*ORIGINAL ARTICLE*

**Case Control Study**

# Comprehensive neurocognitive assessment of patients with anorexia nervosa

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## Abstract

**AIM:** To utilise a comprehensive cognitive battery to gain a better understanding of cognitive performance in anorexia nervosa (AN).

**METHODS:** Twenty-six individuals with AN and 27 healthy control participants matched for age, gender and premorbid intelligence, participated in the study. A standard cognitive battery, the Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery, was used to investigate performance on seven cognitive domains with the use of 10 different tasks: speed of processing [Brief Assessment Of Cognition In Schizophrenia: Symbol Coding, Category Fluency: Animal Naming (Fluency) and Trail Making Test: Part A], attention/vigilance [Continuous Performance Test - Identical Pairs (CPT-IP)], working memory [Wechsler Memory Scale (WMS®-Ⅲ): Spatial Span, and Letter-Number Span (LNS)], verbal learning [Hopkins Verbal Learning Test - Revised], visual learning [Brief Visuospatial Memory Test - Revised], reasoning and problem solving [Neuropsychological Assessment Battery: Mazes], and social cognition [Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions]. Statistical analyses involved the use of multivariate and univariate analyses of variance.

**RESULTS:** Analyses conducted on the cognitive domain scores revealed no overall significant difference between groups nor any interaction between group and domain score [F(1,45) = 0.73, $P$ = 0.649]. Analyses conducted on each of the specific tasks within the cognitive domains revealed significantly slower reaction times for false alarm responses on the CPT-IP task in AN [F(1,51) = 12.80, $P$ < 0.01, Cohen's d = 0.982] and a trend towards poorer performance in AN on the backward component of the WMS®-Ⅲ Spatial Span task [F(1,51) = 5.88, $P$ = 0.02, Cohen's d = -0.665]. The finding of slower reaction times of false alarm responses is, however, limited due to the small number of false alarm responses for either group.

**CONCLUSION:** The findings are discussed in terms of poorer capacity to manipulate and process visuospatial material in AN.

**Key words:** Cognition; Eating disorder; Body image; Spatial processing; Short-term memory

**Core tip:** The findings of this study suggest that individuals with anorexia nervosa (AN) have largely intact cognitive performance, which notably differs to the cognitive profile of other psychiatric illnesses, such as schizophrenia, bipolar disorder and major depressive disorder, which are all associated with significant cognitive deficits. However, a trend for AN participants to perform poorer on the backward component of a spatial span task was revealed. This suggests a poorer capacity to process and manipulate visuospatial information in AN, which may be related to the distortions of body image experienced by these individuals.

## INTRODUCTION

Anorexia nervosa (AN) is a serious psychiatric condition with a mortality rate among the highest of any mental illness[1,2]. Yet, the factors involved in the genesis and maintenance of the illness remain unclear. A common feature of AN is perfectionism, which has been identified as a significant risk factor for the illness, and is a feature found to persist following long-term recovery[3,4]. Thus, cognitive assessments reported in the AN literature often focus on tasks related to perfectionism and rigid thinking patterns, such as cognitive set shifting tasks[5]. Individuals with AN have been found to perform significantly more poorly than healthy individuals during tasks of cognitive set shifting such as the Wisconsin Card Sort Test and certain target detection tasks, displaying stereotyped behaviours with rigid approaches to changing rules[6-8]. However, unlike other psychiatric illnesses, there is a paucity of research employing more comprehensive assessments of cognitive profile in AN.

Studies of cognition in AN have tended to use a range of cognitive assessments rather than utilising a standard cognitive battery; they have consequently reported conflicting findings[9-18]. Therefore, the use of a standard neurocognitive battery, such as the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB)[19], would be advantageous and would also allow for direct comparisons to be drawn between AN and other clinical populations. The MCCB was originally designed to assess cognitive domains most relevant to schizophrenia but has since been applied to assess cognitive impairments in other psychiatric illnesses, including bipolar disorder[20], posttraumatic stress disorder[21] and major depressive disorder[22]. With the use of 10 different tasks, the MCCB assesses the following 7 cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition.

