might suggest, however, that a general attentional deficit existed but that it was a deficit of a specific component of the

attention system. The current research did not suggest what aspect this may be and further research might be necessary to examine this. It could also be argued that further research needs to consider the role of confounders that can impact attention, such as anxiety or medication, as the papers reviewed had not consistently controlled for these.

Executive Function

A number of specific executive functions were examined across the papers with a varied pattern of results. These were focus/execute abilities; decision making/planning; strategy finding; cognitive flexibility; set shifting; and central coherence.

Pendleton Jones et al. (1991) examined 'focus/execute' abilities and found a significant deficit. They were the only paper to separate out this component of executive functioning. There were mixed findings when decision making/planning was examined. The higher rated papers showed contradictory results (Cavedini et al., 2004; Cavedini et al., 2006; Bosanac et al., 2007; Tchanturia et al., 2007), although the majority did report deficits in decision making and planning. Two highly rated papers examined strategy finding and found no significant deficit in this area (Cavedini et al., 2004; Cavedini et al., 2006). Two stated that they have measured cognitive flexibility and again there was variation in the methodological ratings of the papers (Thompson 1993; Tchanturia et al. 2002).

A large number of tests examined set shifting in AN and, as previously, the results were diverse with some papers finding deficits and others finding none. When the papers of higher methodological quality were considered, the picture was still unclear. Tchanturia, Anderluh et al. (2004) and Tchanturia, Morris et al. (2004) reported deficits in set

shifting across a variety of tests. Yet these results should be viewed with caution, as both papers did not consistently and clearly define set shifting and often the tests contained an attentional element, which may have confounded the results.

One paper examined central coherence in AN using a broad range of tests (Lopez et al., 2007). This paper was the highest scoring when rated on methodological quality and made a clear case for AN patients having a good local processing style. The tests used, however, had not been shown to be reliable and valid across a general population and had only previously been applied to patients on the Autistic spectrum; not all the tests used had found impaired central coherence; the paper did not consider the impact of processing speed or attentional deficits; and finally, the patient sample had severe and chronic AN and results may not be generalisable to a wider AN population

There was no clear picture of executive functioning in AN, and this may remain the case until other deficits are fully understood and therefore accountable in the results found on executive tests. Confounders such as anxiety and depression also needed to be systematically accounted for in the analysis of tests. Additionally, it would seem that clearer definitions of executive functions were needed to allow a better understanding of possible deficits.

Perception

Perceptual processing style and perceptual set shifting were examined. Tchanturia et al. (2001) examined perceptual processing style and found a 'rigid processing style' in AN. They defined this as a rigid pattern of responding and an inability to switch response. The same research group then extended this idea and suggested that there may be a

perceptual set shifting deficit in AN. The main limitation with this research was that there was no evidence-base for the paradigm as a neuropsychological test that measures set shifting and it had not been shown to be reliable and valid. Therefore, there did not appear to be any reliable evidence of perceptual deficits in AN. Pendleton Jones et al. (1991) explored broader visuospatial skills and found a significant deficit, however, these results could have been impacted by attentional difficulties and confounded by depression and anxiety.

Motor

Finally, two papers examined motor deficits in AN (Ohrmann et al., 2004; Bosanac et al., 2007). They found contradictory results and both rated well when the methodological quality was assessed. This difference may be due to the tests used and the role of attention and the confounding depression scores. It was not possible therefore to conclude whether or not motor difficulties are present in AN from these papers alone.

General overview

This review aimed to answer the question: what is the evidence for a cognitive impairment in adults with anorexia nervosa? From the papers reviewed there did appear to be supporting evidence for deficits in some aspects of attentional and executive functioning difficulties. The papers did not support the idea that there are memory difficulties and could not agree conclusively on verbal, motor, and perceptual difficulties.

There were a number of general criticisms that were applicable to all the papers reviewed. Multiple papers found that comorbid diagnoses were significantly impacting on the test results, yet there was no consistent attempt to exclude these illnesses or account for this in the analysis. The majority of papers acknowledged the attentional deficits in AN and the reduced processing speed, but few considered this in the tests used or their analysis. As a result meaningful conclusions cannot be drawn from the data until these variables have been considered. There were also some general exclusion criteria that were not considered in any of the papers reviewed: i) English as a second language should have been considered; as the majority of tests used had not been validated on non-English speakers; and ii) prior experience of testing was very relevant as some of the papers had repeatedly used the same patient sample.

Throughout the papers reviewed there was an assumed connection between the tests used and the underlying cognitive domains; however, not all the tests used had been reliably shown to reflect hypothesised underlying mechanisms. It could be argued that, from the papers reviewed, there was evidence of impaired test performance by some AN patients on some tests, but that there were numerous explanations for these results and the impairments were not present in all patients with AN. Related to this was the ambiguity concerning the causal direction; even if it was accepted that the poor test performance was reflective of an underlying deficit, there was a lack of clarity about whether the AN (and potentially the low weight) was impacting the deficit, the deficit impacting the AN, or both.

Given that there was often only a small significant difference between the groups, it needs to be considered whether this level of deficit is clinically meaningful and whether

it can be suggested to reflect causal and maintaining mechanisms for AN. It could also be argued that if there is a true cognitive deficit then it should be present across all the tests measuring it and across all the patients. This was not the case, however, in the papers and tests reviewed.

Limitations of this review

There were a number of limitations of this review. Firstly the inclusion/exclusion criteria for the papers used has limited the quality of the review itself. Papers where the neuropsychological test was not the main component might have been excluded in addition to studies comparing AN to other disorders. Furthermore, papers examining the neuropsychology in adolescents or recovered AN only had been excluded. Whilst this review excluded papers that had adolescent populations it did not exclude papers that included adults whose AN had started during adolescence. It could be argued that the cognitive impact of adolescent onset AN may still be evident in adults suffering from the illness. It may be that the variability in test performance is associated with the age of onset, severity and length of illness during this critical phase for frontal lobe development (Frampton and Hutchinson, 2007). There was not enough illness information given in the papers reviewed to allow an examination of this. It can be argued that the requirement of a BMI below 17.5 is not a core component of AN and is an arbitrary cut off. This ties in with wider ongoing discussions concerning the appropriateness of the diagnosis criteria for AN (Fairburn and Cooper, 2007). It was not within the scope of this review to debate the definition of AN and it was felt that some consistency between the papers reviewed was necessary to get the most accurate description of the neuropsychological profile of adults with active AN.

The second area that has limited the review were the methodological scoring criteria used. Papers were only scored on information that was available and extra or additional information was not sought from authors. This meant that papers might have been unnecessarily marked down based on the absence of information rather than evidence of methodological weakness. Finally, effect sizes were not calculated or considered fully within this review as they were not stated in the majority of the papers reviewed and it was out with the scope of this review to calculate effect sizes for all the tests used. This is reflective of a wider issue; effect size does not seem to be routinely stated or calculated in AN research. This is unhelpful as it could lead to inappropriate, subtle or small, effects being researched in depth to help understand the cause, maintenance and symptoms.

This review had focused on the impaired performance on neuropsychological testing and the assumption that this was reflective of underlying cognitive impairments in adults with AN. There are, however, a number of possible explanations for impaired test performance including the impact of comorbidities such as anxiety or depression, or the role of trauma during childhood on neurological development. This review had not focused on these and this has limited the conclusions that can be reached, this is reflective of the wider research into neuropsychological performance in AN and may explain the range of findings. It might be that future research into impaired test performance should consider a broader range of explanations rather than assuming an underlying deficit was being measured.

Implications for future research and clinical practice

This review showed that there is still need for further research into the neuropsychological profile of AN. There are a broad number of areas that need to be considered to ensure that research is as thorough as possible: confounding comorbidities need to be excluded or accounted for; lower level processes need to be acknowledged or accounted for when results are examined, specifically the roles of attentional difficulties and processing speed needs to be accounted for in all neuropsychological test in AN; the links between tests used and underlying cognitive domains need to be either clearly supported by an evidence-base or discussed rather than assumed; and the patient group used needs to be as homogenous as possible with consideration given to the impact of teenage onset on the neuropsychology. The neuropsychological profile is still relatively unknown with definitive conclusions very hard to reach. The areas that have the strongest evidence of a deficit are those of attention and executive function. Future research into these areas would be beneficial.

The primary suggestion for clinical practice is for clinicians to be aware of the possibility of attentional deficits in AN and consider this when structuring sessions. The results of this review would not suggest that talking therapies are inappropriate for AN, but would suggest that there is thought given to length and speed of sessions along with the formats used to share information. Secondly, if clinicians are performing any routine neuropsychological test with patients suffering from AN then they need to consider the impact that possible attentional deficits may have across all aspects of testing, along with the impact of any comorbid illnesses. Finally, the mixed pattern of findings might suggest that routine neuropsychological screening, especially of executive functions, would be beneficial when working with patients with AN. This might then allow an

individual understanding of patients' strengths and weaknesses and to ensure that treatment is designed appropriately.

The final question to consider is whether the deficits found explain the symptoms of AN. It is perhaps easier to explain the possible impairments through the symptoms and the bigger picture of AN, rather than trying to explain the symptoms of the illness by the impairments. Attentional deficits could be explained through the effects of medication or low weight for example, rather than the deficits being a core part of AN. It could also be conceived that, what is measured as an attentional deficit, is driven by the cognitive processes that have been documented in AN. Perhaps, it is the obsessive thoughts about food, weight and shape that act as distracters and impact attention. The executive functioning difficulties have been considered as an explanation for the symptoms of AN; for example the difficulties with central coherence have been proposed to explain the perfectionism and obsessionality that is often seen (Lopez et al., 2008). The lack of consistent research to support the executive function deficits, alongside the relatively small size of the impairments that have been found, make it seem unlikely that these deficits are driving the symptoms of AN.

Tchanturia et al. (2005) proposed that research into the cognitive profile of AN either be hypothesis driven or a general cognitive battery approach. Papers in this review had used both approaches, although the majority had been driven by neurostructural or neurochemical hypotheses, rather than looking for impairments that might explain the symptoms. Future research into this area that uses an hypothesis driven approach might benefit from further clarity and discussion around the relationship between the cognitive abilities that are being examined and symptoms, development and maintenance of AN.

