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Performance and brain activity during the Wisconsin Card Sorting Test in adolescents with obsessive-compulsive disorder and adolescents with weight-restored anorexia nervosa

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Abstract

Anorexia nervosa (AN) and obsessive-compulsive disorder (OCD) both show a peak age of onset during adolescence and share a number of phenotypic features, such as rigid rule-bound behavior and perseverative thinking. There is evidence of difficulties with set shifting or task switching in adults with each disorder, but evidence in adolescents is limited. Further, no studies have previously directly compared AN and OCD on this cognitive process or examined comparative neural correlates. This study provides exploratory analyses to address this gap by measuring brain activity with functional magnetic resonance imaging (fMRI) during a computerized version of the Wisconsin Card Sorting Test (WCST) in female adolescents with weight-restored AN (WR-AN) (n=14), OCD (n=11) and healthy controls (n=24). Results revealed greater perseverative errors in the OCD group than healthy controls and WR-AN, but no difference between WR-AN and healthy controls. Greater activity in the right front pole, inferior frontal gyrus, and middle frontal gyrus during the task (compared to a control matching task) was associated with more perseverative errors in the OCD group, but not healthy controls. The correlation between perseverative errors and brain response to the task in the WR-AN group was not different from either comparison group. These findings propose an hypothesis that behavioral similarities between OCD and AN, as well as difficulties with set shifting in adults with AN, are driven by obsessive-compulsive features present in AN rather than a shared underlying neurocognitive signature. This notion should be tested in larger samples in future studies.

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Ethical standards: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki declaration and its later amendments. Informed consent and assent was obtained from all individual participants in the study.

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Keywords

obsessive compulsive disorder; anorexia nervosa; Wisconsin Card Sorting Test; set shifting; cognitive flexibility; adolescents

1. Introduction

Anorexia nervosa (AN) has long been observed to demonstrate symptoms in common with obsessive-compulsive disorder (OCD), a condition featuring perseverative thinking and compulsive behaviors in attempt to alleviate distress from obsessive thoughts [1]. Overlap between the phenotypic characteristics expressed in AN and OCD, such as cleanliness, perfectionism, orderliness, and rigidity is substantial [2, 3]. Heritable traits found in individuals with AN (e.g., neuroticism, harm avoidance, low novelty seeking) [4, 5] are also associated with anxiety disorders, which previously included OCD [6], and there is evidence of high familial rates of OCD in AN [7]. In addition, reports show between 4.5% and 62% of patients with AN have a comorbid lifetime diagnosis of OCD, greater than the general population, [8–11] and between 0.7% and 9.7% of patients with OCD have a comorbid lifetime diagnosis of AN [11–14]. Despite the considerable shared phenotypic expression and heritability between AN and OCD, potential neurocognitive mechanisms have never been directly compared. Specifically, the two disorders may share a neural signature of cognitive inflexibility. Examining neural mechanisms of these symptoms is important when the clinical presentations that we can observe appear otherwise similar leading us to use similar, but possibly inappropriate treatment approaches. Independent studies of AN and OCD have used inconsistent methodologies, making comparisons challenging because differences between findings may result from the method utilized in the study. Thus, a direct comparison of the two disorders in the same study is critical.

Set shifting is an executive function reflecting cognitive flexibility. Set shifting difficulties are thought to relate to the phenotypically observed behaviors of rigid, rule-bound thinking present in AN and OCD [15, 16]. Although, there is evidence of difficulties with set shifting in both AN [17] and OCD [18, 19], a systematic review of reviews on set shifting in eating disorders revealed inconsistent findings, with smaller effect sizes for adolescents with AN versus adults [20]. One of the most widely used tasks to measure set shifting is the Wisconsin Card Sorting Test (WCST) [21]. In this test, participants are presented with a number of cards and asked to match the cards using some rule, but are not told what the rule is. With feedback, the participants learn the sorting rule, which is subsequently changed without notice, and participants must again try to learn the new sorting rule. Perseverative errors on the WCST occur when participants continue to apply the old rule despite negative feedback.

