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RESEARCH ARTICLE

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The neural correlates of a central coherence task in young women with anorexia nervosa

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Abstract

Objective: Heightened detail-processing and low levels of central coherence are common in individuals with anorexia nervosa (AN) and predict poorer prognosis. However, it is unclear whether these processing styles predate the disorder or, rather, emerge during later stages of AN. The current study aimed to address this question by investigating central coherence, and the neural correlates of central coherence, in a sample of young women with AN with shorter duration of illness than previous studies recruiting adult samples.

Methods: We recruited 186 participants, including: 73 young women with AN, 45 young women weight-recovered from AN, and 68 age-matched controls. Participants completed the Embedded Figures Task during an fMRI scan.

Abbreviations: AAN, Acute anorexia nervosa; ADHD, Attention deficit hyperactivity disorder; AN, Anorexia nervosa; ASD, Autism spectrum disorders; AQ10, Autism quotient-10 item version; BMI, Body mass index; BOLD, Blood-oxygen-level-dependent; DSM, Diagnostic and Statistical Manual of Mental Disorders; EFT, Embedded Figures Task; FEAT, FMRI Expert Analysis Tool; fMRI, Functional magnetic resonance imaging; HC, Healthy control; MRI, Magnetic resonance imaging; ROI, Region-of-interest; RT, Reaction time; WR, Weight-recovered from anorexia nervosa.

Monica Leslie and Daniel Halls contributed equally to the manuscript.

Results: There were no significant differences between the participant groups in performance accuracy or reaction time. There were no other between-groups differences in neural response to the Embedded Figures Task.

Conclusions: These findings contrast with evidence from older adults demonstrating differences in the neural underpinning of central coherence amongst participants with AN versus control participants. The current study adds to an increasing literature base demonstrating the resilience of neuropsychological traits and associated brain systems in the early stages of AN.

KEYWORDS
anorexia nervosa, central coherence, eating disorders, fMRI, neuropsychology

Key points

- Performance on the Embedded Figures Task did not differ in young women with a history of anorexia nervosa compared to control participants.
- The neural correlates of central coherence did not differ in young women with anorexia nervosa compared to control participants.
- Duration of anorexia nervosa was not correlated with neural response to the Embedded Figures Task.

1 | INTRODUCTION AND AIMS

Anorexia nervosa (AN) is a severe psychiatric disorder characterised by restricted eating and other weight-loss behaviours leading to excessively low body weight, intense fear of gaining weight or becoming fat, and disturbances in the perception of body weight and shape or disturbances in the perception of the seriousness of the individual's low weight (American Psychiatric Association, 2013). AN has a complex aetiology with numerous risk and maintenance factors leading to the onset and persistence of the disorder, respectively.

One factor that has been suggested to contribute to the development and maintenance of AN are autistic traits. For example, autism-spectrum disorders are over-represented in populations with AN versus the general population (Westwood et al., 2017) and autistic traits have been found to correlate with greater levels of disordered eating even in non-clinical young adult populations (Carton et al., 2014). In particular, a neuropsychological phenotype characterised by a rigid and detail-focused cognitive processing style, characteristic of autism spectrum disorders (ASD) (Cribb et al., 2016), has been posited to contribute to the maintenance of restrictive eating behaviour in AN (Treasure & Schmidt, 2013).

Later evidence has supported this hypothesis, finding weaker levels of central coherence in adults with both AN and bulimia nervosa (Lang et al., 2014, 2016), where central coherence is defined by inefficiencies in global processing in combination with a greater propensity for detail-focused processing. Evidence suggests that the obsessionality associated with a rigid and detail-focused processing style impedes response to treatment-as-usual and is associated with a poorer prognosis in AN (Lo Sauro et al., 2013). However, the extent to which these traits reflect an inherited endophenotype, versus state-related consequences of starvation, is currently unclear.

One line of research attempting to clarify the origins of weak central coherence in AN has focused on assessing cognitive factors in children and young adults with the disorder. Children and young adults with AN, on average, have shorter durations of illness than older adults with AN (Fisher et al., 2001), thus, any cognitive differences detected in this population are therefore more likely to reflect pre-existing vulnerability to the disorder rather the effects of prolonged starvation. A systematic review conducted by Lang and Tchanturia (Lang & Tchanturia, 2014) found evidence of weaker central coherence in some studies of children and adolescents with AN, compared to age-matched control participants. However, several studies included both children and adults in the same subsample, thus preventing the assessment of central coherence in youth populations alone (Lang & Tchanturia, 2014). Further research in children and young adults with AN is therefore needed to clarify whether deficiencies in central coherence are present at earlier stages of the disorder.

