RESEARCH ARTICLE

Cognitive Set-Shifting in Anorexia Nervosa

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Abstract

Objective: Adult anorexia nervosa (AN) is associated with inefficient cognitive flexibility and set-shifting. Whether such inefficiencies also characterize adolescent AN is an important area of research.
Method: Adolescents with AN and matched controls were administered a computerized task that required initial learning of an explicit rule using corrective feedback and learning of a new rule after a set number of trials. Adult patients with AN and controls were also examined.
Results: Adolescents with AN did not differ from matched controls with respect to set-shifting cost (decrease in performance after rule change), whereas adults with AN had significantly greater set-shifting cost compared with controls.
Discussion: This study suggests that set-shifting inefficiencies may not be a vulnerability factor for AN development in adolescents with AN, but might become an important aspect of the disorder at later age, and could point towards developmental neurobiologic brain changes that could affect AN at different ages. Copyright © 2012 John Wiley & Sons, Ltd and Eating Disorders Association.

Keywords
anorexia nervosa; neurobiology; childhood; set shifting; cognitive flexibility

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Research in anorexia nervosa (AN) has indicated that treating youth with the disorder is more successful than treating older individuals with AN (Fisher, 2003), but the reasons for this phenomenon are unknown. The generally young age of onset of AN suggests potential developmental aspects of this disorder (i.e. specific vulnerabilities) relating to the developing brain and body. However, such factors that distinguish younger from older individuals with AN have not been well studied.

Recently, the concept of endophenotypes has been developed, which aims to move from the overt behavioural symptoms of an illness to more stable and genetically determined phenotypes (Gottesman & Gould, 2003). By definition, endophenotypes must be associated with the illness, heritable, primarily state independent and familial. The identification of such endophenotypes in AN can potentially guide the development of more specific and effective treatments. For AN, inefficient cognitive set-shifting is a potential endophenotype (Tenconi et al., 2010) Set-shifting is a neurocognitive concept that refers to the ability to switch tasks flexibly or the mental ability to change behaviour in relation to changing rules. Several studies found that women ill with AN have set-shifting inefficiencies (Tchanturia et al., 2011) in that they tend to perseverate on previously applicable rules (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007). Such findings are consistent with the clinical observation that these patients tend to be cognitively rigid and persistent (Brewerton, Hand, & Bishop, 1993). Recent evidence suggests that set-shifting inefficiencies not only occur across adults with AN but also other subtypes of eating disorders, such as bulimia nervosa (Roberts, Tchanturia, & Treasure, 2010). Reduced set-shifting has also been found in unaffected relatives of AN patients (Roberts, Tchanturia, & Treasure, 2012) and seems to persist after individuals with AN have restored weight (Tchanturia et al., 2004). Individuals who have maintained long-term recovery from AN (i.e. maintained a stable weight and resumed menses for 1 year; Hambrook et al., 2010; Roberts, Tchanturia, & Treasure, 2010) have also shown set-shifting impairments compared with age-matched healthy controls. These findings further suggest that set-shifting inefficiencies may be an endophenotype of this disease. Given that set-shifting has been associated with brain dopamine (DA) function (Floresco, Magyar, Ghods-Sharifi, Vexelman, & Tse, 2006) and that the pathophysiology of AN may involve DA alterations (Frank et al., 2005; Kaye, Frank, & McConaha, 1999), it is possible that alterations in set-shifting in AN represent changes to the DA system.

An important question that arises is whether such inefficiencies are present at all points of the disease. One approach is to examine whether set-shifting inefficiencies are present in young individuals who later develop AN. Such a study would require an epidemiological approach with random sampling of a large set of non-AN individuals and then following them to the development of the disease. Another more feasible approach is to study in a cross sectional design set-shifting in young individuals who have already developed AN and compare them with an adult sample.

