

RESEARCH ARTICLE

Cognitive Profile of Children and Adolescents with Anorexia Nervosa

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Abstract

Objective: Few studies of cognitive functioning in children and adolescents with anorexia nervosa (AN) have been conducted. The aim of this study was to examine the neurocognitive and intelligence profile of this clinical group.

Method: The study was a matched case–control ($N=188$), multi-centre study including children and adolescents with AN ($N=94$) and healthy control participants ($N=94$).

Results: The results suggest that Full Scale Intelligence Quotient (Wechsler Intelligence Scale for Children-III/Wechsler Adult Intelligence Scale-III) in this patient group is close to the normal population mean of 100. Individuals with AN exhibited significantly worse performance in nonverbal intelligence functions (i.e. Wechsler Intelligence Scale for Children-III/Wechsler Adult Intelligence Scale-III, Perceptual Organization Index) and in verbal memory (Test of Memory and Learning—Second Edition, Memory for Stories) and motor speed (Cambridge Neuropsychological Test Automated Battery, Simple and Choice Reaction Time) compared with healthy control participants. No significant difference in set-shifting ability (Cambridge Neuropsychological Test Automated Battery, Intra-Extra Dimensional Set Shift and Trail Making Test B) was found.

Conclusions: Inefficiency in nonverbal intelligence functions and in specific cognitive functions was found in this study of children and adolescents with AN. © 2014 The Authors. *European Eating Disorders Review* published by John Wiley & Sons, Ltd.

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Keywords

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Introduction

Although most studies on children and adolescents with anorexia nervosa (AN) found no evidence of cognitive inefficiencies (Andres-Perpina et al., 2011; Buhren et al., 2012; Calderoni et al., 2013; Lang, Stahl, Espie, Treasure, & Tchanturia, 2014a), some studies have suggested specific cognitive impairments. Andrés-Perpiña et al. (2011) found a significant increase in time spent on visuoconstruction on The Rey Osterreith Complex Figure Test (RCFT). Similar findings have been made by Rose, Frampton, and Lask (2013), who also found a significantly longer time spent on construction along with a more detailed approach to the design. In terms of sensory-motor speed, it has been proposed that patients with AN perform worse than healthy controls

(HC) (Hatch et al., 2010a). In a recent review of central coherence in children and adolescents with AN, Lang & Tchanturia, 2014 state that the overall findings suggest that children and adolescents had a lower central coherence score when compared with HC groups, indicating a less globally orientated processing style. Impaired set-shifting abilities have also been suggested, although a recent review and meta-analysis has found no significant difference (Lang et al., 2014a). In a case series by Rose, Frampton, & Lask (2012), the authors point to the lack of consensus in the findings of studies on cognitive function in AN. The number of studies and patients included in these studies tends to be relatively small, which may reduce the reliability of the findings. As children and adolescents undergo cognitive maturation, it is possible that AN may have adverse effects on cognitive development, and

existing cross-sectional studies are not able to take this into account. Thus, an important future area of research is to gain more insight into the possible interaction between the neurological development and the progression of AN.

Cognitive functioning in adult patients with anorexia nervosa

The vast majority of studies on cognitive function in AN have been conducted in adults. In these studies, inefficiencies in attention, set-shifting, central coherence, executive function, memory, verbal functioning, cognitive flexibility and visuospatial ability have been identified (Andres-Perpina *et al.*, 2011; Buhren *et al.*, 2012; Calderoni *et al.*, 2013; Hatch *et al.*, 2010a, 2010b; Lang *et al.*, 2014a, 2014b; Lopez, Stahl & Tchanturia, 2010; Lopez *et al.*, 2008a, 2008b; Stedal, Rose, Frampton, Landro & Lask, 2012; Tchanturia *et al.*, 2004; Tchanturia *et al.*, 2011; Tchanturia *et al.*, 2012; Fagundo *et al.*, 2012; Gillberg, Rastam, Wentz, & Gillberg, 2007; Green, Elliman, Wakeling & Rogers, 1996; Jauregui-Lobera, 2013; Kaye, 2008; Kingston, Szmukler, Andrewes, Tress & Desmond, 1996; Lounes, Khan & Tchanturia, 2011; Mathias & Kent, 1998; Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007; Sarrar *et al.*, 2011). In a number of studies conducted in recent years, the focus has been on set-shifting ability, that is, the ability to move flexibly from one task/strategy to another (Lezak, 1995). These studies have shown insufficiencies in the set-shifting ability in adult patients with AN (Tchanturia *et al.*, 2011). Previous findings regarding intelligence have varied (Gillberg *et al.*, 2007). A recent meta-analysis found intelligence quotient (IQ) to be at least as high in the AN group as in the normative population (Lopez *et al.*, 2010). The average IQ in the studies included in the meta-analysis varied from a mean Full Scale IQ (FSIQ) of 96.1 (Mathias & Kent, 1998) to 116.8 (Southgate, Tchanturia, & Treasure, 2008).