Evidence of impaired set shifting in AN is more apparent in adults than in adolescents. A recent meta-analysis of studies of set shifting in adolescent AN found no differences between adolescents with AN and healthy controls on set shifting using the WCST based on only three studies of the task in adolescents with varied findings [22]. In OCD, meta-analyses have found greater perseverative errors on the WCST in patients with OCD

compared to healthy controls [18, 19]. Most studies, however, of cognitive flexibility in OCD have been conducted on adult samples. One study of children and adolescents (mean age of 13) found impaired performance on the WCST in categories and nonperseverative errors but not perseverative errors in those with OCD compared to healthy controls [23], and another found no differences on perseverative errors [24]. The only other study of set shifting in adolescents with OCD examined male adolescents with and without OCD using a task switching test rather than the WCST found more switch errors in the OCD group compared to age-matched healthy controls [25]. Thus, there is also inconsistent evidence of difficulties with set shifting in adolescents with OCD and data are limited.

In addition to the limited data in adolescence, the neural signature of set shifting is not perfectly understood, and to date, no studies have investigated neural function underlying set shifting in adolescents with AN. One neuroimaging study of adults with AN found aberrant brain activity related to WCST, such that patients with AN had greater activity in left middle frontal gyrus, precuneus, and superior parietal lobule when shifting versus maintaining rule-sets compared to healthy controls, but behavioral performance was similar between patients and controls [26]. Another small study of adults with AN found reduced activity in the right ventrolateral prefrontal cortex and bilateral parahippocampal cortex when shifting sets compared to controls, but again no difference on perseverative errors [27]. A third study using a different set shifting task found hypoactivation in the ventral anterior-cingulate-striato-thalamic loop during response shift and greater activation in frontoparietal networks in anorexia nervosa, but not behavioral evidence of set shifting deficits [28].

The prevailing neurobiological model of OCD centers on frontostriatal dysfunction [29] and Milad and Rauch also implicate the dorsolateral prefrontal cortex and parietal cortex in OCD [30]. One study found that performance on the WCST in adults with OCD correlated with regional cerebral blood flow in the left inferior frontal cortex and left caudate at rest (not task-based brain function), and patients made more perseverative errors than controls [31], thus illustrating potential frontostriatal dysfunction related to set shifting. In another study, male adolescents with OCD showed reduced activation in the right and left inferior parietal and superior temporal cortices compared to healthy controls when switching a task compared to repeating a task [25].

In sum, both AN and OCD have evidenced abnormal patterns of brain activity while engaging in set shifting tasks, including the WCST. However, the brain regions implicated in prior research and behavioral results have not been consistent. This may be related to the differences in tasks used, the contrasts selected to determine brain activity during the tasks, as well as performance differences. Given that the tasks are often complex and require more than just set shifting skill, it may be that other functions, such as processing speed, interfere with obtaining consistent neural correlates [32, 33]. Using a behavioral correlate, such as performance measures related directly to set shifting may improve our ability to detect neural correlates. No prior studies have investigated the relation between task-based brain activity and set shifting related performance measures like perseverative errors in AN or OCD.

Both AN and OCD have a peak onset during adolescence [34, 35], with OCD showing two peaks, the earlier during adolescence [36]. Studying this age range allows for examination of processes early in the illness, which reduces the potential for a “scar” effect from the illness on the brain, wherein the brain function is changed as a consequence of having the illness. Furthermore, when considering set shifting as an underlying neural mechanism for observed characteristics in these disorders, it is important to establish these processes across ages [37]. Additionally, studying adolescence has important implications for early intervention.

Examining brain function in adolescents with AN who are currently underweight is problematic because of known brain atrophy as a consequence of malnutrition [38]. Instead, recruiting patients who have regained weight can aid in the identification of cognitive processes that are trait-based and may have been present prior to the illness [39]. Importantly, Tchanturia and colleagues found that weight gain in adult patients with AN did not improve set shifting, suggesting that prior findings of set shifting difficulties were not dependent on malnutrition [15]. Thus, focusing on patients who have regained weight will ensure that effects are not due to malnutrition while still allowing for the identification of differences related to AN.