The literature on cognitive function in youth with AN is not consistent with adult research results. For instance, one study found reduced performance on a sensori-motor task during the underweight state but improved performance with weight restoration. In that same study, adolescents with AN performed superior to healthy controls on working-memory and executive function tasks (Hatch et al., 2010).

In contrast to the well-established set-shifting inefficiencies in adults with AN, few studies have examined set-shifting in younger patients with AN. The studies used different designs with inconsistent results, including worse or normal set-shifting performance compared with controls (Dmitrzak-Weglarz et al., 2011; McAnarney et al., 2011; Sarrar et al., 2011).

We used a novel, but simple, category learning task that required learning of changing rules, which requires set-shifting ability. The task had a set number of trials both prior to and following the rule change (set-shift), thereby allowing to examine the speed of acquisition of the new rule. This is in contrast to other clinical measures that have been used in the past to examine set-shifting in AN, such as the Wisconsin Card Sorting Test (WCST), where the number of trials prior to a shift requirement is not pre-determined, thereby allowing participants to have a different level of exposure to the initial rule. Versions of this task have been used previously to examine category learning inefficiencies in other patient populations (Filoteo, Maddox, Ing, & Song, 2007).

A group of adolescent patients with AN was contrasted with a group of age-matched and gender-matched controls. A group of adult patients with AN was also contrasted with a group of age-matched and gender-matched controls to validate previous results in adult AN. We hypothesized that adolescent AN would display set-shifting inefficiencies similar to adults, with the notion that this cognitive alteration would be an endophenotype independent from age. If adolescent AN patients display similar set-shifting inefficiencies as adult AN patients, it would suggest that this cognitive impairment is observed very early in the course of the disease and may contribute to the development of the disease regardless of age. In contrast, if adolescent AN patients are not impaired, it would suggest that cognitive set-shifting does not contribute to disorder development in the young, whereas still being an important factor for AN in the older age group.

Method

Participants

A total of 90 study participants were recruited: 15 adolescent patients with AN (ADOL-AN) and 16 adolescent controls (ADOL-C), 26 adult patients with AN (ADULT-AN) and 33 adult control women (ADULT-C). Demographic and disease characteristics are displayed in Table 1. The mean age of the ADOL-AN and ADOL-C groups did not differ ($p = 0.11$), nor did the mean age of the ADULT-AN and ADULT-C groups ($p = 0.92$) differ. The age of disease onset was greater in the ADULT-AN group than in the ADOL-AN group, $t(40) = 4.6$, $p < 0.001$, and the duration of illness was greater in the ADULT-AN group than in the ADOL-AN group, $t(40) = 3.9$, $p < 0.001$. The two AN groups did not differ in current body or lowest body mass index (BMI; both p values > 0.50). AN and control groups were matched for education level.

Screening and study inclusion

Participants with AN were recruited through the Eating Disorders Program at Children's Hospital Colorado ($n = 17$), the Eating Disorder Center of Denver ($n = 13$) and the University of California San Diego Eating Disorders programme ($n = 11$). The study included patients in the inpatient, day treatment and outpatient levels of care. Control participants were recruited through local advertisements in the Denver ($n = 25$) and San Diego ($n = 24$) metropolitan areas. Studies at both sites were initiated and supervised by the last author. Written informed consent was obtained for each participant after a complete description of study procedures, and all research procedures were approved by the local Institutional Review Boards. Study participants completed the Temperament Character Inventory (Cloninger, Przybeck, Svarkic, & Wetzel, 1994) and the Eating Disorder Inventory-2 (Garner, 1991). Healthy controls had a lifetime history of body weight between 90% and 110% of ideal body weight since menarche and had no history of psychiatric or major medical illness. Participants with AN met DSM-IV-TR (APA, 2000) criteria for AN, restricting or binge/purging subtype. Healthy individuals under 18 years were interviewed with DISC Predictive Scales (Lucas et al., 2001) to assess for psychological symptoms. Adolescents with AN completed the Clinical Diagnostic Interview Schedule for Children 4.0, to assess all major psychiatric diagnoses (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). ADULT-C and ADULT-AN were assessed with the Structured Clinical Interview for DSM-IV Axis I Disorders (First, Gibbon, Spitzer, & Williams, 1996). Five ADOL-AN and 14 ADULT-AN had comorbid major depressive disorder, 8 ADOL-AN and 12 ADULT-AN had a comorbid anxiety disorder; no individuals had a psychotic, substance use or bipolar disorder. Two of the ADOL-AN and 11 of the ADULT-AN individuals were of the binge/purging subtype, and all other participants were of the restricting subtype. Thirteen of the ADOL-AN and 20 of the ADULT-AN took psychoactive medication, most commonly a serotonin reuptake inhibitor or atypical antipsychotic, or both.