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Figure 1. Flow Diagram for Systematic Review

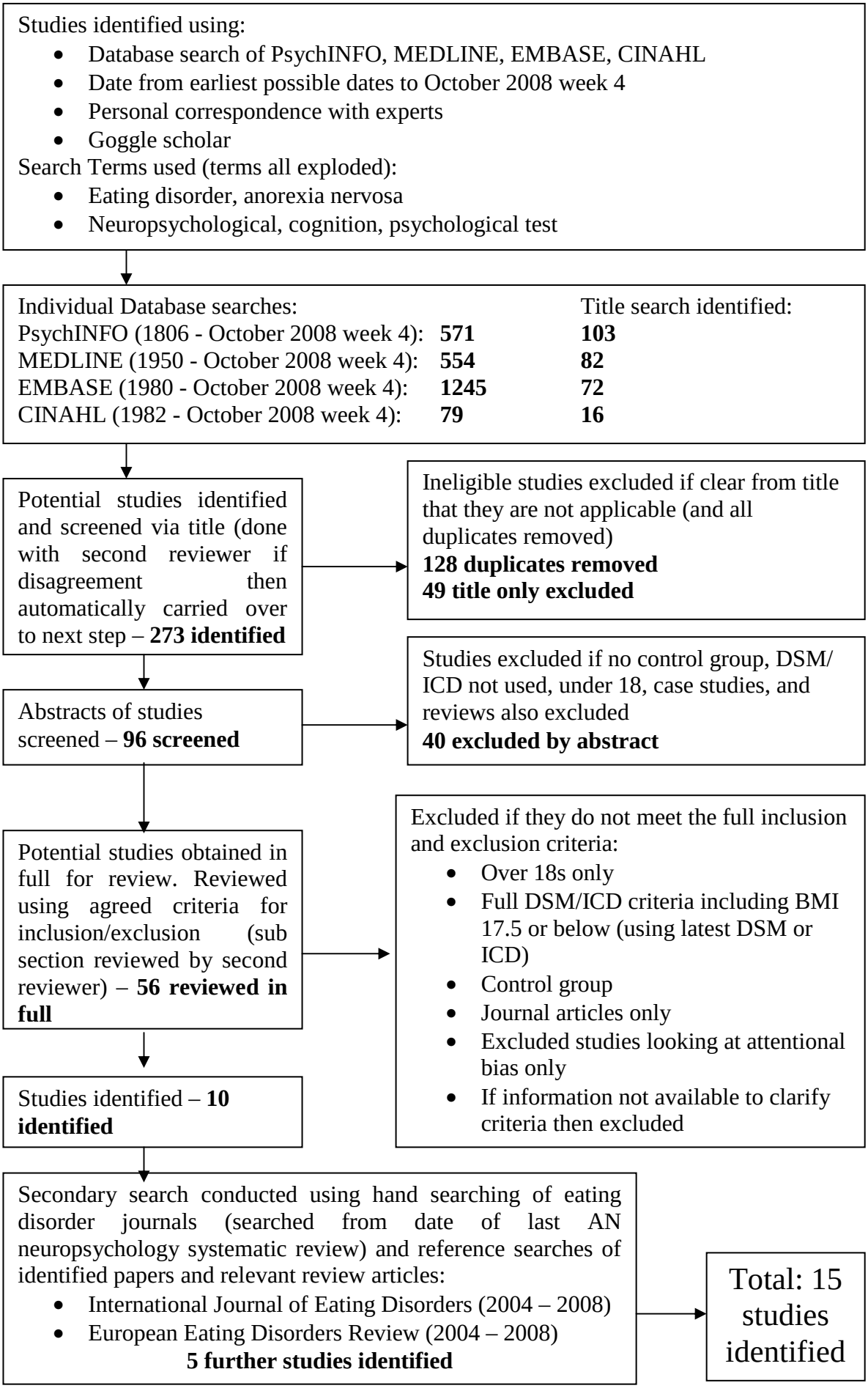

Table 1: Demographic information from the included studies

Paper	N	Age	BMI	Matched	Exclusion Criteria
Bosanac et al. (2007)	AN: 16 AN r: 12 BN: 13 HC: 16	28.94 (9.59) 28.92 (7.73) 28.31 (9.13) 23.81 (6.08)	15.18 (1.37) 20.47 (2.13) 23.52 (5.45) 22.26 (2.75)	Age Intelligence (NART)	Learning Disability
Cavedini et al. (2004)	AN:59 HC: 82	22.8 (3.9) 30.9 (10.7)	ANR 13.5 (1.5) AN BP 15.6 (2.2)	Educational level	Comorbidity Learning Disability Neurological Illness Brain injury/trauma Substance abuse
Cavedini et al. (2006)	AN: 42 HC: 38	24.5 (5.2) 22.6 (4.1)	14.2 (1.7) no data	Age Education	Comorbidity Medical disease Neurological syndromes Brain injury/trauma Substance use Psychotropic medication Receiving other therapy
Lawrence et al. (2003)	AN: 12 HC: 12	25.7 (7.2) 26.7 (6.2)	15.8 (1.4) 24.4 (4.0)	Age Intelligence (NART)	None stated
Lopez et al. (2008)	AN: 42 HC: 42	28.4 (9.6) 26.3 (6.4)	15.8 (1.7) 21.9 (2.7)	Gender Age Intelligence (NART)	Head injury Neurological disease Psychosis Learning Disability
Ohrmann et al. (2004)	AN: 11 HC: 12	22.7 (3.8) 23.9 (4.4)	15.2 (1.22) 23.7 (2.8)	Age Gender	Comorbidity (except depression) Head trauma Neurological Illness Medication
Pendleton Jones et al. (1991)	AN: 30 AN r: 20 BN: 38 HC: 39	24.4 (5.3) 26.0 (6.2) 24.1(4.0) 24.9 (4.4)	59.4 (6.6)* 87.8 (11.2)* 94.0 (7.3)* 98.2 (7.5)*	Age Education Handedness	Medical problems Malnutrition Learning disability Medication
Seed et al. (2000)	AN: 18 HC: 18	27.3 (range 19.3 – 42.7) HC – does not state	15.24 (2.045) 22.133 (1.654)	Age Intelligence (NART)	None stated for AN Controls: psychiatric disorder
Seed et al. (2002)	AN: 20 HC: 20	29.122 (1.880) 29.314	14.210 (0.462) 22.355 (0.699)	Age	None stated for AN Controls: psychiatric disorder

		(1.913)			
Tchanturia et al. (2001)	AN: 15 BN: 15 HC: 28	28.1 (7.3) 25.1 (7.1) 28.2 (5.6)	14.1 (2.2) 20.0 (2.3) 22.3 (2.1)	Age	None stated
Tchanturia et al. (2002)	AN: 30 AN r:16 HC: 23	25.2 (6.7) 30.0 (6.0) 27.6 (6.4)	14.6 (2.1) 20.1 (1.7) 21.3 (1.8)	Age Gender Education	Psychotropic medication Psychiatric Illness
Tchanturia, Anderluh et al. (2004)	AN: 34 AN r:18 HC: 36	27.2 (8.3) 28.4 (6.8) 25.9 (4.8)	13.7 (1.4) 20.4 (1.3) 21.8 (1.6)	Age Ethnicity Education Intelligence (NART)	Control group: any psychiatric illness or brain injury None stated for AN groups
Tchanturia, Morris et al. (2004)	AN: 34 BN: 19 HC: 35	26.7 (7.9) 26.5 (5.7) 24.8 (4.7)	13.7 (1.4) 21.8 (2.1) 21.8 (1.7)	Age Education	Head injury Brain operation Psychosis Substance abuse
Tchanturia et al. (2007)	AN: 29 AN r: 14 HC: 29	28.5 (9.17) 28.9 (7.4) 26.3 (7.9)	15.3 (3.1) 16.2 (2.6) 16.3 (2.6)	Gender Age Intelligence (NART) Education	Head injury Psychosis Epilepsy
Thompson (1993)	AN: 10 HC: 10	25.8 23.2 (standard deviations not stated)	(weight not stated – clarifies that AN group had BMI 15% below normal body weight)	Age Education Social Class Intelligence (NART) Geographic habitation	None stated

AN – anorexia nervosa, BN – bulimia nervosa, AN r – anorexia nervosa recovered, HC – healthy weight controls

* = Percentage of ideal body weight as determined by the Metropolitan Life Insurance Company table

Table 2. Cognitive Domains assessed by Papers in Systematic Review
(Note that some tests could have been placed under more than one heading, for full information regarding the listed tests refer to Lezak et al., 2004)

Cognitive Domain		Paper	Tests Used to assess	Significant
Language	Verbal intelligence	Ohrmann et al. (2004)	WAIS-R Vocabulary	Significant
		Pendleton Jones et al. (1991)	Verbal o WAIS-R Similarities, Comprehension, Vocabulary	Significant
		Thompson (1993)	WAIS-R Information subtest**	Significant
		Thompson (1993)	WAIS-R Similarities and Comprehension subtests**	N.S.
Memory	Verbal learning	Bosanac et al. (2007)	CDR immediate word recall	Significant
		Ohrmann et al. (2004)	Auditory verbal learning test – immediate recall	Significant
		Seed et al. (2000)	Auditory verbal learning test – immediate recall	N.S.
		Seed et al. (2002)	CDR word recognition – reaction time	N.S.
		Seed et al. (2002)	CDR word recognition - sensitivity	Significant
		Seed et al. (2002)	CDR immediate word recall - number	N.S.
		Seed et al. (2002)	CDR immediate word recall – errors	Significant
		Thompson (1993)	Auditory Verbal Learning Test - immediate	Significant
	Verbal memory	Bosanac et al. (2007)	CDR delayed word recall	Significant
		Ohrmann et al. (2004)	Auditory verbal learning test – delayed recall	N.S.
		Seed et al. (2000)	Auditory verbal learning test – delayed recall	Significant
		Seed et al. (2002)	CDR delayed word recall - number	N.S.
		Seed et al. (2002)	CDR delayed word recall - errors	N.S.

		Pendleton Jones et al. (1991)	Memory o Babock Story recall Test o Wechsler Memory Scale o Buschke Selective Reminding Test	Significant
		Thompson (1993)	Auditory Verbal Learning Test - delayed	N.S.
	Visual learning	Lawrence et al. (2003)	Visual discrimination learning suite – initial learning stage	Significant
		Ohrmann et al. (2004)	Figural Learning Task	N.S.
		Seed et al. (2000)	CANTAB paired associate learning**	N.S.
		Seed et al. (2002)	CDR picture recognition - sensitivity	Significant
		Seed et al. (2002)	CDR picture presentation	N.S.
	Visual memory	Lawrence et al. (2003)	Pattern recognition memory	N.S.
		Seed et al. (2000)	CANTAB pattern spatial recognition; **	N.S.
		Seed et al. (2002)	CDR picture presentation	N.S.
	Working memory	Bosanac et al. (2007)	CDR quality of working memory	N.S
		Bosanac et al. (2007)	CDR speed of memory	N.S.
		Seed et al. (2002)	CDR spatial working memory – reaction time	Significant
		Seed et al. (2002)	CDR spatial working memory - sensitivity	Significant
		Seed et al. (2002)	CDR memory scanning – reaction time	Significant
		Seed et al. (2002)	CDR memory scanning - sensitivity	N.S.
		Seed et al. (2000)	CANTAB spatial working memory **	N.S.
		Thompson (1993)	WAIS-R Digit Span subtest	N.S.

Attention		Bosanac et al. (2007)	Cognitive drug research (CDR) power of attention	Significant
		Ohrmann et al. (2004)	Divided attention task	Significant
		Seed et al. (2002)	CDR simple reaction time	Significant
		Seed et al. (2002)	CDR choice reaction time	Significant
		Seed et al. (2002)	CDR digit vigilance - accuracy	Significant
		Seed et al. (2002)	CDR digit vigilance – reaction time	N.S.
		Seed et al. (2002)	CDR digit vigilance – false alarms	N.S.
		Thompson (1993)	Paced Auditory Serial Addition test**	N.S.
		Thompson (1993)	Trail Making Test A**	N.S.
	Vigilance	Pendleton Jones et al. (1991)	Vigilance o Continuous Performance Test	N.S
		Seed et al. (2000)	Computer based vigilance task	Significant
Executive Functions	Focus/execute	Pendleton Jones et al. (1991)	Focus/execute o WAIS-R digit symbol o Trail Making Test o Talland Letter Cancellation Test Revised	Significant
	Decision Making/Planning	Bosanac et al. (2007)	Iowa Gambling Task	N.S
		Cavedini et al. (2004)	Iowa Gambling Task	Significant
		Cavedini et al. (2006)	Iowa Gambling Task	Significant
		Seed et al. (2000)	CANTAB tower of London**	N.S.
		Tchanturia et al. (2007)	Iowa Gambling Task	Significant
	Strategy Finding	Cavedini et al. (2004)	Object Alternation Test	N.S.
		Cavedini et al. (2006)	Object Alternation Test	N.S
	Executive Functioning	Thompson (1993)	Controlled Oral Word Association Test**	N.S.