Previous studies have identified differences in neural functioning associated with central coherence in adults with AN. For example, our previous study, which included

an older sample with a longer duration of AN, found less activation of the right precuneus and greater activation of the right fusiform gyrus among adults with AN versus healthy control participants during the completion of a task measuring central coherence (Fonville et al., 2013). However, this study observed a pattern of behavioural effects in the opposite direction to that generally observed in adults with AN, such that participants with AN exhibited lower accuracy on an Embedded Figures Task (EFT), which requires participants to identify a geometric shape within the context of a more complex image. These findings therefore indicate stronger central coherence amongst participants with AN compared to controls.

One potential explanation for this finding is that the functional magnetic resonance imaging (fMRI) version of the EFT is different from the version used outside of the scanner due to the addition of a forced choice component between two candidate figures, rather than the identification of the target shape within a single complex figure. However, this design feature is necessary to avoid introducing excessive noise into the fMRI signal caused by the participant pointing at the location of the identified geometric shape, as per the version of the task administered outside of scanner conditions. Furthermore, although the fMRI version of the EFT has previously been found to be associated with minimal performance differences in autistic populations as compared to control populations (Ring et al., 1999; Damarla et al., 2010; Manjaly et al., 2007; Spencer et al., 2012), it has nonetheless yielded important contributions to our understanding of differences in the neural underpinnings of local detail processing in autism. We, therefore, believe that the task warrants similar use to expand our knowledge of the neural correlates of local detail processing in populations with AN as well.

Furthermore, a follow-up study later found that, following a course of cognitive remediation therapy aimed at increasing cognitive flexibility and global thinking patterns, participants with AN exhibited greater task-related reductions in activation in the fusiform gyrus and the middle occipital gyrus, and a greater increase in activation within the medial frontal gyrus extending into the precuneus, compared to a control group of healthy participants over the same period of time (Fonville et al., 2014). It is not surprising to find that these regions are associated with a visual search task, given that transcranial magnetic stimulation evidence has demonstrated that the right precuneus contributes to visual short term memory capacity (Kraft et al., 2015) and the fusiform gyrus is associated with processing visual stimuli and identifying this pattern with a previously defined object category (e.g., a face, house, etc.) (Tarr & Gauthier, 2000). This pattern of effects therefore suggests that cognitive remediation therapy is associated with rectification of initial differences in the neural underpinnings of detail-focused processing in adults with AN. A separate study also found that central coherence in women with AN was positively associated with functional connectivity within somatosensory neural networks at rest, and may be related to body checking behaviours (Favaro et al., 2012).

However, to date, no study has examined whether young adults with AN also exhibit differences in activation of the neural circuits involved in global versus detail-focused processing. These differences in neural activation may occur at an earlier stage of illness even in the absence of demonstrated differences in performance. The current study therefore aimed to address this gap in the literature, by investigating differences in the neural correlates of central coherence in young women with, versus without, AN on the EFT. In line with the majority of central coherence findings observed in adults, we hypothesised that young women with AN would similarly demonstrate faster reaction times and greater accuracy on the EFT. However, given that our previous study administering the EFT in adults with AN did not replicate these behavioural findings (Fonville et al., 2013), we therefore hypothesised that we would observe differences in the activation of the same regions previously observed in adults with AN, the right fusiform gyrus and the right precuneus, but that the direction of these differences may differ in line with our anticipation of stronger, rather than weaker, performance on the EFT. Given that superior detail-focused processing is strongly associated with autistic features (Cribb et al., 2016), we also hypothesised that greater levels of autistic traits would predict blood-oxygen-level-dependent (BOLD) response within the right precuneus and right fusiform gyrus in young women with AN and across the entire participant sample.

2 | METHODS

2.1 | Participants

We recruited 186 young women to take part in the current study. Seventy-three women met DSM-5 criteria (American Psychiatric Association, 2013) for AN at the time of the study, 23 women were weight-restored from AN but exhibited continuing elevated levels of eating disorder symptoms, 22 women were in full recovery from AN, and 68 comparison women had no current or prior history of an eating disorder. Demographic characteristics associated with the sample, separated by clinical status, are presented in Table 1. Given the low sample sizes for the weight-recovered and fully recovered participant samples, these groups' data were pooled into a single weight-recovered participant group for all analyses.