Stimuli

The category learning task was adapted from that used by Filoteo et al. (2005) to study explicit category learning and set-shifting in patients with basal ganglia disorders. Two different sets of computer-generated stimuli presented colour images of either cartoon 'castles' or 'houses'. Examples of stimuli from each of the eight sets are shown in Figure 1. For each set, four possible binary-valued dimensions could vary from trial to trial. These four dimensions and the binary values for each stimulus set were the following: *castle stimuli*—shape of foundation (diamond or square), location of ramparts (above walls or sunken into walls),

Table 1 Demographic and clinical information of adults with anorexia nervosa (ADULT-AN), age-matched adult controls (ADULT-C), adolescents with anorexia nervosa (ADOL-AN) and age-matched adolescent controls (ADOL-AN)

	ADULT-AN		ADULT-C				ADOL-AN		ADOL-C			
	M	*SD*	*M*	*SD*	*p*	η_p^2	*M*	*SD*	*M*	*SD*	*p*	η_p^2
Age (years)	26.2	7.2	26.0	5.3	*ns*	0.00	14.8	1.1	14.0	1.6	*ns*	0.09
Age at onset (years)	16.8	0.4	—	—	—	—	13.6	2.1	—	—	—	—
Duration of illness (years)	9.1	8.4	—	—	—	—	0.9	0.8	—	—	—	—
Body mass index (kg/m^2)	16.4	1.3	21.8	1.8	ADULT-C > ADULT-AN**	0.75	16.2	1.1	20.5	2.2	ADOL-C > ADOL-AN**	0.63
Lowest body mass index	14.7	2.2	—	—	—	—	14.8	1.7	—	—	—	—
TCI												
Novelty seeking	15.9	6.2	19.8	5.2	ADULT-C > ADULT-AN*	0.11	15.3	5.1	23.5	4.6	ADOL-C > ADOL-AN*	0.44
Harm avoidance	21.9	7.2	8.6	3.3	ADULT-AN > ADULT-C*	0.61	20.8	8.8	9.2	3.3	ADOL-AN > ADOL-C*	0.44
Reward dependence	15.0	4.1	18.4	3.2	ADULT-C > ADULT-AN*	0.19	13.9	3.3	16.3	2.6	ADOL-C > ADOL-AN*	0.15
Persistence	5.7	2.0	5.2	1.8	*ns*	0.02	5.8	1.9	5.0	1.6	*ns*	0.05
EDI-2												
Drive for thinness	14.0	5.9	0.7	1.6	ADULT-AN > ADULT-C**	0.73	15.3	6.4	1.1	1.7	ADOL-AN > ADOL-C*	0.70
Bulimia	4.7	5.4	0.2	0.9	ADULT-AN > ADULT-C**	0.29	2.3	5.1	0.1	0.4	*ns*	0.08
Body dissatisfaction	15.0	8.9	1.5	3.1	ADULT-AN > ADULT-C**	0.54	13.0	8.4	1.5	2.1	ADOL-AN > ADOL-C*	0.48
Ineffectiveness	11.4	7.7	0.3	0.8	ADULT-AN > ADULT-C**	0.55	9.9	7.7	0.7	1.4	ADOL-AN > ADOL-C*	0.42
Perfectionism	10.2	4.8	3.9	3.3	ADULT-AN > ADULT-C**	0.39	9.4	6.0	6.1	4.2	ADOL-AN > ADOL-C*	0.10