The current study aims to provide preliminary findings on set shifting performance and neural processes to inform future research on adolescent set shifting in OCD and AN, as it is the first direct comparison on set shifting between adolescents with these disorders. Adolescent females age 12-19 with a diagnosis of OCD, AN (weight-restored), or healthy controls free from psychopathology were recruited to participate in a neuroimaging study where they completed a computerized version of the WCST while undergoing functional magnetic resonance imaging (fMRI).

We hypothesized that set shifting would be impaired in the OCD group compared to healthy controls, in line with prior research in OCD. Additionally, we anticipated similar set shifting performance between AN and both OCD and healthy controls given the inconsistent previous findings in adolescents with AN. We expected similar neural processes associated with perseverative errors on the WCST to be present in the two patient groups based on the adult literature, although this aim is exploratory given the lack of any prior neuroimaging studies in adolescent AN. Given limited evidence of disruptions in frontostriatal and frontoparietal networks in AN and OCD these regions were expected to show aberrations in these data.

2. Methods

2.1. Participants

Adolescent (age 12-19) females were recruited from clinics and the community, leading to our final sample of 14 adolescents with weight-restored AN (WR-AN), 11 adolescents with OCD, and 24 healthy controls (mean age 15.4 years across groups). We recruited healthy controls from the community via flyers, online advertisements, and local community email lists. The study only recruited females due to the high prevalence of AN in females and the potential for sex differences to influence group differences on study measures [40, 41]. All participants with WR-AN previously met DSM-IV-TR [42] criteria (the current diagnostic

manual at the time data collection for the study began), but were weight restored at the time of the study (greater than 85% of median body weight, defined as the weight associated with the 50th percentile BMI for the age, sex, and height). This was to ensure that current low weight did not result in a confound impacting brain function. Although weight restored at time of data collection, all participants with WR-AN previously met low weight criterion. Additionally, loss of menses were not required to meet diagnosis of AN. Diagnoses were assessed by trained assessors with the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) for participants under age 18 and the Structured Clinical Interview for DSM Disorders (SCID) for participants 18 and over (two participants in each group completed the SCID), AN diagnoses were made with the Eating Disorder Examination (EDE; [43]). Participants were excluded if they had comorbid AN and OCD in order to establish clear differentiation of brain processes for each diagnosis. All healthy adolescents were free from any mental health disorder. Of the adolescents with WR-AN, 2 were diagnosed with AN-binge/purge type and 12 with AN-restricting type, 50% had a comorbid illness, including 4 with major depressive disorder, 2 with post-traumatic stress disorder, and 1 with agoraphobia. Of the adolescents with OCD, 45.5% had a comorbid illness, including 3 with generalized anxiety disorder, 1 with specific phobia of crowds, and 1 with social phobia. Fifty-three participants underwent neuroimaging scans for this study, but four (one adolescent with WR-AN/OCD, two adolescents with OCD, and one healthy control) were excluded: three due to technical problems that resulted in insufficient scan data and one due to comorbid AN and OCD. There were no differences between groups on age or percent of median body weight.

2.2. Procedures

2.2.1. Protocol—After providing informed consent and assent, participants completed a diagnostic evaluation utilizing the K-SADS or SCID (depending on age). Patients with AN completed the the EDE, and patients with OCD completed the Children's Yale-Brown OC Scale (CY-BOCS; [44]). On a separate visit, participants underwent magnetic resonance imaging, where they completed structural scans and functional scans while performing the WCST. All study activities were approved by the local institutional review board.

2.2.2. Task—The WCST used during the fMRI scan was presented using E-Prime software (Psychology Software Tools, Pittsburgh, PA), Visual stimuli were displayed on a reverse projected screen viewed via a mirror. The fMRI version of the WCST [45] was presented in block design with a sort block and match block. Three reference cards were presented at the top of the screen and a target card presented below. Sort blocks were in line with the classic WCST, and participants were to select the card on top that was associated with the target card according to a rule, which they determined via trial and error plus feedback. Possible rules to sort the cards included having the same color, shape, or number of objects on the card. Cards included red, green, and blue stars, circles, and triangles in groups of 1, 2, or 3 shapes. The target cards were drawn from a 60-card pool and always differed from the reference cards during the sort block. If participants answered 4 consecutive trials correctly, the rule for sorting changed. Match blocks provided a contrast condition controlling for motor, visual, and task demand characteristics, but did not require set-shifting. Participants were asked to simply find the reference card that was identical to