	Set shifting	Cavedini et al. (2004)	Weigl's sorting task	N.S.
		Cavedini et al. (2004)	WCST	N.S
		Cavedini et al. (2006)	Weigl's sorting test	N.S
		Ohrmann et al. (2004)	Modified WCST	N.S.
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – motor time	Significant
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – motor errors	N.S.
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – alphabet time	Significant
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – alphabet errors	N.S.
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – shifting time	Significant
		Tchanturia, Anderluh et al. (2004)	Trail Making Task – shifting errors	N.S.
		Tchanturia, Anderluh et al. (2004)	BSAT	Significant
		Tchanturia, Anderluh et al. (2004)	Picture Set Test	Significant
		Tchanturia, Anderluh et al. (2004)	FAS	N.S.
		Tchanturia, Anderluh et al. (2004)	FAS Perseveration	N.S.
		Tchanturia, Anderluh et al. (2004)	CatBat – time	Significant
		Tchanturia, Anderluh et al. (2004)	Bat – time	Significant
		Tchanturia, Anderluh et al. (2004)	CatBat – errors	N.S.

		Tchanturia, Morris et al. (2004)	Trail Making Task – motor time	Significant
		Tchanturia, Morris et al. (2004)	Trail Making Task – motor errors	N.S.
		Tchanturia, Morris et al. (2004)	Trail Making Task – alphabet time	Significant
		Tchanturia, Morris et al. (2004)	Trail Making Task – alphabet errors	N.S.
		Tchanturia, Morris et al. (2004)	Trail Making Task – shifting time	Significant
		Tchanturia, Morris et al. (2004)	Trail Making Task – shifting errors	N.S.
		Tchanturia, Morris et al. (2004)	BSAT	Significant
		Tchanturia, Morris et al. (2004)	Picture Set Test	N.S.
		Tchanturia, Morris et al. (2004)	FAS	N.S.
		Tchanturia, Morris et al. (2004)	FAS Perseveration	N.S.
		Tchanturia, Morris et al. (2004)	CatBat – time	Significant
		Tchanturia, Morris et al. (2004)	Bat – time	Significant
		Tchanturia, Morris et al. (2004)	CatBat – errors	Significant
	Cognitive flexibility	Tchanturia, Morris et al. (2004)	CatBat - perseverations	Significant
		Tchanturia et al. (2002)	CatBat – time taken	Significant
		Thompson (1993)	Trail Making Test B**	Significant
		Thompson (1993)	WCST**	N.S

	Central coherence	Lopez et al. (2007)	Rey complex figure – Copy Accuracy	N.S.
		Lopez et al. (2007)	Rey complex figure – Copy Order	Significant
		Lopez et al. (2007)	Rey complex figure – Copy Style	Significant
		Lopez et al. (2007)	Rey complex figure – Recall accuracy	N.S
		Lopez et al. (2007)	Rey complex figure – Index copy	Significant
		Lopez et al. (2007)	Rey complex figure – Percentage recall	N.S.
		Lopez et al. (2007)	Rey complex figure - organisational strategy	Significant
		Lopez et al. (2007)	Embedded figure test – total time taken	N.S
		Lopez et al. (2007)	Embedded figure test – number time out failures	Significant*
		Lopez et al. (2007)	Sentence completion task – local processing score	Significant
		Lopez et al. (2007)	Homograph reading task	N.S
Perception	Visuospatial	Pendleton Jones et al. (1991)	Visuospatial o Rey-Osterrieth Complex Figure Test o Embedded Figures Test o WAIS-R Block design	Significant
		Thompson (1993)	Rey Complex Figure Test: Copy trial and Delayed recall	N.S.
		Thompson (1993)	WAIS-R Block Design and Object Assembly subtests	N.S.
	Perceptual processing style	Tchanturia et al. (2001)	Fixed set paradigm (Haptic) –number of illusions	Significant
		Tchanturia et al. (2001)	Fixed set paradigm (Haptic) – absolute fluctuations	Significant
		Tchanturia et al. (2001)	Fixed set paradigm (Haptic) – relative fluctuations	Significant
	Perceptual set shifting	Tchanturia et al. (2002)	Haptic – number of illusions	Significant

		Tchanturia, Anderluh et al. (2004)	Haptic	Significant
		Tchanturia, Morris et al. (2004)	Haptic	Significant
Motor	Motor speed	Bosanac et al (2007)	CDR morse tapping	Significant
		Ohrmann et al. (2004)	FAIR	N.S.
		Ohrmann et al. (2004)	Go-No Go	N.S.

**Tests not associated with specific domain in the paper – Lezak et al. (2004)/CANTAB website www.camcog.com used as reference

Table 3. Individual Methodological Scores for Papers in Systematic Review

Threat	Bosanac et al. (2007)	Cavedini et al. (2004)	Cavedini et al. (2006)	Lawrence et al. (2003)	Lopez et al. (2008)	Ohrmann et al. (2004)	Pendleton Jones et al. (1991)	Seed et al. (2000)	Seed et al. (2002)	Tchanturia et al. (2001)	Tchanturia et al. (2002)	Tchanturia, Morris et al. (2004)	Tchanturia, Anderluh et al. (2004)	Tchanturia et al. (2007)	Thompsom (1993)
Low statistical power	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
Violation of assumptions of statistics	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0
Unreliability of dependent or independent variable measures	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Unreliability of treatment implementation	1	1	1	0	1	0	0	0	1	0	0	0	0	0	1
Heterogeneity of participants	1	0	1	1	1	1	1	1	0	0	1	1	1	1	1
History: malnutrition	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
History: medication	0	0	1	0	0	1	1	0	0	0	1	0	0	0	0
History: co-morbidity	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0
History: head injury	0	1	1	0	1	1	0	0	0	0	0	0	1	1	0
History: substance abuse	0	1	1	0	0	0	0	0	0	0	0	0	1	0	0
History: learning disability	1	1	0	0	1	0	1	0	0	0	0	0	0	0	0
Instrumentation	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0
Selection AN bias	1	0	0	0	1	0	1	1	1	0	1	1	1	1	1
Selection Control bias	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1
Exclusion criteria	0	1	1	0	1	1	1	0	0	0	1	0	1	1	0
Inadequate preoperationalisation explication	1	1	1	1	1	0	1	0	0	1	1	1	1	1	0
Mono-operation bias	1	1	0	0	1	1	1	0	0	0	0	0	1	0	1
Experimenter expectancies	1	1	1	1	0	0	0	0	1	0	0	0	0	0	0
Interaction of treatments	0	1	0	0	0	0	0	0	1	1	0	0	0	1	0
Interaction of selection and treatment	0	1	1	0	1	0	0	0	0	1	1	1	1	1	0
Interaction of history and treatment	1	1	1	0	1	1	0	0	0	0	0	0	0	1	0
Final Score	**10**	**13**	**12**	**4**	**15**	**7**	**10**	**3**	**5**	**5**	**8**	**6**	**9**	**9**	**5**

Chapter 2

Major Research Project

An Investigation of Set Shifting in Anorexia Nervosa

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Written according to guidelines for submission to Psychological Medicine
(Appendix 5.0 Instructions to contributors)

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Abstract

Background: Recent research has examined the possibilities that deficits in cognitive processes, in particular set shifting, might contribute to the development and maintenance of anorexia nervosa (AN). Results of studies of set shifting have been mixed. There has been considerable variability in tests used to measure set shifting and a lack of homogeneity of populations sampled.

Methods: This study investigated set shifting abilities within a restrictive sub type AN population using the intra-extra dimensional set shift (IED) sub-test of the Cambridge Neuropsychological Test Automated Battery (CANTAB) and the Brixton Spatial Anticipation Test (BSAT). Participants with AN were matched with healthy controls.

Results: There was no significant difference found between the groups on the BSAT or the number of stages that were completed on the IED. The AN group made significantly more errors on the IED. Anxiety scores for the AN group were significantly correlated with this error measure The two measures of set shifting were not significantly correlated.

Conclusion: Possible explanations were considered for the significant difference on only one of the measures, including that the IED may be a more difficult test or that the tests may be measuring different cognitive abilities. The role of anxiety on the results was also acknowledged. The possibility that previous, contradictory, research has captured aspects from different AN subgroups and the usefulness of the diagnosis of AN was discussed. Whilst it appears that patients with AN made significantly more errors on the IED, there is not currently enough conclusive evidence to support the idea that this is indicative of a deficit in set shifting.

Introduction

Anorexia Nervosa[2] (AN) is a severe mental illness with currently no evidence-based primary choice medical or psychological treatment (NICE Guidelines, 2004). Historically, psychological models aimed to understand the causes and maintenance of AN through maladaptive or distorted thoughts and beliefs; there is no evidence to support any one model (Fairburn et al., 2003).

Recent research has begun to focus on cognitive processes rather than thought content to better understand the cause and maintenance of AN. Research has investigated the neurobiology and neuropsychology of AN (Key et al., 2006; Steinglass and Walsh, 2006), finding a variety of cognitive deficits (Kingston et al., 1996; Roberts et al., 2007).

Tchanturia, Morris et al. (2004) summarised the neuropsychological impairments found in AN as deficits in attention and executive functioning. Interest has been focused on the role of set shifting/mental flexibility deficits and the possible relationship that these deficits may have with the cognitive characteristic of AN such as rigid thinking (Fassino et al. 2002). Research has shown that set shifting deficits remain after weight restoration and are present in sister siblings of sufferers of AN; implying there may be a genetic contribution towards these deficits and possibly a genetic endophenotype. (Holliday et al., 2005)

Both set shifting and mental flexibility are used interchangeably to supposedly describe the same cognitive ability, though different papers use differing terms and definitions. Lezak et al. (2004) define mental flexibility problems as difficulties with rigidity or perseveration

[2] See appendix 1.0 for DSM IV definition of AN (APA, 1994)

that primarily present behaviourally and encompasses the capacity to shift thinking, the capacity for flexibility and shifting relates to perceptual, cognitive and response dimensions. In this paper the term set shifting will be used, referring to the Lezak et al. (2004) definition.

Roberts et al. (2007) conducted a meta-analysis of the role of set shifting difficulties in AN and concluded there were deficits in set shifting in AN. Fifteen studies were examined that investigated set shifting using a variety of assessment tools. The studies reviewed used relatively heterogeneous populations of AN patients, with variability between AN samples in weight, age, length of illness, age of onset and amongst how matched they were to the control groups. This suggests that future research may benefit from having more thorough inclusion/exclusion criteria. The studies also used different definitions of set shifting and highlighted the discrepancies that exist around defining set shifting and the validity of the tests that supposedly measure this ability. The tests of set shifting used in this meta-analysis may all be influenced by speed of processing. Pieters et al. (2003) have shown that, whilst there exists debate as to its underlying pathology, there is an attentional impairment in AN that can result in an apparent reduction in processing speed. This impaired processing speed can then result in impaired performance on many neuropsychological tests and needs to be considered in research examining any cognitive ability in AN.

