Cross-sectional study of cognitive function in women with a history of eating disorders in the UK Biobank cohort

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Declaration of Conflicts of Interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Abstract

Objective: The present study aimed to compare the cognitive functions of women who reported a history of eating disorders (ED) with women who did not report any such history. Within the group of women who reported a history of ED, it aimed to compare the cognitive functions of those who met anorexia nervosa body mass index (BMI) criteria at the time of assessment with those who did not meet such criteria.

Method: The sample in this observational cross-sectional study belonged to the UK Biobank cohort, and consisted of 260,601 women in middle to older age, of whom 347 had a lifetime history of ED. Participants underwent sociodemographic, medical and psychological evaluation, and were assessed with four computerized cognitive tasks. Multiple regression analyses were conducted to take account of covariates.

Results: Slower reaction time was found in those with an ED history: differences of small effect size were found across different levels of model adjustment ($d = -.096$ [95% CI $-.201, .009$] to $-.150$ [95% CI $-.249, -.052$]). Reasoning, visuospatial memory and prospective memory were not significantly different between those with and without a history of ED. A consistent pattern of results was not found when comparing the sub-sample of participants with ED split according to current BMI criteria.

Discussion: The findings suggest that an ED history may correlate with slower processing speed in middle to older age, but this may be partly accounted for by clinical covariates. Further research in population-representative cohorts is required.

Keywords

Cognition; mental processes; eating disorders; cohort studies; women

Introduction

The National Institute of Health and Clinical Excellence (NICE, 2019) calculates that approximately 1.25 million people in the UK have an eating disorder, although these numbers likely underestimate reality. Eating disorders (ED) are complex conditions that affect the individual as a whole. Research has paid particular attention to psychological, family and social factors surrounding these illnesses, but there has been less research on neuropsychological associations.

The literature shows that people with ED manifest cognitive differences compared with the general population. Children and adolescents with ED do not always present cognitive deficits compared with matched controls, yet impairments within the adult population are highly evident (Hirst et al., 2017). Research focused on women has shown consistent difficulties in executive functions, in particular in cognitive flexibility, central coherence, decision-making and inhibitory control (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Buzzichelli et al., 2018; Giannunzio et al., 2018; Hamatani et al., 2018; Harper et al., 2017; Hirst et al., 2017; Kanakam, Krug, Collier, & Treasure, 2017; Overas, Kapstad, Brunborg, Landro, & Ro, 2017; Smith, Mason, Johnson, Lavender, & Wonderlich, 2018; Steward et al., 2016; Weinbach, Perry, Sher, Lock, & Henik, 2017; Zegarra-Valdivia & Chino-Vilca, 2018), and in social functions, mainly in theory of mind and affect recognition (Bentz, Jepsen, Pedersen, et al., 2017; Bora & Kose, 2016; Brockmeyer et al., 2016; Dapelo et al., 2017; Fujiwara, Kube, Rochman, Macrae-Korobkov, & Peynenburg, 2017; Postorino et al., 2017; Zegarra-Valdivia & Chino-Vilca, 2018). In contrast, language (Overas et al., 2017; Spitoni et al., 2018) and orientation (Spitoni et al., 2018) frequently appear to be preserved. Meanwhile, results for measures of attention (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Buzzichelli et al., 2018; Giannunzio et al., 2018; Spitoni et al., 2018; Terhoeven et al., 2017), processing speed (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Buzzichelli et al., 2018; Giannunzio et al., 2018; Terhoeven et al., 2017), memory (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Hamatani et al., 2018; Overas et al., 2017; Terhoeven et al., 2017) and verbal fluency (Spitoni et al., 2018; Zegarra-Valdivia & Chino-Vilca, 2018) tend to be more variable.