TABLE 1 Descriptive demographic statistics

	Healthy Control ($n = 69$)			Acute AN ($n = 68$)			Weight-restored AN ($n = 49$)					
	Mean (SD)	Median (IQR)	Skew	Mean (SD)	Median (IQR)	Skew	Mean (SD)	Median (IQR)	Skew	F	df	p
Age (Years)	19.44 (3.13)	18.50 (17.33–22.61)	0.52	19.04 (2.79)	18.52 (17.01–21.52)	0.36	19.78 (3.12)	18.99 (17.35–22.42)	0.21	1.35	2	0.262
BMI	22.72 (3.32)	22.20 (20.39–24.35)	1.05	16.60 (1.55)	16.79 (15.59–18.02)	−0.66	21.06 (2.37)	20.07 (19.42–21.94)	1.12	101.23	2	<0.001
IQ	108.23 (7.02)	109.12 (103.75–112.83)	−0.81	108.02 (6.86)	107.88 (104.16–112.21)	−0.06	111.66 (6.31)	110.77 (106.84–116.34)	0.23	2.52	2	0.084
EDE-Q global score	0.51 (0.54)	0.32 (0.14–0.60)	1.43	3.43 (1.55)	3.77 (1.98–4.82)	−0.42	2.80 (1.70)	2.81 (1.13-4.47)	−0.14	77.90	2	<0.001
HADS	7.71 (4.90)	6.50 (5.00–10.00)	1.14	18.50 (7.11)	20.00 (14.75–23.00)	−0.69	15.39 (7.25)	14.00 (11.50–19.25)	1.17	41.54	2	<0.001
AQ-10	2.27 (1.54)	2.00 (1.00–3.00)	0.74	4.41 (2.12)	4.00 (3.00–6.00)	0.45	3.61 (2.21)	3.00 (200–5.00)	0.88	11.82	2	<0.001

Abbreviations: AN, anorexia nervosa; AQ-10, autism quotient - 10 item version; BMI, body mass index; EDE-Q, eating disorder examination - questionnaire version; HADS, hospital anxiety and depression scale; IQ, intelligence quotient; IQR, interquartile range.

This analysis choice, thus, allows us to compare two groups that have experienced similar predisposing factors to AN but current normal weight status, thus allowing us to more clearly identify neural changes associated with temporary state condition during the acute phase of the illness (observed only in participants with current AN), as opposed to a more enduring endophenotype (observed in participants with, and weight-recovered from, AN). Twenty-two women with current AN, 22 weight-restored women, and two healthy control women were taking psychiatric medication at the time of the study. This amounted to 24.73% of the total sample taking psychiatric medication at the time of the study.

Thirteen women with current AN were taking an antidepressant, one was taking an antipsychotic, five were taking both an antidepressant and an antipsychotic, one was taking an antiepileptic, one was taking an antidepressant and antiepileptic, and one was taking an anxiolytic drug. Of the women who were weight-recovered from AN, 14 were taking an antidepressant, three were taking an antipsychotic, two were taking an antiepileptic, two were taking an antidepressant and an antipsychotic, and one was taking an antidepressant and anxiolytic drug. One healthy control woman was taking an antidepressant and one was taking ADHD medication at the time of the study. The average illness duration of participants with current AN was 3.10 years (SD = 2.56 years) and the average illness duration of participants weight restored from AN was 4.53 years (SD = 2.78 years).

All participants were required to be female and between the ages of 16 and 25 years old. Participants in the current AN participant group were required to meet DSM-5 criteria for AN at the point of recruitment and have a BMI less than 90% of the median BMI for age and gender or a body mass index (BMI) less than 18.5. Participants in the weight-recovered AN group must have previously been diagnosed with AN, but have a BMI within the healthy weight range (18.5–25) at the time of the study. Participants' history of an eating disorder was verified using the Structured Clinical Interview for DSM-5 (First et al., 2015), which was checked against their weight-for-height status in the laboratory. Participants in the healthy control group were required to have no current eating disorder or history of an eating disorder. Participants in the healthy control group were also required to have a BMI within the healthy weight range (18.5–25). Exclusion criteria for the study included any neurological impairment (e.g., epilepsy), serious brain injury or learning difficulties, and MRI incompatibility (e.g., pregnancy, claustrophobia, inability to lie down flat, and any metal in or on the body which could not be removed). Participants with current AN were recruited

from the South London and Maudsley National Health Service Foundation Trust. The healthy control and recovered AN participant groups were recruited via social media, via the website for BEAT (the largest UK charity for eating disorders), and through advertisements in the local community. All participants provided written informed consent to take part in the study, and for participants under the age of 18, parental consent was also obtained. Ethical approval for the study was granted by the London–Surrey Borders Research Ethics Committee (REC Reference: 17/LO/0271). All study activities were in completed in accordance with the Declaration of Helsinki.

