Neuropsychological Aspects of Eating Disorders

Nancy Zucker, PhD; Ashley Moskvich, MA; and Adrienne Soo

EDUCATIONAL OBJECTIVES

1. Describe the temporal stages of attention and how they relate to clinical symptom expression in eating disorders.

2. List assessment tools appropriate for the measurement of visually guided attention in eating disorders.

3. List the most frequently documented deficits in neuropsychological functioning in anorexia nervosa.

There have been impressive advances in the study of neurocognition in those with eating disorders (ED), despite some unique challenges posed by this clinical population. Since eating disorders typically onset in adolescence, an important transitional period in brain development, there is concern that the physical sequelae associated with (or constituting) eating disorders alters prior developmental trajectories; it is important to determine if changes in cognition and behavior are more accurately construed as disease scars rather than pathophysiological markers.

The study of unaffected family members, investigation of those with variable illness duration and at different phases of recovery, assessment of those at different developmental stages, and study of larger sample sizes are helping to establish more thoroughly the robustness of neuropsychological find-
ings. Further, the field has advanced from general neurocognitive batteries to more strategic, hypothesis-driven testing guided by documented aberrations in neurotransmitter systems, disorder phenomenology, and persisting behavioral features characteristic of the diagnosis.

Because the bulk of neuropsychological evidence has been conducted on samples with anorexia nervosa (AN) and a recent review of such findings in those with bulimia nervosa (BN) concluded that no coherent pattern of neurocognitive findings could be discerned, given the limited state of evidence, this review necessarily focuses predominantly on those with AN.

**PERCEPTUAL AND VISUOSPATIAL ABILITIES**

Concerns with symmetry and excessive concern with detail have long characterized the clinical presentation of those with AN. Such clinical features have prompted systematic investigation of the presence of biases in visually guided attention that may affect memory and general function. The construct of weak central coherence has been the most systematically investigated, given the limited state of evidence. According to this model, originally identified in autism spectrum disorders (ASD), visually guided attention is captured or biased by local or feature-based aspects of a stimulus rather than global or configuration-based gestalts.

Early iterations of this model proposed that such local biases may interfere with configuration-based processing. This would lead, in theory, to there being potential implications for deciphering complex social stimuli such as faces, and for extracting prototypes from exemplars. Recent iterations of this model emphasize that such styles of visually guided attention are more accurately construed as a bias and related superiority in extracting local details, rather than a core deficit in gestalt-processing. This latter conclusion was based on evidence that in ASD, global-processing can be obtained depending on the manipulation of task instructions or various contextual variables.

Taking a lead from this body of work in ASD, study of visual perception in ED is at a more preliminary stage limited to characterizing styles of visually guided attention, and defining the robustness of a given style across diagnoses, stages of illness, and in unaffected relatives. A meta-analysis by Lopez and colleagues examined evidence of weak central coherence, summarized results from 16 studies and concluded that data were insufficient to adequately adjudicate the model in AN or BN.

**Impact of Global Bias**

Although there was consistent evidence of performance decrements on tasks that would benefit from a “global bias,” data failed to support superiority in local processing, as has been demonstrated in ASD. Since that review, several studies employing larger samples have been conducted. For example, Tenconi and colleagues examined weak central coherence in a sample of 153 patients with a lifetime history of AN (60 with active illness, 63 weight-restored, 30 with sustained symptom remission) and 28 healthy sisters.

The AN group, regardless of phase of illness or recovery, demonstrated worse performance on tasks that benefit from a global bias (eg, the Object Assembly subtest of the Wechsler Intelligence Scale), and showed decrements in visuospatial memory in the Recall subtest of the Rey Complex Figure, a task consistently employed across laboratories to assess this feature.

The latter task requires the individual to first draw a copy of a complex figure constructed of organizing global elements (eg, a large rectangle) and more detailed non-organizing elements. At 3- and 30-minute intervals, participants are then again asked to draw the figure completely from memory (uncued). Several scoring systems have been devised. The order in which an individual copies and recalls these elements is a way to order biases in visual attention.