the target card during trials of this block. Visual feedback was provided on each trial for both blocks (“incorrect” or “correct”), followed by an interval of 4-seconds. Each block consisted of 16 trials, and each trial lasted 4 seconds. Four blocks of each type were presented, and instructions to “SORT” or “MATCH” were presented at the onset of each block. Because this version of the WCST was created for fMRI, there are no available community norms for behavioral data. Comparisons to healthy control adolescents are thus utilized as the comparison to a norm score in this study.

2.2.3. Functional MRI—Imaging was conducted on a 3.0 Tesla General Electric MR750 scanner (gehealthcare.com) using an 8-channel head coil. fMRI scans used a spiral in/out pulse sequence [46] with the following parameters: 30 axial slices (3mm thick, 1mm skip) parallel to the AC-PC line and covering the whole brain. TR=2000 msec, TE=30msec, flip angle=90°, FOV=22cm², 64×64 matrix, in-plane spatial resolution of 3.125mm. Shimming reduced blurring and signal loss from field inhomogeneities.

We conducted image pre-processing using FMRIB Software Library (FSL), www.fmrib.ox.ac.uk/fsl. This included motion correction, skull stripping, spatial smoothing of 5mm full-width/half-maximum Gaussian kernel, mean-based intensity normalization of all volumes by the same factor, and high-pass temporal filtering with 60s cutoff. We did not utilize slice-timing correction in order to avoid interpolation of data. We coregistered functional images of each participant to corresponding structural images in native space (2-step registration, which included a high-resolution T1-weighted 3D inversion recovery spoiled gradient-recalled acquisition scan, as well as a matched-bandwidth T1-weighted image collected in the same plane as the functional scans), and registered structural images to structural standard images, defined by the Montreal Neurological Institute averaged 152 standard brain.

2.3. Statistical analysis

Whole brain analyses were performed using mixed-effects modeling to account for inter-subject variability. We conducted whole brain analyses due to limited existing data on the neural processes underlying set shifting in adolescence. Cluster-based correction in FSL was used with a $z > 3.1$ and $p < 0.05$, in line with recent standards to address concerns about inflated false-positive inferences in fMRI analyses [47]. FEAT software (FMRI Expert Analysis Tool; FSL) was used for analyses. FSL’s MCFLIRT tool was used to correct for motion. If relative motion was greater than 1.5mm, we used FSL’s tool for removing motion outliers, using DVARS (RMS intensity from volume to volume). This was done on three patients with AN, one with OCD, and three health controls. If motion consisted of more than just these outliers (spikes), the data were not used, although we did not have to exclude any data for this reason. Contrasts were conducted between sort and match blocks. Group comparisons on timeseries contrasts were examined in higher-order analyses using an omnibus ANOVA. Perseverative errors, calculated as the proportion of trials during the sort block in which participants kept sorting cards according to the rule of the previous set after receiving an error feedback, were also entered in FEAT at the group level to examine the relation between the overall behavioral performance based on perseverative errors and the BOLD signal during the overall task. Perseverative errors indicate difficulty shifting to a

new set of rules while relinquishing the old one. This analysis allows us to determine whether individuals who show this difficulty by committing more perseverative errors have differential neural processing when attempting to sort vs. match.

3. Results

3.1. Behavioral data

Demographic data are presented in Table 1. Groups did not differ on age or percent median body weight. One-way analysis of variance (ANOVA) did not reveal a significant effect of group on perseverative errors ($F(2,46) = 2.92, p = 0.064, \eta_p^2 = 0.113$), Figure 1 displays the means for each group (OCD: $M = 0.03, SD = 0.011$; healthy controls: $M = 0.018, SD = 0.017$; WR-AN: $M = 0.018, SD = 0.010$). Although the omnibus ANOVA was not significant, due to the exploratory nature of the study and the medium effect size of the omnibus test, as well as specific a priori interest in the separate group differences, we conducted independent t-tests of the differences between each group. There was a significant difference between the OCD and WR-AN group with a large effect size ($t(23) = -2.798, p = 0.010$, Cohen's $d = 1.11$). The difference between the OCD group and healthy controls was also large ($t(33) = -2.063, p = 0.047$, Cohen's $d = 0.81$). The WR-AN group and healthy controls performed similarly ($t(36) = -0.074, p = 0.942$, Cohen's $d = .02$).