One study by Fowler et al. (2005) using the intra-extra dimensional (IED) set shift task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Cambridge Cognition, 2004) to investigate set shifting, found no significant difference between AN

and healthy controls. This was a surprising find, contradictory to most of the other papers reviewed. The participant sample, however, was an adolescent one with a relatively brief duration of illness. Kingston et al. (2006) suggest that as the teenage brain is still developing, AN onset in these years might result in a different pattern of neuropsychological deficits. The diagnosis of AN is also thought to be less stable in teenage years (Roberts et al., 2007). The IED is a standardised and validated test that is not timed and so may be less affected by potential deficits in speed of processing; therefore it would merit being applied again to a more homogenous adult AN population. There is debate in the literature regarding the appropriate age to distinguish child and adolescent AN populations and adult populations (Lask and Bryant-Waugh, 2000). Some research has divided the population at age 16 and there is considerable research into the neuropsychological impact of child and adolescent AN under16 (Frampton and Hutchinson, 2007). In this study the term adult is used to mean anyone 18 years of age or older. Whilst this may still capture elements of an adolescent or teenage population it is a clinically meaningful divide; adult and child services in Britain are generally split at this age.

There are three studies that have used the Brixton Spatial Anticipation Test (BSAT) (Burgess and Shallice, 1997) to examine set shifting differences (Tchanturia, Anderluh et al., 2004, Tchanturia, Morris et al., 2004; Holliday et al., 2005). Overall, there was found to be a small but significant difference between the AN samples and healthy normal participants; however, there was considerable variation in the effect size found in the three studies. The BSAT is a well validated and reliable measure and it is interesting to note that overall only a small effect size was found using this measure. It would be interesting to

reapply this measure to a more homogenous population. There is also an argument that different set shifting tests could actually be measuring different cognitive abilities so it is interesting to compare two tests that are purportedly measuring the same ability.

When researching any aspect of AN it is important to consider the potential differences between the restrictive and binge-purge sub types as it has been hypothesised that they may have different neuropsychological profiles. A small scale study investigating this did not find any difference (Tchanturia, Anderluh et al., 2004), though other research suggests there may be differences between the sub groups across a number of domains including brain structure and core beliefs (Goethals et al. 2007; Unoka et al., 2007). It would seem advisable that until this question has been addressed, research investigating the neuropsychological profile of AN should consider the sub types separately to reduce the risk of possible confounding factors. It has been theorised that the binge-purge sub type may have similarities with the neuropsychological profile of bulimia nervosa (BN), which does not show the same set shifting deficits (Tchanturia et al., 2001). Therefore this study will examine the restrictive sub type of AN.

It is clear that further research examining the role of set shifting in AN is necessary, and that this research needs to be thorough and replicable. Weaknesses evident in previous research need to be addressed, and there needs to be discussion around the definition of set shifting and an examination of whether the various tests that supposedly assess this are measuring the same cognitive functions.

Aims and Hypothesis

This study investigated set shifting abilities in a restrictive sub type AN population. There were two hypotheses:

1. There would be a measurable deficit in performance of a restrictive sub type AN population on executive functioning set shifting tasks compared to a matched control sample, comparing both the BSAT and the IED subtest of the CANTAB with matched healthy controls; and

2. There would be a correlation between performance on the BSAT and on the IED subtest of the CANTAB.

Method

Participants:

Estimation of required sample size - when comparing AN samples with controls, previous studies into set shifting difficulties have found a variety of effect sizes, ranging from small (CANTAB/ BSAT /Trail Making) to medium (CatBat/Wisconsin Card Sorting) to large (Haptic Illusion Task) (Roberts et al., 2008). The CANTAB has only been used once on a possibly inappropriate sample so data from that study may not reflect an accurate effect size. Furthermore, many of the other studies have used a heterogeneous population and this may also have influenced effect size. In the present study efforts were made to increase power by rigorous sample selection and the use of tests less dependent on speed of processing and therefore sample size required was based on an expectation of a large effect

size. As such the appropriate power calculation was performed assuming the following: statistic – One-tailed t-tests; effect size – large (d=0.8); alpha – 0.05; power – 0.80. Total sample size is: 42 - 21 in the group with AN and 21 controls

Participants were recruited for the AN group from two locations: a specialist NHS clinic for eating disorders and a private in-patient facility for eating disorders. The control group (CG) participants were recruited from staff within the NHS clinic and from a clinical psychology interest group (see Appendix 6.0 for a full description of the recruitment process). All participants were female. Ethical approval was obtained from NHS Lothian Research Ethics Committee 2 and subjects gave informed written consent.

Inclusion/exclusion criteria:

There is high comorbidity in AN with depression and anxiety and it would not be possible to recruit an adequate sample size if depression and anxiety were exclusion criteria (Wade et al., 2000). Participants from the AN group were therefore eligible for inclusion if they had a primary diagnosis of AN restrictive sub type (DSM-IV diagnosis), they did not have any comorbid disorders other than depression and anxiety, their body mass index (BMI) was below 17.5, and they were in active treatment or post assessment stage on waiting list to ascertain initial suitability for inclusion.

Participants from the CG were eligible for inclusion if they did not have a diagnosable eating disorder or history of eating difficulties, they did not have any other psychiatric illness and their BMI was between 20 and 25[3].

Participants were excluded from the study if they met any one of the following criteria as this would impact on their performance on neuropsychological testing: any visual or motor impairment, a history of epilepsy, neurological illness, brain injury or substance use, a learning difficulty as defined by an estimated National Adult Reading Test (NART) IQ score of under 70, were under eighteen, or had prior experience of being tested on any of the assessments used. Participants taking medication that may have influenced cognitive processing were assessed on a case-by-case basis by consultant psychiatrists at a health clinic.

Recruitment Procedures

Participants from the AN group were recruited through clinicians within the services. Clinicians were made aware of inclusion/exclusion criteria and asked to give an information letter to suitable candidates inviting them to contact the lead researcher if interested in participating. Participants from the control group were recruited either via a poster (NHS staff) or a presentation (psychology interest group) requesting they contact the lead researcher for further information if interested in participating.

[3] The British Nutrition Foundation (2005) defines this as the healthy weight range for adults.

Once participants contacted the lead researcher expressing interest they were given further information over the telephone about the study and their rights, and the suitability for inclusion was ascertained. They were then invited to the clinics for a one off appointment.

Current height and weight for the AN participants were gathered from clinicians prior to testing (with the participants' permission); this information was gathered from the CG at the beginning of the session along with the completion of structured exclusion questions. Both groups then completed the Structured Clinical Interview for DSM Axis I Disorders (SCID-I), Structured Clinical Interview for DSM Axis II Personality Disorders Personality Questionnaire (SCID-II PQ), Hospital Anxiety and Depression Scale (HADS), Eating Disorder Examination Questionnaire (EDE-Q) and National Adult Reading Test (NART). If any participants were found to have any co-morbid diagnoses (other than depression or anxiety) or a learning difficulty then the session ended at this point. Prior to the neuropsychological component the participant's postcode was recorded to assess their socio-economic status using the Carstairs and Morris Deprivation Index. Participants were also offered the opportunity to have a break before completing the neuropsychological component to prevent fatigue. It should be noted that only one participant asked for a break and there was no noticeable or reported fatigue with any other subjects.

The neuropsychological component of the session consisted of the BSAT and IED CANTAB scale. The session took no more than an hour and a half to complete. The administration protocol for all the measures was followed and the lead researcher administered all tests.

Measures

Diagnostic measures were used to establish inclusion/exclusion criteria and measures examining set shifting were used to explore the research hypothesis.

Diagnostic measures:

Eating disorder – The Eating Disorder Examination Questionnaire (EDE-Q) (Fairburn and Beglin, 1994) is a valid and reliable self-report measure for screening for eating disorders. The full version (EDE) has been used in previous research and the EDE-Q has been validated against this, allowing for some comparison of data (Luce and Crowther, 1999).

Psychiatric illness – Both groups were screened for DSM-IV diagnosable psychiatric illnesses using the Structured Clinical Interview for DSM Axis I Disorders (SCID-I) (First, Spitzer et al., 1997) and the Structured Clinical Interview for DSM Axis II Personality Disorders Personality Questionnaire. (SCID-II PQ) (First, Gibbon et al., 1997). These have been shown to be reliable, valid and again have been used in previous research. The SCID-II PQ has been shown to be a reliable diagnostic tool in place of the full SCID-II interview for excluding personality disorders (Ekselius et al., 1994)

Premorbid IQ – This was assessed using the National Adult Reading Test (NART) (Nelson and Willison, 1991). This is not the most recent assessment tool for measuring premorbid IQ however the CANTAB uses this for co-varying for IQ and it has been shown to be reliable, valid and used in previous research (Crawford et al., 2001).

Mood and anxiety –These were measured in all participants using the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) as this is a brief self-report measure that is reliable, valid and used in previous research (Bjelland et al., 2002).

Socio-economic Status – Socio-economic status (SES) was assessed as it has been shown that a possible SES bias exists within patients with AN and therefore this needs to be accounted for and excluded as a possible source of variability (Hoek, 2002). The Carstairs and Morris deprivation index was used for this (McLoone, 2004).

Illness information - The severity of illness, age of onset and illness duration was recorded to enable the characteristic of the AN group to be recorded.

Set shifting measures:

Intra-extra dimensional (IED) set shift task from the Cambridge Neuropsychological Test Automated battery (CANTAB) - This is a test of rule acquisition and reversal, participants progress through stages by correctly selecting a stimuli on a touch screen computer six consecutive times, they then move to a new rule. If at any stage a participant makes 50 incorrect guesses the test finishes. Participants are told after each guess whether they were correct to enable them to learn the rule. There are nine different stages that a participant can complete. Participants are scored on the number of stages they complete and the number of incorrect guesses that they make. It is important to note that this test is less speed dependent than other measures of set shifting, which allows speed of processing difficulties to be excluded from the measurement

Brixton Spatial Anticipation Test (BSAT) –This is also a test of rule acquisition. Participants are asked to predict where a blue circle will move on a grid, there is a pattern

they can learn. The pattern occasionally changes and participants are required to switch to this new pattern to ensure they continue to predict the movement correctly. The raw score is the number of incorrect predictions a participant makes. It has been shown to be a valid and reliable test.

Design

This was a quasi-experimental, between subjects design. The variables measured were: BMI; years of education; socio-economic status; premorbid IQ; IED CANTAB score; BSAT score; and HADS score.

Results

Participants

Participants with AN and healthy weight controls were matched in terms of age, years of education, estimated IQ, gender and socio-economic status. 22 participants were initially included in the AN group: three were excluded as their weight increased between initially volunteering and their appointment, three were excluded as they became medically unstable over the recruitment process and five changed their minds about participating after initially agreeing. Two participants were taking psychotropic medication, it was decided that due to the stability and quantity of the dosage this would not impact on performance. Analysis was therefore undertaken with 11 participants in the AN group. 22 participants were also initially included in the CG: four were excluded as English was a second language and three were excluded as they had prior experience of the neuropsychological tests that were being used. Analysis was therefore undertaken with 15 participants in the CG group. No

participants were excluded due to co-morbidities, the SCID-I and SCID-II-PQ revealed no co-morbidities other than depression and anxiety in either group.

Data analysis

Due to the size of the recruited sample, non-parametric analysis was used (Pett, 1997); Mann-Whitney U tests were used to compare the scores on the set shifting tests between the groups and to compare the groups to ensure they were matched on the following variables: age; years of education; estimated IQ; and socio-economic status. The relationships between potential confounders and the set shifting measures were analysed using Spearman's Rank Correlation; the relationship between the BSAT and CANTAB was also analysed using this test. Means and standard deviations are reported.

Demographic and Clinical Information

The demographic characteristics of the samples are provided in Table four. There was no significant difference found between the groups on any of the matching criteria: age; years of education; socioeconomic status (Carstairs and Morris deprivation score – DEPCAT); or NART estimated global full scale IQ. There was a significant difference between the groups on BMI, depression (HADS score), anxiety (HADS score) and eating disorder characteristics (EDE-Q Global score).