The use of local strategies has been proposed to be less efficient, contributing to less visual groupings and, hence, to decrements in visuospatial memory. Accordingly, across stages of illness, Tenconi and colleagues documented both lower scores on the Coherence Index (indicative of more local bias), and worse visuospatial memory in those with AN. No differences between AN subtypes and an intermediate level of difficulty in unaffected sisters were also noted.

Although such findings are suggestive of the persistence of this neuropsychological feature with symptom remission, further study with larger samples is needed to understand both the nature of visually guided attention, the contexts in which a local vs. global bias can be manipulated, and the specific clinical implications of such biases. For instance, whether such biases are related systematically to perceptual or experiential aspects of body image has yet to be established.

Such a link would be critical because disturbance in the experience of the body and somatic preoccupation are hallmark features of those with ED. Clinical features such as feeling fat despite low weight or perceiving one’s physical image as larger than actuality (though data have been mixed) has validity for putative deficits in perceptual, proprioceptive, visuospatial, and kinesesthetic capacities.

Although the most research in this area has focused on attitudinal features toward appearance (eg, body dissatisfaction), there is increasing evidence that such negative experiences may
result from more basic aberrations in sensorimotor processes.

**Sensorimotor Effects**

To date, the estimation of sensorimotor capacities in ED has largely been determined by judgments of stimuli outside the body (eg, grooved pegboard, weighted haptic balls).8 In contrast, the body schema, the sense of the body that initiates and guides behavior, is constituted of one’s direct sense of body experience. For example, Guardia and colleagues9 examined body-scaled actions in adults with AN examining whether they could accurately judge their capacity to fit through an aperture of randomly presented sizes. Those with AN were severely impaired on this task, even though the authors carefully controlled for a general overestimation bias. Degree of impairment also was associated with both duration of illness and body dissatisfaction.

Examination of motor skills and coordinated movements has shown mixed results. Participants from a population-based cohort study of AN demonstrated persisting dysdiadochokinesis up to 10 years post-diagnosis that continued despite weight restoration.10-12 Tchanturia and colleagues have documented difficulties with haptic discrimination in both AN and BN in paradigms designed to examine whether patients could shift sets to experience novel haptic stimuli after habituation to a prior stimulus.13 Bosanac and colleagues14 report persisting motor deficits on a finger-tapping task in patients with both AN and BN irrespective of weight status. However, there have also been a number of studies that show motor-speed improvements with weight restoration.15 Complicating such study is that neuroendocrine changes that often accompany the starved state (eg, changes in leptin) have been reported to alter movement patterns greatly. There is also accumulating evidence that those with AN do not evidence subjective body ownership; patterns of blood-oxygenation levels, measured during functional neuroimaging, indicate that those with AN process images of others in a similar manner to which they process images of themselves.

Although such findings may certainly be a result of “self-conditioning” (ie, repeatedly orienting to oneself and one’s biological needs as objective criteria rather than informative motivational drives), such alterations in perspective may result from more primitive alternations in vestibular, kinesthetic, and proprioceptive senses. Since body image disturbance is the most persistent feature in ED, increasing vulnerability to relapse, it is important to understand the neurobiology and related subjective features beyond attitudes.

**LANGUAGE AND INTELLIGENCE**

Study of intellectual functioning in ED has been limited despite clinical impressions of excessive effort applied to academic pursuits and extreme importance placed on academic achievement. However, the role of effort relative to ability in driving such achievement has been a limited focus of study. Lopez, Stahl, and Tchanturia16 conducted an elegant and comprehensive review and meta-analysis of studies that incorporated a measure of intelligence in those with AN (studies in BN were too limited to perform such a review). Their findings revealed some method variance with estimated IQ. Specifically, studies using the National Adult Reading Test yielded larger effect sizes than those employing various forms of the Wechsler Intelligence Scale. The authors hypothesized that this discrepancy may be due to the various cognitive capacities tapped by these measures.

