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BRIEF COMMUNICATION

Set shifting deficit in anorexia nervosa

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Abstract

Anorexia nervosa (AN) is a severe mental illness characterized in part by rigid thinking and ritualized behaviors involving eating and weight. Cognitive rigidity may play a role in the perpetuation of symptoms, and may provide information as to important brain-based abnormalities. Neuropsychological studies of patients with AN have shown cognitive dysfunction, but few have focused on cognitive flexibility. This study assessed set shifting in patients with AN, as a measure of cognitive flexibility. In this study, 15 patients with AN were compared with 11 healthy controls using a neuropsychological battery including the Wisconsin Card Sort Test (WCST). While patients with AN did not differ from controls on 5 measures of neuropsychological function, they made significantly more perseverative errors on the WCST, indicating a problem in set shifting. This finding suggests that patients with AN have a specific neurocognitive abnormality that may play a role in the development and persistence of this disorder.
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Keywords: Wisconsin Card Sort Test, Cognition, Neuropsychology, Eating disorders, Cognitive flexibility, Neuropsychological tests

INTRODUCTION

Anorexia nervosa (AN) is characterized by significantly low body weight together with a relentless preoccupation with concerns about body shape and weight. AN is a serious mental illness: the mortality rate is estimated at 5.6% per decade of illness and an average of 30–50% of patients require rehospitalization within one year of discharge (Pike et al., 2003). The clinical phenomena seen in patients with AN include intrusive ideation and stereotyped behaviors suggestive of a cognitive disturbance contributing to perpetuation of the illness. Cognitive deficits have long been described in AN. The most common findings indicate impairment at low weight in attention, short-term memory, verbal and visual memory, and visuospatial construction. While some studies have shown improvement in these areas with weight normalization, other studies have demonstrated persistent impairments (Green et al., 1996; Kingston et al., 1996).

Patients with AN have long been noted to demonstrate high levels of perfectionism and obsessionality (Strober, 1980) that are maladaptive around issues of eating, shape, and weight. The repetitive and stereotyped cognitions and behaviors of patients with AN share features with obsessive-compulsive disorder (OCD). For example, patients may develop specific rules around cutting their food, or around what foods are considered "safe" and "unsafe," and their eating behavior becomes highly ritualized. Even when they express a desire for change, patients demonstrate great difficulty changing these behaviors. These core clinical features raise questions about patients' neuropsychological characteristics and suggest that studies of cognitive flexibility, defined as the ability to change mental sets or responses, would be of interest.

One model of AN (Steinglass & Walsh, in press) posits that the inability to alter these perseverative eating behaviors is an important clue to the mechanism of perpetuation of AN. This model proposes that, as in a model of the

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neurobiology of OCD, these behaviors are mediated by nondeclarative learning, which is mediated through corticostriatal circuits (Graybiel & Rauch, 2000). Neuroimaging findings consistent with this hypothesis include structural (Husain et al., 1992) and metabolic (Delvenne et al., 1999) differences in the striatum in patients with AN compared to controls, and differences in dopamine receptors in the striatum in patients with a history of AN compared to controls (Frank et al., 2005). While these findings do not necessarily clarify the etiology of AN, they suggest that neurocognitive studies may identify brain-based abnormalities that underlie the perpetuation of eating disordered behaviors.

The few studies that have addressed cognitive flexibility in AN are provocative. One group has conducted several studies in patients with AN, using cognitive and perceptual tasks (Tchanturia et al., 2001, 2002, 2004). In the perceptual tasks, balls of different sizes were placed in the hands of participants with closed eyes, and the participants were asked to indicate the relative sizes of the balls. The extent to which a participant's response was influenced by prior presentations suggests cognitive rigidity. In the cognitive task, participants were presented with a story in which they were asked to complete the initial letter for certain words (i.e., "_at" could be "cat" or "bat"). The extent to which participants erroneously chose a letter from the previous portion of the story suggests cognitive rigidity. In the first study, the perceptual task was administered to 15 patients with AN, 15 patients with bulimia nervosa (BN), and 28 healthy controls. Patients with AN and BN made more perceptual errors than controls (Tchanturia et al., 2001). These findings were replicated in a larger sample, using both the cognitive and perceptual tasks (Tchanturia et al., 2004). In this study, patients with AN ($n = 34$) and BN ($n = 19$) made more errors than controls ($n = 35$). The same group compared both tasks in a group of acutely ill, underweight patients with AN ($n = 30$), a group of patients recovered from AN ($n = 16$) (defined as stable weight and regular menses for 1 year), and healthy controls ($n = 23$). Both acutely ill and recovered AN patients showed significantly poorer performance on both tasks compared to controls (Tchanturia et al., 2002).