3.2. Imaging: Group Differences

Analyses of brain activity differences between sort and match conditions within each group revealed significant regions in all three groups where activity was greater during sort compared to match. There were also regions with greater activity during match compared to sort within the healthy control and WR-AN groups, but not the OCD group. Brain regions in these within group analyses are presented in Table 2.

An ANOVA revealed no significant differences in brain activity during sort vs. match blocks between patient or control groups.

3.3. Imaging: Perseverative Errors

When adding perseverative errors to the whole brain FEAT group level analyses, there were no significant interactions between group and perseverative errors. There was a trend such that brain activity during sort vs. match blocks was greater with more perseverative errors in the OCD group, but not the healthy control group (Figure 2). This trend was found in the right frontal pole, right inferior frontal gyrus, and right middle frontal gyrus. Percent signal change from these regions was extracted from the brain maps for each participant to explore the relationship between these values and perseverative errors in SPSS. Although the FEAT analyses did not reveal a significant interaction (due to the methods involved in whole brain cluster-based thresholds in FSL), there was a significant interaction between group and perseverative errors on the percent signal change extracted from these brain regions ($F(9,39) = 3.61, p = 0.002, \eta_p^2 = 0.455$). The association between perseverative errors and brain activity in these regions in the WR-AN group appeared to be somewhere between healthy controls and OCD groups.

4. Discussion

In light of the study aim to provide preliminary findings to inform future hypotheses, the discussion will focus on a summary of these findings followed by implications for refining our understanding of set shifting in OCD and AN. In line with hypotheses, we found that adolescents with OCD exhibited more perseverative errors than adolescents with WR-AN and healthy controls, suggesting possible difficulty with set shifting. Additionally, adolescents with WR-AN did not show significantly more perseverative errors compared with healthy controls. There were no differences in neural activity during sort vs. match blocks of the WCST between any of the groups. Within group analyses showed many overlapping regions of activation. Finally, adolescents with OCD showed a positive correlation between perseverative errors and activity in the right frontal pole, right inferior frontal gyrus, and right middle frontal gyrus, which was not present for healthy controls, although these correlations did not reach significance when examining the whole brain. The relation between perseverative errors and brain activity in the WR-AN group was not significantly different from either the OCD group or healthy controls.

Given prior research on set shifting deficits in adult patients with AN, but not consistently in adolescents [22], the pattern of behavioral data on the WCST showing the greatest perseverative errors in adolescents with OCD, may suggest that adolescents with WR-AN would develop more deficits over time. One study of neurocognitive function in adolescents with AN showed an age effect on cognitive flexibility, in line with this possible explanation [48]. However, another explanation could be that similarities in symptoms observed in AN and OCD are due instead to comorbid obsessive-compulsive symptoms or features present in AN rather than inherent features of the illness itself. In support of this, adults with AN have more obsessive and compulsive features than do adolescents, particularly adolescents who have achieved weight restoration [49]. AN in adulthood often has had a long duration, and obsessive compulsive personality traits predict a more enduring course of illness [49]. Additionally, studies of adolescents with AN have also found that obsessive compulsive features of AN symptoms predict poor prognosis in treatment, particularly those with longer inpatient hospital stays [50]. Thus, deficits in set shifting may be more characteristic of OCD than AN, and their presence in adults with AN may be due to comorbid OC traits rather than overlapping deficits or a shared phenotype between the two disorders. Further, enduring AN may reinforce or generate obsessive-compulsive features over time leading to the observed set shifting differences in adults with AN. A third explanation could be more directly related to the weight restored status of our sample, suggesting that partial recovery is associated with better set shifting. Perhaps weight gain was possible for these adolescents because they had normal set shifting performance. Indeed, some evidence of clustering in AN is present suggesting the presence of subgroups of patients with AN for whom neurocognitive functioning is more impaired than others [51]. Perhaps a cluster of patients with poor set shifting ability would be less likely to show weight restoration during adolescence and be recruited for this investigation. Thus, a longitudinal examination of set shifting over the course of the illness in adolescents and in different clusters of neurocognitive function would be necessary to rule out this explanation.

