nature mental health

Article

https://doi.org/10.1038/s44220-023-00199-6

Transdiagnostic neurocognitive dysfunction in children and adolescents with mental illness

Received: 13 July 2023

Accepted: 20 December 2023

Published online: 22 January 2024

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Robust evidence from adult samples indicates that neurocognitive dysfunction is a hallmark of many mental illnesses, contributing to the loss of daily function and quality of life that these illnesses cause. However, it is still unclear whether neurocognitive deficits associated with mental illnesses begin to manifest well before adulthood or impact treatment response. Here we address this gap by evaluating neurocognitive function in four groups of children and adolescents with different mental illnesses compared to their matched healthy peers. Our team evaluated the neurocognitive performance of youth diagnosed with attention deficit and hyperactivity disorder ($N = 343$), anorexia ($N = 40$), first onset psychosis ($N = 25$) and functional neurological disorder ($N = 56$) versus age-matched healthy controls ($N = 483$), cross-sectionally. Performance was assessed using an objective assessment battery designed for use across diagnoses and settings and validated for its correlations with underlying brain structure and function. The following cognitive domains were assessed: sustained attention, cognitive flexibility, decision speed, executive function, information processing speed, psychomotor response speed, response inhibition, verbal memory and working memory. Distinct profiles of neurocognitive dysfunction were detected for each diagnosis relative to the healthy reference group. Youth with first onset psychosis displayed the most severe and generalized impairments across domains of sustained attention, verbal memory, response inhibition, cognitive flexibility, information processing speed and working memory. Children and adolescents with attention deficit and hyperactivity disorder showed impairments in multiple domains of at least moderate severity with the most pronounced impairments in executive function, sustained attention and working memory. Children and adolescents with anorexia displayed more specific moderate impairments limited to cognitive flexibility, response inhibition, sustained attention, decision speed and verbal memory. Impairments in functional neurological disorder were also relatively specific and moderate, limited to executive function, working memory, cognitive flexibility, decision speed and information processing speed. These findings suggest that neurocognitive impairment in mental illness is transdiagnostic and can be detected as early as childhood or adolescence with standardized computerized testing.

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Table 1 | Study demographics

	ADHD		Anorexia		First onset psychosis		Functional neurological disorder	
	Clinical	Control	Clinical	Control	Clinical	Control	Clinical	Control
N	343	343	40	41	25	42	56	57
Age range (years)	6–18	6–18	12–18	12–18	11–18	11–18	8–18	8–18
Age mean and s.d. (years)	11.78±3.20	11.87±3.08	15.23±1.61	15.25±1.58	16.23±1.63	16.19±1.37	13.49±2.12	13.60±2.31
Sex	76 F (22.2%), 267 M (77.8%)	76 F (22.2%), 267 M (77.8%)	40 F (100%), 0 M (0%)	41 F (100%), 0 M (0%)	10 F (40%), 15 M (60%)	12 F (28.6%), 30 M (71.4%)	40 F (71.4%), 16 M (28.6%)	41 F (71.9%), 16 M (28.1)
Site								
Adelaide	75	263	0	28	0	0	0	35
Melbourne	40	13	29	2	56	0	6	0
Sydney	228	67	11	11	0	57	19	7

Age and sex compositions are shown for each clinical group and their matched healthy controls. F, female; M, male; s.d., standard deviation.

Cognitive dysfunction is a concurrent feature of multiple mental illnesses among adults and youth. Patients' performance on neuropsychological tests can be used to quantify cognitive dysfunction. These tests involve performing tasks and can provide objective measurements of cognitive domains such as set shifting, response inhibition, working memory, fluency, planning, verbal memory, nonverbal memory, processing speed, attention and visuospatial function[1].

Regarding findings in adults, a 2021 systematic review of meta-analyses[2] compared cognitive performance in 97 samples of individuals suffering from various psychiatric disorders to cognitive performance in healthy reference data. Results indicated an impairment in at least one cognitive domain in patients with autism spectrum disorder, bipolar disorder, eating disorders, depression, schizoaffective disorder, obsessive-compulsive disorder, personality disorders, post-traumatic stress disorder, schizophrenia, substance use disorders and Tourette's syndrome, with effect sizes ranging from 0.4 to 0.6 (ref. 2). In particular, disorders characterized by psychotic symptoms, such as schizophrenia, showed the largest deficits in cognitive performance. This is in line with previous evidence showing that speed of processing, verbal learning and memory, visuospatial learning and memory, working memory, attention and problem solving all show medium to large impairments in patients with psychosis compared to healthy samples[3–15]. Conversely, eating disorders and substance use disorders showed the smallest cognitive deficits, although these were detectable across all examined domains[2]. This is consistent with previous findings showing that patients with anorexia nervosa ('anorexia' hereafter), at least in the acute state, perform worse than controls in particular in tasks involving attention, processing speed, memory and visuospatial construction[16–20].

Overall, these results suggest that cognitive deficits are a transdiagnostic feature of mental illness, that is, a feature that cuts across traditional diagnostic boundaries. Therefore, they are not limited to disorders using cognitive dysfunction as part of their diagnostic criteria. So far, studies of clinical samples have largely investigated cognitive impairments in adults with mental illness, despite the majority of mental illnesses emerging in childhood and adolescence[21–24]. Mental illnesses are the leading cause of disability in children and adolescents, affecting an estimated 13.4% of youth worldwide[25,26]. Evidence suggests that cognitive deficits associated with mental illnesses begin to manifest before adulthood[27–32]. For example, in youth suffering from bipolar disorder, research using multiple assessments has shown moderate to large impairments in verbal learning, verbal memory, working memory, visual learning and visual memory[33,34]. In early onset schizophrenia, studies have found large deficits in general intellectual ability, processing speed, working memory, verbal memory and learning; medium deficits in rule discovery and perseveration, planning and problem solving; and minimal deficits in attention[35]. In youth with attention deficit and hyperactivity disorder (ADHD), performance on neurocognitive tests has consistently shown decreased overall cognitive ability, as well as worse performance across neuropsychological measures of learning, spanning memory and executive function[36–40]. In youth with anorexia, studies have found poorer nonverbal performance, altered attention to disorder-related stimuli, perceptual processing impairment in discriminating body images, weaknesses in central coherence, set-shifting weaknesses at low weight status, decision-making weaknesses and greater neural resources required for working memory[41]. Finally, studies in youth with major depressive disorder have found deficits in psychomotor speed, attention, memory and executive function[42].

Previously, we have added to this literature by using standardized cognitive tests to assess cognitive impairments in youth within individual diagnostic groups, including ADHD[43,44], first onset psychosis[45], anorexia[17] and functional neurological disorder[46]. However, it is unclear how different cognitive domains are affected differently within diagnoses and how the dysfunctions of each cognitive domain in one mental illness compare transdiagnostically to dysfunctions of the same domain in other illnesses. In this Article, a unique focus is a new transdiagnostic evaluation comparing cognitive performance in patients aged 6–18 years diagnosed with ADHD, anorexia, first onset psychosis and functional neurological disorder with the cognitive performance of age-matched healthy controls. Prior findings are based on multiple different types of assessment batteries, but we assessed cognitive performance using the same standardized web-based cognitive battery in all groups[1], thus enabling us to quantify cognitive deficits in each clinical diagnosis consistently. Also, by collecting the same battery of tests across diagnoses, we were able to directly compare the performance in each cognitive domain between every diagnosis pair and, vice versa, the performance between every cognitive domain pair in each diagnosis. We focused on the cognitive domains of attention, planning, response inhibition, verbal fluency, verbal memory, visual memory and working memory to align with previous adult literature. We hypothesized that youth suffering from the included diagnoses would display cognitive deficits compared to age-matched controls and that findings would mirror previous findings in adult clinical populations.