Aim of the study

The main purpose of the present study was to characterize the neuropsychological profile of children and adolescents with AN, in the acute stage of the illness. This was carried out in comparison with a healthy control group. It was the aim of the study to describe both the patients' specific cognitive functions as well as intelligence profile, as indicated by FSIQ, Verbal IQ (VIQ), Performance IQ (PIQ), Verbal Comprehension Index (VCI) and Perceptual Organization Index (POI).

The primary hypotheses of the study were that children and adolescents with AN would

1. display the same intelligence level or one above that found in the HC group;
2. show a different profile of specific cognitive functions than the HC group;
3. demonstrate set-shifting deficits relative to the HC group.

Method

Recruitment

Patients were recruited to the study after being diagnosed with AN. Diagnosis was conducted by medical doctors. Recruitment

of patients took place at three participating centres. Two centres were specialized psychiatric hospital units for inpatients and outpatients with an eating disorder: the Section of Eating Disorders, Psychiatric Department, Aalborg University Hospital, North Denmark Region, Denmark (project holders), and the Mental Health Centre for Child and Adolescent Psychiatry, Bispebjerg Department, Capital Region, Denmark. The third participating centre was Medical Specialist Clinic in Child and Adolescent Psychiatry, in a private setting, Copenhagen, Denmark, which only had outpatients. Recruitment of patients took place from January 2009 to December 2011.

The HC group was recruited from schools. Entire school classes of the relevant age range were invited to participate. Patients and HCs were matched 1:1 on gender and age (i.e. within one grade) and matched at group level on socio-demographic background. Only participants in the HC group received a small incentive of approximately 71 USD.

Patients were diagnosed using the Diagnostic and Statistical Manual of Mental Disorders (DSM), 4th edition (American Psychiatric Association, 1994). Subsequently, the patients were rediagnosed in accordance with the DSM, 5th edition (American Psychiatric Association, 2013). A total of 89 patients met DSM-5 diagnostic criteria for AN. Five patients did not fully meet the diagnostic weight criteria for AN. These patients did, however, meet the diagnostic criteria for Other Specified Feeding or Eating Disorder, Atypical AN.

Ethical aspects

Participation was voluntary, and patients were informed that non-participation would not affect their treatment. Written and oral information about the study was provided before recruitment. Written informed consent was obtained from the holder of custody. The study was conducted in accordance with the Helsinki Declaration and was approved by the local Research Ethics Committee, file number N-20080060MCH, and authorized by the local Data Protection Agency.

Measurement and evaluation techniques

Assessment of psychopathology

The Eating Disorder Examination (EDE) version 16 was used to assess AN symptomatology, onset and development of the eating disorder (Cooper, Cooper, & Fairburn, 1989; Wilfley, Schwartz, Spurrell, & Fairburn, 2000). The EDE has good internal consistency, discriminate and concurrent validity and inter-rater reliability (Fairburn *et al.*, 1993; Williamson, Barker, Bertman, & Gleaves, 1995). For the assessment of psychiatric comorbidity, the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL) (Kaufman, Birmaher, Brent, Ryan, & Rao, 2000; Kaufman *et al.*, 1997) was used, with a cut off score of 3. The Autism Screening Questionnaire, which is a screening questionnaire for Asperger syndrome filled in by parents, was also applied, with a cut off ≥ 19 (Ehlers, Gillberg, & Wing, 1999). A parental interview was conducted to collect anamnestic data. A structured somatic examination included a collection of clinical observations and patient-reported somatic symptoms according to generally recognized somatic complications in AN (Hebebrand & Bulik, 2011; Mitchell & Crow, 2006), including electrocardiogram (ECG) recordings and clinical and paraclinical assessments.