Most of the existing studies included small samples, and examined cognitive performance mostly in adolescents and young adults. The present research aimed to extend the evidence base, by including a larger sample, with older female participants, who were recruited by UK Biobank. UK Biobank is a repository of sociodemographic, medical and psychological data belonging to people from England, Scotland and Wales. It can be accessed by investigators around the globe and seeks to encourage research for enhancing knowledge of health conditions of worldwide interest (Sudlow et al., 2015).

This cross-sectional study hypothesized that women with ED would exhibit cognitive differences compared to women without ED. Firstly, the cognitive performance of participants who self-reported a history of ED was compared with a comparison group who did not report any such history. Secondly, within the group of participants who self-reported a history of ED, the cognitive performance of those who met anorexia nervosa (AN) body mass index (BMI) criteria ($\leq 17.5 \text{ kg/m}^2$, in the International Classification of Diseases, 10th edition) (World Health Organization, 2004) at the time of assessment was compared with those who did not meet such criteria.

Methods

Participants

The UK Biobank began a longitudinal, population-based, cohort study in 2006, which is still ongoing. Men and women aged 40 to 70 were identified from NHS primary care registers and were invited by post to attend one of 22 assessment centers in England, Scotland and Wales. The baseline wave recruited 502,543 participants, all of whom provided written consent, and underwent sociodemographic, medical, psychological and cognitive assessment (Cullen et al., 2019). The inclusion criteria for the present study were female gender, available data on ED history and at least one cognitive test. The sample included 260,601 women, of whom 347 self-reported a history of ED and 260,254 did not report a history of ED. No exclusion criteria were applied. This study included only women due to the insufficient theoretical background related to the male population.

Measures and Procedure

Each participant attended for a single baseline assessment visit, lasting around two hours. Measures were administered using a standardized protocol across all centers. Further details are given in Cullen et al. (2019).

Computerized touchscreen questionnaires collected information on age, gender, educational level, neighborhood deprivation (Townsend Deprivation Index), ethnic group, and country of origin. Participants were asked to complete information on smoking habits and alcohol consumption; and they were asked to report whether they had been diagnosed by a doctor with any medical condition or disability, the age at diagnosis, and the intake of any medication around the time of assessment. The list of comorbid neurological and psychiatric conditions, and of psychotropic medications in the UK Biobank population can be found in Appendices 1 and 2 in the Supplemental Materials.

If in the computerized questionnaire the participant had reported a medical condition and/or a current medication, she was interviewed by a trained nurse, who would confirm the responses and codify them. All reported ED diagnoses were coded into one joint category by the UK Biobank staff.

The BMI (kg/m^2) of the participants was calculated from measures of height and weight taken by trained staff at the Assessment Center during physical examination. For the purpose of this study, data on BMI were used to create dichotomous variables for participants meeting AN BMI criteria ($\leq 17.5 \text{ kg/m}^2$) or not.

The cognitive data were collected from four bespoke instruments, which were designed by the UK Biobank. These were presented in a computerized touchscreen format, without a trained tester. Two of the tasks (Reaction Time and Visuospatial Memory) were included in the assessment battery throughout the recruitment wave, and two of them (Reasoning and Prospective Memory) were added part-way through the recruitment wave when the baseline assessment protocol was extended. Compared to gold standard tests, the validity of the UK Biobank tasks proved to be moderate to strong, and a high

reliability after a four-week interval was found. The Reasoning task showed the highest reliability coefficient ($r_{xx}=.61$), while the Visuospatial Memory task presented the lowest reliability coefficient ($r_{xx}=.41$). The reliability coefficients of the Reaction Time and the Prospective Memory tasks were $r_{xx}=.55$ and $r_{xx}=.45$, respectively (Fawns-Ritchie & Deary, 2019).