Although cognitive batteries have been compiled in past research to assess cognition in AN[12,13], a standardised cognitive battery has rarely been used[23]. Furthermore, although each of the cognitive domains in the MCCB has been investigated in past research in AN, the findings are largely inconsistent. Under the speed of processing domain, intact fluency and symbol

coding performance has typically been found[15,24]. Poorer performance on trail making tasks on the other hand have been reported by some researchers[25], but not by others[8]. In relation to the attention/vigilance domain, performance on a continuous performance task has not been found to differ from healthy individuals[26], though performance on a similar task requiring rapid visual information processing has been found to result in poorer performance in AN patients[27]. Performance on tasks assessing verbal and visuospatial working memory, on the other hand, have also been found to not differ from healthy individuals by some investigators[10,27], whilst others have reported poorer visuospatial working memory in AN[28]. In relation to visual learning, performance has typically been found to be intact in AN[9,29]. Furthermore, although performance on reasoning and problem solving tasks such as mazes has also been found to be largely intact in AN[23], other tasks assessing this domain such as object assembly and block design, have been found to result in poorer performance in AN[11,28]. Finally, studies assessing social cognition in AN also show inconsistent findings, with some reporting poorer performance[30] and others failing to find a significant difference from healthy individuals[31].

Therefore, the aim of this study was to utilise a comprehensive battery of tasks to investigate cognitive performance in AN. We hypothesised that individuals with AN would show poorer performance on tasks assessing each of the cognitive domains, except the tasks assessing speed of processing and visual learning, where the literature has reported intact performance to date. We further completed exploratory analyses of performance of each of the tasks in AN given that the MCCB was originally designed to examine cognitive profile in people with schizophrenia, who are reported to show substantial cognitive problems. Individuals with AN are not expected to show such extreme deficits, and thus may only show impairment at the individual task level rather than at the level of domains overall. As cognitive performance is significantly affected by malnutrition[32] and this is a likely factor in the inconsistent findings to date in AN, we sought to investigate AN participants who were at a uniform phase of their illness trajectory [medically stable but below the healthy body mass index (BMI) range].

## MATERIALS AND METHODS

This study was approved by the Human Research Ethics Departments at the University of Melbourne, Swinburne University of Technology, the Melbourne Clinic, the Austin Hospital and St Vincent's Hospital; all in Melbourne, Australia. Informed written consent was obtained from all participants. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

### Participants
Participants were 26 right-handed females with AN and 27 healthy controls (HC). Groups were matched for age and premorbid intelligence quotient (IQ). HCs were recruited through public advertisements, whereas AN participants were recruited through public advertisements; the Body Image and Eating Disorders Treatment and Recovery Service at the Austin and St Vincent's Hospitals; and The Melbourne Clinic; all in Melbourne, Australia. All patients were required to be medically stable (*i.e.*, not requiring medical attention due to their physical state) prior to inclusion in the study.

All participants were English speaking and had no history of significant brain injury or neurological condition. Controls were required to have no history of an eating disorder or other mental illness; they were also required to not be taking any medications apart from hormonal contraceptives (11 HC participants were taking medications). AN participants were instructed to continue with their normal medications, which were: selective serotonin reuptake inhibitors (11), atypical antipsychotics (12), benzodiazepines (6), serotonin-noradrenaline reuptake inhibitors (SNRIs) (3), hormonal contraceptives (3), melatonergic antidepressants (3), noradrenergic and specific serotonergic antidepressant (1) and cyclopyrrolones (1).

The Mini International Neuropsychiatric Interview, 5.0.0[33] was used to screen all participants for major Axis I psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). It was also used to confirm diagnoses of AN, with the exception of the amenorrhea criterion which is no longer included in the current DSM-5. AN was required to be the primary diagnosis of the AN group. AN participants with comorbid psychiatric conditions, other than psychotic conditions, were not excluded as this would not have represented a typical AN sample.

Premorbid intelligence was estimated using the Wechsler Test of Adult Reading[34]. Eating disorder symptomatology was investigated with the Eating Disorders Examination Questionnaire[35] (Table 1).

### Cognitive battery
With the use of 10 different tasks, the MCCB assesses 7 cognitive domains. Scores on each task are entered into the MATRICS scoring program which produces cognitive domain scores.