Notes: TCI, Temperament and Character Inventory subscales; EDI-2, Eating Disorder Inventory-2 subscales.
[a]The ADULT-AN group had significantly greater scores than the ADULT-C group on the TCI harm avoidance subscale and all of the EDI-2 subscales. The ADULT-C group had greater scores than the ADULT-AN group on the TCI's novelty seeking and reward dependence subscales. The ADOL-AN group had greater scores than the ADOL-C group on the TCI harm avoidance subscale and all EDI-2 subscales, except for the bulimia and perfectionism subscales. The ADOL-C group had greater scores than the ADOL-AN group on the novelty seeking and reward dependence subscales. ADULT-AN and ADOL-AN groups did not differ on any of the investigated scales.
*p value <0.05.
**p value <0.01.

Figure 1 Example of the category learning task that presents two different sets of computer-generated stimuli of either a cartoon castle or a house

number of rings surrounding castle (one or two) and colour of drawbridge (yellow or green); *house stimuli*—colour of door (blue or red), lighting inside window (lights off or lights on), shape of roof (flat or triangular) and nature of plants (shrub or tree). Each stimulus was presented in colour that remained constant except for the altered dimension that was relevant to the categorization task described earlier. Each stimulus was approximately 10 cm in height and from a viewing distance of approximately 60 cm subtended about 9.6° of visual angle.

Procedure

Each participant was randomly administered one set of stimuli (houses or castles). Participants were told that they would be shown individual pictures and were asked to categorize each as either belonging to Category 1 or Category 2 by pressing a specified key. Participants were also told that after they categorized the picture, they would receive feedback on the computer screen in the form of the word 'correct' for correct responses and the word 'wrong' for incorrect responses. Participants were also told that they would be guessing at first and that they should attempt to learn from their errors. For each set of stimuli, four dimensions would vary on a trial-by-trial basis. The task of the participant was to determine the relevant dimension on the basis of the corrective feedback. Participants were presented 160 trials in eight blocks: 80 pre-rule-shift trials and 80 post-rule-shift trials. For the castle stimuli, the relevant dimension prior to the rule shift was the shape of the foundation (Category 1 = square shape, Category 2 = diamond shape), and the relevant dimension after the rule shift was the number of rings around the castle (Category 1 = one ring, Category 2 = two rings). For the house stimuli, the relevant dimension prior to the rule shift was the shape of the roof (Category 1 = flat, Category 2 = triangular), and the relevant

dimension after the rule shift was the nature of the plants (Category 1 = tree, Category 2 = bush). Participants were never informed that a rule shift was going to occur and thus had to infer it on the basis of the corrective feedback.

Each trial began with the presentation of a picture that remained on the screen until the participant made a categorization response. Immediately following a response, correct or incorrect feedback was presented for 0.75 seconds while the stimulus remained on the screen, followed by a blank screen for 1.0 second, and then the presentation of the next stimulus.