Assessment of cognitive functions

Cognitive function was examined using a comprehensive neuropsychological test battery (Table 1). The test battery was composed after a thorough review of the literature. The goal was to assemble a battery that included major cognitive domains and functions of relevance to AN. It was deemed appropriate to administer the complete gold-standard intelligence tests and to avoid short form IQ estimates. The most recent version of the Wechsler Intelligence Scale for Children-III (WISC-III)/Wechsler Adult Intelligence Scale-III (WAIS-III) in Danish was the natural choice. The choice of other cognitive tests used in the study was based on frequently used tests in other published AN studies. Finally, Cambridge Neuropsychological Test Automated Battery (CANTAB) was chosen because of the expediency of using a computerized test battery. CANTAB had at study start only been used in one other AN study but is frequently used in studies of cognitive functions in other psychiatric disorders. Set shifting was assessed with the following tests: Trail Making Test B (TMT B) minus Trail Making Test A (TMT A) and the Intra-Extra Dimensional Set Shift (IED) Extra-Dimensional Stage (EDS) errors from CANTAB.

Depending on age, either the WISC-III (Wechsler, 1991) or the WAIS-III (Wechsler, 1997) was administered: FSIQ, VIQ and PIQ were calculated, as were the four secondary indices, namely, VCI, Working Memory Index, POI and Processing Speed Index.

Rey Osterreith Complex Figure Test (Knight & Kaplan, 2003; Meyers & Meyers, 1995) was used, including copy, immediate recall and delayed recall.

Trail Making Tests (Reitan & Wolfson, 1985) A and B were also administered.

Nine subtests from CANTAB (Lowe & Rabbitt, 1998; Sahakian & Owen, 1992) were used, including the Motor Screening Task (which served solely as an introduction task), Stockings of Cambridge, IED, Spatial Span, Spatial Working Memory, Rapid Visual Information Processing, Simple and Choice Reaction Time (RTI), Pattern Recognition Memory and Spatial Recognition Memory.

Four subtests from the Test of Memory and Learning—Second Edition (TOMAL-2) (Reynolds & Bigler, 1994) were used, including Memory for Stories, Word Selective Reminding, Memory for Stories—delayed recall and Word Selective Reminding—delayed recall.

Assessment of control participants

The HC group were screened for indication of psychiatric disorder during recruitment using the Strengths and Difficulties Questionnaire (Goodman, 1997), a brief behavioural screening questionnaire. Furthermore, the HCs were screened with the Autism Screening Questionnaire (Ehlers et al., 1999), and an identical neuropsychological test battery was administered.

Inter-rater reliability

To achieve high inter-rater reliability, joint personnel training, co-rating and supervision were provided continuously during the study period. Highly trained staff managed all assessment tools. Fully trained clinical psychologists assessed cognitive function and administered the EDE. Somatic assessment was conducted by doctors and medical doctors, and parent interviews were performed by nurses. Ongoing co-rating and supervision was

provided by PhD level psychologists. To ensure high inter-rater reliability for the assessment of cognitive function, co-rating was conducted on the WISC-III/WAIS-III, RCFT, TMT A and B and TOMAL-2 in 15 cases, and inter-rater reliability for the WISC-III/WAIS-III was evaluated in 14 cases. The observed intra-class correlation coefficient for FSIQ was 0.985, which is within a satisfactory range and indicates high uniformity in rating.

Statistical analysis

Data were analysed using either paired *t*-tests or, if data did not fulfil the requirement of normality, the non-parametric equivalent Wilcoxon signed rank tests. Effect sizes were calculated, taking into account the dependence structure of the data by adjusting for the correlation within matched pairs (Dunlap et al., 1996). Linear regression analyses were performed on Memory for Stories and RTI five-choice movement time/RTI simple movement time, with POI and group as explanatory variables. Appropriate transformations were applied to meet regression assumptions. Robust standard errors were estimated in all regression analyses because of the data being matched. For Memory for Stories, RTI five-choice movement time/RTI simple movement time, TMT B minus TMT A, and IED EDS errors, correlation coefficients were calculated using Spearman's rho as not all variables were normally distributed.

The chosen level of significance was 5% in all analyses.

All analyses were carried out in the statistical software Stata version 11.

Results

A total of 188 participants, equally distributed between the AN group ($N=94$) and the HC group ($N=94$), participated in this study. Two HCs were excluded because of psychopathology, and two additional HCs were subsequently recruited.