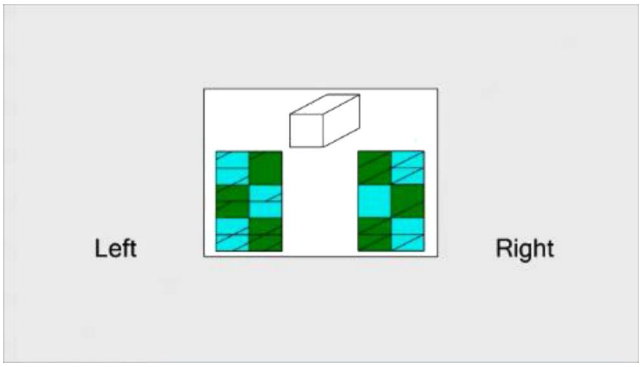

FIGURE 1 An example trial from the embedded figures task

2.2 | Measures

The Eating Disorders Examination - Questionnaire version (Fairburn et al., 2009), the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), the National Adult Reading Test (Nelson, 1982), and the Autism Quotient-10 item version (AQ10) (Allison et al., 2012) were administered to the participants. Details about these measures are presented in the Supplementary Material.

2.2.1 | The embedded figures task

The EFT requires participants to identify a geometric shape within the context of a more complex image. During each trial, participants were presented with one target geometric shape alongside two complex images. Participants used their right hand to press the left or right button on a button box to indicate whether the corresponding left or right complex image contained the target geometric shape. Each trial fell into one of two difficulty categories, simple or complex, depending on the degree of intricacy of the images being searched. An example trial of the EFT is presented in Figure 1.

2.3 | Procedure

Each participant attended two study sessions. During the first session, participants completed the self-report questionnaires and structured clinical interviews. Participants were screened for MRI safety prior to proceeding to the second session. During the second study session, participants completed the EFT during an fMRI scan. Each participant was presented with a total of 18 simple task trials and 18 complex task trials, consisting of six blocks of three trials each, where trial blocks alternated between simple and complex difficulty level. Each trial lasted for 10 s. A black screen with a central white fixation cross was presented for 30 s at the beginning of the task, halfway through the task, and at the end of the task. The total duration of the task was therefore 450 s.

2.4 | fMRI scan acquisition

A total of 225 volumes were acquired during the functional scan. Images within the fMRI scans were acquired with a slice thickness of 3 mm and a slice gap of 3.3 mm. A total of 41 slices were acquired in a top to bottom order. The field of view was 240 mm^2 with a 64 $\times$ 64 matrix and a slice gap of 3 mm. The scan was conducted with an echo time of 30 ms and a repetition time of 2,000 ms. The flip angle was set to 75 degrees. A 3D high-spatial-resolution, Magnetisation Prepared Rapid Acquisition (3D MPRAGE) T1-weighted scan was also acquired. Field of view was 270 mm^2 with a 256 $\times$ 256 matrix size. The T1-weighted scan was conducted with an echo time of 3.016 ms and a repetition time of 7.312 ms. The flip angle was set to 11 degrees.

2.5 | Statistical analysis

2.5.1 | Behavioural data analysis

We captured accuracy and reaction time data during the EFT, and subsequently analysed these data using a 3 (Acute AN vs. Weight-Recovered AN vs. Healthy Control) x 2 (Simple vs. Complex) mixed-design ANOVA.

2.5.2 | MRI Data Pre-processing

We conducted pre-processing of the MRI data using fMRIprep 1.2.6-1 (Esteban et al., 2017, 2019), which is based on Nipype 1.1.7 (Gorgolewski, 2017; Gorgolewski

et al., 2011). The full boilerplate associated with fMRI-Prep containing extensive details of pre-processing is presented in the Supplementary Material.

2.5.3 | MRI Data Analysis

We conducted both first- and second-level processing using FSL FEAT (FMRI Expert Analysis Tool) Version 6.00 (Smith et al., 2004; Jenkinson et al., 2012). At the single subject level, the data were modelled using the general linear model framework. We operationalised the 'Central Coherence' regressor as a binary contrast comparing complex against simple task trials (Complex - Simple) and a separate binary contrast comparing simple against complex task trials (Simple - Complex). This approach allowed us to isolate neural processes associated with local visual search processes while subtracting out the confounding influence of early visual perceptual processes. However, in order to determine the extent to which any differences observed between our results and the results of our previous study conducted in an older adult population with AN (Fonville et al., 2013) were associated with true population differences, rather than the result of a different analysis approach, we also repeated our previous analysis approach in a separate analysis we report in the Supplementary - Material. In this analysis, we compared BOLD activation associated with both simple and complex EFT trials against BOLD activation associated with viewing a fixation cross.

The BOLD signal was modelled by convolving our design matrix with a Double Gamma function. We included global signal, derivatives of motion parameters, squares of motion parameters, and a scrubbing variable excluding volumes with a framewise displacement >0.9 as confound variables at the single-subject level. A multivariate analysis of variance for all motion parameters and the scrubbing variable revealed that head motion did not significantly differ between the three participant groups ($F = 0.83$, $df_1 = 28$, $df_2 = 338$, $p = 0.714$, partial $\eta_2 = 0.064$).

