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Restrictive Anorexia Nervosa And Set-Shifting in Adolescents: A Biobehavioral Interface

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Abstract

PURPOSE—Set-shifting is a neurocognitive concept defined as the ability to switch tasks flexibly. Set-shifting scores are worse in adults with Restrictive Anorexia Nervosa (AN-R) than in controls. Adolescence is a developmental period when young people must respond flexibly to new situations. The purpose of this study is to compare the set-shifting scores of 24 adolescent females with AN-R and 37 matched normal adolescent controls (ages 14–20).

METHODS—Methods included sociodemographic, psychological and biologic data, and neurocognitive testing using the Behavior Rating of Executive Function – Self- and Parent-Reports, the Cambridge Neuropsychological Automated Battery, and the Wisconsin Card-Sorting Test. Statistical analyses included t-tests, multiple analysis of variance, and correlations.

RESULTS—Study and control subjects were similar on sociodemographic data and intelligence quotient. There were differences in Body Mass Index and the Eating Disorder-3 evaluation. Significant differences in the composite score of set-shifting between the study and control groups were found using multiple analysis of variance.

CONCLUSIONS—Adolescent females with AN-R had significantly worse set-shifting scores than did control subjects. Future studies of adolescent AN-R subjects should include biologic (fMRI) and neurocognitive measures to determine the mechanisms at the brain-behavioral interface so that treatment can be directed specifically to set-shifting deficits.

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INTRODUCTION

Individuals who have restrictive anorexia nervosa (AN-R) are underweight, fearful of gaining weight, and have perceptual distortions of their body image. Set-shifting is a neurocognitive construct defined as the ability to switch tasks flexibly. Set-shifting scores are worse in adults with AN-R than in controls [1]. Examples of set-shifting statements from the Behavior Rating Inventory of Executive Function-Student (BRIEF-S) [2] are: "I have trouble getting used to new settings; I get upset with a change in plans."

Studying set-shifting in adolescents with AN-R is important because: (1) Adolescence is a developmental period when young people must respond flexibly to multiple, new demands; inability to do so, may result in developmental challenges for the adolescent; (2) set-shifting capacity has not been examined in adolescents with AN-R; and (3) understanding the biobehavioral construct of set-shifting may provide a useful framework for future studies of the etiology and treatment of AN-R utilizing modern neurocognitive and neuroimaging methods. The effects of malnutrition on set-shifting appear to be minimal.

The hypothesis for this study is that adolescents with AN-R have worse set-shifting scores on formal neurocognitive testing than do normal adolescent controls.

METHODS

The AN-R group consisted of 24 adolescent females, ages 14–20, who met the DSM-IV criteria for AN-R. Exclusions included the diagnoses of bulimia nervosa, eating disorder not otherwise specified, gastrointestinal conditions, major psychiatric conditions (schizophrenia, bipolar disorder, and severe depression), developmental conditions, and use of psychotropic medications. We chose to study only AN-R subjects as the neurobiologic bases of AN-R and bulimia nervosa may differ.

The control group consisted of 37 healthy females ages 14–20 with no history of eating disorders or other chronic illnesses. AN-R and control subjects were matched by group for age, ethnicity, socioeconomic status (health insurance status and parental education level), and intelligence quotient (IQ). Informed consent was obtained by a trained team member from both the adolescent and the accompanying parent. The Institutional Review Board at the University of Rochester Medical Center (URMC) approved this study.

Set-shifting was determined using the Behavior Rating Inventory of Executive Function, Self and Parent-Reports (BRIEF-SR and PR) [2], by the adolescent's performance on both the computerized versions of the Wisconsin Card Sorting Test (WCST- Revised and Expanded) [3], and the Intra/Extradimensional Set Shift EDS subtest of the Cambridge Neuropsychological Test Automated Battery (CANTAB) [4]. In both the WCST and CANTAB, subjects identified rules and responded to stimuli based on those rules. Ability to respond appropriately to change in rules on these tests is related to their ability to switch tasks flexibly (set-shifting). Psychological evaluation included the Kaufman Brief Intelligence Test-2 [5], the Eating Disorder Inventory-3 (EDI-3) [6] and measures of depression and obsession-compulsion. Biological and sociodemographic data were also collected.