********** INSERT TABLE FOUR HERE **********

Illness information was collected from the AN group and is shown in Table five; the age of onset of AN ranged from 8 – 59 (mean 23.27), the length of the current episode ranged from 1 – 16 years (mean 4.82), the number of previous episodes of AN ranged from 0 -10 (mean 1.42) and the number of inpatient admission went from 0 -10 (mean 2.55). AN participants also reported if they had a history of other eating disorders, three reported a history of bulimia nervosa and two reported a history of AN binge purge sub type.

********** INSERT TABLE FIVE HERE **********

Neuropsychological Results

The BSAT data were examined using a Mann Whitney U test to assess differences between both the raw error scores and scaled scores from the two groups; both measures showed no significant difference between the groups. BSAT error scores: U = 72, n.s. (AN n = 11, CG n = 15), mean AN = 12.09, CG = 11.47, range AN = 3 – 23, CG = 5 - 19, effect size: d = 0.11; BSAT scaled score: U = 76, n.s. (AN n = 11, CG n = 15), mean AN = 6.45, CG = 7.27, range AN = 4 – 10, CG = 5 – 10, effect size: d = 0.13

The IED CANTAB results were examined by looking at participants' standard scores on the number of stages completed and the total number of errors made (adjusted). The standard score is derived using the CANTAB normative database; it shows how many standard deviations the subject's score varies from a sample matched on age and NART FSIQ. Whilst the groups are matched on these, they are not individually matched, therefore it is more rigorous to use the standard scores. The adjusted error scores reflect the potential

number of errors a participant could have made had they completed all trials. There was no significant difference between the groups when the stages completed standard scores were compared using a Mann Whitney U test (U = 78, n.s., AN n = 11, CG n = 15, mean AN = -0.65, mean CG = -0.14, range AN = -3.88 – 0.54, CG = -3.88 – 0.6, effect size d = 0.34). When the total errors adjusted standard scores were compared between the groups using a Mann Whitney U test there was a significant difference found between the groups (U = 38.5, $p < 0.05$, AN n = 11, CG n = 15, mean AN = -0.49, mean CG = 0.13, range AN = -2.67 – 0.48, CG = -2.48 – 0.69, effect size d = 0.60).

When the total errors adjusted standard scores for the AN group were examined individually eight fell within one standard deviation of the mean, one was within two standard deviations and two were more that two standard deviations away from the mean; in comparison in the CG group 15 fell within one standard deviation of the mean, one was within two standard deviations and one was more than two standard deviations of the mean.

Impact of Comorbidity on Results

There was a significant difference found between the groups on the anxiety and depression scores from the HADS. The CG did not meet criteria on either the depression or anxiety scales whilst the AN group had mean scores that showed mild depression and moderate anxiety. The impact of these comorbidities on the significant total errors adjusted score from the IED CANTAB was examined further in the AN group using Spearman's rank correlation coefficient. Depression scores were not found to be significantly correlated (r = -0.26, n.s.), the anxiety scores were found to be significantly correlated with the adjusted

errors standard scores ($r = -0.67$, $p < 0.05$). Depression and anxiety scores were also compared with the BSAT error scores and no correlation was found (anxiety $r = -0.49$ n.s. depression $r = 0.51$ n.s.)

Relationship between the Neuropsychological Measures

The relationship between the two neuropsychological tests was assessed using a Spearman's rank correlation coefficient; the total errors adjusted standard score from the IED CANTAB was compared with the number of errors from the BSAT. There was not found to be a significant correlation ($r = 0.16$ n.s.)

Discussion

The aim of this study was to investigate set shifting abilities in a restrictive sub type AN population. Specifically, it was hypothesised that performance on two set shifting tasks in an AN group would be significantly impaired compared with healthy controls. It was also hypothesised that there would be a correlation between the two measures used. The results have not fully supported these hypotheses. Whilst there was a significant difference found on the number of errors made in the IED CANTAB task it was not possible to exclude the impact that anxiety has had on this result. This might have also impacted on the lack of correlation between the two groups.

Firstly, the BSAT task showed no significant difference between the two groups on either the raw error score or the scaled score and the effect size found for both measures was very small. This was not consistent with previous research (Tchanturia, Anderluh et al., 2004;

Tchanturia, Morris et al., 2004), which had shown a wide range of effect sizes for the BSAT and suggested that the variability found might be due to differing AN populations being used. It has been hypothesised that a deficit on the BSAT may only be present in acutely unwell patients with AN (Roberts et al., 2007); however, no clear definition of acute AN is given by the authors. The patients that have been classified as acute were both inpatients and outpatients and had a mean BMI of approximately 13. It may be that malnutrition in the acute (low weight) phase of AN could account for the previous significant findings. It is also possible that the BSAT is an easier measure of set shifting and that there has been a ceiling effect in the scores. The majority of the AN group scored in the 'high average' or above range, it may be that the BSAT is not challenging enough to detect the subtle nature of the set shifting deficit.

The results from the IED task of the CANTAB were more varied. On overall stages completed of this task, there was no significant difference found between the groups. Yet when the errors made during the task were examined in more detail, accounting for a person's intelligence and age, there was a significant difference found between the groups and a medium to large effect size. Whilst the significant result contradicts previous research, as stated in the introduction, this may be due to an older, more homogeneous population being used. There was a significant relationship found between the number of errors made and the levels of anxiety in the AN group and this needed to be considered as an explanation for the significant difference between the groups. Anxiety levels have been shown to impact on performance in neuropsychological tests and it could be this that resulted in a poor performance and not a specific difficulty with set shifting (Pendleton

Jones et al., 1991). It is interesting to note that anxiety only appeared to be playing a role on the IED and not the BSAT. There are a number of possible explanations for this. The IED could be perceived as a more difficult test and may thus lead to increased performance anxiety. When a wrong answer is elicited on the IED the computer flashes red and emits a loud beep. This might have made the task more anxiety provoking and potentially tied in with the perfectionism that is found in the AN population (Fairburn et al., 2003). A measure of perfectionism might be useful to include in future research into this area. The IED was always administered before the BSAT and it could be that participants were more anxious because this task was first (again, future research might benefit from reversing the administration order on tests to account for this). Thus, there are a variety of possible explanations for the increased role of anxiety in the IED task. Whatever the explanation, the impact of anxiety cannot be ignored and implies that the significant difference found may not be truly reflective of a difficulty with set shifting.

The second hypothesis was not been supported. When the relationship between the two set shifting measures was examined, there was no significant correlation found between the tasks. This could have a number of possible explanations. As discussed above only the IED appeared to be influenced by anxiety and this could explain the difference. It might also be that the tests are different levels of difficulty; both groups appeared to be impacted by ceiling effects on the BSAT and this might have masked a possible correlation between the scores. It is possible that the two tasks could also be measuring different cognitive abilities, or different aspects of set shifting. This leads to a broader issue that exists in the research into set shifting; it is a poorly defined concept and consequently there exists a range of tests

that purport to measure this ability that can appear to be quite different tasks. Whilst it is not within the scope of this paper to address this issue conclusively, the difference found between the tasks, which is indicative of the variety of findings throughout previous research, suggests that further clarification needs to be given regarding what the different tests are measuring and whether this qualifies as set shifting.

This paper used strict inclusion and exclusion criteria to obtain as homogenous a group from the AN population as possible. It was not possible, however, to exclude all potential confounders that occur within different aspects of the illness and therefore it is worth considering the population that was used and how this may have influenced the results. As discussed in the introduction only AN restrictive patients were used but it is important to note that five of the group had a history of either bulimia nervosa or AN binge purge sub type.

Secondly, the age of onset of the group needs to be considered; there is considerable research into the impact of adolescent onset AN on neuropsychological functioning (Frampton and Hutchinson, 2007). Ideally this study would only have included participants who developed the illness in adulthood; however, it was felt that this would have been too limiting on the recruitment procedure and therefore adolescent onset participants were included and this also may have affected the results. The study also defined adults as anyone 18 or older in order to have a clinically meaningful sample. By including young adults within the AN group the sample might have been biased as the frontal lobes, and

consequently executive functions, are not considered to be fully developed until early twenties (Sowell et al., 1999).

Discussed above are a number of possible explanations for the individual results that were found, but it is important that the results are considered in a broader context. Specifically the subtle nature of neuropsychological deficits in AN and what this implies, and the use of the diagnostic term 'anorexia nervosa' need to be examined. Previous research has discussed the subtle nature of neuropsychological deficits in AN (Tchanturia et al., 2005) and it needs to be considered whether such small deficits are playing a role in the symptoms, cause or maintenance of this illness. In this study there were a comparable number of participants in each group that were below the threshold of average scores on the error measure of the IED CANTAB. It could be hypothesised that perhaps this relatively small deficit acts as a catalyst and that this, combined with a wide range of difficulties and past experiences, plays an important role in the development and/or maintenance of AN and that without this deficit a different set of symptoms would have occurred. This clearly needs further investigation. It could equally be hypothesised that researchers are examining a deficit that is not critical or core to any part of AN development, maintenance or symptoms and that the deficits can actually be attributed to other underlying difficulties such as anxiety. It might be that the perfectionism often found in AN resulted in increased anxiety when performing on the more difficult IED task from the CANTAB. This leads to a broader argument that the underlying psychopathology of AN that has been well established could be impacting on performance on a range of neuropsychological tests. It would interesting to compare AN patients with a non-clinical sample that shared some of

the underlying psychopathology on a battery of neuropsychological tests to allow the cognitive impact of AN to be better understood.

Another broader issue that this research highlights is around the definition of AN. As discussed above, the role of age of onset of AN can appear to play a critical role in brain development and the course and outcome of the illness, and there is debate about whether early onset AN is a different disorder (Frampton and Hutchinson, 2007). This is just one example of a potential division that could be drawn within the wider AN population. There is also debate about fully separating AN restrictive and AN binge purge. Perhaps, the wide variety of results from neuropsychological testing that are reported in the literature are reflective of research capturing different aspects of different AN populations; the label 'anorexia nervosa' may be an umbrella term for a wide range of illnesses and difficulties.

The strengths of the research have already been discussed in some detail when considering the individual results that were found. There are also a number of general points that need be considered. This research had a larger number of exclusion criteria and accounted for a wider variety of confounders than previous research, these have included having English as a first language and having no prior experience of testing (Wheeler, unpublished) The two samples were also well matched across a wide range of factors that could again have impacted on the results. Whilst this study had small participant numbers, reflective of the general difficulties recruiting in AN research, it did find a medium to large effect size on the IED CANTAB errors measure, which could be suggestive of a clinically meaningful deficit on this task. Although, as discussed above the explanation for this deficit may not be

poor set shifting. This study also used a homogenous AN group by only examining restrictive AN. Whilst there is still no definitive argument as to whether the two sub groups should be viewed separately or not, this research allows for a greater clarity of possible cognitive deficits within this specific population. Finally, by using the CANTAB and BSAT to examine set shifting, the influence of speed of processing has been accounted for and excluded unlike previous research, which did not account for the possible role that this may have played.