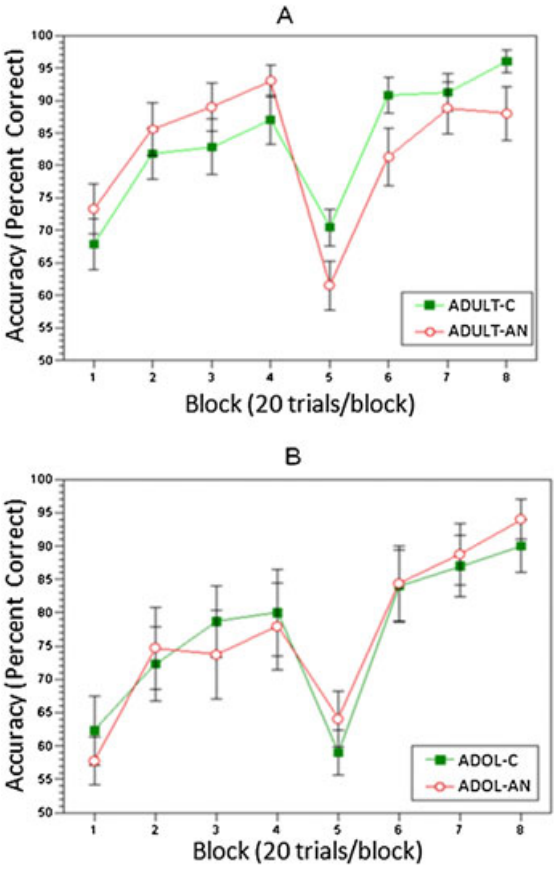
Statistical analysis

Demographic and disease-related variables were compared using independent sample *t*-tests. Accuracy performances on the category learning task were examined separately for the adults and the adolescents by using two separate 2 (group) × 8 (blocks) mixed-design analyses of variance (ANOVAs). To determine the impact of the actual shift, we computed a shift-cost score was computed by subtracting each participant's accuracy on Block 5 from their accuracy on Block 4 (higher scores equalled a greater shift cost). The shift-cost scores for the patient and control groups were then compared using independent sample *t*-tests. To examine the impact of both age and diagnosis simultaneously on shift cost, we conducted a 2 (adult versus adolescent) × 2 (AN versus controls) between-participants ANOVA using the shift-cost index as the dependent variable. Correlation analyses were conducted using Pearson's correlation analysis. All statistical tests were two-tailed and considered reliable at the $p < .05$ level. Effect sizes are reported as partial eta squared η_p^2.

Results

Accuracy results

Accuracy (per cent correct) across the 160 trials in eight trial blocks are depicted in Figure 2A for the adult and Figure 2B for the adolescent groups. For the adult groups, there was a significant group by block interaction, $F(7, 399) = 2.7$, $p < 0.05$, $\eta_p^2 = 0.045$, and a significant main effect of block, $F(7, 399) = 19.6$, $p < 0.001$, $\eta_p^2 = 0.255$. The main effect of group was not significant, $F(1, 57) = 0.06$, $p = 0.80$, $\eta_p^2 = 0.001$. To follow up the significant interaction, we contrasted the groups separately on Blocks 1–4 (pre-shift blocks) and Blocks 5–8 (post-shift blocks) using two separate 2 × 4 ANOVAs to determine if there were any differences between the groups in pre-shift learning and post-shift learning curves. The results for Blocks 1–4 revealed an effect of block, $F(3, 171) = 22.9$, $p < 0.001$, $\eta_p^2 = 0.287$, but no effect of group, $F(1, 57) = 1.4$, $p = 0.24$, $\eta_p^2 = 0.024$, and no Group Block interaction, $F(3, 171) = 0.13$, $p = 0.94$, $\eta_p^2 = 0.002$. The results for Blocks 5–8 revealed an effect of block, $F(3, 171) = 55.0$, $p < 0.001$, $\eta_p^2 = 0.491$, a trend towards an effect of group, $F(1, 57) = 3.6$, $p = 0.06$, $\eta_p^2 = 0.059$, but no Group × Block interaction, $F(3, 171) = 1.0$, $p = 0.39$, $\eta_p^2 = 0.017$. The mean shift cost for the ADULT-AN group was 31.7% ($SD = 21.8$), and for the ADULT-C group, it was 16.2% ($SD = 27.0$). These means were significantly different, $t(57) = 2.4$, $p < 0.05$, $\eta_p^2 = 0.09$. These findings indicated that the ADULT-AN group's accuracy rate was impacted to a larger extent than that of the ADULT-C group.