Although the National Adult Reading Test estimates IQ based largely on verbal abilities, the Weschler scales assesses a broader range of cognitive processes (eg, visuospatial abilities) that have been found to be impaired in AN. Despite such variation, findings were supportive that those with AN have average to above average IQ, relative to population norms and comparison samples. The authors reported a significant trend between the association of body mass index (BMI) and premorbid IQ (lower BMI associated with lower premorbid IQ), but there were not significant associations of BMI with current IQ. Although the number of studies was limited, the authors did a qualitative examination of the relation of IQ and symptoms recovery. They found that the average IQ of recovered samples was significantly greater than population means.

Intelligence can be independent of effort. An early study of adolescents with AN examined achievement relative to IQ scores.17 The authors report higher school achievement than would
be predicted by IQ. While it certainly could be argued that anything that can be achieved is in the realm of that person’s capabilities, one concrete boundary to guide health care providers and caregivers in this regard is that achievement should be constrained by functional limitations — ie, what one can attain without interfering with mental or physical health.

Given documented elevations on trait features in AN, such as perseverance and deficits in executive functioning that may enhance persistence (due to inability to shift sets as summarized below), concrete limitations on effort may be clinically necessary. The relative clinical value of such constraints is an area where neuropsychological findings and clinical interventions may be investigated and integrated.

**TEMPORAL PHASES OF ATTENTION**

The study of executive functioning has been the most widely researched and replicated domain of impairment in neurocognition in ED. Strauss, Sherman, and Spreen define executive functioning as encapsulating “part of a system that acts in a supervisory capacity in the overall hierarchy of brain processing and encompasses skills necessary for goal-directed behavior.”

There has been increased emphasis on diagnostic crossover in those with ED (migrating from one eating disorder diagnosis to another); a transdiagnostic framework for classification in those with ED has repeatedly been proposed. However, data show that there may be differentiation in executive functioning between those whose disorder is characterized by a more dysregulated behavioral style (eg, binge eating with forms of purgative behavior) relative to those who severely restrict their food intake and maintain an unhealthy low weight for a sustained period. Posner and Rothbart divide these temporal phases of attention into alerting, orienting, and executive.

**Alerting**

Alerting refers to achieving and maintaining high sensitivity to incoming stimuli. Such awareness constitutes the state of the individual and likely fluctuates throughout task performance. It also influences such cognitive variables as sustained attention. The study of changes in cognition when an individual is anticipating threat such as ED-related stimuli (eg, anticipating seeing pictures of provocative foodstuffs) has, to our knowledge, not been routinely conducted using neuropsychological testing. Still, the nature of ED poses some interesting considerations for the study of cognitive performance as fluctuations in nutritional status compromise alertness and other cognitive functions.

There has been wide recognition of the possibility of such cognitive alterations during acute phases of starvation in AN; those with ED have unique psychological relationships to states of satiety and hunger that differentially may affect cognition relative to typically developing controls. An example of the attempts to control such state variability is the work of Nikendei and colleagues.

This study compared the performance of those with AN with two control groups: one that fasted before testing, and one that did not. Findings indicated that, on a test of memory recall, those with AN more closely resembled the fasted group. It is unclear, however, whether the directionality of nutrition and cognitive performance operates the same in those with ED. For example, being sated may enhance performance in typically developing controls but compromises executive attention in those with ED due to increases in somatic preoccupation. Future studies of alerting in ED could review the acute effects (or subjective perceived effects) of nutritional deprivation on cognition, as well as performance across the testing session.