Multivariate analyses of variance (MANOVA) were conducted to identify significant differences between the two groups (AN-R and controls) in set-shifting outcomes: BRIEF-SR Shift Composite (composed of the Behavioral and Cognitive Shift subscales), BRIEF-PR Shift, number of Total and Perseverative Errors on the WCST, and the standardized number of Extra-Dimensional Stage Errors (EDS) on the CANTAB IED. Post-hoc analyses were

carried out to examine individual measures using univariate, two-sample t-tests or Wilcoxon AN-Rk Sum test, where appropriate, using SAS 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

Our study and control subjects' sociodemographic and IQ scores were similar, whereas Body Mass Index (BMI), EDI-3, depression, and compulsion and obsession scores were worse for those with AN-R compared to control subjects (Table 1). Significant group differences on set-shifting between the AN-R and control groups were found using a MANOVA on the composite set-shifting score (Wilk's $\lambda = 0.77$, $F(1, 25.5) = 4.04$, $p < .006$). Post-hoc analyses on individual scores are summarized in Table 2 with p-values from univariate, two-sample t-tests provided. Both BRIEF-SR composite and BRIEF-PR set-shifting scores were significantly different between groups (60.8 ± 11.0 vs. 48.4 ± 11.0, $p<0.001$ and 54.5 ± 9.6 vs. 47.1 ± 10.6, $p< 0.008$ respectively) (higher scores are worse scores) with both AN-R subjects and their parents reporting that AN-R subjects had more set-shifting problems than controls. On the WCST, the AN-R group had significantly fewer Total Errors (57.7 ± 10.6 vs. 63.0 ± 5.0, $p=0.011$, respectively) and nearly significantly fewer Perseverative Errors (60.5 ± 11.0 vs. 64.8 ± 6.4, $p=0.057$, respectively) on the WCST (lower scores are worse). There were no differences in EDS errors on the CANTAB. There was no relationship between nutritional status (BMI) and any of the individual set-shifting items.

DISCUSSION

These data support our hypothesis that adolescent females who have AN-R have worse set-shifting scores than do normal controls. Set-shifting deficits in adults with AN-R have been demonstrated with multiple neuropsychological tests including the WCST which we used. [1] Set-shifting deficits may be a marker for AN-R as it has been shown that women who have anorexia nervosa and their unaffected female siblings have worse set-shifting scores than do healthy controls, raising the question of whether set-shifting is an endophenotype for anorexia nervosa. [7]

Further understanding the cognitive and neural mechanisms of set-shifting deficits in adolescent AN-R subjects may provide insights into the etiology and treatment of this condition. In a recent study, 15 adult women with anorexia nervosa and 15 control women underwent event-related functional magnetic resonance imaging (fMRI) while performing a task that involved both cognitive (rigid approaches to changing rules) and behavioral (stereotyped or perseverative behaviors) components of set-shifting [8]. AN-R participants made significantly more errors in the behavioral component, but not in the cognitive component. Behavioral shifting was associated with reduced activation of the ventral anterior cingulate striato-thalamic loop and activation in the frontal and parietal brain regions on fMRI. Our results from the BRIEF-SR indicate that AN-R subjects had significantly worse scores on both the behavioral and the cognitive components of the BRIEF-SR Shift than did the controls (Table 2). We question whether the degree of an adolescent's set-shifting deficits predicts poorer long- and short-term outcome. That is, is a higher score on set-shifting on initial presentation (more set-shifting deficits) associated with poorer outcome?