At the group level, we conducted region-of-interest (ROI) analyses using featquery within the right precuneus and the right fusiform gyrus. We created the ROI masks based on the WFUpickatlas toolbox (Maldjian, http://www.nitrc.org/projects/wfu_pickatlas) in SPM12 (Penny et al., 2011) and re-sliced the masks into subject space. We subsequently conducted exploratory whole brain analyses using cluster level inference with a cluster threshold of $Z > 3.1$ and $p < 0.05$, corrected for multiple comparisons using Gaussian random field theory.

3 | RESULTS

3.1 | Behavioural data analyses

Descriptive statistics associated with the accuracy and reaction time (RT) data are presented in Table 2. There were four outliers ($|Z| > 3.0$) in the accuracy data for simple trials, two outliers in the accuracy data for complex trials, three outliers in the RT data for simple trials, and one outlier in the RT data for complex trials. These cases were excluded from relevant analyses. The 3 × 2 ANOVA for Accuracy data revealed a significant main effect of Complexity, such that participants were more accurate in responding to simple versus complex trials, $F(1,175) = 897.36$, $p < 0.001$, partial $\eta_2 = 0.837$. However, there was not a significant main effect of participant group ($F(2,175) = 0.49$, $p = 0.613$, partial $\eta_2 = 0.006$) or a significant interaction between trial complexity and participant group ($F(2,175) = 0.72$, $p = 0.486$, partial $\eta_2 = 0.008$).

The 3 × 2 ANOVA for the RT data also revealed a main effect of Complexity, such that participants responded more quickly on simple versus complex trials, $F(1,175) = 4160.06$, $p < 0.001$, partial $\eta_2 = 0.960$. There was not a significant interaction between trial complexity and participant group, $F(2,175) = 2.18$, $p = .117$, partial $\eta_2 = 0.024$. However, there was a trend towards a significant main effect of participant group ($F(2,175) = 2.42$, $p = 0.092$, partial $\eta_2 = 0.027$). A post hoc Fisher's LSD test revealed that this trend was driven by faster RT of healthy control participants versus participants with acute AN (mean difference = 185.27, SE = 86.298, $p = 0.033$). There were no significant differences in RT for the healthy control versus weight-recovered participant groups (mean difference = 55.36, SE = 98.723, $p = 0.576$) or between the acute AN and weight-recovered participant groups (mean difference = 129.92, SE = 96.748, $p = 0.181$).

3.1.1 | Results of ANOVAs investigating the relationship between autistic traits and performance on the EFT

We investigated whether autistic traits predicted performance on the EFT using a 2 (Low autistic traits vs. high autistic traits) x 2 (Simple vs. Complex) mixed design ANOVA. The median AQ10 score for the sample was 3. We therefore divided the sample into two groups, such that the group with low autistic traits was defined by an AQ10 score ≤ 3, while the group with high autistic traits was defined by an AQ10 score > 3. Descriptive statistics associated with the accuracy and reaction time (RT) data for each group are presented in Table 3. The 2 × 2 ANOVA for

TABLE 2 Descriptive statistics associated with the accuracy and reaction time scores in the embedded figures task for each participant group

	Simple Trials: Accuracy Mean (SD)	Complex Trials: Accuracy Mean (SD)	Simple Trials: Reaction Time Mean (SD)	Complex Trials: Reaction Time Mean (SD)
Healthy control	0.98 (0.037)	0.70 (0.144)	1585.97 (393.854)	5031.89 (805.374)
Acute AN	0.98 (0.047)	0.68 (0.113)	1660.58 (483.538)	5360.64 (708.246)
Weight-restored AN	0.97 (0.046)	0.71 (0.120)	1627.53 (472.016)	5115.18 (716.909)

Note: Accuracy data is presented as the proportion of correct responses. Reaction time data are presented in milliseconds.
Abbreviation: AN, anorexia nervosa.

TABLE 3 Descriptive statistics associated with the accuracy and reaction time scores in the embedded figures task, divided by high versus low AQ10 scores

	Simple Trials: Accuracy Mean (SD)	Complex Trials: Accuracy Mean (SD)	Simple Trials: Reaction Time Mean (SD)	Complex Trials: Reaction Time Mean (SD)
Low AQ10 group	0.98 (0.036)	0.70 (0.123)	1669.58 (438.383)	5249.20 (735.568)
High AQ10 group	0.97 (0.055)	0.69 (0.124)	1610.91 (470.801)	5141.81 (761.951)

Notes: Accuracy data are presented as the proportion of correct responses. Reaction time data are presented in milliseconds.
Abbreviation: AQ10, autism quotient – 10-item version.