Although accumulating research demonstrates the persistence of cognitive impairment with weight restoration in AN, as well as a lack of correlation between many forms of cognitive impairment and BMI, the subjective experience of the individual is not routinely taken into account. As such, patients may subjectively experience a sharpened sense of alertness and enhanced performance when calorically restrained. This experience may add to the reinforcing value of eating disorder symptoms and provide novel targets for intervention — regardless of actual changes in cognition.

**Attention Orienting**

Attention orienting indexes the motivational salience of particular stimuli for a given organism. Studies of attention blindness indicate that although an individual may believe he or she perceives complete information when gazing on complex scenes (as in everyday experience), in fact, much visual information escapes conscious awareness. Thus, what an individual orients atten-
tion to provides important information regarding what that individual considers salient. In ED, as in other psychiatric disorders, the study of attention orienting has focused on the study of attention biases toward illness-related content. Such studies only indirectly address issues of core cognitive deficits or assets, but these investigations highlight the contexts (eg, hunger, emotional arousal) in which cognitive deficits may manifest or become exacerbated. Further, although such biases cannot speak to disorder etiology, they may be relevant for disorder maintenance and, thus, highlight targets for treatment.

Executive Attention

Tests of executive attention in ED often employ illness-related content. For example, the Stroop task has been the most widely used test of cognitive bias in those with ED. Although considered a task of attention bias, it encapsulates other executive capacities such as inhibitory control. In the original version of this task, participants must inhibit a prepotent response of reading a word and instead name the conflicting color ink in which the word is written (eg, the word “red” printed in blue ink). Illness-related variants of this task use words hypothesized to cue illness-related cognitions and affect, and thus, to interfere with processing and hence reaction time (eg, food words, body shape).

A meta-analytic review of attention bias to food stimuli reported small effect sizes in those with AN and medium effect sizes in BN in response to food words using Stroop methodology. However, although these results support differences in the attention processing of illness-relevant stimuli, the results cannot delineate the precise temporal differences in attention (whether those with eating disorder are orienting more to illness-related content or have trouble shifting attention away from such content).

Technological advances have permitted more precise temporal delineation of aberrations in attention orienting. For example, Giel and colleagues examined early attention orienting via use of ocular-tracking methodology. They found no evidence of differences in early stage processing in food stimuli in those with AN relative to controls; however, they found differences in later stages of processing, showing decreased sustained attention to food cues.

Such findings were also reported in several studies employing the dot probe task, a laboratory measure of attention orientation and disengagement in which participants respond to a probe that is placed behind one of two visual stimuli (eg, an illness-related stimuli versus a control stimuli). More rapid speed in responding to the probe reflects a bias toward the stimuli that preceded the probe. A mixed sample of those with ED demonstrated visual avoidance of food pictures with a significant medium effect size. Negative, high-calorie food images caused visually guided avoidance in ED, with a large effect size and visual orienting to low calorie food images, with a medium significant effect size.

Brooks and colleagues concluded that those with ED, regardless of diagnosis, have an attention bias toward food stimuli. Those with AN may not differ from healthy controls in initial orienting to food, but demonstrate greater sensory disengagement/avoidance at the latter temporal stages of emotional processing.

Zucker and Harshaw hypothesize that such sensory disengagement may be compensatory due to aberrations in executive attention. As shifts in attention are one way to regulate arousal/emotional experience, deficits in executive attention may compromise the ability to use such attention shifting as an emotion regulatory strategy. This, in turn, would necessitate or reinforce the use of attention avoidance of motivationally salient (and potentially distressing) contexts.

SET SHIFTING

Aberrations in executive attention have been the most robustly documented deficit in those with ED. The accumulated data provide the most consistent evidence for aberrations in capacities to shift cognitive sets in those with AN. Set-shifting is defined as the ability to move back and forth between tasks, operations, or mental sets. In the largest sample to date, Tchanturia and colleagues examined executive attention in a sample of 216 patients diagnosed with AN; 72 with AN, weight-restoration, and symptom improvement; 69 with BN; and 216 typically developing controls. Performance was examined on the Brixton task, a test that assesses the capacity to abstract rules governing a set of visual stimuli and the capacity to detect and shift strategy when former rules are ineffective.