Results

A summary of the demographic characteristics of the participants is given in Table 1.

We used a linear mixed model to assess the impact of each diagnosis on performance in our cognitive domains of interest. Consistent with our hypotheses, all diagnoses showed an impairment in at least one cognitive function measure compared to healthy matched controls and each diagnosis showed a distinctive profile of cognitive dysfunction (cognitive domain × diagnosis interaction; $F = 8.148$, $P < 0.001$).

Figures 1 and 2 summarize the performance of each group of participants for each cognitive domain. Table 2 presents the results of all significant comparisons between the cognitive performance in

https://doi.org/10.1038/s44220-023-00199-6

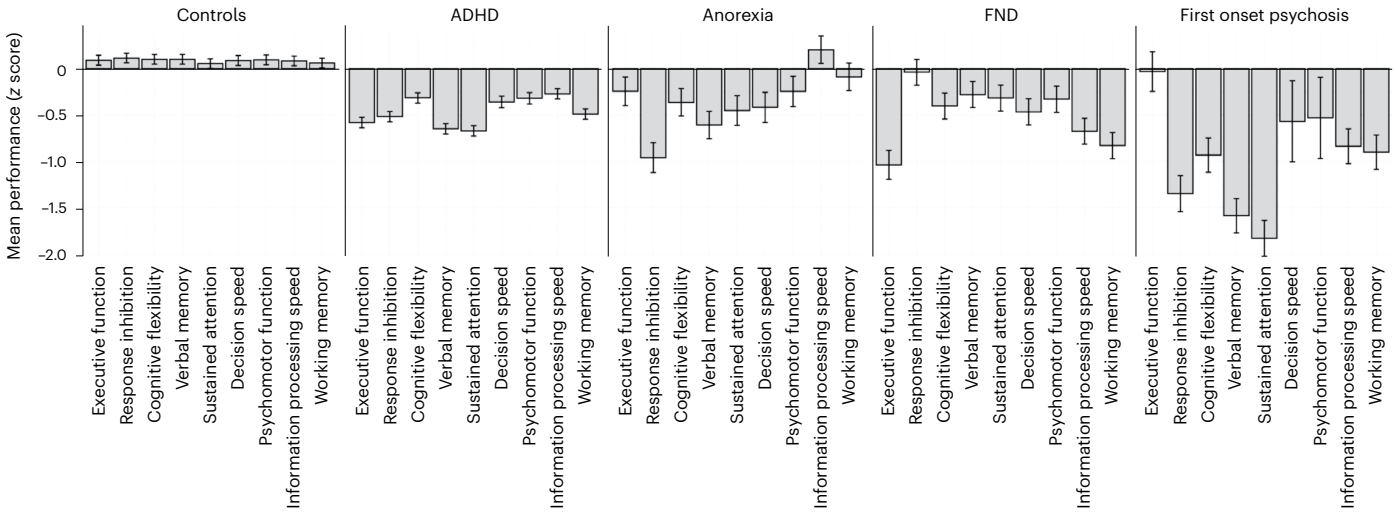

Fig. 1 | Cognitive performance of patients and controls across cognitive domains grouped by diagnosis. The bar plots show the effects estimated by the linear mixed model predicting cognitive performance. Mean predicted cognitive performance is expressed in standard deviations relative to a healthy norm (*z* scores), accounting for model covariates (data collection site) and repeated measures. Controls ($N = 483$), ADHD ($N = 343$), anorexia ($N = 40$), FND ($N = 56$) and first onset psychosis ($N = 25$) independent participants were examined over nine domains of cognitive function. Bars indicate mean effects, and whiskers indicate standard errors. FND, functional neurological disorder.

each diagnosis and healthy controls. Table 3 presents the results of all significant comparisons between each pair of diagnoses within each cognitive domain (see Supplementary Table 1 for all comparisons, including nonsignificant ones). Supplementary Table 2 presents the results of all significant comparisons between each pair of cognitive domains within each diagnosis, and Supplementary Table 3 presents all comparisons, including nonsignificant ones.

The following sections outline the cognitive deficits of each diagnosis in detail.

ADHD

Patients with ADHD performed worse than controls across all domains (see Table 2, Fig. 1 for model effects and Supplementary Fig. 1 for raw data). Deficits within verbal memory (mean difference 0.75, s.e.m. 0.07, $t = 10.42$, $P_{corr} < 0.001$, $d = 1.08$) and sustained attention were the strongest (mean difference 0.73, s.e.m. 0.07, $t = 10.14$, $P_{corr} < 0.001$, $d = 1.048$). The ADHD group was the only group to display significant dysfunction in psychomotor function compared to healthy controls (mean difference 0.42, s.e.m. 0.08, $t = 5.41$, $P_{corr} < 0.001$, $d = 0.598$). Other domains negatively affected include executive function (mean difference 0.67, s.e.m. 0.07, $t = 9.19$, $P_{corr} < 0.001$, $d = 0.970$), response inhibition (mean difference 0.63, s.e.m. 0.07, $t = 8.94$, $P_{corr} < 0.001$, $d = 0.91$), cognitive flexibility (mean difference 0.42, s.e.m. 0.07, $t = 5.87$, $P_{corr} < 0.001$, $d = 0.599$), decision speed (mean difference 0.45, s.e.m. 0.08, $t = 5.69$, $P_{corr} < 0.001$, $d = 0.644$), information processing speed (mean difference 0.36, s.e.m. 0.07, $t = 5.01$, $P_{corr} < 0.001$, $d = 0.513$) and working memory (mean difference 0.55, s.e.m. 0.07, $t = 7.78$, $P_{corr} < 0.001$, $d = 0.794$).

Patients with ADHD performed significantly worse than patients with anorexia in tasks measuring information processing speed (mean difference −0.48, s.e.m. 0.16, $t = -2.96$, $P_{corr} = 0.026$, $d = -0.685$) and worse than patients with functional neurological disorder in response inhibition tasks (mean difference −0.48, s.e.m. 0.16, $t = -3.08$, $P_{corr} = 0.018$, $d = -0.689$; see Table 3, Fig. 2 for model effects and Supplementary Fig. 2 for raw data).

Anorexia

Patients with anorexia displayed dysfunction in five out of the nine total cognitive domains tested (~56%; see Table 2, Fig. 1 for model effects and Supplementary Fig. 1 for raw data). Performance was worst in tasks measuring response inhibition (mean difference 1.07, s.e.m. 0.18, $t = 6.14$, $P_{corr} < 0.001$, $d = 1.548$) and verbal memory (mean difference 0.71, s.e.m. 0.16, $t = 4.33$, $P_{corr} < 0.001$, $d = 1.021$). Other domains negatively affected include cognitive flexibility (mean difference 0.46, s.e.m. 0.16, $t = 2.84$, $P_{corr} = 0.037$, $d = 0.668$), sustained attention (mean difference 0.51, s.e.m. 0.17, $t = 2.90$, $P_{corr} = 0.031$, $d = 0.73$) and decision speed (mean difference 0.51, s.e.m. 0.18, $t = 2.85$, $P_{corr} = 0.036$, $d = 0.728$).

Patients with anorexia performed significantly worse than the functional neurological group in tasks testing response inhibition (mean difference −0.92, s.e.m. 0.20, $t = -4.56$, $P_{corr} < 0.001$, $d = -1.327$; Table 3 and Fig. 2).