The strengths of this study include an exclusive focus on adolescent females who have AN-R, a matched healthy control group, and the use of behavioral and self-report evaluations, and parental measures of set-shifting deficits. Limitations of the study include the small study sample and minimal biological data.

CONCLUSIONS

Future set-shifting studies of AN-R subjects should use both behavioral and cognitive set-shifting evaluations simultaneously with functional resonance imaging (fMRI). Use of neuroimaging and computerized cognitive evaluations may clarify the mechanisms at the brain-behavioral interface that underlie this complex condition. Such technologies might also be used to test potential interventions to modify set-shifting deficits [9]. Additionally, we question whether scores on set-shifting screening predict outcomes of AN-R.

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TABLE 1

Demographic and Psychological Characteristics of Study Population

Characteristic	AN-R Subjects (N =24)	Control Subjects (N=37)	*p* value
Chronological age in years, mean (± SD)	16.3 (± 1.2)	15.9 (± 1.5)	0.302
Age at menarche in years, mean (± SD)*	12.9 (± 0.8)	12.5 (± 1.4)	0.338
Race (% Caucasian)	96.0	92.0	1.00
Health insurance (% with private insurance)	100.0	100.0	1.00
Parental education, median [range]	2.9 [1–4]	2.9 [1–4]	0.915
IQComposite score *(KBIT-2)*, mean (± SD)	111.6 (± 10.7)	113.1 (± 10.2)	0.637
Body Mass Index, mean (± SD)	16.7 (± 1.3)	22.3 (± 3.7)	**< 0.001**
Eating Disorder Inventory-3 (EDI-3), mean (± SD)**			
Eating Disorder Risk Composite	50.5 (± 11.5)	35.6 (± 6.1)	**< 0.001**
General Psychological Maladjustment Composite	48.0 (± 9.8)	35.0 (± 4.4)	**< 0.001**
Beck Depression Inventory-II (BDI-II), mean (± SD)***			
Total score	21.6 (± 13.6)	4.4 (± 4.6)	**< 0.001**
Child Yale-Brown Obsessive-Compulsive Scale (cY-BOCS), mean (± SD) ***			
Compulsions	7.1 (± 5.6)	3.2 (± 3.6)	**0.002**
Obsessions	6.1 (± 4.0)	3.8 (± 4.9)	**0.047**

Results were considered significant at $p < 0.05$.

* Two study subjects had not started their menarches at the time of the study visit.

** Mean T-scores, standardized-for-age

*** Higher scores are poorer scores.

TABLE 2

Set-Shifting Assessments

Set -Shifting Neurocognitive Measure	AN-R Subjects (N =24) Mean T-Score (± SD)	Control Subjects (N=37) Mean T-Score (± SD)	*p* value
Behavior Rating Inventory of Executive Function-Self Report (BRIEF-SR)			
Shift (composite)*	60.8 (± 13.5)	48.4 (± 11.0)	< **0.001**
Behavioral Shift	64.1 (± 13.5)	48.5 (± 11.2)	< **0.001**
Cognitive Shift	54.9 (± 13.4)	48.7 (± 10.5)	< **0.050**
Behavior Rating Inventory of Executive Function-Parent Report (BRIEF-PR)			
Shift*	54.5 (± 9.6)	47.1 (± 10.6)	**0.008**
Wisconsin Card Sorting Test (WCST)			
Total Errors**	57.7 (± 10.6)	63.0 (± 5.0)	**0.011**
Perseverative Errors**	60.5 (± 11.0)	64.8 (± 6.4)	*0.057*
Cambridge Neuropsychological Test Automated Battery: Intra/Extra-Dimensional Set Shift (CANTAB IED)			
Extra-Dimensional Stage (EDS) Errors*	8.7 (± 10.0)	7.6 (± 9.3)	*0.661*

Results were considered significant at $p < 0.05$.

* Higher T-scores indicate poorer performance.

** Lower T-scores indicate poorer performance.