Accuracy data revealed a significant main effect of Complexity, such that participants were more accurate in responding to simple versus complex trials, F (1,165) = 836.47, $p < 0.001$, partial $\eta_2 = 0.835$. However, there was not a significant main effect of autistic traits (F (1,165) = 0.56, $p = 0.457$, partial $\eta_2 = 0.003$) or a significant interaction between trial complexity and autistic traits (F (1,165) < .001, $p = 0.999$, partial $\eta_2 < 0.001$).

The 2 × 2 ANOVA for the RT data investigating the effect of autistic traits also revealed a main effect of Complexity, such that participants responded more quickly on simple versus complex trials, F (1,165) = 3976.01, $p < 0.001$, partial $\eta_2 = 0.960$. There was not a significant interaction between trial complexity and autistic traits, F (1,165) = 0.19, $p = 0.666$, partial $\eta_2 = 0.001$, nor was there a main effect of autistic traits on RT, F (1,165) = 1.09, $p = 0.299$, partial $\eta_2 = 0.007$.

3.2 | ROI analyses

3.2.1 | ROI analysis for the right precuneus

We conducted a between-groups ANOVA comparing mean BOLD activation for the EFT complexity contrast within the right precuneus for the participant groups with acute AN (AAN), weight recovered from AN (WR), and healthy control participants (HC). There were three outliers (|Z| > 3.0) in the extracted parameters for the precuneus data, which were excluded from the analysis. There were no significant differences between the three participant groups, F (2,175) = 0.14, $p = 0.867$, partial $\eta_2 = 0.002$. We subsequently added psychiatric medication as a covariate in a between-groups ANCOVA to account for any suppression of between-group differences driven by psychotropic medication. This ANCOVA did not reveal significant differences between the three participant groups, F (2,174) = 0.47, $p = 0.628$, partial $\eta_2 = 0.005$. The difference between participant groups in the mean BOLD activation for the EFT complexity contrast within the right precuneus is depicted in Figure S1.

3.2.2 | ROI analysis for the right fusiform gyrus

We conducted a between-groups ANOVA comparing mean BOLD activation for the EFT complexity contrast within the right fusiform gyrus for the AAN, WR, and HC participant groups. There were two outliers (|Z| > 3.0) in the extracted parameters for the fusiform gyrus data, which were excluded from the analysis. There were no

significant differences between the three participant groups, $F(2,176) = 2.13$, $p = 0.121$, partial $\eta_2 = 0.024$. We subsequently added psychiatric medication as a covariate in a between-groups ANCOVA to account for any suppression of between-group differences driven by psychotropic medication. This ANCOVA also did not reveal significant differences between the three participant groups, $F(2,175) = 1.77$, $p = 0.173$, partial $\eta_2 = 0.020$. The difference between participant groups in the mean BOLD activation for the EFT complexity contrast within the right fusiform gyrus is depicted in Figure S2.

3.3 | Exploratory whole-brain analyses

An initial one-sample *t*-test revealed two clusters associated with the Complex - Simple contrast spanning the left premotor cortex, left dorsomedial frontal cortex, left inferior frontal gyrus, the right dorsomedial frontal cortex, the left middle parietal lobe and the left primary sensory cortex. The full results of this one-sample *t*-test are presented in Table 4. An additional one-sample *t*-test revealed one significant cluster associated with the Simple - Complex contrast spanning the left supplementary motor area, the left medial prefrontal cortex, the left primary sensory cortex, the right medial prefrontal cortex, and the left primary motor cortex. The full results of this one-sample *t*-test are presented in Table 5.

A between-groups ANOVA comparing the BOLD response associated with complexity of the EFT between the three participant groups did not reveal any significant clusters associated with the Complex - Simple or Simple - Complex contrast. We next conducted a sensitivity analysis excluding participants taking psychoactive medication to account for any suppression of between-group differences driven by psychotropic medication. This between-groups ANOVA also failed to detect any significant between-groups differences associated with greater or lesser complexity of the EFT. We subsequently conducted exploratory whole brain analyses across the entire participant sample including AQ10 as a covariate. We also conducted additional exploratory whole brain analyses within the participant group with current AN including AQ10 score and illness duration as a covariate in separate one-sample *t*-tests for the Complex - Simple and Simple - Complex contrasts. There was no association between the AQ10 and BOLD response to the EFT amongst participants with current AN or amongst the entire participant sample. Illness duration was not associated with BOLD response to either the Complex - Simple or Simple - Complex contrasts among the AAN sample.