First onset psychosis

Compared to their healthy counterparts, patients with first onset psychosis displayed significant dysfunction in the majority of cognitive domains tested (six out of nine, ~67%; see Table 2, Fig. 1 for model effects and Supplementary Fig. 1 for raw data). Patients with first onset psychosis displayed striking deficits in sustained attention (mean difference 1.88, s.e.m. 0.20, $t = 9.38$, $P_{corr} < 0.001$, $d = 2.716$), verbal memory (mean difference 1.69, s.e.m. 0.19, $t = 8.77$, $P_{corr} < 0.001$, $d = 2.433$) and response inhibition (mean difference 1.46, s.e.m. 0.20, $t = 7.28$, $P_{corr} < 0.001$, $d = 2.107$). Other domains affected include cognitive flexibility (mean difference 1.03, s.e.m. 0.19, $t = 5.37$, $P_{corr} < 0.001$, $d = 1.489$), information processing speed (mean difference 0.92, s.e.m. 0.20, $t = 4.72$, $P_{corr} < 0.001$, $d = 1.327$) and working memory (mean difference 0.96, s.e.m. 0.19, $t = 5.01$, $P_{corr} < 0.001$, $d = 1.388$).

Compared to other diagnostic groups, patients with first onset psychosis showed particularly pronounced overall cognitive dysfunction. The first onset psychosis group performed significantly worse compared to at least one other diagnostic group in almost every cognitive domain, with the exception of executive function. The most distinctive patterns of differences between patients with first onset psychosis and other diagnostic groups were seen in tasks measuring verbal memory and sustained attention (see Table 3, Fig. 2 for model effects and Supplementary Fig. 2 for raw data).

Functional neurological disorder

Patients with functional neurological disorder displayed deficits in five out of the nine tested cognitive domains (~56%; see Table 2, Fig. 1

https://doi.org/10.1038/s44220-023-00199-6

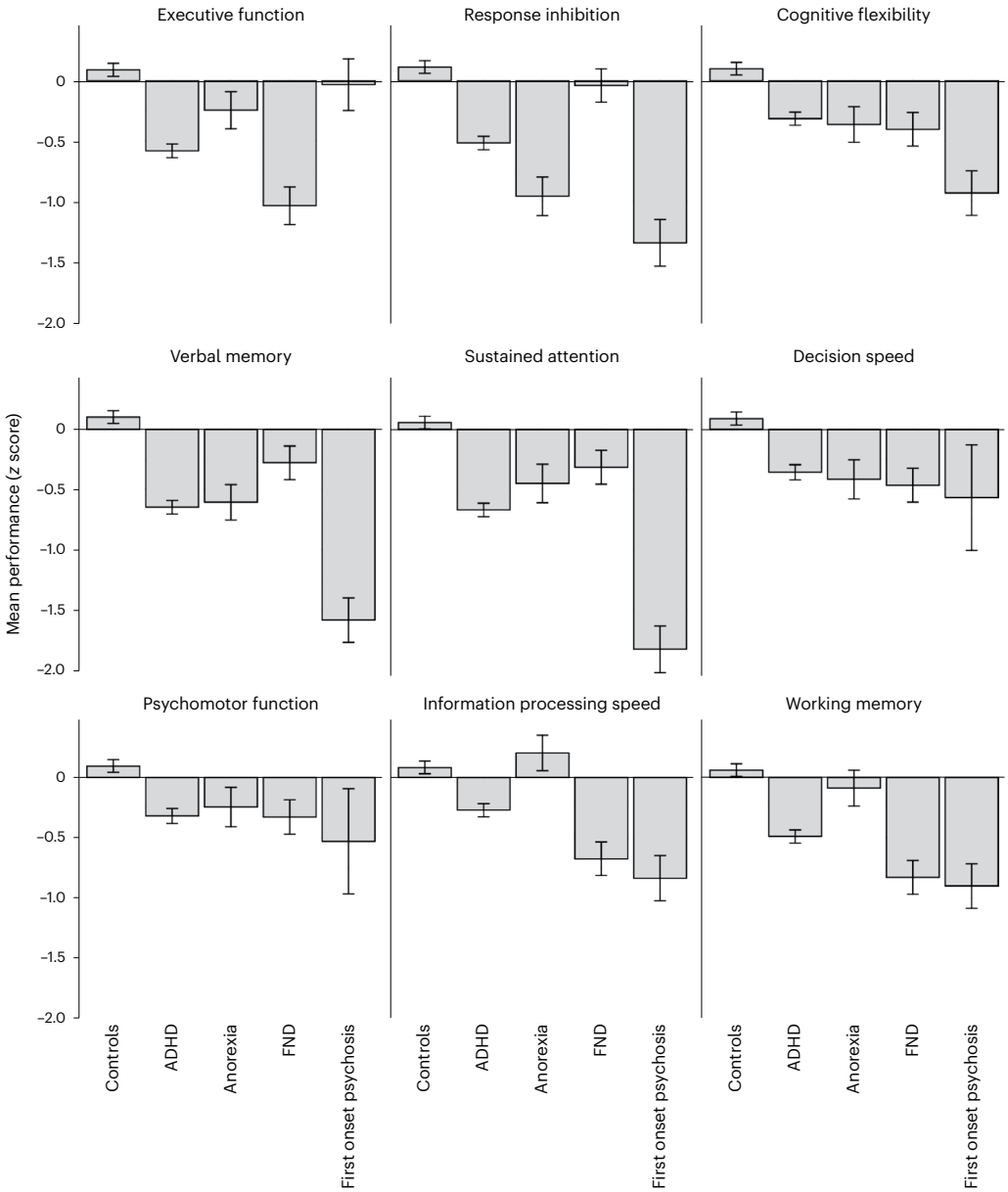

Fig. 2 | Cognitive performance of patients and controls across cognitive domains grouped by diagnosis. The bar plots show the estimate by the linear mixed model predicting cognitive performance. Mean predicted cognitive performance is expressed in standard deviations relative to a healthy norm (*z* scores), accounting for model covariates (data collection site) and repeated measures. Controls ($N = 483$), ADHD ($N = 343$), anorexia ($N = 40$), FND ($N = 56$) and first onset psychosis ($N = 25$) independent participants were examined over nine domains of cognitive function. Bars indicate mean effects, and whiskers indicate standard errors. FND, functional neurological disorder.

for model effects and Supplementary Fig. 1 for raw data). Deficits in executive function appeared to be an exceptional struggle for patients with functional neurological disorder (mean difference 1.13, s.e.m. 0.18, $t = 6.45$, $P_{corr} < 0.001$, $d = 1.627$). Patients with functional neurological disorder also particularly underperformed in tasks challenging working memory (mean difference 0.89, s.e.m. 0.16, $t = 5.54$, $P_{corr} < 0.001$, $d = 1.285$). Other domains affected include cognitive flexibility (mean difference 0.50, s.e.m. 0.16, $t = 3.14$, $P_{corr} = 0.015$, $d = 0.726$), decision speed (mean difference 0.55, s.e.m. 0.16, $t = 3.43$, $P_{corr} = 0.006$, $d = 0.799$) and information processing speed (mean difference 0.76, s.e.m. 0.16, $t = 4.74$, $P_{corr} < 0.001$, $d = 1.094$).

Patients with functional neurological disorder displayed greater dysfunction than patients with anorexia in multiple domains. The functional neurological disorder group performed significantly worse than those with anorexia in tasks measuring executive function (mean difference 0.79, s.e.m. 0.21, $t = 3.78$, $P_{corr} = 0.002$, $d = 1.144$), information processing (mean difference 0.88, s.e.m. 0.19, $t = 4.54$, $P_{corr} < 0.001$, $d = 1.267$) and working memory (mean difference 0.74, s.e.m. 0.20, $t = 3.80$, $P_{corr} = 0.001$, $d = 1.068$; see Table 3, Fig. 2 for model effects and Supplementary Fig. 2 for raw data).

