

Neuropsychological Studies in Anorexia Nervosa

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ABSTRACT

Neuropsychological findings in eating disorders are somewhat inconsistent. This may be because individual studies have used a broad range of tests on relatively small, heterogeneous clinical groups, thus limiting the detection of subtle neuropsychological differences in these patients. Therefore, rather than using broad assessments of a variety of neuropsychological functions, adoption of a more focused, hypothesis-driven approach based on clinical practice is proposed. This will allow more in-depth investigations of

targeted functions and will improve the chances of detecting a problem, of exploring its ecologic validity, and of tailoring a treatment. We have demonstrated this approach using our neuropsychological studies of cognitive flexibility in anorexia nervosa (AN). © 2005 by Wiley Periodicals, Inc.

Keywords: neuropsychology; anorexia nervosa; ecological validity; cognitive flexibility

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Introduction

Neuropsychological tests were developed originally to assess the effects of brain lesions or trauma, but increasingly are being used to examine psychiatric populations for which neuropsychological impairments are likely to be much less severe. Furthermore, neuropsychological tests are now being used to assist with diagnosis, to obtain quantifiable data on the condition, and to develop treatment plans. Therefore, it is timely to reflect on how these neuropsychological tools should be used in the future, particularly for individuals with anorexia nervosa (AN). We have reviewed our own and other data on neuropsychological developments in AN.

Research Studies in Psychiatric Patients Including Those With AN

In psychiatry, neuropsychological testing has typically been directed towards some aspect of cognitive ability. The value of this approach in individuals with psychiatric disorders is relatively well established.¹ This is apparent in several comprehensive reviews of

neuropsychological findings in different psychiatric disorders. For example, Heinrichs and Zakzanis² reviewed 204 studies of schizophrenia and reported moderate to large effect sizes in 22 neurocognitive tests, indicating broad cognitive impairment in schizophrenia with varying degrees of deficit in all ability domains measured by standard neuropsychological tests. Conversely, in a recent systematic review of studies of cognitive impairment in obsessive-compulsive disorder (OCD), it was concluded that there is no clear and specific neuropsychological profile for the OCD patient group, but there is some evidence for dysfunction in visuospatial memory and verbal memory when tasks require effortful encoding strategies. For example, in studies assessing executive functioning such as fluency, set-shifting, planning, and problem-solving abilities, contradictory results have been obtained.^{3,4}

A search of the literature using the terms *neuropsychology*, *anorexia*, *cognitive performance*, and *executive functions* in PsycInfo, Medline, and Web of Science, together with a manual search of specialist eating disorders journals, identified 36 articles of specific relevance to this review. The conclusions that can be drawn are constrained by the fact that there are a number of methodologic limitations inherent in the reports. Basically, there is no consensus on the existence of neuropsychological impairment in AN even though several lines of research indicate that it is accompanied by neurobiologic (e.g., structural) abnormalities.^{5–8} This apparent absence of consistent reports of neuropsychological impairment in AN may reflect the true situation or, alternatively, may reflect the fact that there have been fewer neuropsychological studies of eating disorders than of other major psychiatric disorders. In addition, it may also be

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related to the fact that there is a lack of consistency in the design of the studies, in terms of patient sample (case-control, cross-sectional, or longitudinal) and methodology (e.g., the tests employed to measure the same function). Diagnostic issues are particularly problematic, as 44% of the reviewed studies were published before the introduction of the 4th ed. of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, Washington, DC, 1994) and the transition to the separation of patients into diagnostic subtypes. In addition, some studies suffer from design weaknesses, including small sample sizes, leading to inadequate statistical power, or failure to define case status or recovery. Furthermore, only 12 studies used a follow-up design to investigate whether weight gain affects cognitive performance and only two reported data obtained from long-term recovered patients.⁹

Several comprehensive reviews have focused on neurocognitive functioning in AN.¹⁰⁻¹² For example, Braun and Chouinard¹⁰ set the scene by introducing the question: "Is AN a neuropsychological disorder?" and cautioned that large studies and twin data would be necessary to establish whether neuropsychological characteristics are trait or state characteristics. Touyz and Beumont¹² compared AN and bulimia (BN) patients and found no difference in neuropsychological performance between these groups. More recently, Lauer¹¹ observed that the most robust neuropsychological findings in eating disorders relate to attentional deficits involving selective attention (enhanced distractibility) and flexibility/ inhibition functions (response selection). Lauer noted that only 40% of patients show impairment in these domains and that those individuals do not differ in terms of clinical characteristics from those without such deficits. Furthermore, these authors reported that such neurocognitive impairments tended to disappear in parallel with weight restoration.

Some general limitations exist throughout most of the neuropsychological research conducted on individuals with eating disorders, namely, that most studies have used a broad range of different neuropsychological tests and have involved AN groups that have varied in their clinical severity. Some of these issues make it rather difficult to compare findings and to make generalized statements. One way of overcoming this is to focus research on targeted hypotheses and to investigate a specific neuropsychological function in depth using various tests, rather than looking at all the functions with a single test that might not be sufficiently sensitive to detect differences in an AN population. It is also important to define the clinical groups in a standardized way.