Notes: [a] Significant group by block interaction, $F(7, 399)=2.7$, $p<.05$

[b] Significant main effect by block, $F(7, 399)=19.6$, $p<.001$

[c] Significant main effect by block, $F(7, 203)=17.7$, $p<.001$

Figure 2 Accuracy (per cent correct) for (A[ab]) adults with anorexia nervosa (ADULT-AN, $N = 26$), age-matched adult controls (ADULT-C, $N = 33$), and (B[c]) adolescents with anorexia nervosa (ADOL-AN, $N = 15$), age-matched adolescent controls (ADOL-C, $N = 16$) for eight blocks of trials (20 trials per block)

In contrast to the adult groups, the ANOVA for the adolescent data did not reveal an interaction, $F(7, 203) = 0.50$, $p = 0.83$, $\eta_p^2 = 0.017$, and similar to the adult groups' results, there was an effect of block, $F(7, 203) = 17.7$, $p < 0.001$, $\eta_p^2 = 0.379$, and no main effect of group, $F(7, 203) = 0.00$, $p = 0.97$, $\eta_p^2 < 0.001$. Although there was no significant group by block interaction, pre-shift and post-shift learning curves were nevertheless examined in the same manner as with the adult groups. The results for Blocks 1–4 identified a significant effect of block, $F(3, 87) = 12.7$, $p < 0.001$, $\eta_p^2 = 0.304$, but no effect of group, $F(1, 29) = 0.12$, $p = 0.73$, $\eta_p^2 = 0.004$, and no Group × Block interaction, $F(3, 87) = 0.51$, $p = 0.68$, $\eta_p^2 = 0.017$. The results for Blocks 5–8 also revealed an effect of block, $F(3, 87) = 46.0$, $p < 0.001$, $\eta_p^2 = 0.613$, but no significant effect of group, $F(1, 29) = 0.31$, $p = 0.58$, $\eta_p^2 = 0.01$, and no Group × Block interaction, $F(3, 87) = 0.30$, $p = 0.82$, $\eta_p^2 = 0.01$. The mean shift cost for the ADOL-AN group ($M = 13.4$, $SD = 27.5$) was actually less than that of the ADOL-C group ($M = 21.3$, $SD = 27.0$), but this difference was not significant, $t(29) = 0.81$, $p = 0.43$, $\eta_p^2 = 0.022$.

Finally, to examine both age and diagnosis simultaneously, we conducted a 2 (adult versus adolescent) × 2 (AN versus controls) between-participants ANOVA using the shift-cost index as the dependent variable. This analysis revealed a significant age group by diagnosis interaction, $F(1, 86) = 4.2$, $p < 0.05$, $\eta_P^2 = 0.047$, but no main effects of age group, $F(1, 86) = 1.3$, $p = 0.25$, $\eta_P^2 = 0.015$, or diagnosis, $F(1, 86) = 0.45$, $p = 0.51$, $\eta_P^2 = 0.005$. As noted previously, the shift-cost index differed significantly between the ADULT-AN and ADULT-C groups but not between the ADOL-AN and ADOL-C groups. A comparison between age groups within diagnostic categories revealed that the ADULT-AN groups' shift cost was greater than that of the ADOL-AN group, $t(40) = 2.4$, $p < 0.05$, $\eta_P^2 = 0.125$, but the ADULT-C and ADOL-C groups' shift costs did not differ significantly, $t(46) = 0.61$, $p = 0.55$, $\eta_P^2 = 0.008$.