Discussion

Previous investigations of adults have shown that cognitive dysfunction is a key feature of mental illness regardless of specific diagnosis. We aimed to extend these findings to children and adolescents suffering from ADHD, anorexia, first onset psychosis and functional neurological disorder. Consistent with our hypotheses, all clinical groups displayed impairments within at least one cognitive domain compared to age-matched healthy controls. Our findings suggest that cognitive dysfunction exists as a transdiagnostic feature of mental illness that

Table 2 | Comparisons of the mean cognitive performance of each diagnosis and that of healthy controls

Domain	Diagnosis	Mean difference	s.e.m.	df	t	P_{corr}	Cohen's *d*
Executive function	ADHD	0.672	0.073	3,162	9.188	0.00	0.97
	Functional neurological disorder	1.128	0.175	3,132	6.448	0.00	1.627
Response inhibition	ADHD	0.631	0.071	2,861	8.940	0.00	0.91
	Anorexia	1.073	0.175	3,246	6.138	7.96×10^{-9}	1.548
	First onset psychosis	1.461	0.201	3,548	7.279	4.12×10^{-9}	2.107
Cognitive flexibility	ADHD	0.415	0.071	2,854	5.870	4.71×10^{-8}	0.599
	Anorexia	0.463	0.163	2,634	2.840	3.67×10^{-2}	0.668
	Functional neurological disorder	0.503	0.160	2,372	3.142	1.46×10^{-2}	0.726
	First onset psychosis	1.032	0.192	3,171	5.367	8.50×10^{-7}	1.489
Verbal memory	ADHD	0.749	0.072	2,999	10.418	0.00	1.08
	Anorexia	0.708	0.163	2,644	4.333	1.49×10^{-4}	1.021
	First onset psychosis	1.686	0.192	3,179	8.767	0.00	2.433
Sustained attention	ADHD	0.726	0.072	2,989	10.136	0.00	1.048
	Anorexia	0.506	0.174	3,230	2.901	3.07×10^{-2}	0.73
	First onset psychosis	1.883	0.201	3,556	9.380	4.34×10^{-9}	2.716
Decision speed	ADHD	0.446	0.079	3,812	5.687	1.54×10^{-7}	0.644
	Anorexia	0.505	0.177	3,365	2.848	3.58×10^{-2}	0.728
	Functional neurological disorder	0.554	0.161	2,437	3.430	5.54×10^{-3}	0.799
Psychomotor function	ADHD	0.415	0.077	3,588	5.407	6.87×10^{-7}	0.598
Information processing speed	ADHD	0.356	0.071	2,882	5.011	5.68×10^{-6}	0.513
	Functional neurological disorder	0.759	0.160	2,372	4.740	2.23×10^{-5}	1.094
	First onset psychosis	0.920	0.195	3,291	4.721	2.41×10^{-5}	1.327
Working memory	ADHD	0.551	0.071	2,862	7.782	0.00	0.794
	Functional neurological disorder	0.891	0.161	2,407	5.538	3.38×10^{-7}	1.285
	First onset psychosis	0.963	0.192	3,172	5.005	5.84×10^{-6}	1.388

Mean differences are contrasts estimated in our linear mixed model analysis. Comparisons were conducted using two-sided *t*-tests, followed by Tukey correction for multiple comparisons of *P* values. *P* values are shown in scientific notation. For brevity, only results for which $P_{corr} < 0.05$ are shown. P_{corr}, Tukey-adjusted *P* value; s.e.m., standard error of the mean; df, degrees of freedom.

can be identified with standardized cognitive testing as early as childhood and adolescence.

Each clinical group sampled displayed a distinct pattern of cognitive dysfunction. Children and adolescents with ADHD showed a diffuse pattern of differences in performance with healthy controls, while displaying especially exceptional impairment in verbal memory and sustained attention. This broad impairment found in our sample aligns with results in adult literature, which indicated impairments in response inhibition, working memory and executive function[47–50].

Compared to ADHD, cognitive deficits in youth anorexia were more specific and limited to cognitive flexibility, sustained attention, decision speed, response inhibition and verbal memory. This is consistent with previous findings showing that patients with anorexia have smaller but still detectable performance deficits across several cognitive domains compared to controls[2,16–20].

Youth with first onset psychosis displayed the most severe impairment of any clinical group in the sustained attention, verbal memory, response inhibition, cognitive flexibility, information processing speed and working memory domains. This pattern and intensity of dysfunction was consistent with what has been detected within adult samples[2–15]. Furthermore, it also matched what was found in other previous studies focusing on early onset psychosis in adolescents[51–57]. Importantly, evidence suggests that patients with youth onset schizophrenia have more severe cognitive deficits than those with late onset schizophrenia[54] and that these cognitive deficits are relatively stable over time[57–59]. Thus, early detection of cognitive impairment through behavioral testing could be important to intervene on these impairments early on.

Cognitive dysfunction in youth with functional neurological disorder was limited to executive function, working memory, cognitive flexibility, decision speed and information processing speed. Executive dysfunction compared to healthy controls uniquely distinguished youth with functional neurological disorder from other diagnostic groups. Although sparse, adult literature also suggests impairments in working memory in these patients[60]. Limited evidence also shows that adults with functional neurological disorder also suffer from executive function deficits, particularly planning[60].

Deficits in cognitive flexibility appeared to be the most stable dysfunction across diagnostic groups, as all four clinical groups sampled performed significantly worse than their healthy counterparts. Within the cognitive flexibility domain, first onset psychosis displayed a significant difference in performance compared to patients with ADHD.

Our findings support the assertion that cognitive impairment is a pervasive feature of mental illness, even in diagnoses that do not include cognitive impairment as a core diagnostic criterion (such as anorexia). Importantly, our findings also demonstrate that cognitive impairment in mental illness can be detected as early as childhood or adolescence with standardized computerized testing.

These results additionally present important future research and clinical implications. First, the transdiagnostic nature of overall cognitive dysfunction but unique patterns of specific impairments among diagnoses suggests that objective measurement of cognition can

Table 3 | Comparisons of the mean cognitive performance of each pair of diagnoses within each cognitive domain

Domain	Diagnosis 1	Diagnosis 2	Mean difference	s.e.m.	df	*t*	P_{corr}	Cohen's *d*
Executive function	Anorexia	Functional neurological disorder	0.793	0.210	4,083	3.777	1.51×10^{-3}	1.144
	Functional neurological disorder	First onset psychosis	−1.005	0.266	4,291	−3.773	1.53×10^{-3}	−1.45
Response inhibition	ADHD	Functional neurological disorder	−0.478	0.155	2,498	−3.079	1.79×10^{-2}	−0.689
		First onset psychosis	0.829	0.200	3,737	4.150	3.28×10^{-4}	1.196
	Anorexia	Functional neurological disorder	−0.920	0.202	3,718	−4.561	5.16×10^{-5}	−1.327
	Functional neurological disorder	First onset psychosis	1.307	0.239	3,285	5.469	4.84×10^{-7}	1.886
Cognitive flexibility	ADHD	First onset psychosis	0.617	0.191	3,338	3.228	1.10×10^{-2}	0.89
Verbal memory	ADHD	First onset psychosis	0.938	0.191	3,352	4.901	9.86×10^{-6}	1.353
	Anorexia	First onset psychosis	0.979	0.237	3,165	4.138	3.46×10^{-4}	1.412
	Functional neurological disorder	First onset psychosis	1.307	0.233	3,054	5.610	2.18×10^{-7}	1.885
Sustained attention	ADHD	First onset psychosis	1.157	0.200	3,750	5.781	9.20×10^{-8}	1.668
	Anorexia	First onset psychosis	1.377	0.251	3,720	5.476	4.73×10^{-7}	1.986
	Functional neurological disorder	First onset psychosis	1.512	0.240	3,325	6.293	2.92×10^{-9}	2.181
Information processing speed	ADHD	Anorexia	−0.475	0.161	2,833	−2.958	2.59×10^{-2}	−0.685
		First onset psychosis	0.565	0.194	3,465	2.913	2.96×10^{-2}	0.815
	Anorexia	Functional neurological disorder	0.879	0.193	3,295	4.544	5.61×10^{-5}	1.267
		First onset psychosis	1.040	0.239	3,242	4.357	1.32×10^{-4}	1.5
Working memory	Anorexia	Functional neurological disorder	0.741	0.195	3,367	3.802	1.38×10^{-3}	1.068
		First onset psychosis	0.813	0.237	3,191	3.425	5.62×10^{-3}	1.172