Neuropsychological Issues in AN

A review of the literature shows that a number of questions remain only partially addressed. We have highlighted these questions and discussed the limited extant research that addresses them.

To what extent are neuropsychological impairments in AN due to a malfunction of specific neurologic systems, or represent suboptimal performance as a consequence of more subtle neuropsychiatric dysfunction? Evidence from studies using the Stroop test suggests there are attentional biases in relation to body and weight stimuli in AN,¹³ but it seems likely that these are perturbations in homeostatically constructed normal neural mechanisms, rather than fundamental malfunctions of neurocognitive modules. Alternatively, the discovery of specific impairments in executive function may be due to a more specific neural abnormality.

Are neuropsychological characteristics reflective of traits that are genetic and/or have emerged neurodevelopmentally or are they state related? Trait characteristics should be largely invariant and remain after recovery from illness. Some studies have reported that in acute underweight AN subjects, there is mild impairment in skills such as short-term verbal and visual memory, visuospatial construction problem solving, and reaction time, but that after weight recovery, these cognitive deficits diminish.¹⁴⁻¹⁶ In contrast, however, Green et al.,¹⁷ Kingston et al.,¹⁸ and Tchanturia et al.¹⁹ have not observed such improvements in cognitive function after recovery. Thus, whether these neuropsychological deficits are state or trait related remains unresolved. It is clear that there is a need to investigate neuropsychological function in patients who attain full psychiatric recovery (i.e., recovery should not simply be defined in terms of weight gain).

How can we establish if neurobiologic abnormalities exist premorbidly, and explore whether they are antecedents for AN or are a consequence of the illness? Evidence suggests that there are both neurologic impairments²⁰ and brain structural abnormalities in AN. However, even if structural brain changes can be demonstrated in AN, the functional correlates of these may be more difficult to ascertain. For example, in a recent study, we have reported decreases of approximately 10% in hippocampal volume in AN subjects but that it is not accompanied by neuropsychological changes in hippocampal function.²¹ Currently, attempts are being made to address such issues related to structure and function using neuroimaging techniques in combination with psychological tools. For example, in our functional Magnetic Resonance Imaging (fMRI) studies,²²⁻²⁴

brain reactivity to photographs of high-calorie foods differentiates women with eating disorders from controls. There are three main findings. First, BN and AN subjects share an abnormal reaction to food in the orbitofrontal (OFC) and anterior cingulate cortices (ACC). It is noteworthy that the OFC and ACC are involved in emotional processing^{25,26} and that abnormal activations in these areas are found in response to disease-related stimuli in OCD²⁷⁻²⁹ and addiction,³⁰ two conditions with symptom overlap with eating disorders. Second, in patients with eating disorders, reactivity to food stimuli in lateral associative cortical areas (parietal, lateral prefrontal) is decreased compared with controls. This is especially so in BN patients who show markedly decreased reactivity to food in the lateral prefrontal cortex. As the lateral prefrontal cortex is involved in inhibition and suppression of undesirable behaviors, we interpreted this as corresponding to a lack of control over eating. Finally, women with long-term recovery from AN showed greater lateral and apical prefrontal reactivity to food than age-matched chronic patients. One hypothesis is that this increase in functionality of these regions is associated with therapeutic change. What will be necessary in the future will be longitudinal neuroimaging studies of eating disorder participants as these have the potential to address issues related to cause and effect. Another approach will be to examine unaffected twins and/or siblings.

What are the clinical implications of neuropsychological research in AN? Understanding the neural underpinning of cognitive dysfunction in AN will increase our theoretical knowledge in a general way, but may also provide insights into the day-to-day functioning of people with AN. Currently, relatively little work has been done on neuropsychological rehabilitation in psychiatric patients. To obtain this information, it will be necessary to conduct studies using "ecologically valid" procedures, in other words, laboratory-based tests that attempt to simulate "real world" cognitive demands. In this way, neuropsychological deficits can be defined in terms of disability, with the possibility that new forms of treatment will take this into account. This will mirror developments in the management of other neuropsychiatric disorders.

Studies of Cognitive Flexibility in AN

We have not yet addressed all four of the critical issues outlined above. However, our ongoing neuropsychological studies have begun to address them.