Interestingly, the relation between perseverative errors and brain activity during sort vs. match blocks was significantly different in the OCD group from healthy controls, with no differences between the WR-AN group and either comparison group. Although it could be suggested that this relation between brain and behavior would emerge in healthy controls if there were greater perseverative errors in this group, the trends do not suggest an effect driven by greater errors in the OCD group. Further, the brain regions identified in this analysis included the right inferior frontal gyrus, which is involved in inhibition [52]. That activity in this region was greater for adolescents with OCD who committed more perseverative errors may suggest greater *effort* to inhibit responses despite lack of success. An additional explanation for this finding may be that for healthy adolescents, a variety of impaired processes may lead to perseverative errors, implicating diffuse brain regions. However, for adolescents with OCD, perseverative errors may be more specifically related to difficulties in set shifting, hence the correlation with brain activity in regions related to inhibition and set shifting functions specifically. These findings represent the first evidence of specific brain region activity related to a behavioral measure of set shifting in OCD and suggest the importance of utilizing behavioral data to better understand neural correlates, particularly in light of the lack of an overall neural difference between sorting and matching blocks on the WCST.

Although not significantly different from either healthy controls or the OCD group, adolescents with WR-AN have a slight, but not significant positive relation between brain and behavior in these regions, which could again reflect partial impairment due to weight restoration, a developmental effect that may change with enduring illness, and/or a trait effect of comorbid OCD symptoms in AN. Those who do not recover and continue to struggle with AN into adulthood may have more obsessive-compulsive symptoms initially, as we know that individuals with these traits show poorer recovery rates [49], or they may continue to develop these traits and then show difficulties with set shifting later in the illness.

This study is the first to directly compare adolescents with OCD and weight restored AN on set shifting, which is important to understand whether these illnesses reflect the same underlying neural processes and deficits in set shifting. It is limited by the small sample, however, which may limit the ability to detect differences between groups. Additionally, the version of the WCST used in this study was developed for fMRI and does not have any established norms. Thus, comparisons with healthy controls in the sample were utilized to explore performance differences. Using a test with available norms would allow for improved ability to determine whether performance in the OCD group was truly aberrant or simply different from this particular group of healthy comparisons. Considering the small (yet significant) difference between the groups in perseveration errors, an open question is if and how these differences translate into day-to-day functioning. In order to answer this question, future research should assess the stability of these differences using more measures of set-shifting abilities and examine if these differences also reflected/correlated with self-reports of cognitive flexibility. Another limitation of the current study is the lack of data on duration of illness or on duration of weight restoration for WR-AN. Finally, as noted, the examination of WR-AN limits our ability to detect set shifting difficulties that could be present during the acute stage of the illness that improved with weight gain. We thus

acknowledge that findings are preliminary and exploratory, but the unique sample may offer important insight into future work with adolescent patients.

Difficulty with set shifting is thought to underlie some of the rigidity and rule-bound behavior seen in both OCD and AN [15, 16]. Nevertheless, in our study, adolescents with OCD showed the greatest perseverative errors and greater neural activation in regions associated with set shifting compared to healthy controls. Specifically, the relation between perseverative errors and brain activity in frontal regions commonly associated with set shifting and executive function was only seen in adolescents with OCD. Future research should include longitudinal examinations of these groups with greater focus on obsessive and compulsive symptoms across patient groups as they move from adolescence to adulthood to further disentangle set shifting and the related neural processes in these groups. Direct examination of the hypothesis that set shifting deficits observed in adult patients with AN are due to obsessive-compulsive features will be important to inform treatment approaches that may address these features. Differentiating deficits that develop over the course of the illness versus those that are present and may predict poor prognosis can further improve our ability to both treat the illness and prevent an enduring course.