The Reasoning task assessed verbal and numeric reasoning; participants were presented with thirteen multiple-choice questions in a two-minute time limit. The Reaction Time task assessed processing speed in a go/no-go format: participants completed a timed test of symbol matching, and the final score was the mean response time in milliseconds across trials where matching symbols had appeared. The Visuospatial Memory task assessed visuospatial working memory: participants were asked to memorize the positions of six card pairs, and then locate them from memory while making as few errors as possible. The number of errors made was used as the final score. In the Prospective Memory task, participants were asked to engage in a specific behavior later in the assessment. They were presented with four colored symbols and were asked to touch a blue square, however, they had to touch the orange circle instead, as instructed earlier. The participants scored zero or one, depending on whether they completed the task on the first attempt or not (Cullen et al., 2019).

The data that support the findings of this study are openly available in UK Biobank at <https://www.ukbiobank.ac.uk/>, reference number 11332.

Data Analysis

The data analysis was carried out with Stata v13 and SPSS21 for Windows. Sociodemographic and clinical data from the ED and non-ED groups were summarized and compared. Independent sample t-tests were conducted for scale measures that were continuous and presented a normal distribution, and χ^2 tests were conducted for categorical measures.

The first set of analyses compared the cognitive performance of women who reported a history of ED with the cognitive performance of women who did

not report a history of ED. The second set of analyses divided the ED sub-sample into two groups and compared their levels of performance: one group included participants with a BMI equal to or less than 17.5 (AN diagnostic criteria) at the time of assessment, and the other group included participants with a BMI higher than 17.5 at the time of assessment.

To facilitate interpretation across tests, the raw scores for Reasoning, Reaction Time and Visuospatial Memory tasks were transformed into age-adjusted z-scores, within five-year age bands across the whole UK Biobank cohort. The direction of these scores was reversed if necessary, so that a higher z-score represented better performance in all the tasks (Cullen et al., 2019).

For both sets of analyses, regression models were run for each cognitive test (dependent variable) separately. A simple regression analysis was used to compare the group differences on the cognitive tests without any covariates. A series of multiple regression analyses included additional covariates (age, education, Townsend Deprivation Index, ethnic group, English-speaking country of birth, smoking and alcohol status, BMI, comorbid neurological and psychiatric conditions, and psychotropic medication) to reduce the role of confounding. The z-scores were analyzed using linear regression, and the coefficients were interpreted as Cohen's d effect sizes. The Prospective Memory score was a binary 0/1 score, and so this was analyzed in its raw form using logistic regression, with coefficients reported as odds ratios.

Diagnostic checks were performed for assumptions of linearity, homoscedasticity and normality of residuals in the final adjusted linear regression models, all of which were acceptable. Multicollinearity was checked and found to be in the acceptable range (Variance Inflation Factor values all below 1.81).

G*Power 3.1.9.2 (Erdfelder, Faul, & Buchner, 1996) was used to estimate statistical power based on the available sample sizes on the cognitive tests. With the largest available sample size of 346 for the ED group and

258,997 for the comparison group (Reaction Time task), and the p value threshold set at 0.0125 (two-tailed, taking account of multiple tests across four dependent variables), there was 89% power to detect a group difference in cognitive performance of $d=.2$ (small effect size), in unadjusted analyses. For other cognitive tests with smaller available samples, there was sufficient power (at least 80%) to detect larger effect sizes ($d=.5$).

Statistical power was also estimated for the multiple regression models, in which sample sizes were smaller owing to missing data on covariates. The largest available sample size with complete data for the first set of analyses included 298 for the ED group and 242,659 for the comparison group (Reaction Time task), and with the p value threshold set at 0.0125 (two-tailed, taking account of multiple tests across four dependent variables), there was 83% power to detect a group difference in cognitive performance of $d=.2$ (small effect size). For other cognitive tests with smaller available samples, there was sufficient power (at least 80%) to detect larger effect sizes ($d=.5$). The models would also have similar power even with additional covariates (Green, 1991). The largest available sample size with complete data for the second set of analyses included 34 for the ED group and 264 for the comparison group (Reaction Time task), and with the p value threshold set at 0.0125 (two-tailed, taking account of multiple tests across four dependent variables), there was 97% power to detect a group difference in cognitive performance of $d=.8$ (large effect size). For other cognitive tests with smaller available samples, the power was insufficient (56%) to reliably detect even large effect sizes ($d=.8$).