Limitation of the study

There are a number of limitations to this research that need to be considered and acknowledged. Illness information was recorded from the AN group to allow a description of the characteristics of the group; however, this was only collected through self-report and is open to a number of criticisms. Patients might have misreported or misremembered information and it is very difficult to define when AN starts, so the age of onset information could be incorrect. As discussed above this study had small participant numbers, which means that even though a medium – large effect size was found future research would need to use a larger sample size to ensure an adequate cross section of the population was assessed. Therefore, the results do need to be viewed cautiously and cannot lead to definitive conclusions about set shifting in AN. Due to the small sample, nonparametric statistics were used, as it was not possible to assess the distribution of the data for normality. It might be that by using analysis that ranked the data rather than considering the actual figures, the relatively small differences between the groups had been inflated. When the raw data were examined the majority of the results were within the normal range

expected for the population's age and IQ. It could be that if further data were gathered to enable parametric analysis, the differences between the groups would not be present. Again, due to the nonparametric nature of the data, it was not possible to examine the errors made on the IED CANTAB whilst co-varying for the effect of anxiety. This limits the inferences that can be drawn from this data, as it is not possible to conclusively exclude or acknowledge the possible impact of anxiety on the results. The impact of anxiety on the IED CANTAB scores could have been examined more clearly if the order of presentation of the two set shifting measures had been reversed for half of the participants. This would have allowed the exclusion of the possibility that the IED CANTAB was more anxiety provoking because it was the first test used. Future research would benefit from ensuring that the order of presentation is considered along with possibly introducing a subjective measure of anxiety after each test is completed to further explore the role of this on test performance.

There are a number of areas of future research that might lead on from this study. It would interesting to repeat the study with AN binge purge participants and compare the two groups. This is an area that has been under-researched and would warrant further exploration. It would also be useful to conduct a larger scale study that used a wider variety of tests that claimed to measure set shifting. This might help to clarify the different components of set shifting and how they are affected in AN. Following on from that, this study clearly highlights the difficulties that exist in defining set shifting. There needs to be more exploration of the links between set shifting (using an agreed clear definition) and the brain injured population. This may help to fully understand what set shifting is and why it

may be involved in AN. As discussed above there is debate around the definition of AN and the usefulness of this concept, it would be interesting to compare AN patients with matched psychiatric controls. This would account for comorbidities, such as anxiety and depression, along with psychiatric histories i.e. trauma, abuse etc; which may then help tease out the role that set shifting plays in AN specifically.

As shown by both this study and the previous systematic review (Wheeler, unpublished), further research is needed to fully understand what, if any, cognitive impairments exist in AN and what may be underlying these. There do appear to be, however, measurable difficulties in some patients with AN on some neuropsychological tasks. It could be argued that regardless of the underlying mechanism of these difficulties (i.e. anxiety or cognitive deficit) it is beneficial to explore strategies that may help patients manage them. There is currently research exploring the use of cognitive remediation therapy in AN to help with a range of cognitive difficulties (Tchanturia et al., 2006; Tchanturia et al., 2007). This study could be argued to support this approach; however, it should be noted that it might be that by clarifying the underlying mechanisms of these difficulties, addressing, for example, a patient's anxiety could produce just as effective outcomes.

Conclusion

In conclusion, this study appeared to offer some support for the idea that there was a measurable deficit on some measures of set shifting within an AN population. Further, this study could lead to the hypothesis that the underlying reasons for this deficit might not be related to set shifting difficulties but rather other confounding difficulties such as anxiety or

core psychopathology found in AN. This might help to explain the varied results across the research that has examined patients with AN for possible cognitive impairments (Wheeler, unpublished).

If future research into cognitive impairments can account for these other possible explanations about the underlying mechanisms driving the impairments, then the potential impact of these impairments on AN needs to be considered; the question of what role, if any, such subtle deficits may play on the symptoms, cause or maintenance of AN needs to be answered.

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Table 4: Demographic Information and analysis

Measure	AN Mean	AN Standard Deviation	CG Mean	CG Standard Deviation	Mann-Whitney U score	Significance
BMI	15.05	1.28	22.05	1.41	0	<0.01
Age	29.82	13.30	29.13	8.48	69.5	n.s.
Years of Education	14.91	3.09	16.67	2.77	49	n.s.
DEPCAT Score	3.27	1.49	3.73	1.79	69.5	n.s
Depression HADS	9.10	6.19	0.40	0.51	0	<0.01
Anxiety HADS	12.20	4.87	3.47	2.80	9.5	<0.01
Global EDE-Q	3.31	1.80	0.19	0.25	2	<0.01
NART Estimated FSIQ	104.09	3.75	112.07	5.38	65	n.s.

AN n = 11, CG n = 15 (Depression HADS, Anxiety HADS, Global EDE-Q AN = 10)

Table 5: Clinical Information for the AN group

Characteristic	Range	Mean	Standard Deviation
Age of onset	8 - 59	23.27	14.06
Duration of current episode	1 - 16	4.82	4.24
Previous number of episodes	0 - 10	1.42	3.08
Inpatient admission	0 - 10	2.55	3.17
History of other eating disorders	3 bulimia nervosa 2 AN binge purge	N/A	N/A

Chapter 3

Advanced Clinical Practice I Reflective Critical Account

The Role of Self-Disclosure across Therapeutic Settings

(abstract only)

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Submitted in partial fulfilment of the requirements for the degree of doctorate in clinical psychology (D.Clin.Psy)

Abstract

This account discusses self-disclosure across therapeutic settings using a specific example of self-disclosure as the main point of reflection and then broadening out to address wider issues. Self-disclosure is defined, the professional guidelines and empirical evidence are reviewed and the role of self-disclosure in clinical psychology is explored. Then the background of the specific reflection is given. The specific situation is explored using a model of reflection, which examines the situation, the evidence base supporting it and future issues. In the reflective review the act of reflecting is discussed along with the role of supervision in the context of this account, the implications of this account for the profession, and future developments both individually and more broadly are discussed.

Chapter 4

Advanced Clinical Practice II Reflective Critical Account

Teaching in Clinical Psychology: How are we taught to teach?

(abstract only)

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Abstract

This account examines the relationship between teaching and clinical psychology. The policy and practice guidelines around the role and use of teaching in clinical psychology are discussed along with the evidence around effective teaching. The integral nature of teaching in clinical psychology is described along with the background and context of the reflection. The reflective situation describes my experience teaching in a clinical training session; a model of reflection is used to examine this. In the reflective review, the importance of being evidence-based teachers and trainers and the role of evaluating the quality of teaching are considered. The use of supervision to aid the reflective process is described, the broader professional practice issues that are raised are discussed and the impact of this reflection on future practice is examined.

Appendices

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Appendix 1.0 - Diagnostic criteria for anorexia nervosa (from DSM-IV-TR)

A. Body weight is less than is considered normal for height and age. Weight is consistently less than 85% of that expected, which can be due to either weight loss, or failure to gain weight during growth.

B. Despite being underweight, there is an intense fear of putting on weight and becoming fat.

C. Refusal to accept low body weight as a problem, excessive influence of body weight and shape on self-worth, or a distorted body image perception.

D. Amenorrhea (abnormal absence of a minimum of three successive menstrual cycles).

There are two identifiable types of anorexia nervosa:

Restricting Type: Throughout the present episode of anorexia nervosa, there has been no regular occurrence of binge eating or purging (self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

Binge Eating/Purging Type: Throughout the present episode of anorexia nervosa, there has been a regular occurrence of binge eating or purging.

Appendix 2.0 – Methodological Criteria Scoring Pro Forma

Class of Validity	Threat	Description	Threat or not enough information (0)	No threat (1)
Statistical conclusion validity	Low statistical power	Have they reported a power calculation on prior to starting and got appropriate numbers?		
	Violation of assumptions of statistics	Are statistics assuming normal distribution without checking this and using parametric statistics?		
	Inflated error rate	Are they more likely to have made a type one error (rejecting null when it is true) – is alpha higher than 0.05?		
	Unreliability of dependent or independent variable measures	Have the reported the reliability coefficients? And if reported are they over 0.80?		
	Unreliability of treatment implementation	Were the tests administered consistently: have they reported training people or used computer?		
	Heterogeneity of participants	Have the group been matched (i.e. age, gender, IQ, education level) Need to be matched on two or more criteria for point		
Internal validity	History	Have they considered any of the effects occurring before the testing – prior experience of testing, malnutrition, medication, comorbid disorder? (need all 4 for a point, record which ones tests have considered)		
	Instrumentation	Have these tests been reported to be reliable and valid and is literature cited that has used them in other populations?		
	Selection	1. Is there any bias in how the AN group were selected? i.e. all inpatients/outpatients, from age limited population		

		2. Is there any bias in how the control group were selected? i.e. all students/medical staff		

Construct validity	The main potential confounders are identified and taken into account in the design and analysis	Has speed of processing been accounted for?		
		Have they listed exclusion criteria?		
	Inadequate pre operationalisation explication	Are the key constructs inadequately defined (definition of neuropsychological processes being tested – individual and specific)?		
	Mono-operation bias	Are they assessing a construct (neuropsychological process) with only one measure?		
	Experimenter expectancies	Are raters aware of the research hypothesis and could the construct be potentially manipulated? (manual vs. computerised)		
	Interaction of treatments	Are the participants being exposed to multiple tests, which could potentially lead to inaccurate results? i.e. through fatigue. Have they put in a break, swapping order of tests, should not be testing for longer than approx. 20 minutes without break		

External validity	Interaction of selection and treatment	Limited generalisability of effect to other samples – how well are the AN diagnosed? Binge purge and/or restrictive? Have they separated the diagnoses?		
	Interaction of history and treatment	Limited generalisability of effect to other time frames – Is illness onset and duration given?		
Final Score				

Appendix 3.0

The following criteria were removed from the methodological scoring criteria:

- Inflated error rate
- Speed of processing accounted for
- History – prior experience of testing
- Testing
- Interactions with selection
- Irrelevance in experimental setting
- Maturation
- Statistical regression
- Differential attrition
- Ambiguity of causal direction
- Diffusion of treatment
- Compensatory equalisation of treatments
- Rivalry of participants
- Resentful demoralisation
- Monomethod bias
- Hypothesis guessing within experiment
- Evaluation apprehension
- Confounding of construct with levels of construct
- Restricted generalisability across constructs
- Interaction of setting and treatment

Appendix 4.0 Excluded papers (from full text onwards):

No control group

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Under eighteens

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No standard deviations given

Appendix 5.0: Instructions for Authors - Psychological Medicine

Editorial Policy

Psychological Medicine is a journal aimed primarily for the publication of original research in clinical psychiatry and the basic sciences related to it. These include relevant fields of biological, psychological and social sciences. Review articles, editorials and letters to the Editor discussing published papers are also published. Contributions must be in English.

Submission of manuscripts

Papers for publication from Europe and Australasia, except those on genetic topics, should be addressed to the UK Editor, Professor Robin Murray, Psychological Medicine Editorial Office, Douglas House, 18E Trumpington Road, Cambridge CB2 8AH, UK, E-mail: lgs21@cam.ac.uk.

Papers from the Americas, Asia, Africa and the Middle East, and all papers dealing with genetic topics, irrespective of country, should be sent to the US Editor, Professor Kenneth S. Kendler, MCV, PO Box 980126, Richmond, VA, 23298-0126, USA (Street address: Virginia Biotechnology Center One, Room 1-123, 800E Leigh Street, Richmond, VA, 23219, USA), Email: bherrmann@vcu.edu.

Submissions by email attachments are preferred. Alternatively contributors who wish may send one hard copy of the text, tables and figures, plus an identical copy on computer disk, giving details of format used (e.g. MS Word etc.). Authors should also accompany their submission with a list of 5 or more suggested suitable referees to aid the peer review process.

A covering letter signed by all authors should confirm agreement to submission. The letter should also give full mailing, fax and email contact details of the author who will handle correspondence. Submission of a paper will be held to imply that it contains original work that has not been previously published and that it is not being submitted for publication elsewhere. This should be confirmed in the letter of submission. When an article has been accepted for publication, the authors should email their final version or send a copy on computer disk (indicating format used, e.g. Mac/PC, MS Word/Word Perfect, etc.) together with one hard copy of the typescript and good quality copies of all tables, figures, etc. However, the publisher reserves the right to typeset the material by conventional means if an author's disk proves unsatisfactory.