Our research has been based on the observation that people with AN show, as core features, high harm avoidance, inflexibility of thinking, rigid behaviors around eating, and high perfectionism.³¹ In addition, neuropsychological studies have highlighted a tendency to be inflexible on cognitive tasks and an inability to change past patterns of thinking. These features can be conceptualized as difficulties in set-shifting and we hypothesized that people with AN would demonstrate this inflexibility in an experimental setting. Set-shifting ability is essential for cognitive-behavioral flexibility, allowing the adaptation of behavior in line with changing demands of the environment. Problems in set-shifting may manifest in a variety of forms related to cognitive inflexibility (e.g., concrete and rigid approaches to problem-solving and stimulus-bound behavior) and response inflexibility (e.g., perseverative or stereotyped behaviors). The hypothesis was supported in a series of studies conducted by our group (Table 1). We began with a simple perceptual test, the Haptic illusion task, to establish if people with AN would demonstrate set-shifting difficulties in the perceptual domain.³² We eliminated the possibility that the observed difficulties were due to a broader difficulty on perceptual tasks, as suggested by Grunwald et al.,^{33,34} by conducting a study using both cognitive and perceptual set-shifting tasks. We found that set-shifting difficulties observed in AN were not restricted to the perceptual domain. Furthermore, set-shifting difficulties were also evident in individuals long-term recovered from AN.³⁵ These initial studies suggested that these features are not purely a function of the acute illness state. Subsequently, we developed a broader battery of set-shift tasks, applied to a larger sample of individuals with eating disorders, to explore the specificity of our findings. Broad set-shifting difficulties were evident in individuals with AN both during the acute phase of the illness and after weight restoration (longitudinal data).³⁶ It is noteworthy that a separate comparison between individuals with acute AN and long-term recovered patients (cross-sectional data)¹⁹ showed that normal performance was only present in a subsample of the set-shifting tasks in the long-term recovered group.

We have also extended this research using the same neuropsychological tests in sister pairs discordant for AN. Results suggest that difficulties in set-shifting are shared by the healthy sisters of those with AN.³⁷ This observation raises the intriguing possibility of set-shifting representing a potential endophenotype for genetic studies of AN.

Because of the conceptual similarities between neuropsychological measures of inflexibility and

TABLE 1. Cognitive flexibility in AN: studies by our group over the past 5 years

Study	Tests Employed	No. and Groups of Participants	Age (years)	BMI	Case-Control/Follow-Up	Core Findings
Tchanturia et al. ³²	Perceptual illusions	15 AN 15 BN 28 HC	28.1 25.1 28.2	14.1 20.0 22.3	Cross-sectional	AN and BN had higher perceptual rigidity vs. controls.
Tchanturia et al. ³⁵	Perceptual illusions Cognitive shift	30 AN 16 AN Rec 23 HC	25.2 30.0 27.6	14.6 20.1 21.3	Cross-sectional	AN acute and AN Rec had high perceptual and cognitive rigidity.
Tchanturia et al. ³⁶	Perceptual illusions Cognitive shift Trail making A,B Brixton Picture set	34 AN 19 BN 35 HC	26.7 26.5 24.8	13.7 21.8 21.8	Cross-sectional	AN (acute) demonstrated a wider range of set-shifting difficulties vs. BN and control groups.
Tchanturia et al. ³⁶	Perceptual illusions Cognitive shift Trail making A,B Brixton Picture set	34 AN 18 AN Rec 36 HC	27.2 28.4 25.9	13.7 20.4 21.8	20 patients were followed up after weight gain (inpatient program)	AN and AN Rec had high perceptual rigidity. In cognitive shifting, the AN Rec group was doing better than the AN acute group. Childhood perfectionism was highly associated with inflexibility.
Holliday et al. ³⁷	Perceptual illusions Cognitive shift Trail making A,B Brixton Picture set	47 AN 47 sisters 47 nonrelated controls	26.3 27.6 26.5	17.9 22.8 22.1	Sister pair and HC	Unaffected sisters had higher levels of perceptual rigidity vs. control group.

Note: AN = anorexia nervosa; AN Rec = anorexia long-term recovered; BN = bulimia nervosa; HC = healthy comparison group; BMI = body mass index. Means of the values are shown.

clinical and empirical observations of a rigid and inflexible personality in AN, we explored the relationship between these constructs. From the viewpoint of premorbid childhood traits, childhood inflexibility was found to be highly predictive (40% using the hierarchical regression backward method) of set-shifting difficulties.¹⁹ However, using the temperament scales from the Temperament and Character Inventory revised (TCIR),³⁷ no strong relationship between personality and neuropsychological performance was observed, although harm avoidance had a small effect (12% using regression modeling with standard errors). Therefore, we have concluded that measures of personality vary in the extent to which they tap the features assessed by the neuropsychological tests, with childhood inflexibility showing the strongest association with the variables tested to date.

From the consistent results we have obtained showing reduced cognitive flexibility in AN, we are investigating the efficacy of a flexibility intervention program in an inpatient treatment setting. Our preliminary observations indicate that feedback on neuropsychological assessment and cognitive remediation using a flexibility module is

beneficial for people with AN at a severe stage of illness if they have problems with set-shifting tasks.

Conclusions

There is a general consensus that there are no gross neuropsychological deficits in AN. Reported deficits such as cognitive rigidity are likely to be subtle and may be difficult to formally demonstrate with tools that have been developed for research/assessment of patients with severe brain lesions. Therefore, we propose the adoption of an experimentally driven approach rather than of the use of broad assessments of neuropsychological function. This approach will require the use of substantial sample sizes that will (a) allow the identification of subtle neuropsychological deficits, (b) enable deficits to be related to clinical symptomatology, and (c) establish potential relationships with personality measures and/or biologic measures. By integrating this approach into a longitudinal design, it will also be possible to address issues of state versus trait. This might be followed

by ecologically valid paradigms to examine how putative neuropsychological deficits affect daily functioning and, ultimately, the development of focused intervention programs based on research evidence.

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