**Speed of processing:** Speed of processing is assessed with three different tasks. The Brief Assessment of Cognition in Schizophrenia: Symbol Coding task requires participants to use a key to correctly match and report as many digits that correspond to nonsense symbols as they can within 90 s; the number of correctly matched symbols constitutes the score. The Category Fluency: Animal Naming (Fluency) task requires participants to orally report as many animals as they can in 60 s, which constitutes the task score. The Trail Making Test: Part

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| Table 2 Cognitive domain scores | | | | | |
| --- | --- | --- | --- | --- | --- |
| | AN | HC | F | *P* | Cohen's d |
| | M (SD) | M (SD) | | | |
| Speed of processing | 57.42 (9.75) | 59.85 (7.80) | 1.01 | 0.32 | 0.28 |
| Attention/vigilance | 43.42 (8.08) | 46.85 (8.47) | 2.27 | 0.14 | 0.41 |
| Working memory | 56.12 (9.68) | 58.56 (9.33) | 0.87 | 0.36 | 0.26 |
| Verbal learning | 53.38 (10.33) | 50.33 (8.19) | 1.42 | 0.24 | 0.33 |
| Visual learning | 54.85 (6.25) | 56.59 (9.77) | 0.60 | 0.44 | 0.21 |
| Reasoning and problem solving | 55.15 (8.29) | 58.11 (7.11) | 1.95 | 0.17 | 0.38 |
| Social cognition | 49.42 (6.93) | 48.07 (10.86) | 0.29 | 0.59 | 0.15 |
| Overall composite | 54.31 (7.97) | 56.19 (7.03) | 0.83 | 0.37 | 0.25 |

AN: Anorexia nervosa; HC: Healthy control.

conducted on the seven cognitive domain scores across groups. Secondly, one way analysis of variance was used on each of the task variables to compare group performance, with alpha set at 0.01 to account for multiple comparisons. Statistical review of the study was performed by a biomedical statistician.

## RESULTS

A MANOVA conducted on the cognitive domain scores revealed no overall significant difference between groups nor any interaction between group and domain score [$F_{(1,45)}$ = 0.73, $P$ = 0.649] (Table 2). Analyses conducted on each of the specific tasks within the cognitive domains revealed significantly slower reaction times for false alarm responses on the CPT-IP task in AN [$F_{(1,51)}$ = 12.80, $P$ < 0.01, Cohen's d = 0.982] and a trend towards poorer performance in AN on the backward component of the WMS®-Ⅲ Spatial Span task [$F_{(1,51)}$ = 5.88, $P$ = 0.02, Cohen's d = -0.665] (Table 3). The finding of slower reaction times of false alarm responses is, however, limited due to the small number of false alarm responses for either group.

## DISCUSSION

Overall, the results from this study suggest intact cognitive performance in AN on the majority of the measures studied, despite significantly low BMIs and the potential long- and short-term effects of starvation. The only cognitive measure which showed a trend toward impairment in the AN group was visuospatial working memory. Poorer performance in AN was specifically found during the backward component of the task and not the forward component of the task, or the task overall. A study by Fowler *et al*[27] also reported intact overall spatial span performance in AN, but did not report whether AN and healthy individuals differed in the forward or backward components of the task. The forward component is thought to represent the capacity of the visuospatial sketchpad, whereas the backward component of this task is thought to represent a measure of executive function as it requires additional manipulation within temporary storage[36], suggesting that individuals with AN have specific working memory

difficulties when the cognitive demand is high. This deficit appears to be specific to visuospatial working memory as LNS performance was intact in this cohort. Working memory deficits specific to visuospatial working memory have also been reported by Kemps *et al*[28], who found AN participants were poorer at recalling object locations, but did not differ in the recall of object names compared to healthy individuals. This finding is also in keeping with several studies reporting impairments in immediate recall on visuospatial memory tasks such as the Rey Complex Figure Test[37]. Poorer capacity to manipulate and process visuospatial material may also be related to the specific visuospatial processing deficits experienced in AN, in which patients overestimate the size of their own body[38]; though, this relationship would require specific investigation.