The following information must be given on the first page (title sheet): (1) title and short title for running head (not more than 60 characters): (2) authors' names, (3) department in which the work was done, (4) word count of text excluding abstract, tables/figures and reference list. Generally papers should not have text more than 4500 words in length (excluding these sections) and should not have more than a combined total of 5 tables and/or figures. Papers shorter than these limits are encouraged. For papers of unusual importance the editors may waive these requirements. A structured abstract of no more than 250 words should be given at the beginning of the article using the headings: Background; Methods; Results; Conclusions. The name of an author to whom correspondence should be sent must be indicated and a full postal address given in the footnote. Any acknowledgements should be placed at the end of the text (before the References section). Declaration of Interest: A statement must be provided in the

acknowledgements listing all financial support received for the work and, for all authors, any financial involvement (including employment, fees, share ownership) or affiliation with any organisation whose financial interests may be affected by material in the manuscript, or which might potentially bias it. This applies to all papers including editorials and letters to the editor.

Contributors should also note the following:
1. S.I. units should be used throughout in text, figures and tables.
2. Authors should spell out in full any abbreviations used in their manuscripts.
3. Foreign quotations and phrases should be followed by a translation.
4. If necessary, guidelines for statistical presentation may be found in: Altman, D. G., Gore, S. M., Gardner, M. J. & Pocock, S. J. (1983). Statistical guidelines for contributors to medical journals. British Medical Journal 286, 1489-1493.

References

(1) The Harvard (author-date) system should be used in the text and a complete list of References cited given at the end of the article. In a text citation of a work by more than two authors cite the first author's name followed by et al. (but the names of all of the authors should be given in the References section). Where several references are cited together they should be listed in rising date order.

(2) The References section should be supplied in alphabetical order (authors' names in bold, journal titles in full), following the text. Some examples follow:

Article

Miller PM, Byrne M, Hodges A, Lawrie SM, Johnstone EC (2002). Childhood behaviour, psychotic symptoms and psychosis onset in young people at high risk of schizophrenia: early findings from the Edinburgh high risk study. Psychological Medicine 32, 173-179.

Corporate Author

US DHSS (1993). Social Security Bulletin, 1993, pp. 346-348. U.S. Department of Health and Human Services: Washington, DC.

Supplement

Norman RMG, Lewis SW, Marshall M (2005). Duration of untreated psychosis and its relationship to clinical outcome. British Journal of Psychiatry (Suppl.) 187, S19-S23.

Book

Cleckley HJ (1941). The Mask of Sanity, 2nd edn. Mosby: St. Louis, MO.

Chapter in book

Brewer WJ, Wood SJ, DeLuca C, Pantelis C (2006). Models of olfaction for exploring neurodevelopment. In Olfaction and the Brain (ed. W. J. Brewer, D. Castle and C. Pantelis), pp. 97–121. Cambridge University Press: Cambridge.

Thesis

Mulder LJM (1988). Assessment of cardiovascular reactivity by means of spectral analysis (Ph.D. thesis). University of Groningen, The Netherlands.

(3) Online citations

doi (when published online prior to printed issue)

Lauritsen MB, Pedersen CB, Mortensen CB (2004). The incidence and prevalence of pervasive developmental disorders: a Danish population-based study. Psychological Medicine. Published online: 21 October 2004. doi:10.1017/S0033291704002387.

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World Bank (2003). Quantitative techniques for health equity analysis – Technical Notes (http://siteresources.worldbank.org/INTPAH/Resources/Publications/Quantitative-
Techniques/health.eq tn07.pdf). Accessed 15 February 2006.
[Authors are requested to print-out and keep a copy of any online-only material, in case the URL changes or is no longer maintained.]

(4) 'Other' citations

'In Press' citations: check if published online. The doi number and date can then be included rather than 'In Press'.

'Submitted' and 'in preparation' references should be deleted from Refs section and cited in text as 'unpublished observations' (e.g.: J. Brown et al. unpublished observations).

Figures and tables

Only essential figures and tables should be included. Further tables, figures, photographs and appendices, may be included with the online version on the journal website. Unmounted photographs on glossy paper should be provided. Magnification scales, if necessary, should be lettered on these. Where possible, prints should be trimmed to column width (i.e. 70 mm). Diagrams should not be included in the text and should be submitted in a form suitable for direct reproduction. The printed version will normally be reduced to 70 mm wide, so care should be taken to ensure that lettering and symbols will remain clearly legible. All photographs, graphs, and diagrams should be referred to as figures and should be numbered consecutively in Arabic numerals. Ensure that the figure number is marked on the back of the photograph or artwork together with the name of the author and paper title. Captions for figures should be typed double-spaced on separate sheets. Tables should be numbered consecutively in the text in Arabic numerals and each typed on a separate sheet after the References section. Titles should be typed above the table.

Proofs and offprints

Page proofs will be sent to the author designated to receive correspondence. Corrections other than to printer's errors may be charged to the author. Fifty offprints of each paper are supplied free; additional offprints are available according to a scale of charges if they are ordered on the form supplied when the proof is returned.

(Revised 24/08/07)

Appendix 6.0: Recruitment process

This appendix shows the chronological process of recruitment from the time the study received formal approval from the University of Glasgow, the numbers in bold represent the total number of AN and CG participants recruited:

July 2008: Received approval to commence project from the University of Glasgow

August2008: Submitted project for ethical approval

September 2008: Received preliminary ethical approval and full R&D approval from NHS Lothian

October 2008: Received full ethical approval

November 2008: Commenced recruitment

December 2008: **AN 3**

January 2009: Applied for amendment to place poster which was advertising the study in the recruitment site, considered further recruitment sites. Approached two private inpatient eating disorder facilities and two NHS health boards to potentially recruit.
AN 5, CG 1

February 2009: One NHS board and one in-patient facility agreed to potential recruitment, ethics advised that approval for this should be sought in April as the process was altering and this would be more efficient
AN 5, CG 6

March 2009: Received approval for poster
AN 7, CG 8

April 2009: Applied to second NHS health board for R&D approval to run the study in their area and applied to the private hospital R&D for their permission.
AN 9, CG 12

May 2009: Received permission to recruit from the private hospital and commenced the study
AN 10, CG 14

June 2009: **AN 11, CG 15**

July 2009: Received approval from the second NHS health board to recruit from this site (due to staff changes there was a considerable delay in this approval and unfortunately in arrived on 14th July and there was not sufficient time to recruit from them)

Appendix 7.0 MRP Proposal

Major Research Proposal

An Investigation of Set Shifting in Anorexia Nervosa

Ellie Wheeler
31st March 2008

Research Supervisor: Prof. Jon Evans
Field Supervisor: Dr Patricia Graham

An Investigation of Set Shifting in Anorexia Nervosa

Abstract

Recent research has examined the possibilities that deficits in cognitive processes, in particular set shifting, might contribute to the development and maintenance of anorexia nervosa (AN). Results of studies of set shifting have been modest. There has been considerable variability in tests used to measure set shifting, and a lack of homogeneity of populations sampled. This study will investigate set shifting abilities within a restrictive sub type anorexia nervosa population using the set shifting sub-test of the Cambridge Neuropsychological Test Automated Battery (CANTAB) and the Brixton Spatial Anticipation Test (BSAT) which are reliable and valid tests. Participants with AN will be matched with healthy controls.

Introduction

Anorexia Nervosa[4] (AN) is a severe mental illness with currently no evidence based primary choice medical or psychological treatment (NICE Guidelines, 2004). Historically, psychological models aimed to understand the causes and maintenance of AN through maladaptive or distorted thoughts and beliefs; there is no evidence to support any one model (Fairburn, Cooper and Shafran, 2003).

Recent research has begun to focus on cognitive processes rather than content to better understand the cause and maintenance of AN. Research has investigated the neurobiology and neuropsychology of AN (Key, O'Brien, Gordon, Christie and Lask, 2006; Steinglass and Walsh, 2006), finding a variety of cognitive deficits (Kingston,

[4] See appendix 1 for DSM IV definition of AN (APA, 1994)

Szmukler, Andrews, Tress and Desmond, 1996; Roberts, Tchanturia, Stahl, Southgate and Treasure, 2007).

Tchanturia, Morris et al. (2004) summarised the neuropsychological. impairments found in AN as deficits in attention and executive functioning. Of interest has been the role of set shifting[5] deficits and the possible relationship that these deficits may have with the cognitive characteristic traits of anorexia such as rigid thinking (Fassino et al. 2002). Lezak, Howieson and Loring (2004) define mental flexibility problems as difficulties with rigidity or perseveration that primarily present behaviourally and encompass the capacity to shift thinking. The capacity for flexibility and shifting relates to perceptual, cognitive and response dimensions.

Research has shown that set shifting deficits remain after weight restoration and are present in sister siblings of sufferers of AN; Implying there may be a genetic contribution towards these deficits and possibly a genetic endophenotype. (Holliday, Tchanturia, Landau, Collier and Treasure, 2005)

Roberts et al. (2007) conducted a meta-analysis of the role of set shifting difficulties in AN and concluded there were measurable deficits in set shifting in AN. Fifteen studies were examined that investigated set shifting using a variety of assessment tools. All the studies reviewed used quite heterogeneous populations of anorexia patients; variability occurred in the following areas: weight, age, length of illness, age of onset and amongst the control groups. Future research would benefit from having thorough inclusion/exclusion criteria and larger numbers of participants. A specific gap

[5] Both set shifting and mental flexibility are used interchangeably to describe the same cognitive ability, different papers use different terms.

highlighted was the role that reduced speed of processing may play on influencing test results.

One study by Fowler et al. (2005) using the intra-extra dimensional set shift task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) to investigate set shifting, found no significant difference between AN and healthy controls. This was a surprising find, contradictory to most of the other papers reviewed. The participant sample, however, was an adolescent one with a relatively brief duration of illness. Kingston et al. (2006) suggest that as the teenage brain is still developing, AN onset in these years might result in a different pattern of neuropsychological deficits. The diagnosis of AN is also thought to be less stable in teenage years (Roberts et al., 2007). The CANTAB is a well-standardised and validated test that accounts for speed of processing; therefore it would merit being applied again to a more homogenous adult AN population.

There are three studies that have used the Brixton Spatial Anticipation Test (BSAT) to look for set shifting differences. Overall, there was found to be a small but significant difference between AN sample and healthy normal participants; however there was considerable variation in the effect size found in the three studies. The BSAT is a very well validated and reliable measure and it is interesting to note that overall only a small effect size was found using this measure; it is also a highly clinically valid test as it is relatively cheap and easy to use. It would be interesting to reapply this measure to a more homogenous population. There is also an argument that the different set shifting tests are measuring different skills so comparing two tests would be interesting to assess if they are measuring the same cognitive abilities.

Three published studies employed the BSAT task (Tchanturia, Anderluh et al., 2004; Tchanturia, Morris et al., 2004; Holliday et al. 2005), all of them from our research group. No meta-analysis was calculated for the BSAT task, as there were only four data-points across studies and eating disorder groups. An average standardized effect size of 0.21 was calculated for the BSAT task. It should be noted that wide variation in effect size was noted across samples employing this task. The only group in which the confidence interval did not overlap with zero were people acutely ill with AN (Tchanturia, Morris et al., 2004).