Mean differences are contrasts estimated in our linear mixed model analysis. Comparisons were conducted using two-sided *t*-tests, followed by Tukey correction for multiple comparisons of *P* values. *P* values are shown in scientific notation. For brevity, only results for which $P_{corr} < 0.05$ are shown. P_{corr}, Tukey-adjusted *P* value, s.e.m., standard error of the mean; df, degrees of freedom.

potentially serve as a helpful tool for mental health clinicians for early detection and differentiation of mental illnesses in youth. This is especially important considering our results derived from youth as young as 6 years of age. Traditionally, many mental health diagnostic criteria rely on patients' ability to recognize their dysfunction or emotions and be able to explain them in detail. This reliance on self-reported symptoms presents unique barriers for youth mental health diagnostics due to developmental realities. Future research can build on this work by further investigating cognitive signatures in other widely experienced psychiatric disorders in youth such as anxiety and depression. This study also suggests that cognitive dysfunction could be a target for treatment using strategies such as cognitive remediation that has been identified as effective in disorders such as schizophrenia[61].

Our team's prior work suggests that up to 27% of adult patients suffering from depression display cognitive impairments measured by the same tests used in the current study[62]. These patients are less likely to remit with standard antidepressant treatment and are likely to continue experiencing cognitive impairments despite any improvement in mood symptoms. Future studies should investigate the relationship of cognitive dysfunction and treatment outcomes among various youth mental health diagnoses. Another important future direction would be to investigate whether findings generalize to other widely used cognitive batteries (for example, ref. 63). Finally, these findings could be expanded by investigating the neuroimaging correlates of cognitive dysfunction in children and adolescents with mental illness[64,65]. For example, impaired segregation of task-positive and task-negative brain networks has been found in ADHD and could explain the diffuse performance deficit in this disorder[66]. In first onset (as well as chronic) psychosis, efficiency of the frontoparietal network and cingulo-opercular networks was associated with worse performance on standardized tests of general cognition[67]. Cognitive deficits in anorexia have been found to be associated with disruption of connectivity between the thalamus and prefrontal cortex[68]. Children and adolescents with functional neurological disorder showed altered connectivity in several brain networks, but to the best of our knowledge, how this relates to cognitive performance has not yet been investigated. Extending these neuroimaging insights could help advance future precision approaches for early treatment of developmental and mental health disorders.

The current study is subject to limitations. First, as referenced earlier, the sample analyzed features of only four clinical diagnoses, since these were the only ones available in the BrainNet database, namely ADHD, anorexia, first onset psychosis and functional neurological disorder. Future studies should extend investigations of cognitive impairments to other mental illnesses common in childhood and adolescence, such as mood (for example, bipolar disorder and major depressive disorder) and anxiety disorders. As every diagnostic group in our sample featured some degree of cognitive impairment, we anticipate that future studies investigating other diagnoses will produce similar results. Also, even though our dataset allowed us to compare results across several diagnoses, the sample sizes for each were heterogeneous. In particular, future studies investigating cognitive performance in anorexia, first onset psychosis and functional

neurological disorder using larger samples than ours might be able to detect subtle performance deficits in these diagnoses that we could not detect. Next, the current study was not able to consider the impact of social determinants relevant to brain health such as education access and quality, economic stability and social and community context due to inconsistent reporting of relevant data from the included protocols. Future studies should make the effort to collect and examine these important demographic factors related to brain development and overall brain health. Additional limitations include the cross-sectional nature of the current results. This is particularly pertinent for disorders such as anorexia and first onset psychosis that often worsen over time. Future endeavors should include longitudinal analyses to evaluate the effect of illness duration on cognition. Finally, another limitation was that we could not consider the potential confounding effects of treatment in analyses. Future studies should account for the potential impact of treatments on cognitive performance by clinical diagnosis and assess if these treatments improve cognitive deficits.

Methods

Participants

The data used in the present work were downloaded from BrainNet, a large database for mental health research, which combines data from a number of separate studies (access to BrainNet can be requested[69]). In particular, the current sample was recruited through clinical services associated with the University of Sydney, University of Adelaide and University of Melbourne and through advertising and self-referral. Inclusion criteria were age between 6 and 18 years old; diagnosis of ADHD, anorexia, first onset psychosis and functional neurological disorder (clinical groups) or no psychiatric diagnosis (controls); capacity to undergo a computerized test; normal (or corrected to normal) vision; and ability to use a keyboard. No data from minors with other diagnoses were available in BrainNet; therefore, we focused on ADHD, anorexia, first onset psychosis and functional neurological disorder. The only exception to this was one single minor with post-traumatic stress disorder and two matched controls from the same site, which we removed from our analyses. In this sample, with 'first onset psychosis' we mean minors who had experienced their first episode of a psychosis with onset before 18 years. Participants were excluded if they had a developmental delay (assessed by intelligence quotient testing), a known medical condition such as epilepsy, a history of head trauma causing a loss of consciousness for 10 min or more or substance dependence. Each included dataset and corresponding study was approved by the Sydney West Area Health Service's and Children's Hospital at Westmead's human research ethics committees. Approval numbers are as follows: psychosis sample and corresponding healthy controls ('the first episode project'), WSAHS HREC 98/12/3.3(682); ADHD sample and corresponding healthy controls, HREC 2006/12/4.5(2502); functional neurological disorder and corresponding healthy controls, HREC/2006/8/4.15(2415); and anorexia and corresponding health controls, HS/TG HREC2003/12/4.14 (1785). All participants and parents/guardians, as appropriate, signed and dated an approved informed consent form. Where participants consented, their data were made available for open sharing in BrainNet. All research complies with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Diagnosis of clinical groups was confirmed by consensus from clinicians using the following criteria and scales. For ADHD, Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-IV) and Conners' Rating Scale[70] were used; for details see ref. 43. For anorexia, Structured Clinical Interview (DSM-IV) and physical conditions were used; for details see ref. 17. For first onset psychosis, Structured Clinical Interview (DSM-IV) and Positive and Negative Syndrome Scale[71] were used; for details see ref. 45. For functional neurological disorder, Structured Clinical Interview (DSM-IV) was used; for details see ref. 46. For each clinical group, an age- and sex-matched sample of healthy individuals was recruited as a control group (Table 1).

Race, ethnicity and other socially relevant groupings were not included in the current analysis. This is because the data sourced for this study were archival data and race, ethnicity and other socially relevant groupings were not present in all available data.