Contrary to expectations, individuals with AN did not differ from healthy individuals in performance on any other task. Though the AN group were found to make false alarm responses of longer reaction time than the control group, this finding is limited due to the small number of false alarm responses for either group, thereby not allowing accurate statistical analyses to be undertaken. The existing research utilising the same or similar tasks is particularly inconsistent with many studies reporting no cognitive deficits, while others report significantly poorer cognitive performance in AN. The inconsistency in findings may be largely related to differences in methodology, particularly the participants examined. Malnutrition certainly effects cognitive function as reported in studies of induced starvation[32]. Studies in AN patients often recruit individuals currently undergoing inpatient treatment as they are often easily accessible to researchers. The primary role of most inpatient treatment services is medical stabilisation. Therefore, patients admitted to such services are typically very physically unwell. The majority of patients in this study were outpatients at the time of testing. Furthermore, the few inpatients included were required to be medically stable. Despite all patients recruited for this study being medically stable, their BMIs were significantly below normal and their eating disorder symptomatology significantly high, suggesting that they were in an acute phase of the illness but were physically well enough to function. Therefore, the sample recruited

| Table 3  Specific task scores | | | | | |
| --- | --- | --- | --- | --- | --- |
| | AN<br>M (SD) | HC<br>M (SD) | F | *P* | Cohen's d |
| Speed of processing | | | | | |
| BACS SC | 63.23 (9.80) | 68.11 (9.19) | 3.50 | 0.07 | 0.51 |
| Fluency | 28.19 (6.43) | 27.19 (5.54) | 0.37 | 0.54 | 0.17 |
| TMT-A | 23.62 (57.50) | 21.30 (4.83) | 2.54 | 0.12 | 0.44 |
| Attention/vigilance | | | | | |
| CPT-IP | | | | | |
| Hits proportion | 0.82 (0.10) | 0.86 (0.09) | 1.65 | 0.21 | 0.42 |
| Hits reaction time | 550.25 (60.43) | 533.05 (51.08) | 1.26 | 0.27 | 0.31 |
| False alarms proportion | 0.11 (0.05) | 0.09 (0.06) | 1.04 | 0.31 | 0.36 |
| False alarms reaction time | 508.08 (147.39) | 369.98 (133.55) | 12.80 | < 0.01 | 0.98 |
| Random responses proportion | 0.01 (0.01) | 0.01 (0.01) | 1.96 | 0.17 | 0.00 |
| DPRIME score | 2.55 (0.54) | 2.78 (0.56) | 2.37 | 0.13 | 0.42 |
| Working memory | | | | | |
| WMS®-Ⅲ | | | | | |
| Forward score | 9.65 (2.30) | 10.3 (1.88) | 1.25 | 0.27 | 0.31 |
| Backward score | 9.12 (1.80) | 10.3 (1.75) | 5.88 | 0.02 | 0.67 |
| Total score | 18.77 (3.54) | 20.59 (2.94) | 4.18 | 0.05 | 0.56 |
| LNS | 17.38 (2.82) | 16.74 (2.97) | 0.66 | 0.42 | 0.22 |
| Verbal learning | | | | | |
| HVLT-R™ | | | | | |
| Total recall | 29.38 (4.01) | 28.07 (3.82) | 1.48 | 0.23 | 0.34 |
| Delayed recall | 13.42 (17.74) | 9.96 (1.63) | 1.02 | 0.32 | 0.23 |
| Delayed retention | 92.80 (14.13) | 91.98 (14.59) | 0.04 | 0.84 | 0.06 |
| Delayed recognition | 11.04 (0.96) | 10.93 (1.33) | 0.12 | 0.73 | 0.10 |
| Visual learning | | | | | |
| BVMT-R™ | 28.62 (3.98) | 29.78 (6.23) | 0.65 | 0.42 | 0.22 |
| Reasoning and problem solving | | | | | |
| NAB®: Mazes | 22.46 (3.43) | 23.70 (2.63) | 2.20 | 0.14 | 0.41 |
| Social cognition | | | | | |
| MSCEIT™: Managing emotions | 96.98 (5.92) | 95.41 (9.57) | 0.51 | 0.48 | 0.20 |