As shown in Table 2, the gender distribution was 84 females and 10 males in each group. The average age in the AN group was 14.9 years (SD 1.8) with a range of 10.2–17.9 years. The patients in the study cohort were seriously ill, with an average body mass index of 15.8 (SD 1.8), a mean resting pulse of 59.6 (SD 13.4), Lanugo hair in 38 and peripheral cyanosis in 33 of the patients with AN.

Eighty-three patients had AN, restricting type, whereas 11 patients had AN, binge-eating/purging type. A total of 30 patients had a family history of eating disorders. Symptoms of comorbidity were found in 34 patients. The mean duration of disease, measured by self-reported duration of changes in eating behaviour, was 1.2 years (SD 1.2), with a range of 0.1–6.4 years.

A highly significant difference was observed between groups in the POI (Table 3) (mean = -5.4 , $p=0.009$), with better scores in HCs. A nearly significant between-group difference was found in PIQ (mean = -4.0 , $p=0.051$), with patients performing poorer than HCs. No significant differences were found for the VCI, Working Memory Index or Processing Speed Index indices. Likewise, no significant between-group difference was found in FSIQ or VIQ (Table 3).

Findings suggested that the intelligence profile was significantly more uneven in the AN group compared with the HC group, such that a significantly larger difference was found between VCI and POI in the AN group relative to the HC group (mean = 8.1, $p < 0.001$; Table 3).

Table 1 Assessment battery

Cognitive function	Test	Sub test	Purpose
Intelligence	Wechsler Intelligence Scale for Children-III (WISC-III) or Wechsler Adult Intelligence Scale—III (WAIS-III)	Full Scale Intelligence Quotient (FSIQ)	Overall level of general cognitive and intellectual functioning. Measure of the global intellectual functioning (FSIQ) is derived from the total combined performance on the VCI, PRI, WMI and PSI (Wechsler, D, 1991; Wechsler, D, 1997)
		Verbal Intelligence Quotient (VIQ)	Measure of the spoken language capabilities and limitations and the overall verbal intellectual abilities. Measures acquired knowledge, verbal reasoning and attention to verbal materials. VIQ is a composite of the VCI and WMI scores (Wechsler, D, 1991; Wechsler, D, 1997)
		Performance Intelligence Quotient (PIQ)	Measure of mental capacity in dealing with nonverbal skills, and a measure of overall visuospatial intellectual abilities. Assesses fluid reasoning, spatial processing, attentiveness to details and visual-motor integration. PIQ is derived from the POI and PSI (Wechsler, D, 1991; Wechsler, D, 1997)
		Verbal Comprehension Index (VCI)	Measure of verbal reasoning and verbal acquired knowledge, that is, crystallized intelligence. Includes language comprehension and production, listening and communication ability, general knowledge of facts and cultural knowledge (Wechsler, D, 1991; Wechsler, D, 1997)
		Working Memory Index (WMI)	Measure of the ability to attend to information presented verbally, manipulate that information in short-term immediate memory and formulate a response (Wechsler, D, 1991; Wechsler, D, 1997)
		Perceptual Organization Index (POI)	Measure of visuospatial organization and visual-motor skills within a time limit, that is, fluid reasoning (Wechsler, D, 1991; Wechsler, D, 1997)
		Processing Speed Index (PSI)	Measure of speed of cognitive processes and response output. Measures attention to visual material, visual perception and organization, visual scanning and hand-eye coordination (Wechsler, D, 1991; Wechsler, D, 1997)
Executive functions	Rey Osterreith Complex Figure Test (RCFT) Trail Making Test (TMT)	Copy	Measure of visuoconstruction (Meyers, J & Meyers, K, 1995)
		B	Measure of visual attention and set-shifting abilities (Reitan, RM & Wolfson, D, 1985)
	Cambridge Neuropsychological Test Automated Battery (CANTAB)	Stockings of Cambridge (SOC)	Measure of spatial planning
Working memory	CANTAB	Intra-Extra Dimensional Set Shift (IED)	Test of rule acquisition and reversal. It features visual discrimination and attentional set formation maintenance, shifting and flexibility of attention. The test is a computerized analogue of the Wisconsin Card Sorting test
		Spatial Span (SSP)	Measure of working memory capacity. SSP is a visuospatial analogue of the Digit Span test (Lowe, C, & Rabbitt, P, 1998; Sahakian, BJ & Owen, AM, 1992)
Attention	CANTAB	Spatial Working Memory (SWM)	Measure of the ability to retain spatial information and to manipulate remembered items in working memory
		Rapid Visual Information Processing (RVP)	Measure of sustained attention
Processing speed	TMT	A	Measure of visual attention and speed (Reitan, RM & Wolfson, D, 1985)
	WISC-III/WAIS-III	Digit Symbol Coding	Measure of perceptual-motor speed (Wechsler, D, 1991; Wechsler, D, 1997)
Visual memory	CANTAB	Simple and Choice Reaction Time (RTI)	Measure of response latency and movement time
	CANTAB	The Pattern Recognition Memory (PRM)	Measure of visual pattern recognition memory in a two-choice forced discrimination paradigm
	RCFT	Immediate recall	Measure of visuospatial abilities and short-term memory (Meyers, J & Meyers, K, 1995)