The current study assesses cognitive flexibility with a more commonly used measure, the Wisconsin Card Sort Test (WCST) (Berg, 1948), which has been widely used in psychiatric populations as an assessment of executive functioning and cognitive flexibility, and set shifting in particular. Notably, this task has not been well studied in AN. A single study by Fassino et al. (2002) administered the WCST to 20 patients with AN and 20 healthy controls and reported that patients with AN performed less well, making more errors and achieving a significantly lower number of categories of classification. Patients in this study were underweight at the time of assessment, and demonstrated impaired attention, which may have influenced performance.

The goal of the current study is to assess cognitive flexibility and set shifting in AN, using the WCST. This study included patients at different stages of illness to better evaluate core problems in the disorder.

METHODS

Participants were patients with AN ($n = 15$), and healthy volunteers ($n = 11$). All participants were women. In the patient group, 10 out of 15 were inpatients whose body mass index (BMI) ranged from 17.7 kg/m^2 to 20.2 kg/m^2. Five were studied as outpatients, with BMI ranging from 16.7 kg/m^2 to 19.8 kg/m^2. Participants were screened using a semi-structured interview for Axis I pathology Structured Clinical Interview for DSM-IV (SCID-I; First et al., 1995) and a semi-structured interview to assess eating disorder pathology in detail (Eating Disorder Examination; Fairburn & Cooper, 1993). Because of symptom overlap between disorders, patients with AN often meet criteria for depressive or anxiety disorders, therefore these participants were not excluded. Participants were excluded if they had an Axis I disorder that required treatment in addition to treatment of AN. At the time of entry into treatment at the Eating Disorders Research Clinic, patients met DSM-IV criteria for AN. Patients who were menstruating were included, as amenorrhea does not increase the specificity of the diagnosis of AN. All participants were medically stable. This study was approved by the New York State Psychiatric Institute Institutional Review Board, and all participants gave written informed consent.

Participants were administered a neuropsychological test battery and self-report questionnaires. The test battery included the Weschler Abbreviated Scale of Intelligence (WASI), the California Verbal Learning Test (CVLT), the Stroop test, the Trail Making Test, Parts A and B, the Controlled Oral Word Association test (COWA), and the Wisconsin Card Sort Test (WCST). The WASI provided an estimate of IQ, as well as verbal and performance IQ estimates. Attention was measured by the Stroop and the Trail Making Test. Explicit memory was measured by the CVLT short-term and long-term recall scores. In addition, the COWA measured verbal fluency. The self-report questionnaires measured symptom severity. These included the Beck Anxiety Inventory (BAI) for anxiety symptoms, the Beck Depression Inventory (BDI) for depressive symptoms, and the Eating Disorder Inventory (EDI). The EDI is a standard, self-report questionnaire about eating disorder symptoms that measures drive for thinness, perfectionism, maturity fears, bulimia, body dissatisfaction, ineffectiveness, interpersonal distrust, and interoceptive awareness.

Cognitive flexibility was assessed using the WCST (Computer Version 4, Psychological Corporation). Participants are instructed to match stimulus cards with one of four category cards. The category cards include a single red triangle, two green stars, three yellow crosses, and 4 blue circles. Thus, the correct matching rule could be color, number, or shape. The participant receives feedback after each trial as to whether they have matched the card correctly. However, the correct sorting rule changes unpredictably

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during the course of the task. The version administered uses 128 stimulus cards.

Data were analyzed using SPSS (SPSS version 12.0.1). Given the hypothesis that patients with AN have a problem in set shifting, the primary outcome measure was performance on the WCST. All other comparisons were secondary analyses. Comparisons between groups were made using the independent samples *t* tests. The alpha level was set at $p = .05$.

RESULTS

The mean duration of illness among patients with AN was 10.8 ± 5.8 years. The mean BMI of patients with AN was 19.0 ± 1.0 kg/m^2, whereas normal controls mean BMI was 22.1 ± 1.8 kg/m^2. Clinical characteristics and measures of neuropsychological function of patients and controls are summarized in Table 1. Patients and controls did not differ in age, years of education, or estimated IQ. As expected, patients differed from controls on all symptom measures, including BAI, BDI, and EDI.

The results from SCID-I at the time of testing showed that 9 patients (60%) had no other Axis I diagnosis. Two patients met criteria for current major depression (13%) and 1 patient (7%) met criteria for dysthymia. Four patients (27%) met criteria for an anxiety disorder. Of these, one patient met criteria for social phobia and obsessive-compulsive disorder, one met criteria for post-traumatic stress disorder and generalized anxiety disorder, one met criteria for generalized anxiety disorder only, and one met criteria for post-traumatic stress disorder and social anxiety disorder.