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Fig. 1.

Mean proportion of trials with perseverative errors during the sort blocks for each group (calculated as the number of trials during which participants kept sorting cards according to the rule of the previous set after receiving an error feedback divided by the total number of trials in the sort blocks). Error bars represent SD.

Fig. 2. Correlations between brain activity during sort vs match blocks and perseverative errors. Brain regions (right frontal pole, right inferior frontal gyrus, and right middle frontal gyrus) and correlation for OCD, WR-AN, and healthy control groups

Table 1.

Demographic and Clinical Means (SD)

Measure	AN (n=14)	OCD (n=11)	Health Controls (n=24)
Age	15.79 (1.93)	15.64 (2.01)	15.29 (1.65)
%MBW	99.14 (7.44)	99.81 (13.61)	103.28 (11.23)
EDE Global Score	1.79 (1.47)		
CY-BOCS Severity		18.7 (5.33)	

%MBW = percentage of median body weight based on CDC curves of expected growth, EDE = eating disorder examination (only available for AN group), CY-BOCS = Children's Yale-Brown OC Scale (only available for OCD group)

Table 2.

Brain regions (MNI coordinates of cluster peaks) and corresponding max Z-scores for within group comparisons

x	y	z	Max Z	Brain Region
Healthy Controls: Sort > Match				
6	-12	28	6.44	Bilateral posterior cingulate
12	-22	14	5.79	Bilateral thalamus
38	24	36	7.36	Bilateral frontal pole/middle frontal gyrus/inferior frontal gyrus/paracingulate gyrus
-32	-68	-18	7.34	Bilateral temporal occipital fusiform gyrus/precuneus/lateral occipital cortex
Healthy Controls: Match > Sort				
8	-54	16	4.18	Right precuneus
40	-26	68	4.94	Right postcentral gyrus
38	18	-32	4.15	Right temporal pole
-22	-14	-18	4.87	Left hippocampus
-6	-60	22	5.21	Left precuneus
38	-20	8	4.84	Right central opercular cortex/insula
0	46	-10	5.69	Bilateral paracingulate gyrus (inferior)/anterior cingulate/frontal pole
-60	0	8	5.29	Left precentral gyrus/insula/middle temporal gyrus
OCD: Sort > Match				
4	-74	12	4.18	Right intracalcarine cortex
30	26	-4	4.6	Right orbitofrontal cortex/insula
-30	26	-4	4.59	Left orbitofrontal cortex/insula
-8	24	32	4.37	Bilateral paracingulate gyrus
-28	-2	54	4.74	Left middle frontal gyrus
40	24	32	6.41	Right middle frontal gyrus
-48	2	34	5.02	Left precentral gyrus
34	-58	40	6.15	Bilateral precuneus/lateral occipital/superior parietal
WR-AN: Sort > Match				
4	16	54	3.72	Right superior frontal gyrus
14	-66	44	4.13	Right precuneus
36	-80	16	4.2	Right lateral occipital cortex
-24	-82	12	4.74	Left lateral occipital cortex
-40	4	32	4.45	Left precentral gyrus/middle frontal gyrus
32	4	46	4.17	Right middle frontal/precentral gyrus
-42	-60	-6	4.65	Left inferior temporal gyrus
40	30	24	5.16	Right middle frontal gyrus
-38	-50	46	5.28	Left superior parietal lobule/angular gyrus/lateral occipital cortex
36	-52	44	5.02	Right angular gyrus/superior parietal lobule/lateral occipital cortex
WR-AN: Match > Sort				
-54	-72	28	4.39	Left lateral occipital cortex
-38	-22	6	4.3	Left Heschl's gyrus/insula

x	y	z	Max Z	Brain Region
-6	10	0	4.26	Bilateral caudate
42	-12	4	4.73	Right insula
-22	-34	-16	4.46	Left hippocampus
-26	10	-34	4.82	Left temporal pole
40	-4	-22	4.43	Right temporal pole
-42	-4	-10	5.12	Left insula
-8	-60	24	5.57	Bilateral precuneus
6	36	0	5.62	Bilateral anterior cingulate/paracingulate