(Continues)

Table 1 (Continued)

Cognitive function	Test	Sub test	Purpose
		Delayed recall	Measure of visuospatial abilities and long-term memory (Meyers, J & Meyers, K, 1995)
Spatial Memory	CANTAB	Spatial Recognition Memory (SRM)	Measure of visuospatial recognition memory in a 2-choice forced discrimination paradigm
Verbal memory	Test of Memory and Learning—Second Edition (TOMAL-2)	Memory for Stories	Measure of short-term verbal memory and executive function (Reynolds, CR & Bigler, ED, 1994)
		Word Selective Reminding	Measure of short-term verbal memory (Reynolds, CR & Bigler, ED, 1994)
		Memory for Stories—delayed recall	Measure of long-term verbal memory and executive function (Reynolds, CR & Bigler, ED, 1994)
		Word Selective Reminding—delayed recall	Measure of long-term verbal memory (Reynolds, CR & Bigler, ED, 1994)

This table displays an overview of the complete neuropsychological assessment battery included in the study.

Table 2 Description of patient cohort

Age (mean, SD)	14.9	1.8
Female (n, %)	84	89.4
Male (n, %)	10	10.6
Duration of illness, years (mean, SD)	1.2	1.2
Country of birth (n, %)		
Denmark	90	95.7
Other European	3	3.2
Africa	1	1.1
Weight (mean, SD)	42.9	7.3
Height (mean, SD)	164.5	7.9
Body mass index (mean, SD)	15.8	1.8
WHO guideline \geq 5th percentile (n, %)	30	31.9
WHO guideline <1st percentile (n, %)	34	36.2
Blood pressure (mean, SD)		
Systolic	105.8	10.7
Diastolic	68.0	8.9
Pulse (mean, SD)		
Resting	59.6	13.4
Lanugo (n, %)	38	40.4
Peripheral cyanosis (n, %)	33	35.1
ASSQ (n, %)		
\geq 19	5	5.3
<19	82	87.2
NA	7	7.4
KSADS (n, %)		
Affective Disorders	19	20.2
Anxiety Disorders	21	22.3
Psychosis	5	5.3

This table displays selected patient descriptors, including demographics, somatic variables and information regarding duration of illness and comorbidity. KSADS, Kiddie-Schedule for Affective Disorders and Schizophrenia.

The patients with AN showed decreased motor speed, as significant differences were found in the RTI subtests simple movement time (mean = 43.70, $p = 0.038$) and five-choice movement time (mean = 57.11, $p = 0.001$). There were no significant differences between the AN group and the HC group in the remaining processing speed subtests. However, there was a highly significant

between-group difference in verbal short-term memory on the TOMAL-2 task Memory for Stories (Table 3): patients performed more poorly than HCs on immediate recall of the stories (mean = -3.7 , $p = 0.009$). The AN group showed decreased long-term verbal memory, as a trend towards significance was found for delayed recall on the TOMAL-2 Memory for Stories (mean = -2.7 , $p = 0.077$). There were also signs of executive function inefficiencies in the domain of spatial planning in the AN group, as a marginally significant difference was detected for the problems solved in minimum moves measure on the CANTAB Stockings of Cambridge subtest (mean = -0.48 , $p = 0.069$). For visuoconstruction ability, measured with the copying task RCFT, the AN group scored significantly better than the HC group (mean = 1.2, $p = 0.003$). There were no significant differences found between the AN group and the HC group in set-shifting measured with TMT B minus TMT A (mean = -0.8 , $p = 0.594$) and IED EDS errors (mean = -2.6923 , $p = 0.097$). No significant differences were found in the remaining subtests.