On the neuropsychological tests, patients and controls did not differ on measures of attention, memory, or verbal fluency (see Table 1). However, on the WCST, patients made significantly more errors than controls, and had significantly fewer correct responses (see Table 2). Patients made significantly more perseverative errors, but the difference in nonperseverative errors was not significant. Perseverative errors occur when the participant persists in attempting to make a match using the prior category matching rule. Comparing the scores to age and education matched norms, the control group score for perseverative errors was in the 53rd percentile, whereas the patient group was in the 36th percentile (mean). In the patient group, none of the WCST measures were significantly correlated with BMI, or with scores on the EDI, BDI, or BAI.

Anorexia nervosa is defined, in part, as weight less than 85% of ideal, which corresponds approximately to a BMI of 18.5 kg/m^2. In the patient group, 3 of the participants were underweight at the time of testing. Therefore we reanalyzed the data including only the 12 patients whose BMI's were greater than 18.5 kg/m^2. The differences between patients and normal controls persisted. Patients had a mean total correct of 69.5 ± 9.6 *versus* controls 79.9 ± 7.6, $t(21) =$

Table 1. Clinical characteristics and neuropsychological function

	Normal Controls ($n = 11$) Mean ± *SD*	Patients ($n = 15$) Mean ± *SD*	*t*	df	*p*	Cohen's *d*
Clinical Characteristics						
Age (yrs)	24.0 ± 3.1	25.6 ± 6.0	−0.81	24	.424	−0.34
Education (yrs)	16.6 ± 2.0	15.3 ± 1.9	1.75	24	.093	0.67
BMI (kg/m^2)	22.1 ± 1.8	19.0 ± 1.0	5.40	24	.000	2.13
Beck Depression Inventory	1.7 ± 1.8	21.0 ± 13.2	−4.74	24	.000	−2.05
Beck Anxiety Inventory	4.3 ± 3.7	13.8 ± 11.3	−2.52	20	.020	−1.13
Eating Disorders Inventory	13.9 ± 14.2	86.9 ± 43.6	−5.35	24	.000	−2.25
Neuropsychological Tasks						
Estimated IQ	115.5 ± 6.6	109.8 ± 12.1	1.40	24	.174	0.58
Estimated Verbal IQ	113.6 ± 5.6	111.3 ± 11.3	0.61	24	.545	0.26
Estimated Performance IQ	113.5 ± 8.9	105.7 ± 14.6	1.55	24	.135	0.65
Stroop, Interference Score	0.18 ± 6.5	3.9 ± 7.6	−1.24	20	.231	−0.53
COWA	45.6 ± 8.7	49.5 ± 11.3	−0.96	23	.349	0.39
COWA repetitions	0.45 ± 0.7	0.64 ± 1.1	−0.50	23	.620	0.21
Trails A	22.9 ± 5.8	25.5 ± 7.6	−0.95	24	.350	−0.38
Trails B	45.9 ± 15.5	54.8 ± 27.6	−0.96	24	.347	−0.40
Trails test ratio B:A	2.0 ± 0.4	2.1 ± 0.8	−0.44	24	.662	−0.16
CVLT, immediate recall	53.0 ± 7.3	54.8 ± 7.1	−0.63	24	.533	−0.25
CVLT, short delay recall	12.4 ± 2.5	12.5 ± 1.8	−0.21	24	.839	−0.05
CVLT, long delay recall	12.5 ± 2.5	13.0 ± 2.2	−0.58	24	.564	−0.21
CVLT, learning score	1.4 ± 0.42	1.5 ± 0.70	−0.23	24	.821	−0.17
CVLT, total repetitions	3.8 ± 2.7	3.9 ± 3.2	−.098	24	.923	−0.03

Note. BMI = Body Mass Index, COWA = Controlled Oral Word Association, CVLT = California Verbal Learning Test. The following data are missing: for BAI, one control and three patients; for EDI, one control; for Stroop, one control and three patients; and for COWA, one patient.

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Table 2. WCST results of patients with AN and controls

	Normal Controls ($n = 11$) Mean ± *SD*	Patients ($n = 15$) Mean ± *SD*	*t*	df	*p*	Cohen's *d*
Trials administered	85.5 ± 14.9	98.6 ± 20.1	−1.83	24	.080	−0.74
Total correct	79.9 ± 7.6	69.7 ± 8.8	3.08	24	.005	1.24
Errors, Total	15.3 ± 7.5	28.9 ± 20.8	2.06	24	.050	−0.87
Errors, Perseverative	8.2 ± 3.7	13.8 ± 7.7	2.23	24	.035	−0.93
Errors, Nonperseverative	7.1 ± 4.3	15.1 ± 14.1	1.80	24	.084	−0.77
Categories completed	6.0 ± 0.0	5.4 ± 1.4	1.41	24	.172	0.61
Trials to complete 1st category	13.1 ± 5.1	12.8 ± 3.0	0.18	24	.291	0.07

2.86, $p = .009$. Patients mean perseverative errors were 14.9 ± 8.1 compared to controls 8.2 ± 3.7, $t(21) = -2.52$, $p = .020$. In addition, patients total errors differed significantly from controls, mean = 31.3 ± 22.5 *versus* controls 15.3 ± 7.5, $t(21) = -2.26$ $p = .035$.