4 | DISCUSSION

The current study aimed to investigate differences in the neural correlates of central coherence in young women with, versus without, AN on the EFT. We hypothesised that young women with AN would demonstrate faster reaction times and greater accuracy on the EFT. With regards to the fMRI data, we hypothesised that young women with AN would exhibit different levels of task-related activation in the right precuneus and the right fusiform gyrus, as compared to control participants during the EFT. We also hypothesised that the greater levels of autistic traits would predict BOLD response within the right precuneus and right fusiform gyrus in young women with AN and the entire participant sample.

The data did not support our hypotheses regarding the behavioural measures, as there were no significant differences between participant groups for the accuracy data. Furthermore, there was a trend effect for the RT data in the opposite direction to our hypothesis, such that AAN participants demonstrated numerically slower, rather than faster, reaction times than HC participants for complex trials of the EFT. Our ROI analyses did not reveal significant differences between the participant groups in the mean activation of the right fusiform gyrus or right precuneus in response to completing complex versus simple task trials. There were no between-group differences associated with the trial-complexity contrast in any other brain regions. We did not observe an association between autistic traits and neural response to the task amongst the AAN participant group or the entire participant sample.

Our behavioural data add to a limited and mixed set of previous findings assessing central coherence in adolescents and young adults with AN. While evidence in older adults with a more chronic course of illness has suggested a pattern of weaker central coherence amongst participants with AN (Lang et al., 2014), previous studies conducted in adolescents have not demonstrated a clear pattern of effects (Lang & Tchanturia, 2014). As mentioned previously, it is worth noting that the version of the EFT used in fMRI studies involves presenting a forced-choice task, such that participants must choose which of two presented figures contained the target shape (Fonville et al., 2013). By contrast, versions of the EFT administered outside of the fMRI scanner only require participants to indicate when they have found the target shape within a single complex figure (Lang et al., 2014). Findings observed in relation to differences in central coherence may be specific to the measure used and it is therefore worth noting that our findings are in line with those of our previous fMRI study, which administered the same version of the EFT to adults with AN, including the

TABLE 4 Results of the one-sample *t*-test exploratory whole brain analysis for the neural activation associated with the embedded figures task contrast comparing complex to simple trials

CLUSTER Number	Hemisphere	k	p_{FWE}	Peak Coordinates x	y	z	Description
CLUSTER 1	Bilateral	7,504	<0.001	−26.5	−0.5	59.5	Left premotor cortex, left dorsomedial frontal cortex, left dorsolateral frontal cortex, and right dorsomedial frontal cortex
				−24.5	−2.5	53.5	
				−0.5	15.5	49.5	
				−50.5	3.5	33.5	
				9.5	23.5	37.5	
				−50.5	29.5	25.5	
CLUSTER 2	Left	222	0.001	−48.5	−32.5	39.5	Left middle parietal lobe and left primary sensory cortex
				−54.5	−28.5	45.5	
				−58.5	−28.5	47.5	
				−62.5	−16.5	37.5	

Notes: A $Z > 3.1$ cluster-forming threshold was used. We report significant clusters at the $p < 0.05$ threshold.

TABLE 5 Results of the one-sample *t*-test exploratory whole brain analysis for the neural activation associated with the embedded figures task contrast comparing simple to complex trials

CLUSTER Number	Hemisphere	*k*	P_{FWE}	Peak Coordinates *x*	*y*	*z*	Description
CLUSTER 1	Bilateral	23,600	<0.001	−4.5	−16.5	49.5	Left supplementary motor area, left medial prefrontal cortex, left primary sensory cortex, right medial prefrontal cortex, and left primary motor cortex
				−4.5	59.5	−6.5	
				3.5	59.5	−6.5	
				−22.5	−28.5	63.5	
				−28.5	−28.5	57.5	
				−10.5	59.5	25.5	

Notes: A $Z > 3.1$ cluster-forming threshold was used. We report significant clusters at the $p < 0.05$ threshold.

forced-choice component of the task. The current study makes a significant contribution to evidence examining central coherence in young people and young adults, as it is the first highly-powered study to measure central coherence on the EFT in young adults with a history of AN versus age-matched controls and the first study to examine to examine associations between EFT-related neural activation and autistic traits in a sample with AN. Taking the current study into account, in contrast to adult samples, the evidence to date does not support the existence of consistent deficiencies in central coherence in female adolescents and young women with AN.