Correlations between the POI and scores derived from the Memory for Stories subtest and the two measures of RTI were highly significant for the AN group but not for the HC group. Also, higher POI was associated with higher scores in Memory for Stories ($\beta = 0.16$, $SE = 0.06$, $p = 0.004$), faster motor speed, as measured by RTI five-choice movement time ($\beta = 0.01$, $SE = 0.00$, $p = 0.008$), and RTI simple movement time ($\beta = 0.01$, $SE = 0.00$, $p = 0.001$) in patients (with HCs as the reference group).

Finally, significant correlations were observed for POI and the two set-shifting measures, TMT B minus TMT A and IED EDS errors. A significant but weak correlation was observed between TMT B minus TMT A and POI ($\rho = -0.20$, $p = 0.012$) and likewise between IED EDS errors and POI ($\rho = -0.22$, $p = 0.003$).

Discussion

One aim of the study was to describe the level of intelligence in patients with AN. This was carried out through a comparison with the intelligence level of the HC group. It was expected that patients with AN would have the same intelligence level or one above that found in the HC group. No significant between-group

Table 3 Neuropsychological test scores at baseline—all participants

	AN-P		HC		Paired		
	Mean	SD	mean	SD	Mean diff	<i>p</i> -value	ES
WISC-III/WAIS-III							
Full Scale IQ (FSIQ)	101.1	16	102	13.4	−0.8	0.695	−0.058
Verbal IQ (VIQ)	104.6	16.9	103	13.3	1.7	0.444	0.114
Performance IQ (PIQ)	96.3	14.4	100.3	13.3	−4	0.051	−0.284
Difference (VIQ − PIQ)	8.3	14.9	2.7	14	5.7	0.007	0.393
Verbal Comprehension Index (VCI)	106.2	16.7	103.6	12.7	2.7	0.226	0.18
Working Memory Index (WMI)	98.2	15.5	97.9	14	0.2	0.914	0.016
Perceptual organization Index (POI)	93	14.6	98.3	13.5	−5.4	0.009	−0.381
Processing speed Index (PSI)	108.2	17.6	108.7	19.2	−0.2	0.945	−0.01
Difference (VCI − POI)	13.2	16.2	5.4	15	8.1	<0.001	0.517
RCFT							
copy	33.5	2.4	32.3	2.7	1.2	0.003	0.45
Time to copy	201.3	86.6	191.4	68.2	9.5	0.397	0.127
Immediate recall	21.5	6.4	21.4	5.4	0.2	0.798	0.037
Delayed recall	21.5	6.5	21.2	5	0.3	0.721	0.049
Trail making							
A	32.1	13	27.6	10.6	0.8	0.505	0.066
B	69.2	31.3	63.4	25.5	0	0.814	0
Difference (B − A)	37.1	25.7	35.8	21.7	−0.8	0.594	−0.036
TOMAL-2							
Memory for Stories	28.3	10.1	31.6	7.8	−3.7	0.009	−0.402
Memory for Stories—delayed recall	24.3	10.6	26.8	8	−2.7	0.077	−0.287
Word Selective Reminding	60.3	9.6	61.4	5.6	−0.9	0.349	−0.142
Word Selective Reminding—delayed recall	10.6	1.8	10.5	1.5	0.1	0.547	0.098
CANTAB							
IED stages completed	8.5824	1.3087	8.5745	0.7827	0	0.375	0.135
IED total errors adjusted	23.5714	31.544	24.9362	19.7619	−1.0659	0.369	−0.13
IED EDS errors	7.1429	8.4716	9.9468	10.4154	−2.6923	0.097	−0.256
PRM number correct	21.5889	2.398	21.6383	1.6188	−0.1222	0.892	0.02
SRM number correct	17.0333	1.9282	17.4468	1.8527	−0.4444	0.127	−0.235
RTI five-choice movement time	382.62	103.03	331.92	75.86	57.11	<0.001	0.633
RTI five-choice reaction time	353.92	143.39	333.97	43.59	−3.31	0.678	−0.066
RTI simple movement time	395.39	129.61	356.02	114.07	43.7	0.038	0.354
RTI simple reaction time	325	88.99	309.29	40.76	−6.86	0.418	−0.143
RVP A	0.8737	0.0472	0.8696	0.0507	0.0036	0.602	0.074
SOC problems solved in minimum moves	8.2584	1.9973	8.7447	1.8076	−0.4831	0.069	−0.254
SOC mean initial thinking time 5	5642.96	4716.04	5933.35	5299.95	−425.01	0.726	−0.053
SOC mean moves 5	7.0534	1.7236	6.7029	1.2147	0.3519	0.132	0.238
SOC mean subsequent thinking time 5	827.75	1152.29	875.68	905.92	−127.47	0.332	−0.145
SSP span length	6.7528	1.5542	6.9574	1.1996	−0.2135	0.312	−0.152
SWM strategy	30.9659	5.1135	31	5.3581	0.1136	0.875	0.022
SWM total errors	180.568	172.643	182.979	149.032	0.1477	0.946	0.009