Level of accuracy analyses

An examination of Figure 2A suggests that one possible reason the ADULT-AN group displayed a greater shift cost than the other groups was that they learned the rule prior to the shift to a larger extent. A correlation between participants' accuracy in Blocks 4 and 5 was conducted to examine this possibility. If it is the case that the ADULT-AN group's shift cost was due to the level of accuracy achieved prior to the rule shift, then there should be a significant negative correlation between accuracy rates in Blocks 4 and 5. These correlations, however, were not significant for the ADULT-AN group, ($r(26) = 0.11$, $p = 0.58$), the ADULT-C group, [$r(33) = 0.01$, $p = 0.94$], the ADOL-AN group, [$r(16) = 0.23$, $p = 0.40$], nor the ADOL-C group, [$r(15) = 0.12$, $p = 0.68$].

Clinical correlates

We further tested relationships between performances on the experimental task and variability in participants that might impact performance. We found no significant correlations between shift-cost index and age, age of disease onset, duration of illness, current BMI, or lowest BMI for the ADULT-AN or the ADOL-AN group. Similarly, for the control groups, there were no correlations between the shift-cost index and age or current BMI. To determine if a diagnosis of depression or anxiety, or the use of psychotropic medications impacted set-shifting, we correlated the shift-cost index with those variables separately in the ADULT-AN and ADOL-AN groups and found no relationship of those variables with set shift-cost index. For all correlation tests, Spearman's rho was between 0.01 and 0.3, p between 0.2 and 0.99.

Discussion

This study is unique in that it directly compares set-shifting performance in adolescent versus adult AN and controls. On the basis of the results from this specific category learning measure, it seems that set-shifting is normal in ADOL-AN compared with ADOL-C but impaired in ADULT-AN versus ADULT-C. This finding could suggest that set-shifting is not necessary to develop AN in youth but may be an important factor in adult AN development and prognosis.

Adult AN set-shifting inefficiencies

The observed set-shifting inefficiencies in the ADULT-AN group compared with ADULT-C support the previously found inefficiencies in adults (Tchanturia et al., 2011; Tchanturia et al., 2012). The ADULT-AN groups did not have problems with the initial learning of a novel rule and, in fact, tended to perform somewhat better than controls (although this was not statistically different). Results also indicate that the cognitive set-shifting inefficiencies displayed by the ADULT-AN group was not due to learning performance of the initial rule (i.e., the level of performance on the final block before rule shift did not correlate with performance on the block just after rule change). Rather, the inefficiencies we observed are specific to the rule change and independent of these other factors.

Normal set-shifting in adolescent AN

The lack of set-shifting inefficiencies in youth with AN raises several interesting and important questions. Set-shifting inefficiencies are proposed endophenotypes of AN (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005). This study provides preliminary evidence that such inefficiencies may be highly related to age. Recently, Sarrar et al. (2011) found worse set-shifting performance in adolescent AN in the context of neuropsychological tests, and these impairments improved with weight gain. McAnarney et al. (2011) found that AN youth compared with healthy adolescent controls performed worse on the WCST. Although a highly useful task, the WCST is somewhat limited because of its complexity, stressful nature, time requirements and the fact that individual examinees are often administered a different number of trials prior to the set-shift, thereby not allowing each subject to be equally exposed to the initial rule. Another recent study that also studied WCST response in adolescent AN found normal performance in the AN group compared with control youth (Dmitrzak-Weglarz et al., 2011). All in all, the literature on set-shifting in AN is inconsistent and requires further study.

This current study used a task that measures initial rule learning, cognitive set-shifting and subsequent learning of a new rule and is a more simple task than those that have been used in previous studies demonstrating set-shifting inefficiencies in AN. Using a simpler task with a standard number of trials, as carried out in the present study, allowed for examination of initial-rule and post-rule acquisition in a standard, efficient and non-stressful manner, which is considered a strength of the this study. Another recent study found subtle impairments in set-shifting ability in adolescent AN compared with healthy controls.