The study reported deficits across groups, with larger effect sizes in those with purging as a diagnostic feature. Such diagnostic differentiation is consistent to a previous study that showed worse performance on tasks of cognitive control (Stroop) among the binge/purge eating disorder subtype. This study also endorsed temperamental features indicative of deficits in self-regulatory capacities. Patterns of neural activation differed across AN subtypes on a functional neuroimaging task that required behavioral inhibition and executive attention (a go/no-go task). Combined, these results suggest that the binge/purge subtype of AN may evidence greater deficits in executive attention, and that the strategies employed to achieve goal-directed behavior may differ among AN diagnostic subtypes with important implications for the development of intervention methods.
EVIDENCE OF NEUROCOGNITIVE ENDOPHENOTYPE

Deficits in executive attention, specifically the capacity to shift cognitive and/or behavioral sets, has been proposed as a neurocognitive endophenotype of those with ED. An endophenotype is a feature along the path between genotype and phenotype that is quantifiable, meaningfully associated with illness pathophysiology, persists with illness remission, and is seen in biological relatives of the affected individual and conceivably could facilitate gene identification.29 Recent work has examined the persistence of set-shifting during sustained periods of ED symptom improvement and in unaffected relatives. The limited work in this area belies the ability to make definitive conclusions on the persistence of set-shifting deficits, but findings across laboratories are suggestive of both sustained impairment and the clinical significance of these cognitive features.

Roberts, Tchanturia, and Treasure21 examined the persistence of set-shifting deficits across a battery of tasks in a sample of 270 patients, including a sample of unaffected siblings, restricting and binge/purge subtypes of AN who were actively ill who had achieved symptom remission for a sustained duration, and those with BN. Although aberrations in set-shifting were found transdiagnostically, greater impairment was indexed in binge-purging subtype. The recovered group was within normal limits on most tasks, but moderate effect sizes remained evident on the number of categories completed on the Wisconsin card-sorting task, a neuropsychological task of executive functioning. The pattern of deficit in executive functioning differed in siblings of those with BN relative to siblings of AN. Most notable was that although deficits in set-shifting were not associated with BMI, they were associated with a longer duration of illness and ritualized eating behavior.

Using a larger sample with AN, Tenconi and colleagues23 found comparable levels of set-shifting difficulties across subgroups of AN whether actively ill, weight-restored, or with sustained symptom remission. Consistent with Roberts and colleagues,21 unaffected siblings demonstrated worse performance on executive functioning tasks relative to typically developing controls; however, the pattern of impairment was more pronounced.21

‘Tower of London’

Finally, in the longest follow-up study to date, Gillberg and colleagues23 examined cognitive ability 18 years after initial AN diagnosis in a sample of 51 patients with adolescent-onset AN. Results from this population-based cohort study revealed persistent deficits in processing speed on the Tower of London task, a test of executive functioning in which participants are asked to build a tower structure from a set of disks placed in a designated starting position. The goal is for the participant to build the tower in as few moves as possible while following certain constraints; it is a task that requires planning, behavioral inhibition, and the capacity to follow guidelines. Several indices of planning style are provided, such as time to initiate the first move, total processing speed, and error scores. Those with AN were significantly slower than typically developing controls to execute goal-directed behavior.

The theme of processing speed is noteworthy. The study by Roberts and colleagues21 controlled for processing speed, and consequently, perhaps, only reported differences on the Trail-making test, a measure of behavioral and cognitive set-shifting, in those with active BN and unaffected sisters of patients with BN. In contrast, Tenconi and colleagues6 did not control for processing speed and documented deficits in those with AN across the temporal spectrum from active to robustly recovered. Future studies may benefit from probing the limits of neurocognitive function by manipulating contextual variables such as task speed to discern whether performance in more real-world contexts (as when multiple streams of data rapidly change) is compromised.