Results

Sociodemographic, lifestyle, physical and medical characteristics of the sample are shown in Table 1, and Table 2 shows the results of the cognitive assessment tasks.

Table 3 shows the results of the regression analyses of the performance of the ED sample in each of the cognitive tasks, considering history of an ED as the independent variable. The regression analyses were conducted through six

models, which added the covariates gradually. The coefficients for the covariates in the fully adjusted models are shown in Appendices 3, 4, 5 and 6 in the Supplemental Materials.

The ED sample presented mild difficulties in the Reaction Time task, suggesting their processing speed was slower compared to the non-ED sample, although with very small effect sizes ($d = -.096$ to $-.150$ across different levels of adjustment). The relationship between the Reaction Time task and a history of ED was statistically significant in the adjusted models until model 5 (all $p < .0125$); however, in model 6 the relationship became non-significant ($p = .074$). The regression analyses showed extremely small effect sizes in the Reasoning task ($d = -.072$ to $.081$ across different levels of adjustment) and in the Visuospatial Memory task ($d = -.017$ to $-.066$ across different levels of adjustment). The relationship between these two tests and a history of ED was non-significant along the models (all $p > .0125$). Lastly, results in the Prospective Memory task demonstrated that in general the ED sample and the non-ED sample had similar odds of being correct. The ED group showed slight differences, and after adjusting for the covariates, the odds of being correct were 12% lower, but this was non-significant ($p = .616$).

Table 4 shows the results of the regression analyses of the performance within the ED sub-sample in each of the cognitive tasks, considering AN BMI criteria as the independent variable. The regression analyses were conducted through six models, which added the covariates gradually. The coefficients for the covariates in the fully adjusted models are shown in Appendices 7, 8, 9 and 10 in the Supplemental Materials. After adjusting for the covariates, results appeared highly variable. ED participants who met AN BMI criteria showed small to medium effect sizes indicating slightly better performance on the Reasoning task ($d = .2$ to $.5$ across models), Reaction Time task ($d = .1$ to $.2$ across models) and Visuospatial Memory task ($d = .3$ across models). On the contrary, in the Prospective Memory task, the odds of being correct of the ED group who met AN BMI criteria were around 5% lower (fully adjusted model) than the ED group who did not meet the AN BMI criteria. Nonetheless, the

confidence intervals were wide and none of these results were statistically significant (all $p > .0125$).

Discussion

This study aimed to determine if women with a history of ED showed different cognitive performance compared to women without such history in four cognitive tasks assessing Reasoning, Reaction Time, Visuospatial Memory and Prospective Memory. It also aimed to investigate if, within the ED group, women meeting AN BMI criteria at the time of assessment had a different performance in the cognitive tasks compared to women who did not meet such criteria.

In this large sample taken from the UK Biobank cohort, the women with a history of ED and the comparison group presented a similar cognitive performance overall. However, small but statistically significant group differences were observed in the Reaction Time models, indicating mild difficulties in the ED group. These differences remained after adjustment for multiple demographic and lifestyle covariates, but when clinical covariates were added in the final model, the effect size reduced slightly and the results were no longer statistically significant. Differences in the Reasoning, Visuospatial Memory and Prospective Memory tasks between both groups were not statistically significant.

Results within the ED sub-sample were more variable. Possibly due to insufficient statistical power and small sample sizes, the models failed to reliably detect any correlation between cognitive performance and BMI criteria. Although the true effect of BMI is likely to be small, the analysis did have enough power to detect the large effects of some other important covariates, and these therefore came through more strongly in the models.