It should be noted that the current neuroimaging findings, observed in a young adult sample with a mean age of 19.46 years, are in contrast with those found in an older adult sample, with a mean age of approximately 24 years (Fonville et al., 2013). We did not find evidence of between-group differences in the right fusiform gyrus or the right precuneus, between the AAN participant group, the WR participant group, or HC participants. Our current findings, thus, contrast with our previous research conducted in a sample with a longer duration of AN, such that Fonville and colleagues (Fonville et al., 2013) rather found evidence of increased activation in the right fusiform gyrus and a lesser BOLD response in the right precuneus among participants with AN, versus HC participants. This contrast also reflects differences in behavioural findings, such that we observed trend level differences in group RT to the EFT, while our previous study observed greater accuracy of HC participants on the EFT, versus participants with AN. Thus, both studies indicate at least trend-level differences for better central coherence amongst participants with AN versus the general population, with stronger evidence of better central coherence observed in our sample of slightly older adults with AN.

As an alternative interpretation, however, given that no difference in accuracy was found between any of the participant groups in response to the EFT, it should be considered that the slower RT of AAN participants in the current study could reflect difficulties with attentional processing or motor speed, as opposed to an enduring cognitive style. In support of this hypothesis, Kjaersdam Telléus and colleagues (Kjaersdam Telléus et al., 2015), in a sample of 188 children and adolescents, found that participants with AN demonstrated reduced motor speed compared to HC participants, which could reflect a direct effect of malnourishment.

However, it should be noted that there were significant differences in the methodology of the current study as compared to our previous study investigating differences in the neural correlates of central coherence in AN (Fonville et al., 2013). First, given that we recruited an older sample of adults in our previous study (Fonville et al., 2013), it may be the case that differences in the activation of the right precuneus and right fusiform gyrus only appear amongst participants with AN, versus HC participants, at later stages of the disorder or as a function of alterations in the natural synaptic pruning process associated with maturation (Penzes et al., 2011). Additionally, the current study used a different analysis approach such that, rather than comparing neural activation during the EFT to the passive viewing of a fixation cross, we instead compared neural activation during complex task trials to that observed during simple task trials.

However, we conducted a supplementary analysis using the same contrast analysed in our previous study (Fonville et al., 2013), such that we compared neural activation during both simple and complex trials of the EFT to neural activation associated with the passive viewing of a fixation cross. This analysis also failed to detect significant between-group differences in an exploratory whole-brain analysis. We did use different neuroimaging software (FSL rather than XBAM) and a more aggressive de-noising procedure than in our previous study (Fonville et al., 2013). However, greater de-noising, including controls for derivatives and squares of motion parameters, should produce a greater signal-to-noise ratio and thus more sensitive identification of between-group differences, rather than the fewer whole-brain clusters observed in the current study. Therefore, our failure to replicate previous findings observed in adults cannot be attributed to our different analysis approach alone.

Strengths of the current study include the large sample size and relatively narrow age range of participants recruited (16–25 years), which allows us to draw firmer conclusions about central coherence in young adults with AN, as this data is not confounded by the inclusion of children or older adults, as in previous studies of central coherence in populations with AN. However, this study is not without limitations. We chose to compare complex against simple EFT trials for our primary BOLD contrast because the figures presented in the EFT are significantly more visually complex than a fixation cross; therefore, contrasting BOLD response during the task against BOLD response to viewing the fixation cross is likely to reflect the confounding effect of greater stimulus complexity (Marcar et al., 2004), rather than capturing cognitive activity associated with visual search processes alone. Our analysis plan therefore erred on the side of avoiding false positive results. However, it is possible this conservative analysis plan may have failed to detect additional true neural effects associated with the EFT by comparing complex versus simple trials rather than comparing against the passive viewing of an equally complex visual figure. We therefore recommend that future studies administering the EFT instead contrast BOLD response during EFT trials to BOLD response during passive viewing of equally complex images to minimise the probability of both Type I and Type II errors. Furthermore, as this study was conducted exclusively in young women, these results should not be generalised to men or other age groups with AN.

Finally, it should be noted that our participant group which was weight-restored from AN was heterogeneous, including both participants who were fully recovered from AN and participants who were weight-restored from AN but continuing to exhibit elevated levels of eating disorder psychopathology. While we deemed the merging of these two clinical groups appropriate on theoretical grounds, and necessary due to the low sample size of both groups, it should be noted that this analysis choice contributed to greater levels of within-group variation on measures of eating disorder psychopathology and BMI.

Overall, the current study has not found evidence of deficiencies in central coherence amongst young women with AN, nor have we identified differences in the neural basis of central coherence between participants with AN and HC participants. The current study adds to an increasing literature base demonstrating the resilience of neuropsychological traits and associated brain systems in the early stages of AN (Leslie et al., 2020). Longitudinal research in future will be helpful in mapping the changes in neuropsychological traits over the course of illness to better understand the time course of disorder progression and optimal time windows in which treatment is most likely to be effective.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Neurovault at https://identifiers.org/neurovault.collection:9197, reference number 9197.

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