Such persistent attention deficits in those with ED suggest overlapping neurocognitive deficits and diagnostic comorbidity with psychiatric disorders such as attention-deficit/hyperactivity disorder (ADHD) or attention-deficit disorder. Of importance, investigation of bulimic behaviors (eg, body dissatisfaction, purgative behavior, and binge eating) was conducted as part of a longitudinal study examining 337 boys and 95 girls with ADHD and 211 boys and 53 girls without ADHD.29 Reassessment occurring in mid-adolescence (mean age, 16.4 years), 8 years after original recruitment, revealed elevated bulimic symptomatology among adolescents with ADHD relative to matched controls. Childhood impulsivity, as opposed to hyperactivity or inattention, best predicted adolescent BN symptoms, particularly for girls. Among youth with ADHD, treatment received during the follow-up period was not associated with BN pathology.

MEMORY

Most memory studies in those with ED have focused on the content rather...
er than the components of memory. There have been excellent reviews largely confirming memory biases for illness-related content in those with AN and BN. Such findings demonstrate that illness-related content facilitates memory storage and acquisition, which may be a contributing illness maintenance factor. Furthermore, if the storage and acquisition of neutral content is impaired, then ED symptoms may be promoting an experience of enhanced cognition (ie, improvements in memory), which may further reinforce disordered behavior.

General deficits in memory have long been postulated in AN as hypercortisolemia, a neuroendocrine feature associated with starvation that has been shown to affect memory and learning in other clinical conditions. In addition, reduced hippocampal volume, a key neural structure in neural circuits implicated in memory and learning, has been demonstrated in AN. There is accumulating evidence of deficits in working memory in those with AN. Working memory refers to the short-term, limited capacity storage of information with deficits in working memory indicating a reduced memory span or rapid loss of new information. Gillberg and colleagues reported that working memory correlated with global outcome in their 18-year follow-up study of those with AN; the proportion of those with AN with a memory index less than 85 had a significantly worse global outcome.

Castro-Fornieles and colleagues examined working memory in adolescents with AN during the acute ill state and following weight restoration (approximately 7 months later). Although ill, those with AN demonstrated increased metabolism in distributed neural circuits implicated in memory and learning, a pattern of activation that was negatively correlated with BMI and that remitted with weight restoration. The authors interpreted this pattern as indication that those with AN worked harder to remember while ill.

This interpretation is notable considering the phenomenology of ED, disorders characterized by extreme self-focus. Disorders such as AN and BN share conceptual, neurobiological, and elevated comorbidities with anxiety disorders more generally, but EDs are somewhat unique in that the primary object of their fear is an omnipresent stimulus: the body. Thus, it is interesting that several studies of working memory in AN examining the role of illness-related distracters or the degree of intrusive illness-related cognitions on working memory have found that both impaired working memory capacity. It is conceivable that working memory deficits are related to, or secondary to, deficits in executive attention, as patients have difficulty disengaging from the illness-related content (ie, their bodies) which constrains working-memory capacity.

CONCLUSION
Patterns of neuropsychological assets and deficits may help in the development of focused intervention strategies and inform disorder pathophysiology. For instance, Gillberg and colleagues describe two patterns of neuropsychological deficits in their 18-year follow-up study, one characterized by working memory deficits and another group that evidence longer processing time and worse performance on tasks of social perception. Both groups had worse outcomes relative to groups without these patterns. Yet, several studies do not find evidence of neuropsychological deficits — or find that neuropsychological impairment improves with weight restoration. To date, such diverse findings equal a lack of consensus over whether neuropsychological deficits identify a particularly high-risk group, or whether early identification and treatment can improve neurocognitive capacities. Larger samples and longitudinal studies are needed to address these issues. However, findings point to the importance of neuropsychological assessment in informing the clinical presentation of those with ED.

REFERENCES
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