Evidence in the literature regarding reaction time performance in the ED population is mixed. Similar to the present study, Buzzichelli et al. (2018) found that adults with ED presented slower reaction times. However, other authors (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Giannunzio et al., 2018;

Terhoeven et al., 2017) emphasized the link between illness stage and processing speed: they concluded that patients in the acute phase present more severe impairments than recovered patients, noting that processing speed deficits frequently reverse after treatment. In the present study, it was found that processing speed difficulties were significantly related to a history of ED in most of the adjusted models, but the inclusion of the clinical covariates in the final model suggested that some of this relationship was accounted for by BMI, comorbid neurological and psychiatric conditions, and/or psychotropic medication. Unfortunately, UK Biobank did not have available information to determine if the participants were ill or not at the time of assessment, or if they had undergone treatment.

The Reasoning task was designed to assess problem-solving abilities which reflect general intelligence and executive function. Surprisingly, ED participants in this sample obtained slightly better scores on the Reasoning task, though these results were not statistically significant. Previous studies have covered the executive function domain extensively, yet studies focused specifically on reasoning skills were not found. Nevertheless, two studies (Rose et al., 2017; Spitoni et al., 2018), which used the Tower tests to assess problem-solving abilities, reached similar conclusions, and observed that the performance of the ED samples in this domain lay within the normal range.

Women with and without a history of ED did not present significant differences in visuospatial memory, and the majority of participants of both groups answered correctly in the Prospective Memory task. However, two studies (Hamatani et al., 2018; Overas et al., 2017) that assessed visual memory in ED participants found that adults showed impairments in immediate and delayed recall. Discrepancies could be explained by different ages, stages of the illness and assessment tools. Unfortunately, no previous studies examining prospective memory were found.

To date, researchers have not been able to elucidate whether neuropsychological impairments in people with ED are premorbid factors or consequences of ED symptomatology. Malnourishment interferes with normal

brain development, and it causes severe, long-term damage if present particularly during childhood and adolescence (Bentz, Jepsen, Pedersen, et al., 2017; Steward et al., 2016). Some authors support the argument that cognitive deficits are risk factors for ED onset, and influence their maintenance, noting that they are exacerbated by starvation and might persist after treatment. Other authors argue that cognitive difficulties are primarily a result of starvation and, therefore, tend to reverse after weight restoration (Bentz, Jepsen, Kjaersdam Telleus, et al., 2017; Bentz, Jepsen, Pedersen, et al., 2017; Brockmeyer et al., 2016; Overas et al., 2017; Spitoni et al., 2018; Steward et al., 2016).

Contrary to other studies, the major strength of the present research is that it included larger samples composed of women in middle to older age groups. Nevertheless, important limitations must be acknowledged. The UK Biobank cohort is known to have selection bias as it included healthier and highly motivated individuals who do not represent the general population or clinical populations (Fry et al., 2017). Additionally, the cognitive tasks used during assessment were designed by UK Biobank to be as brief as possible for administration at scale, therefore, they do not have psychometric properties that are as robust as clinical test batteries. History of ED was self-reported on a retrospective basis, with no primary care data available for corroboration at the time this study was conducted. It should also be acknowledged that the AN BMI criterion is an indirect proxy for an active ED.

Future research should include representative samples along the ED continuum. These conditions are often associated with the female population, yet a great number of men also present altered eating behaviors. Longitudinal studies are also encouraged. UK Biobank did conduct follow-up assessments after baseline with some participants, which may reveal interesting results in the future, but ideally longitudinal studies in ED would also have data available from the time of the initial illness onset. Finally, it is recommended that this study is replicated in other UK cohorts, such as the Avon Longitudinal Study of Parents and Children (University of Bristol).