This table provides a complete overview of the study results of cognitive measures with mean and standard deviation (*SD*) for the patients with anorexia nervosa and HC as well as paired mean difference (mean diff), *p*-values and effect size (ES).

RCFT, Rey Osterreith Complex Figure Test; TOMAL-2, Test of Memory and Learning—Second Edition; CANTAB, Cambridge Neuropsychological Test Automated Battery; IED, Intra-Extra Dimensional Set Shift; EDS, Extra-Dimensional Stage; PRM, Pattern Recognition Memory; SRM, Spatial Recognition Memory; RTI, Simple and Choice Reaction Time; RVP, Rapid Visual Information Processing; SOC, Stockings of Cambridge; SSP, Spatial Span; SWM, Spatial Working Memory; IQ, Intelligence Quotient.

difference in FSIQ was found. In the conclusion of a meta-analysis, Lopez (Lopez *et al.*, 2010) stated that IQ in patients with AN was at least as high as the average IQ in the normative population. The results of this study suggest that FSIQ among children and adolescents with AN is close to the normal population mean of 100, but the study provides no evidence that IQ is elevated above the normal mean in the AN group. The findings of this

study are consistent with the results of several other studies (Bayless *et al.*, 2002; Gillberg, Gillberg, Rastam, & Johansson, 1996; McDowell *et al.*, 2003), including two of the largest studies conducted in patients with AN, McDowell (*N* = 98) (McDowell *et al.*, 2003) and Bayless (*N* = 59) (Bayless *et al.*, 2002). Those studies found an average WAIS IQ of 98.2 (*SD* 12.1) (McDowell *et al.*, 2003) and 103.6 (*SD* 12.1) (Bayless *et al.*, 2002).

However, the results indicated a significant difference between VIQ and PIQ scores and between the VCI and POI, demonstrating an intelligence profile that is less even in the AN group than the HC group. Similar findings with an uneven intelligence profile, with lower performance in the PIQ than in the VIQ, have also been found in several other studies conducted with the WAIS and/or WISC (Bayless *et al.*, 2002; Connan *et al.*, 2006; McCormick *et al.*, 2008; Small, Teagno, Madero, Gross & Ebert, 1982). Likewise, results showed a significant group difference in the POI, with lower performance in the AN group compared with the HC group. Fluid intelligence (*Gf*) (Cattell, 1971) is a central component of POI (Kaplan & Saccuzzo, 2005). *Gf* includes non-verbal fluid reasoning skills, consisting of mental operations used to organize thoughts and examine novel problems. *Gf* allows one to work in complex situations, as well as the capacity to think logically and analyse and solve problems in new situations without the use of previously acquired knowledge (Cattell, 1971). An impaired ability to manage complex situations corresponds well with deficits described in patients with AN, such as inhibitions in central coherence and decreased set-shifting ability; both of which are cognitive functions related to abstract and flexible thinking. Thus, inefficiency in *Gf* may explain some of the cognitive impairments found in the AN group.

On the basis of the findings of studies on set-shifting abilities conducted among adults with AN, one would expect to find similar insufficiencies among children and adults with AN. Thus, one of the hypotheses of the study was that children and adolescents with AN would demonstrate set-shifting deficits relative to the HC group. No significant difference in set-shifting ability was found in children and adolescents with AN and HCs in this study. This finding is consistent with the conclusions in the recent meta-analysis of set-shifting ability in children and adolescents with AN by Lang *et al.* (2014a) mentioned earlier. This meta-analysis concluded that the inefficiencies apparent in the adult AN literature do not appear to be as pronounced in children (Lang *et al.*, 2014a).

Between group differences of visuoconstruction were identified in the RCFT copy test, in which the AN group performed significantly better than HCs. The AN group performed non-significantly slower than the HC group, which may suggest a more perfectionistic and detail-oriented approach. This finding is consistent with that of similar studies of patients with AN (Andres-Perpina *et al.*, 2011; Rose *et al.*, 2013) where increased time spent on visuoconstruction of the task has been found along with a more detailed approach to the design.