Neurocognitive assessments

Cognitive performance was assessed using a standardized, computerized test battery, 'IntegNeuro', which has established norms across nine decades of the healthy lifespan, test–retest reliability[72], construct validity with respect to traditional neuropsychological batteries and brain measures[73], and utility in distinguishing cognitive impairments in psychiatric groups[1,74]. IntegNeuro assessed nine cognitive domains (and tests): executive function (Maze), response inhibition (Go-No-Go), cognitive flexibility (Stroop), verbal memory (Verbal Learning and Memory), sustained attention (Continuous Performance Test), decision speed (Choice Reaction Time), psychomotor function (Motor Tapping), information processing speed (Switching of Attention) and working memory (Digit Span). All tests were visual. See Supplementary Table 4 for a description of these tests. IntegNeuro provides performance measures for each of the tests named above, expressed on the basis of their deviation from a reference healthy population and matched by sex and age. A score for each cognitive domain was then obtained by averaging performance on each test within each of the nine domains (Supplementary Table 4). Scores >5 s.d. from the norm were considered outliers and removed (number of values removed: executive function, 11, 1.16%; response inhibition, 16, 1.69%; cognitive flexibility, 0, 0%; verbal memory, 0, 0%; sustained attention, 1, 0.11%; decision speed, 7, 0.74%; psychomotor function, 15, 1.58%; information processing speed, 1, 0.11%; and working memory, 0, 0%).

Statistical analysis

All analyses were conducted in RStudio 2022.07.2, R version 4.1.3, running on macOS Ventura 13.2. Code for these analyses is available at ref. 75.

Mixed linear model. We modeled the cognitive domain scores for each participant using a mixed linear model to take into account the fact that performance in all nine cognitive domains was measured in each participant. The model independent variables were diagnosis (factor with levels: control, ADHD, anorexia, first onset psychosis and functional neurological disorder), cognitive domain (factor with levels: sustained attention, cognitive flexibility, decision speed, executive function, information processing speed, psychomotor response speed, response inhibition, verbal memory and working memory) and site (factor with levels: Adelaide, Melbourne and Sydney); one random intercept was fit for every participant, and the dependent variable was the IntegNeuro performance score.

In mathematical notation, the model can be written as follows:

$$\begin{aligned}\text{Performance}_{ijk} = {} & \beta_0 + u_i + \beta_1 \times \text{Diagnosis}_{ijk} + \beta_2 \times \text{Domain}_{ijk} \\ & + \beta_3 \times (\text{Diagnosis}_{ijk} \times \text{Domain}_{ijk}) + \beta_4 \times \text{Site}_{ijk} + \epsilon_{ijk}\end{aligned}.$$

In this formula:

- β_0 is the average intercept across all subjects.
- u_i is the random intercept for the ith subject.
- $\beta_1, \beta_2, \beta_3$ and β_4 are the fixed effect coefficients for diagnosis, domain, the diagnosis × domain interaction and site, respectively.
- Diagnosis_{ijk} is the value of the predictor variable 'diagnosis' for the ith subject, measured for the jth domain at the kth site.
- Domain_{ijk} is the value of the predictor variable 'domain' for the ith subject, measured for the jth domain at the kth site.

- $Site_{ijk}$ is the value of the predictor variable 'site' for the ith subject, measured for the jth domain at the kth site.
- ϵ_{ijk} is the residual error for the ith subject, measured for the jth domain at the kth site, assumed to follow a normal distribution $\epsilon \sim N(0, \sigma^2)$.

After fitting our mixed linear model, we used F tests to assess the significance of the main effects of all our predictors, as well as of the cognitive domain × diagnosis interaction, to test whether different diagnoses had different profiles of cognitive dysfunction across domains. We considered significant tests for which $P < 0.05$. We followed up the significant cognitive domain × diagnosis interaction by comparing the performance in each cognitive domain between each pair of diagnoses using t-tests. These tests were adjusted for multiple comparisons by using Tukey's method and were considered significant if $P_{corr} < 0.05$.

Power simulation. To determine our power to detect a significant cognitive domain × diagnosis interaction using our mixed linear model given our sample size, we conducted a simulation (see Supplementary Methods for details). The simulation showed that, given a mean difference in cognitive performance between clinical participants and controls of at least 0.3 and given a number of dysfunctional cognitive domains in each clinical group between 2 and 6, using an $\alpha = 0.05$, we would achieve >80% power to detect our interaction of interest (Supplementary Fig. 3).

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Data used in this study are available on request from Stanford BrainNet at https://www.stanfordpmhw.com/datasets. The BrainNet repository meets the requirements for being public but also aligns with the procedures of other official public and scientific repositories such as HCP, ABCD and NDA. This choice is in line with the FAIRness guidelines, and it respects the original funders' requirements, allowing for appropriate source contributions and citations. Our approach is specifically designed for scientific use, which includes limiting access to for-profit entities to comply with the original funders' stipulations and the consent forms. Therefore, total open access is not feasible. Our intention is to provide public access that is consistent with the consent agreements and the original funders' intentions, similar to the data shared through NIH repositories. On Stanford BrainNet, we established a data access request form that screens users, similar to other public repositories.

Code availability

Code for the analyses is available at https://github.com/leotozzi88/cognition_minors_2023.

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Acknowledgements

We would like to extend our appreciation to the participants in the studies from which source data are drawn. The data are drawn from Stanford BrainNet, which includes data acquired with support from the National Health and Medical Research Council (project grant 1004822 to L.M.W. and A.H.; project grant 457424 to L.M.W., S.C. and M.R.K.) and Australian Research Council (Discovery Projects DP120104496, DP077394 and DP0345481 to L.M.W.), and a Pfizer Foundation Senior Research Fellowship (L.M.W.). We acknowledge the support of the Gustavus and Louise Pfeiffer Research Foundation, which allowed us to analyze cognitive profiles in young individuals experiencing mental health disorders.

Author contributions

K.K., M.R.K., A.H. and S.C. were a part of original data collection for the study. S.N., L.T., R.A.H. and L.M.W. developed the study. L.T. and R.A.H. performed the data analysis. L.M.W., S.N., L.T. and R.A.H. wrote the manuscript, and all authors (S.N., L.T., R.A.H., L.M.W., K.K., M.R.K. and S.C.) reviewed and approved the manuscript.

Competing interests

A.H. has received consultancy fees from Lundbeck Australia and Seqirus. He has received payments for educational sessions run for Lundbeck Australia and Servier. He has developed educational material for Servier. He is the recipient of an investigator-initiated grant from the Balnaves Foundation and Takeda Pharmaceutical Company. He is an investigator on an industry-sponsored trial by Alto Neuroscience. He is the recipient of funding from the Australian Research Council, the Medical Research Future Fund and the National Health and Medical Research Council. He has received philanthropic funding from the Balnaves Foundation. He is the chair of One Door Mental Health. L.M.W. declares US patent applications 10/034,645 and 15/820,338: systems and methods for detecting complex networks in MRI image data. The other authors declare no competing interests.

Ethics approval and consent to participate

The institutional review board approved the protocols of the studies that contributed source data. A study coordinator thoroughly explained the protocol to participants and answered any questions before they provided written informed consent to begin the study. The study was conducted according to the principles of the Declaration of Helsinki.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44220-023-00199-6.