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Tables

Table 1. Characteristics of the sample

	Eating Disorders	Comparison	Statistic (df)	p value
N	347	260254		
Sociodemographic				
Age (years) [†]				
Mean (SD)	51 (7)	56 (8)	13.933 (347.168)	<0.001
Age categories, n (%)				
40-44	75 (21.6)	26525 (10.2)	144.956 (6)	0.001
45-49	83 (23.9)	35177 (13.5)		
50-54	79 (22.8)	41316 (15.9)		
55-59	57 (16.4)	48216 (18.5)		
60-64	41 (11.8)	62960 (24.2)		
65-69	12 (3.5)	44939 (17.3)		
70-74	0 (0.0)	1121 (0.4)		
Has a degree, n (%) [‡]				
Yes	171 (49.6)	80748 (31.6)	51.513 (1)	<0.001
No	174 (50.4)	174891 (68.4)		
n (%) missing	2 (0.6)	4615 (1.8)		
Townsend Deprivation Index				
Mean (SD)	-0.77 (3.34)	-1.35 (3.03)	-3.582 (260283)	<0.001
Townsend quintile [§] , n (%) [‡]				
Qu1 (least deprived)	58 (16.7)	52216 (20.1)	15.289 (4)	0.004
Qu2	58 (16.7)	52127 (20.1)		
Qu3	59 (17.0)	52798 (20.3)		
Qu4	83 (23.9)	52607 (20.2)		
Qu5 (most deprived)	89 (25.6)	50190 (19.3)		
n (%) missing	0 (0.0)	316 (0.2)		
Ethnic group, n (%) [‡]				
White	339 (98.8)	245566 (94.6)	12.812 (4)	0.01
Asian/Asian British	1 (0.3)	4298 (1.7)		
Black/Black British	0 (0.0)	4448 (1.7)		
Chinese	0 (0.0)	938 (0.4)		
Mixed & Other background	3 (0.9)	4228 (1.6)		
n (%) missing	4 (1.2)	776 (0.3)		
English-speaking country of birth, n (%) [‡]				
Yes	334 (96.3)	240786 (92.7)	6.597 (1)	0.01
No	13 (3.7)	19087 (7.3)		
n (%) missing	0 (0.0)	381 (0.1)		
Lifestyle and physical				
Smoking status, n (%) [‡]				
Never	202 (58.2)	154557 (59.6)	2.933 (2)	0.23
Previous	105 (30.3)	81581 (31.5)		
Current	40 (11.5)	23105 (8.9)		
n (%) missing	0 (0.0)	1011 (0.4)		

Table 1. Characteristics of the sample

	Eating Disorders	Comparison	Statistic (df)	p value
Alcohol frequency, n (%)‡				
Daily/Almost daily	75 (21.6)	41976 (16.1)	95.979 (6)	<0.001
3-4 times per week	45 (13.0)	53619 (20.6)		
1-2 times per week	59 (17.0)	67117 (25.8)		
1-3 times per month	28 (8.1)	33960 (13.1)		
Special occasions only	71 (20.5)	38995 (15.0)		
Former	37 (10.7)	9300 (3.6)		
Never	32 (9.2)	14932 (5.7)		
n (%) missing	0 (0.0)	271 (0.1)		
Body Mass Index				
Mean (SD)	22.62 (4.93)	27.07 (5.17)	15.913 (259422)	<0.001
BMI categories, n (%)‡				
Underweight	62 (18.1)	1939 (0.7)	1441.839 (5)	<0.001
Normal	199 (58.0)	101110 (39.0)		
Overweight	54 (15.7)	95203 (36.7)		
Obese class I	23 (6.7)	40516 (15.6)		
Obese class II	2 (0.6)	14082 (5.4)		
Obese class III	3 (0.9)	6231 (2.4)		
n (%) missing	4 (1.2)	1173 (0.5)		
AN BMI criteria, n (%)‡				
Yes	36 (10.5)	570 (0.2)	1551.989 (1)	<0.001
No	307 (89.5)	258511 (99.8)		
n (%) missing	4 (1.2)	1173 (0.5)		
Neurological and mental health				
Comorbid neurological condition¶, n (%)‡				
Yes	16 (5.0)	9926 (3.8)	1.166 (1)	0.28
No	305 (95.0)	249415 (96.2)		
n (%) missing	26 (7.5)	913 (0.4)		
Comorbid psychiatric condition¶, n (%)‡				
Yes	162 (47.9)	22160 (8.5)	669.544 (1)	<0.001
No	176 (52.1)	238094 (91.5)		
n (%) missing	9 (2.6)	0 (0.0)		
Any psychotropic medication, n (%)‡				
Yes	134 (40.6)	26556 (10.5)	315.150 (1)	<0.001
No	196 (59.4)	225514 (89.5)		
n (%) missing	17 (4.9)	8184 (3.1)		