When researching any aspect of AN it is important to consider the potential differences between the restrictive and binge-purge sub types; it has been hypothesised that they may have different neuropsychological profiles. A small scale study investigating this did not find any difference, however there were various methodological flaws (Tchanturia, Anderluh et al., 2004). Other research suggests there may be differences between the sub groups across a number of domains including brain structure and core beliefs (Unoka, Tolgyes and Czobor, 2007; Goethals et al., 2007). It would seem advisable that until this question has been addressed, research investigating the neuropsychological profile of AN should consider the sub types separately to reduce the risk of possible confounding factors. It has been theorised that the binge-purge sub type may have similarities with the neuropsychological profile of bulimia nervosa (BN), which does not show the same set shifting deficits. Therefore this study will examine the restrictive sub type of AN.

It is clear that further research examining the role of set shifting in AN is necessary, and that this research needs to be thorough, robust and replicable. Weaknesses evident in previous research need to be addressed, a clear definition of set shifting used and a reliable and valid test of this are necessary.

Aims and Hypothesis

This study will investigate set shifting abilities in a restrictive sub type AN population. The primary hypothesis is that there will be a measurable deficit in performance of a restrictive sub type AN population on executive functioning set shifting tasks compared to a matched control sample, comparing both the BSAT and the IED subtest of the CANTAB with healthy controls. The secondary hypothesis is that this deficit will be evident using both the BSAT task and the IED subtest of the CANTAB

Plan of investigation

Participants:

Participants will be matched in terms of age, years of education, estimated IQ, gender and socio-economic status.

AN group:

Participants will primarily be recruited from the Cullen Centre (NHS Lothian) – a specialist clinic for eating disorders. Secondary recruitment from NHS Lanarkshire may also occur. Cullen Centre patients will be recruited from the waiting list and active treatment. Following a triage assessment patients are placed on the waiting list according to the severity. During this assessment process diagnostic criteria are examined and enough information will be known to ascertain if they are suitable for

inclusion. If participants are recruited from NHS Lanarkshire then only active cases will be taken to ensure they meet inclusion criteria.

Control group:

Participants will be recruited from staff within NHS Lothian; further participants may be recruited from the East of Scotland Psychology Affiliates Group (ESPAG).

Inclusion/exclusion criteria:

The following exclusion/inclusion criteria will be considered:

AN Group:

- Primary diagnosis of AN (DSM-IV diagnosis) – restrictive sub type
- No comorbid disorders other depression and anxiety
- Body mass index (BMI) below 17.5
- Active treatment or post assessment stage on waiting list

Control Group:

- No diagnosable eating disorder or history of eating difficulties
- No psychiatric illness
- BMI between 20 and 25

All participants:

- Participants taking medication that may influence cognitive processing will be assessed on a case-by-case basis by the consultant psychiatrists at the Cullen Centre using agreed guidelines for suitability

- No visual or motor impairments
- No history of epilepsy, neurological illness or substance use
- No learning difficulties as defined by estimated National Adult Reading Test (NART). IQ score of 70 or over.
- No history of brain injury
- Over eighteen
- No prior experience of being tested on the NART, BSAT or CANTAB

Recruitment Procedures

Participants from the AN group will be recruited through clinicians within the service. Clinicians will be made aware of inclusion/exclusion criteria and be asked to give an information letter to suitable candidates inviting them to contact the lead researcher if interested in participating. This will either be done at the end of the triage assessment process or during active treatment. Participants from the control group will be recruited either via a poster (NHS staff) or a presentation (ESPAG) requesting they contact the lead researcher for further information if interested in participating.

If participants contact the lead researcher expressing interest they will be given further information over the telephone about the study and their rights. If willing to take part they will be invited to the Cullen Centre for a one off appointment (AN group) or assessment session followed by second appointment (control group).

Measures

Diagnostic measures will be used to establish inclusion/exclusion criteria and measures examining set shifting will be used to explore the research hypothesis.

Diagnostic measures:

Eating disorder – The Eating Disorder Examination Questionnaire (EDE-Q) is a valid and reliable measure for screening for eating disorders. The full version (EDE) has been used in previous research and the EDE-Q has been validated against this, this allows for some comparison of data.

Psychiatric illness –Both groups will be screened using the Structured Clinical Interview for DSM Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM Axis II Personality Disorders Personality Questionnaire. (SCID-II PQ). It is hoped that CG participants will be without any psychiatric difficulties (initial recruitment information will state this clearly) and following the triage assessment process any co-morbidities in the AN group should have been highlighted, so administering these test should not be a lengthy process. This has been shown to be reliable, valid and again has been used in previous research.

Premorbid IQ – This will be assessed using the National Adult Reading Test (NART). This is not the most recent assessment tool for measuring premorbid IQ however the CANTAB uses this for co-varying for IQ; it has been shown to be reliable, valid and used in previous research.

Mood and anxiety – These will be measured in all participants but will not be exclusion criteria due to the high incidence of comorbidity in AN. They will be co-varied in analysis if necessary. They will be measured using the HADS as this is a brief measure that it reliable, valid and used in previous research.

Socio-economic Status – Socio-economic status will be assessed as it has been shown that a possible SES bias exists within the anorexic population and therefore this needs to

be accounted for and excluded as a possible source of variability (Hoek, 2002). The Carstairs and Morris deprivation index will be used for this.

Illness information - The severity of illness, age of onset and illness duration will be recorded to enable the characteristic of the AN group to be assessed.

Set shifting measures:

Cambridge Neuropsychological Test Automated battery (CANTAB) – only the specific sub test addressing set shifting will be used. This is the intra-extra dimensional set shift (IED). The reasons for using this test of set shifting have been discussed in the introduction. It is important to note that these tests are less speed dependent than other measures of set shifting which allows speed of processing difficulties to be excluded from the measurement

Brixton Spatial Anticipation Test (BSAT) – The reasons for using this measure have been discussed in the introduction. It has been shown to be a validated and reliable test.

Design

This will be a quasi-experimental between subjects design. The variables that will be measured are: BMI, years of education, socio-economic status, premorbid IQ, IED CANTAB score, BSAT score and HADS score.

Research procedures

Current height and weight for the AN participants will be gathered from clinicians prior to testing (with the participants' permission); this information will be gathered from the CG at the beginning of the session along with the completion of structured exclusion

questions. Both groups will then complete the SCID-I and SCID-II PQ, if any participants are found to have any co-morbid diagnoses then the session will end at this point. Prior to the neuropsychological participant's postcodes will be recorded to assess their socio-economic status using the Carstairs and Morris deprivation Index

The neuropsychological component of the session will consist of the following: NART[6], HADS, EDE-Q, BSAT and IED CANTAB scale. The session should not take more than an hour and a half to complete. The administration protocol for all the measures will be followed.

Justification of sample size

Previous studies into set shifting difficulties in AN have found a variety of effect sizes ranging from small to large. The following measures have been used and have shown the stated effect sizes (e.s.):

CANTAB	small e.s.
BSAT	small e.s.
Trail Making Test	small e.s.
CatBat Task	medium e.s.
Wisconsin Card Sort Test	medium e.s.
Haptic Illusion Task	large e.s.

[6] Whilst clinicians should be excluding patients with learning disabilities some could potentially still be recruited. It is easier for both the researcher and participant if they only have to attend one session, premorbid IQ will be measured at the start of the session and if necessary the data will be excluded. For accurate comparison the same process will also be conducted for the control group

The CANTAB, as previously discussed, was only used once on a possibly inappropriate sample so may not reflect an accurate e.s. Many of the other studies have used a heterogeneous population and this may also have influenced e.s.

This study will take account of speed of processing and have a better more rigorous sample selection controlling for more variability so can expect a large effect size. As such the appropriate power calculation has been performed assuming the following:

Statistic: One-tailed t-tests

Effect Size: Large (0.8)

Alpha: 0.05

Power: 0.80

Total sample size is: 42: 21 in the AN group and 21 controls

The Cullen Centre waiting list is currently 24 months so recruiting an appropriate sized sample should not be problematic. If necessary, recruitment within NHS Lanarkshire will occur.

Settings and equipment

All assessments and interventions will be performed within the Cullen Centre (NHS Lothian) or in health clinics in NHS Lanarkshire. The CANTAB, BSAT, HADS and NART can be supplied by the University of Glasgow. All other relevant diagnostic assessments are available through NHS Lothian.

Data analysis

Data will be analysed using SPSS. Assuming assumptions for parametric analysis are met, the mean scores on the sub test for set shifting for the AN and control groups will be compared for difference using t-tests.

There is high comorbidity in AN with depression and anxiety and it would not be possible to recruit an adequate sample size if depression and anxiety were exclusion criteria (Wade et al., 2000; Kaye et al., 2004). Depression and anxiety may influence the test results; therefore in the event that there are differences in mood or anxiety scores then these will co-varied in the analysis using an ANCOVA

Health and Safety Issues

Researcher safety issues

All work will be done in health clinics within normal hours of practice. Standard risk protocols will be followed and administrative staff will be aware of appointment times and length. This should minimise any potential risk to the researcher.

Participant safety issues

Participants will be attending health clinics and should not be in any high-risk situation.

Ethical issues

Ethical approval will be sought from NHS Lothian with a secondary site specified as NHS Lanarkshire.

The following ethical issues need to be considered before commencing the study:

1. It is not anticipated that the procedures should cause any distress in either group. If any of the participants become distressed at any point during the procedures then the testing will stop and their distress will be managed within the session. If they require further assistance then they will be offered the opportunity to speak to a clinician on site.
2. If any mental health difficulties are highlighted for the control group then they will be encouraged to contact their GP. This will be discussed with them before consenting to the study.
3. If further difficulties are highlighted for the AN group then these will be shared with their clinician, or GP if on the waiting list. This will have been discussed prior to commencing the study.
4. It will be clearly highlighted to potential participants that their involvement is completely optional and that opting out would in no way impact on their treatment or their place on the waiting list.
5. Data storage – data will be stored securely and anonymously. A locked filing cupboard within the Cullen Centre will be used for all data storage and where possible it will not be removed from there. All participants will be given a number as an identifier and only the lead researcher will have access to the corresponding names. If data is stored electronically it will be password protected and stored on a secure access computer. If any data is moved it will be kept in a locked briefcase and if necessary stored in a locked boot. This is in keeping with NHS Lothian protocol for the transport of patient information.

Financial issues

The measures will not need to be purchased however the recording sheets may need to be. There may be minimal costs for administrative purposes, including paper, envelopes and stamps. Otherwise there are no foreseeable extraordinary costs involved. Trainee travel costs should be minimal and will be covered by NHS Lanarkshire.

Timetable

August 2008

- Apply for ethics

September 2008

- Earliest possible date to begin recruitment of AN group
- Start to perform assessment sessions

October 2008

- Start to recruit matched controls
- Start to perform diagnostic interviews and assessment sessions
- Research Progress Meeting

November 2008

- If recruitment is slow for AN group then consider commencing secondary site recruitment

January 2009

- Research Progress Meeting
- Complete Recruitment

February 2009

- Begin analysis

- Begin writing up

April 2009

- First draft handed in

May 2009

- Research Progress Meeting

July 2009

- Final submission deadline

Practical Applications

This study would help to provide further clarity about the neuropsychological profile of AN. It may also help highlight the more specific deficits of set shifting that occur and provide further evidence of the differences between the different sub types of AN. This research could then help influence both further research and direct clinical practice. This may help understanding of the disparity that can exist between an AN patient's thoughts and their behaviour and possibly suggest new directions for future treatment. It would also help to evidence the current use of cognitive remediation therapy that is being trialled as a treatment approach and may suggest ways in which this work can be adapted (Tchanturia, Whitney, and Treasure, 2006; Tchanturia, Davies and Campbell, 2007).

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