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Peer review information *Nature Mental Health* thanks Ruben Gur and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	The data used in the present work was downloaded from Stanford BrainNet, a large database for mental health research which combines data from a number of separate studies. https://www.stanfordpmhw.com/datasets
Data analysis	RStudio 2022.07.02, R version 4.1.3, running on MacOS Ventura 13.2 code available at: https://github.com/leotozzi88/cognition_minors_2023

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Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The study reported biological sex. Because the data used from this study is archival data sourced from multiple prior investigations, we reported sex data as the respective prior investigations reported it. Consent was obtained to share individual level data for all participants. Outside of stating sex as a demographic variable, we did not include gender or sex in our analyses because sex or gender were not relevant to our current research question or hypothesis.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, and other socially relevant groupings were not included in the current study. This is because the data sourced for this study is archival data. Race, ethnicity, and other socially relevant groupings were not present in all available data. One source of ADHD participants reported that the sample was 63% Caucasian, and the rest "were Asian".
Population characteristics	samples are representative of the population in major metropolitan areas in Australia. Age range of total sample: 6-18 years old , Sex breakdown of total sample: female= 336, male= 611
Recruitment	This is archival data sourced from a series of prior clinical studies which were designed to assess cognition across multiple diagnoses in mental health using identical assessments, with the goal of integrating data into a mental health database known as BRAINnet. Participants were recruited from public health and community clinics working together in a collaborative manner within the BRAINnet network. This series of studies recruited participants directly from public health and community clinics in partnership with clinic personnel. Participants with ADHD were recruited from the adolescent medicine clinic at Westmead Hospital attached to the University of Sydney, and equivalent community clinics attached to Flinders University, Adelaide and the University of Melbourne, Melbourne. Patients were referred by two pediatricians specifically. Participants with psychosis were recruited as part of the Western Sydney First Episode Psychosis Project, a network of first contact with mental health services for young people with first presentation of psychotic symptoms. Referrals from Western Sydney and Wentworth area mental health services (combined population base of approximately 950 000 people) were screened for individuals presenting with a first episode of psychosis. Both areas operate early intervention programs targeted to young people with their first episode of a significant mental illness. In addition to community based early intervention services, subjects were referred from an inpatient unit for adolescents with a significant mental illness at Westmead Hospital. Local private psychiatric practitioners and a private psychiatric hospital were also contacted though only two referrals were received from private practitioners. Family members were present for most consenting procedures. Participants with anorexia were recruited through the eating disorders program at the Children's Hospital at Westmead attached to the University of Sydney. All sample participants presented to the hospital for their first admission for a DSM-IV diagnosis of anorexia nervosa. Control participants were recruited from the general community and screened using a web-based questionnaire to ensure that they did not violate the inclusion and exclusion criteria. Participants with functional neurological disorder were recruited through the FND program at the Children's Hospital at Westmead attached to the University of Sydney. Patients were recruited at a paediatric tertiary care hospital in the state of New South Wales, Australia. The sample was drawn from referrals of children presenting with conversion symptoms. Healthy controls were drawn from the BRAINnet database (www.brainnet.net) and had complete data on the same measures as the clinical sample.
Ethics oversight	This is archival data sourced from a series of prior clinical studies. Each protocol represented in the archival data used receive IRB approval prior to recruitment of participants. Each included dataset and corresponding study was approved by the Sydney West Area Health Service's and Children's Hospital at Westmead's Human Research Ethics Committees. Below are the corresponding ethical review approval numbers for each included dataset. Psychosis sample and corresponding healthy controls ("the first episode project"): approval number (WSAHS HREC 98/12/3.3(682)) ADHD sample and corresponding healthy controls: Study 2502]HREC Approval No2006/12/4.5(2502) Functional Neurological Disorder, and corresponding healthy controls: approval number HREC/2006/8/4.15(2415) Anorexia and corresponding health controls sample: approval number HS/TG HREC2003/12/4.14 (1785)

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

The current study is a quantitative study using data from multiple prior studies. Although multiple of the studies representing our dataset included follow-up or multiple data collection points, our current study focused on using the first time point (baseline) data collected. Our team evaluated the neurocognitive performance of youth diagnosed with ADHD (N=343), anorexia (N=40), first onset psychosis (N=25), and functional neurological disorder (N=56) with age-matched healthy controls (N=483). Performance was assessed using an objective assessment battery designed for use across diagnoses and settings and validated for its correlations with underlying brain structure and function. The following cognitive domains were assessed: sustained attention, cognitive flexibility, decision speed, executive function, information processing speed, psychomotor response speed, response inhibition, verbal memory, working memory.

Research sample

The data used in the present work was shared by investigators who participated in the BRAINnet network, and that BRAINnet was founded and led by senior author LM Williams. BRAINnet is a large database for mental health research which combines data from a series of studies specifically designed to use identical assessments. In particular, the current samples were recruited through clinical services associated with the University of Sydney, University of Adelaide and University of Melbourne, and through advertising and self-referral. The representative sources stated the samples were largely representative of the clinical groups included in metropolitan Australian areas and were chosen due to their availability and representativeness of clinical care populations.

ADHD Sample
INCLUSION:
• IQ of 80 or above, assessed using the full scale IQ (WISC-III) or spot the real word test, respectively
• primary diagnosis of attention deficit hyperactivity disorder
EXCLUSION:
• personal or family history of Axis 1 psychiatric disorder (other than as listed above for ADHD subjects), physical brain injury, neurological disorder, genetic disorder or other serious medical condition, and/or a personal history of drug or alcohol addiction.
OTHER DETAILS:
Each patient's diagnosis was confirmed using two assessments: a semi-structured interview based on DSM-IV criteria for ADHD and the Conner's Parent Rating Scales (based on the criteria of T-scores 1.5 S.D. above the norm in either inattentive or hyperactivity/impulsivity indices). Comorbid diagnoses (oppositional defiant disorder, learning disorder, conduct disorder, depression, and anxiety) were accepted. Attention deficit hyperactivity disorder and control participants were also matched on grade at school and intelligence quotient, as estimated by the Spot the Word Test of premorbid intelligence. All participants spoke English. All participants were asked to refrain from drinking caffeinated beverages and smoking cigarettes for 2 hours before a study session. Participants were either medication-naïve or withdrawn from stimulant medications at least 2 days before testing.
Ages:
• ADHD sample: range 6-18 years, mean age 11.78, SD 3.20
• healthy controls: range 6-18 years, mean age 11.87, SD 3.08
Sex Breakdown:
• ADHD sample: female = 76, male = 267
• healthy controls: female = 76, male = 267

FND Sample
INCLUSION:
• diagnosis of conversion disorder/functional neurological disorder
• organic illness had been excluded by the referring medical team-neurology, pediatrics, or neurosurgery
EXCLUSION:
• conversion/FND symptoms had resolved
• having a developmental disability
• did not speak English
• having concomitant organic brain disease such as brain injury or cerebral lupus
OTHER DETAILS
All FND participants had the presence of one or more conversion symptoms (M = 2.60, range, 1–7) – non-epileptic seizures (n = 19, 51%), sensory symptoms (n = 31, 54%), and motor symptoms (n = 38, 67%) – that were sufficiently disabling to require treatment in hospital in 95% (54/57) of cases. Comorbidities: anxiety (54% [31/57]), depression (14% [8/57]), or mixed anxiety/depression (14% [8/57]; defined by DSM-IV-TR). Fifty-eight per cent (33/57) had comorbid medically unexplained pain, and 54% (31/57) suffered from comorbid, nonspecific somatic symptoms (14% [8/57], nausea; 30% [17/57], dizziness; 23% [13/57], breathlessness; and 28% [16/57], fatigue). The majority of participants in the present sample had been healthy prior to onset of the conversion symptoms. Other commonplace illnesses included past episode of depression (n = 3), conduct problems (n = 1), post-traumatic stress disorder (PTSD) symptoms predating the conversion presentation (n = 1), a history of asthma (n = 3), congenital heart disease that had needed surgical repair in infancy (n = 1), coeliac disease (n = 1), keratoconus (n = 1), and past medical or surgical interventions for a range of miscellaneous problems (appendicitis, hernia, back operation, glomerulonephritis, or foot drop [n = 5]). Premorbid functioning of all participants in the present sample fell within the normal IQ range. According to these clinically sourced data, 10 children (18%) were estimated to function in the superior range (IQ 120+), 43 (75%) in the average range (IQ 80–119), and 4 (7%) in the borderline range (IQ 70–79).5 of 57 children had disclosed past sexual abuse, and three other children had a past history of maltreatment (physical/emotional abuse) documented by child protection services. Sixty-three per cent of participants came from intact biological families, 14% lived in blended families, 19% with a single parent, and 4% (two participants) lived with a grandparent. In terms of socioeconomic class, 33% of families were professional, 40% white collar, 14% blue collar, and 2% unemployed (a single mother).
Ages:
• FND sample: range 8-18 years, mean age 13.49, SD 2.12