Notes: AN, anorexia nervosa; BMI, body mass index; Qu, quintile; SD, standard deviation

[†] No missing data.

[‡] Missing excluded from denominator.

[§] Based on data distribution in the whole UK Biobank cohort.

[¶] Apart from eating disorders; not possible to distinguish between missing data and self-report of no condition, therefore both classified as No.

Table 2. Results of cognitive assessment tasks

Cognitive assessment	Eating Disorders	Comparison
N	347	260254
Reasoning task, z-score		
Mean (SD)	-0.19 (0.89)	-0.28 (0.94)
Median (25 th , 75 th)	-0.18 (-1.06, 0.23)	-0.23 (-1.04, 0.41)
n (%) [†] missing	239 (68.9)	171381 (65.9)
Reaction Time task, z-score		
Mean (SD)	-0.18 (0.97)	-0.08 (0.94)
Median (25 th , 75 th)	-0.20 (-0.84, 0.44)	-0.08 (-0.71, 0.55)
n (%) missing	1 (0.3)	1257 (0.5)
Visuospatial Memory task, z-score		
Mean (SD)	0.18 (1.14)	0.20 (1.04)
Median (25 th , 75 th)	0.13 (-0.71, 0.95)	0.13 (-0.52, 0.95)
n (%) missing	8 (2.3)	8213 (3.2)
Prospective Memory task, n (%) [‡]		
Correct first time, n (%)	88 (80.7)	69838 (75.9)
Incorrect first time, n (%)	21 (19.3)	22176 (24.1)
n (%) [†] missing	238 (68.6)	168240 (64.6)

Notes: SD, standard deviation

A higher z-score means a better performance in the task.

[†] High percentage of missing data due to task not included in baseline battery for first three years of recruitment.

[‡] Missing excluded from denominator.

Table 3. Regression results for eating disorder and cognitive tasks

Models	Reasoning task			Reaction Time task			Visuospatial Memory task			Prospective Memory task		
	N	Beta Coefficient (95% CI)	p value	N	Beta Coefficient (95% CI)	p value	N	Beta Coefficient (95% CI)	p value	N	Odds Ratio (95% CI)	p value
1 [†]	88981	.081 (-.097, .259)	.37	259343	-.100 (-.198, -.001)	.05	252380	-.017 (-.127, .094)	.77	92123	.752 (.467, 1.210)	.24
2 [‡]	88227	.001 (-.169, .171)	.99	254786	-.137 (-.236, -.038)	.007	250104	-.050 (-.160, .060)	.37	91121	.909 (.562, 1.469)	.70
3 [§]	88089	.008 (-.160, .177)	.92	254480	-.126 (-.224, -.027)	.01	249800	-.044 (-.154, .066)	.44	90978	.895 (.552, 1.450)	.65
4 [¶]	87765	-.072 (-.235, .092)	.39	253596	-.150 (-.249, -.052)	.003	249028	-.066 (-.176, .045)	.24	90553	1.050 (.641, 1.720)	.85
5 ^{††}	87427	-.051 (-.213, .112)	.54	252543	-.133 (-.231, -.035)	.008	248053	-.058 (-.168, .053)	.31	90145	1.003 (.611, 1.646)	.99
6 ^{‡‡}	85694	-.008 (-.172, .156)	.93	242957	-.096 (-.201, .009)	.07	238794	-.048 (-.166, .071)	.43	88228	.880 (.534, 1.450)	.62

Notes: CI, Confidence Interval

Reasoning task, Reaction Time task, Visuospatial Memory task: a higher z-score means a better performance in the task; beta coefficients can be interpreted as Cohen's d effect size.