Developmental aspects of set-shifting

Set-shifting alterations in AN may become prominent and important for AN prognosis in older AN, but this altered cognitive performance might not play a significant role in adolescents with AN. Set-shifting abilities continue to improve during adolescence (Kalkut, Han, Lansing, Holdnack, & Delis, 2009), whereas others suggested that it may plateau around the 11 years of age (Klimkeit, Mattingley, Sheppard, Farrow, & Bradshaw, 2004). However, it remains uncertain when set-shifting inefficiencies in AN develop. It is unclear whether set-shifting inefficiencies are a factor of illness duration, develop during late adolescent or young adulthood,

or whether the youth with AN have protective factors that compensate for such difficulties. Studies in unaffected siblings of individuals with AN suggest that altered set-shifting is familial (Holliday et al., 2005). Altogether, the ADOL-AN data suggest that set-shifting inefficiencies are not necessary to develop AN. If it is the case that set-shifting inefficiencies somehow contribute to poorer treatment prognosis (Roberts et al., 2010) and set-shifting inefficiencies develop over time in AN as this study suggests, then it becomes even more important to identify and treat AN at a younger age before the development of set-shifting inefficiencies. This might also be consistent with previous findings that show treatment of younger AN patients is associated with better prognosis compared with that of older patients (Fisher, 2003). However, longitudinal studies will be best suited to address those questions.

The finding that adults with AN are impaired on a simpler task than previously used indicates how profound set-shifting inefficiencies can be in adults with this disorder. The cognitive set-shifting inefficiencies observed in the ADULT-AN group was independent of eating disorder symptom severity. This lack of correlation is consistent with other studies, although a relationship of a composite score of various set-shifting tasks and duration of illness has been shown in at least one study (Roberts et al., 2010), although that study did find a relationship with low BMI and AN core feature. Thus, the actual meaningfulness of such inefficiencies from a clinical perspective is not currently known. The DA system has repeatedly been suggested to be altered in adult AN (Frank et al., 2005; Kaye et al., 1999) but is uncertain if such inefficiencies also exist in AN youth. The brain DA system undergoes significant changes during development (Suzuki et al., 2001), and it has been suggested that the youth have a more sensitive DA reward system (Galvan, 2010). Thus, it could be possible that the higher plasticity of brain DA function in youth protects from DA-related set-shifting inefficiencies compared with higher age, when DA response is less flexible.

Limitations

The main limitation of the present study is its small sample size. The effect size of the main difference (i.e. the shift-cost index) between ADULT-AN and ADULT-C groups, however, was medium, whereas a small effect size was found for the comparison between the ADOL-AN and ADOL-C groups. Thus, the lack of a difference between the latter two groups does not appear to be a power issue. The two AN groups differed in age of AN onset and duration of illness, and one could argue that they had two different forms of AN, that is, early and late onset of the disorder. There was also a greater number of binge/purging type AN in the adult AN group, which could have affected the results. However, the two AN groups did not differ significantly on weight, eating disorder behaviour or temperament measures and appear to have a very similar illness presentation and similar to other AN samples (Klump et al., 2004), suggesting overall comparable AN study groups. A second limitation is that a specific test for general intellectual functioning was not administered, which calls into question whether the group differences in the adults and the lack of group differences in the younger adults are due to differences in general cognitive functioning. The education levels across groups were matched, and the task itself is intentionally simple, however, suggesting that baseline levels of cognitive functioning did not likely account for the findings. We did not add a neuropsychological test battery that might have found differences across the AN groups on neurocognitive function such as memory or attention (Hatch et al., 2010; Nikendei et al., 2011). Whether the worse performance in the adult AN group was a normal performance in the adolescent AN group was driven by such factors will need further study in a larger sample.

Implications for research, policy and practice

Results from this current study suggest that (i) if AN is not treated early, set-shifting inefficiencies are likely to emerge and may be an important factor impacting treatment resistance and relapse, (ii) there is a need to identify and treat AN as early as possible and (iii) future research should target biologic factors that determine the development of altered set-shifting in AN in late adolescence and early adulthood.

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