A highly significant between-group difference was found for short-term verbal memory, as was a trend level difference in long-term verbal memory. The HC group performed significantly better than the AN group on the TOMAL-2 Memory for Stories, demonstrating impaired verbal memory in the AN group. The Memory for Stories subscale only measures the number of remembered items and does not reflect the organization of the items recalled. As such, results from the memory tests suggested that it is most likely verbal inculcation or encoding and not verbal long-term memory that is impaired in the AN group. Results of a systematic review of verbal memory in patients with AN found conflicting results (Lao-Kaim *et al.*, 2014). Only a limited number of studies have been conducted on verbal memory. Lao-Kaim

et al. (2014) identified a total of 17 studies. These were conducted among both adolescent and adult patients with AN. In regard to short-term verbal memory, only one study found that patients with AN performed better than a healthy control group (Hatch *et al.*, 2010a), whereas seven found no difference between the two groups (Lao-Kaim *et al.*, 2014). In three studies by Castro-Fornieles *et al.* (2009), Green *et al.* (1996) and Kingston *et al.* (1996), patients with AN performed worse than healthy control subjects, which is in accordance with the insufficiencies in short-term verbal memory observed in the current study.

Deficits in motor speed were demonstrated by significant performance differences between the AN group and the HC group on the RTI motor subtest of CANTAB. This finding corresponds with a previous study in which patients with AN performed more poorly than HCs on sensory-motor speed tasks (Hatch *et al.*, 2010a). However, because there was no difference in vigilance, it could be suggested that it is actually motor speed that is impaired in the AN group. The highly significant correlation in the AN group but not HCs between POI and both Memory for Stories and RTI indicates that the inefficiencies in verbal memory and motor speed are not independent measures of cognitive dysfunction but possibly related to POI.

The results of this study suggest that FSIQ among children and adolescents with AN is close to the normal population mean. Individuals with AN perform significantly worse in nonverbal intelligence tasks, verbal memory and motor speed tasks compared with HC participants and show greater difference between their verbal and nonverbal intelligence.

Increased knowledge regarding the cognitive profiles of children and adolescents suffering from AN could impact clinical practice. For example, nonverbal intelligence deficits should be taken into account during treatment. The organization of cognitive assessment and cognitive training of patients with AN may be guided by these findings. It cannot be determined solely from these baseline data whether the developmental course of cognitive function in patients with AN corresponds to that of HCs or to what extent the observed deficits are reversible. These are important topics for future research.

Strengths and limitations

This is the largest case-control study of cognitive function in children and adolescents with AN. The credibility of the findings is increased because of the large number of participants in the study, the comprehensive, internationally recognized, neuropsychological test battery and high observed intra-class correlation coefficients.

Although the WISC-III and the WAIS-III are standardized and predominantly similar, these are two separate tests. It may be more advantageous to use a single test covering the full age span of the participants, but such a test was not available in Danish at the time of data collection. However, in terms of between-group comparisons, this was less of a problem as matched HCs and the AN group were assessed using the same test version because of 1:1 participant matching. Another limitation was that height and weight information was not obtained in HCs, without which the between-group difference in body mass index could not be calculated.

Conclusion

At the time of writing, this study is the largest case–control study conducted in children and adolescents with AN. The study found that children and adolescents with AN had an FSIQ close to the normal range, comparable with that observed in healthy controls. Thus, this result suggests that children and adolescents with AN have a normal intelligence level close to the population mean. At the same time, patients with AN performed significantly worse on the nonverbal intelligence aspects of the intelligence tests relative to the healthy control participants. There was also evidence of impairments in verbal memory and motor speed. These deficits were correlated with the POI in patients with AN, but not in healthy controls. No evidence of impairment in set-shifting in children and adolescents with AN was found in this study.

Further research should be conducted to examine the course of cognition function over time in those with AN. It is currently unclear how cognitive functions in children and adolescents with AN are affected over time and how the major physical and psychological effects associated with AN is associated with cognitive functions. Increased knowledge regarding nonverbal intelligence insufficiencies in children and adolescents suffering from AN could have an impact on clinical practice and can be important for the organization of cognitive assessments and training in patients suffering from AN.

Disclosures

The authors report no competing interests.

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