Prospective Memory task: score of 1 means correct answer, score of 0 means incorrect answer.

[†] Unadjusted.

[‡] Adjusted for age and degree.

[§] Adjusted for age, degree and Townsend Deprivation Index.

[¶] Adjusted for age, degree, Townsend Deprivation Index, ethnic group and English-speaking country of birth.

^{††} Adjusted for age, degree, Townsend Deprivation Index, ethnic group, English-speaking country of birth, smoking status and alcohol frequency.

^{‡‡} Adjusted for age, degree, Townsend Deprivation Index, ethnic group, English-speaking country of birth, smoking status, alcohol frequency, Body Mass Index, comorbid neurological conditions, comorbid psychiatric conditions and any psychotropic medication; the coefficients for the covariates in these fully adjusted models are shown in Appendices 3, 4, 5 and 6 in the Supplemental Materials.

Table 4. Regression results for anorexia nervosa body mass index criteria and cognitive tasks, within the eating disorder sub-group

Models	N	Reasoning task		N	Reaction Time task		N	Visuospatial Memory task		N	Prospective Memory task	
		Beta Coefficient (95% CI)	p value		Beta Coefficient (95% CI)	p value		Beta Coefficient (95% CI)	p value		Odds Ratio (95% CI)	p value
1 [†]	108	.239 (-.285, .763)	.37	342	.106 (-.233, .445)	.54	335	.313 (-.087, .713)	.13	109	.667 (.137, 3.234)	.62
2 [‡]	108	.416 (-.089, .922)	.11	340	.130 (-.208, .468)	.45	334	.335 (-.064, .733)	.10	109	.652 (.131, 3.254)	.60
3 [§]	108	.506 (.002, 1.011)	.05	340	.132 (-.207, .471)	.44	334	.324 (-.076, .723)	.11	109	.611 (.117, 3.187)	.56
4 [¶]	107	.472 (-.033, .977)	.07	336	.118 (-.222, .458)	.50	330	.314 (-.087, .716)	.13	108	.629 (.120, 3.297)	.58
5 ^{††}	107	.521 (.006, 1.037)	.05	336	.206 (-.085, .605)	.14	330	.395 (-.016, .806)	.06	108	.451 (.077, 2.638)	.38
6 ^{‡‡}	106	.454 (-.053, .962)	.08	298	.177 (-.179, .532)	.33	293	.366 (-.066, .798)	.10	107	.461 (.075, 2.858)	.41

Notes: CI, Confidence Intervals

Reasoning task, Reaction Time task, Visuospatial Memory task: a higher z-score means a better performance in the task; beta coefficients can be interpreted as Cohen's d effect size.

Prospective Memory task: score of 1 means correct answer, score of 0 means incorrect answer.

[†] Unadjusted.

[‡] Adjusted for age and degree.

[§] Adjusted for age, degree and Townsend Deprivation Index.

[¶] Adjusted for age, degree, Townsend Deprivation Index, ethnic group and English-speaking country of birth.

^{††} Adjusted for age, degree, Townsend Deprivation Index, ethnic group, English-speaking country of birth, smoking status and alcohol frequency.

^{‡‡} Adjusted for age, degree, Townsend Deprivation Index, ethnic group, English-speaking country of birth, smoking status, alcohol frequency, comorbid neurological conditions, comorbid psychiatric conditions and any psychotropic medication; the coefficients for the covariates in these fully adjusted models are shown in Appendices 7, 8, 9 and 10 in the Supplemental Materials.