AN: Anorexia nervosa; HC: Healthy control; BACS SC: Brief Assessment of Cognition in Schizophrenia: Symbol Coding; Fluency: Category Fluency: Animal Naming; TMT-A: Trail Making Task Part A reported in seconds; CPT-IP: Continuous Performance Test - Identical Pairs; WMS®-Ⅲ: Wechsler Memory Scale (WMS®-Ⅲ): Spatial Span; LNS: Letter Number Span; HVLT-R™: Hopkins Verbal Learning Test - Revised; NAB®: Mazes: Neuropsychological Assessment Battery Mazes task; MSCEIT™: Managing Emotions: Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions; reaction times on the CPT-IP reported in milliseconds.

is a significant strength of this study, especially as they were age, gender and IQ matched to the HC cohort, resulting in a homogenous sample which is often not achieved in research in AN.

The study is, however, not without its limitations. The MCCB is a standard cognitive battery originally compiled to assess the areas of cognition most relevant to schizophrenia and related disorders. Therefore, cognitions often associated with AN, such as cognitive set shifting[8,39,40], were not investigated. As the aim of the study was to investigate general cognition in AN, and the existing cognitive battery was already lengthy, an additional cognitive set shifting task was not considered feasible. Future research in AN would benefit from including set shifting tasks. Although the MCCB provides a comprehensive profile of basic cognitive tasks, a battery also including tasks related to the specific cognitive traits commonly associated with AN, and tasks allowing more detailed exploration of executive function would be beneficial in future research. Furthermore, the modest sample size may have contributed to the lack of significant differences between groups. Thus, further research utilising the same measures in a larger sample

may reveal statistically significant group differences, rather than the trends reported in the current study. A further potential limitation is that the majority of patients were on medication at the time of testing, which may have influenced the findings.

The findings of this study suggest a cognitive profile in AN different to that of other psychiatric illnesses, such as schizophrenia, bipolar disorder and major depressive disorder, which are all associated with significant cognitive deficits on the MCCB[20,22,41]. Similar findings to the current study have, however, been reported in obsessive compulsive disorder (OCD). Intact performance on a range of cognitive tasks have been reported in OCD. Similarly to the current study, poorer performance on tasks of spatial working memory[42], but not specifically spatial span[43], have been reported in OCD patients. Similarly, poor visuospatial working memory has also been reported in body dysmorphic disorder (BDD), another psychiatric illness within the OCD-spectrum with prominent body image disturbance[44,45]. Though, unlike the current findings, poorer performance on tasks of verbal working memory and executive function have also been reported in BDD[45,46]. Unlike the current

study, however, the spatial span task components in these studies were not separated to better investigate visuospatial working memory. The deficits in visuospatial working memory and otherwise intact cognitive performance in OCD illustrates the overlap in clinical presentation that is often reported in AN, and may provide support for the long-proposed hypothesis that AN and OCD share overlapping psychopathology[47].

Overall, visuospatial working memory was the only cognitive measure that groups were found to differ on in this study, and this may be related to AN patients' difficulties in evaluating their own bodies. As cognitive functioning in general appears to remain largely unaltered in AN, it may suggest that the limited cognitive deficits observed may arise from quite restricted brain regions which may also be involved in the psychopathology of AN.

## ACKNOWLEDGMENTS

## COMMENTS

### Background
Anorexia nervosa (AN) is a psychiatric condition associated with perfectionism and rigid thinking patterns. Investigations of cognitive performance in AN have often focused on related measures. However, comprehensive assessments of cognition in AN have rarely been undertaken and findings have been inconsistent. Therefore, this study utilised a comprehensive cognitive battery to gain a better understanding of cognitive performance in AN.

### Research frontiers
Individuals with AN appear to have largely intact cognitive function, but demonstrate difficulties with complex visuospatial processing.

### Innovations and breakthroughs
Findings in acute AN have rarely utilised a comprehensive set of cognitive tasks and have consequently tended to report conflicting findings. Employing a comprehensive set of cognitive assessments in a group of medically stable patients with acute AN suggests that AN may not be associated with significant cognitive deficits, but with subtle difficulties in manipulating visuospatial information.

### Applications
As only limited cognitive deficits were observed, they may arise from relatively restricted brain regions which may also be involved in the psychopathology of AN.

### Peer-review
The research is interesting and the manuscript is well written.

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