DISCUSSION

In this study, patients with AN showed a problem in cognitive flexibility despite otherwise normal cognitive functioning. More specifically, patients' poor performance on the WCST can be attributable to set shifting difficulties, indicating that patients were less able than controls to adjust to changing rules. As some studies have linked set shifting in the WCST to activation in the prefrontal cortex and the ventral striatum (Monchi et al., 2001; Shafritz et al., 2005), these results are consistent with a model of AN involving abnormalities in corticostriatal circuits (Steinglass & Walsh, in press). This study is also consistent with the work of Tchanturia et al. (2002) who reported cognitive rigidity in patients with AN and recovered from AN. Furthermore, these results confirm the findings of Fassino et al. (2002) and extend them to show that deficits are not exclusive to the underweight state.

Interestingly, in this study patients did not differ from controls on measures of cognitive rigidity that focus on perseveration (Trails B, CVLT, or COWA repetitions). The Trails B task relies on multiple cognitive domains and cognitive flexibility is not necessarily the primary determinant of performance (Lezak et al., 2004). Similarly, repetitions on the CVLT and COWA are reflective of perseveration more than set shifting. The WCST is a purer measure of set shifting, thus these findings further support the hypothesis that the problem in AN is specific to set shifting.

In the current study, even patients with AN whose weights had been restored to the normal range exhibited poorer performance in set shifting relative to controls. The presence of a cognitive problem at normal weight, and in the absence of attention deficits, suggests that there may be neuropsychological disturbances in AN that are not attributable simply to being underweight. Set shifting problems may be a neuropsychological correlate of the traits of rigidity and perfectionism observed in patients with AN. Such problems may be an effect of prior starvation, or suggest a preexisting predisposition to development of AN. In this sample, we were unable to demonstrate a correlation between EDI scores and performance on the WCST. This may be due to the truncated range of EDI scores in this small sample size. Regardless, a set shifting problem may be important in understanding the perpetuation of behaviors and the high relapse rate. In future study it would be interesting to know if a set shifting problem in patients with AN correlates with clinical phenomena that may be related to cognitive rigidity, such as obsessionality and perfectionism.

Several patients in this study met SCID criteria for depressive or anxiety disorders. Abnormalities on the WCST have been shown in many psychiatric populations; however, the neuropsychological deficits tend to be more extensive. In studies of patients with major depression, the WCST deficits occurred in the presence of other deficits (Grant et al., 2001), or were associated with poor performance on all measures of the WCST (Merriam et al., 1999). There are fewer reports of the use of WCST in patients with anxiety disorders, but the published findings do not indicate a problem in this population (Sachs et al., 2004). It is particularly intriguing that, in the current study, problems were observed in a population of patients who demonstrated normal performance on all other cognitive tasks, and that the problem in WCST performance related specifically to perseveration. The pattern of problems, and the absence of a correlation between depression and anxiety scores and WCST performance, suggests that the findings in this study cannot be explained simply by the presence of comorbid disorders.

While the findings of this study are suggestive, the study is limited in several ways. As with many studies of neuropsychological performance in AN, the sample size is small. In addition, while many of the participants are weight restored, they were not at normal weight for sufficient time to be considered fully recovered. The high EDI scores in this sample indicate that these patients continue to have psychological symptoms. Thus, these findings do not fully address the question of whether cognitive rigidity in AN is a "state" or "trait" impairment. Further studies are needed

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to expand the sample size and to directly compare patients at low weight with patients who have recovered from AN, to confirm that set shifting problems are not an artifact of starvation.

Nonetheless, this study demonstrates poor performance by patients with AN on a task of set shifting. This population of patients with AN did not differ from controls in attentional ability, or verbal memory, indicating that global cognition was intact. Set shifting difficulty in patients with AN suggests the possibility of an underlying brain-based abnormality that may help to explain patients' difficulty with changing established cognitions and the stereotyped, ritualized eating behavior patterns that are particularly maladaptive. Further study in a larger sample and involving functional neuroimaging is needed to investigate whether set shifting dysfunction in this population correlates with abnormalities in corticostrial circuits. In addition, further neurocognitive research to explore and elaborate these specific problems over the course of the illness is needed to elucidate their possible role in the development and persistence of AN.

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