• healthy controls: range 8-18 years, mean age 13.60, SD 2.31
Sex Breakdown:
• FND sample: female = 40, male = 16
• healthy controls: female = 41, male = 16

First onset psychosis sample
INCLUSION:
• aged from 13 to 25 years inclusive
• first contact with mental health services with psychotic symptoms (prior contact for non-psychotic problems was acceptable)
• presence of psychotic symptoms as defined by hallucinations, delusions, formal thought disorder or prominent negative symptoms present for a minimum of 3 days
EXCLUSION:
• treatment with electroconvulsive therapy in the 6 months prior to referral
• gross neurological disease
• developmental delay (IQ < 75)
• a history of head injury causing unconsciousness for at least one hour
• thought disorder ≥5 on the Positive and Negative Symptom Scale (PANSS) Conceptual Disorganization item
OTHER DETAILS:
Most participants were currently being treated with antipsychotics. 44% were diagnosed with schizophrenia, 14% bipolar disorder, 14% with a substance induced psychotic disorder, 12% with a schizophreniform disorder, 5% with major depression with psychosis, 5% with psychosis not otherwise specified, 4% with a brief psychotic disorder and 1% with schizoaffective disorder. All subjects were within the first three months of attending a mental health service for the treatment of psychosis. Diagnosis was made by means of a consensus conference of three qualified psychiatrists that drew upon all available information including project assessment, information from family and case manager and case notes some 6–9 months after initial contact with the subject. Diagnoses were made according to DSM-IV and ICD-10.
Age:
• psychosis sample: range 11-18 years, mean age 16.23, SD 1.63
• healthy controls: range 11-18 years, mean age 16.19, SD 1.37
Sex breakdown:
• psychosis sample: female = 10, male = 15
• healthy controls: female = 12, male = 30

Anorexia sample:
INCLUSION:
• normal (or corrected to normal) hearing and vision
• normal premorbid IQ estimate within the normal range
• first hospital admission for DSM-IV anorexia nervosa
EXCLUSION:
• physical brain injury (causing loss of consciousness for 10 min or more)
• neurological disorder, serious medical, or genetic condition (other than AN), or substance use disorders
OTHER DETAILS
Age range:
• anorexia sample: range 12-18 years, mean age 15.23, SD 1.61
• healthy controls: range 12-18 years, mean age 15.25, SD 1.58
Sex breakdown: all female sex

Healthy control samples overall inclusion exclusion criteria
INCLUSION:
• Fluent in English
• Scored within the healthy range on the Somatic and Psychological Health Report (SPHERE-12; Hickie et al., 2001). The SPHERE-12 has equivalence with the General Health Questionnaire and is used to screen for undiagnosed common psychiatric disorders, with six questions relating to psychiatric symptoms (PSYCH-6) and six relating to somatic symptoms (SOMA-6).) Criteria for screening healthy was a score of <2 on PSYCH-6 and < 3 on SOMA-6. Reference: Hickie I.B., Davenport T.A., Naismith S.L., & Scott E.M. (2001). On behalf of the SPHERE National Secretariat. SPHERE: A National Depression Project. The Medical Journal of Australia, 175, S2-S55.
• IQ of 80 or above, assessed using the full scal IQ (WISC-III) or spot the real word test, respectively.
EXCLUSION:
• Record of Attention Deficit Hyperactivity Disorder (ADHD), Schizophrenia, Bipolar Disorder or other psychological and/or psychiatric disorder
• Family history of Attention Deficit Hyperactivity Disorder (ADHD), Schizophrenia, Bipolar Disorder or other psychological and/or psychiatric disorder
• A personal history of having received a blow to the head that resulted in unconsciousness for >10 minutes, within the last 5 years.
• A personal history of neurological disorder
• A personal history of serious medical conditions that could impact assessments
• A severe impediment to vision, hearing, or hand movement that could impact assessments
• Substance dependence of heavy current consumption or illicit drugs or alcohol

Sampling strategy

The current study relied on archival data representing multiple sources. The source data were acquired using a convenience sampling strategy over an extended interval of multiple years to allow for sufficient representation of clinical participants attending each of the referring clinics.

We computed implied power given our total sample size of 947, the consideration of effects for six groups, an alpha of .05, a beta

	of .2 and a conservative small effect size of f=.1. With these parameters our implied power to detect significant group differences is 0.92.
Data collection	Cognitive performance was assessed using a standardized, computerized test battery, "IntegNeuro", which has established norms across nine decades of the healthy lifespan, test-retest reliability26, construct validity with respect to traditional neuropsychological batteries and brain measures27, and utility in distinguishing cognitive impairments in psychiatric groups1,28. IntegNeuro assessed nine cognitive domains (and tests): executive function (Maze), response inhibition (Go-No-Go), cognitive flexibility (Stroop), verbal memory (Verbal Learning and Memory), sustained attention (Continuous Performance Test), decision speed (Choice Reaction Time), psychomotor function (Motor Tapping), information processing speed (Switching of Attention), and working memory (Digit Span). See Supplementary Table 1 for a description of these tests. IntegNeuro provides performance measures for each of the tests named above expressed based on their deviation from a reference healthy population, matched by sex and age. A score for each cognitive domain was then obtained by averaging performance on each test within each of the nine domains (Supplementary Table 1). Scores > 5 standard deviations from the norm were considered outliers and removed (number of values removed: executive function: 11, 1.16%; response inhibition: 16, 1.69%; cognitive flexibility: 0, 0%; verbal memory: 0, 0%; sustained attention: 1, 0.11%; decision speed: 7, 0.74%; psychomotor function: 15, 1.58%; information processing speed: 1, 0.11%; working memory: 0, 0%).
Timing	The data for the included first onset psychosis sample was collected between 2002-2004. The data for the included ADHD sample was collected between 2002-2006 The data for the included anorexia and FND samples were collected between 2006-2010. The FND sample data was specifically sampled from August 16, 2006 through August 16, 2010.
Data exclusions	Some behavioral data was excluded from the final analysis. Scores > 5 standard deviations from the norm were considered extreme scores and removed (number of values removed: executive function: 11, 1.16%; response inhibition: 16, 1.69%; cognitive flexibility: 0, 0%; verbal memory: 0, 0%; sustained attention: 1, 0.11%; decision speed: 7, 0.74%; psychomotor function: 15, 1.58%; information processing speed: 1, 0.11%; working memory: 0, 0%).
Non-participation	Below is the information that was available to the current study team. Psychosis sample: Over a two-year period 224 referrals were made to the project from which 104 subjects initially consented and met all the inclusion criteria. Subjects did not take part for a variety of reasons which included refusal to take part in research (n = 48), refusing all services (n = 11), uncontactable (n = 16), moved out of area (n = 8), working full-time (n = 7) and did not make criteria for study (n = 30). A further 10 subjects dropped out because of illness related factors and were unable to complete more than one arm of the study. They were excluded from further analysis. No subject was excluded because of the unavailability of a parent or guardian. FND sample: 7 participant declined participant in all arms of the study
Randomization	Participants were not randomized or allocated into groups. Clinical participants were recruited by the respective research teams and healthy control participants were recruited to match the clinical sample, therefore controlling for potentially differing covariates such as age, sex, and years of schooling.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A