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ORIGINAL RESEARCH

The Intelligence Structures of School-Age Children with Attention Deficit Hyperactivity Disorder: A Multicenter Cross-Sectional Study in China

Lin Zhu[1,*], Feiyong Jia[2,*], Aihua Cao[3,*], Yan Hao[4], Fei Li[5], Ruizhuo Liu[6], Honghua Li[2], Xiaoxiao Yu[3], Jinzhu Zhao[4], Feng Li[5], Yu Zhang[1], Yang Yu[1], Hua Wei[1], Ying Dai[1], Xuan Zhang[1], Xiao Liu[1], Bin Peng[7], Tingyu Li[1], Li Chen[1]

[1]Growth, Development and Mental Health Center of Children and Adolescents, Children's Hospital of Chongqing Medical University, Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders, Chongqing Key Laboratory of Child Neurodevelopment and Cognitive Disorders, Chongqing, 400014, People's Republic of China; [2]Department of Developmental and Behavioral Pediatric, the First Hospital of Jilin University, Changchun, 130021, People's Republic of China; [3]Department of Pediatrics, Qilu Hospital of Shandong University, Jinan, 250012, People's Republic of China; [4]Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, People's Republic of China; [5]Developmental and Behavioral Pediatric Department, Brain and Behavioral Research Unit of Shanghai Institute for Pediatric Research and Ministry of Education-Shanghai Key Laboratory for Children's Environmental Health, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, 200092, People's Republic of China; [6]The Second Affiliated Hospital of Chengdu, Chengdu, 610017, People's Republic of China; [7]College of Public Health, Chongqing Medical University, Chongqing, 401331, People's Republic of China

*These authors contributed equally to this work

Correspondence: Li Chen, Growth, Development and Mental Health Center of Children and Adolescents, Children's Hospital of Chongqing Medical University, Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders, Chongqing Key Laboratory of Child Neurodevelopment and Cognitive Disorders, No. 136, Zhongshan 2nd Road, Yuzhong District, Chongqing, 400014, People's Republic of China, Email chenli@cqmu.edu.cn

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Purpose: There is no consensus on whether cognitive measures among attention deficit hyperactivity disorder (ADHD) subtypes exhibit more similarities or differences, and most of them have been conducted on English-speaking subjects, lacking cross-cultural perspectives. The present study was aimed at investigating the intelligence structures of school-age children with ADHD who speak Chinese, using a multicenter and large sample size approach, offering some references for clinicians.

Patients and Methods: 772 children aged 6 to 12 years with ADHD took part in the cross-sectional study. All participants underwent the Chinese Wechsler Intelligence Scale for Children-Third Edition assessment. Statistical Package for the Social Sciences (SPSS) Statistics 24 was used for statistical analyses.

Results: No significant differences were found in full intelligence quotient (FIQ), verbal IQ (VIQ), performance quotient (PIQ), as well as most subtest scores among ADHD subtypes. The analysis of variance showed that the boys' scores were higher than girls' scores in PIQ ($P < 0.05$), information ($P < 0.01$), vocabulary ($P < 0.05$) and block design ($P<0.01$) from the perspective of sex, but lower in the coding ($P < 0.01$). From the perspective of age, the senior group (aged 9–12) scored higher in block design ($P < 0.01$) and object assembly ($P < 0.05$) than the junior one (aged 6–8), but lower in VIQ ($P < 0.05$) and verbal comprehension (VC) factor.

Conclusion: Our study supported that ADHD substyles shared more similarities in intelligence structures. Boys outperformed girls in PIQ and some subtests, suggesting that the importance to consider the gender differences and the distribution of intellectual strengths and weaknesses. Older children outperformed in block design and object assembly, but underperformed in VIQ and VC factor. This indicated the need to focus on language development and screen for specific learning disabilities in managing school-age children with ADHD.

Keywords: school-age children, ADHD, intelligence structures, intellectual strengths and weaknesses, language development

Introduction

Attention deficit hyperactivity disorder (ADHD) refers to a common chronic neurodevelopmental disorder starting in childhood and continuing into adulthood. It is mainly characterized by attention deficit and/or hyperactivity impulsivity, which are

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not consistent with the developmental level of children.[1] The prevalence of ADHD is estimated at 7.2% among children worldwide and 6.26% observed among children in China.[2,3] Approximately 65% of children with ADHD have one or more comorbidities.[1] It is evident that ADHD features high prevalence, frequent comorbidities, chronic nature and the complexity of diagnosis and treatment, which underscores the importance of standardizing and ensuring uniformity in the early recognition and diagnostic processes of ADHD. In view of this, the Chinese expert consensus dictates that the first physician should not only select the assessment tools for symptoms, comorbidities and functional impairments in clinical practice based on children's specific circumstances but also incorporate a cognitive assessment into his evaluation.[1] The Wechsler Intelligence Scale for Children (WISC) is indeed considered to be the gold standard for assessing intellectual functioning.[4] Clinically, it serves as an important tool for assessing cognitive function in children with ADHD. It can not only assess the intelligence strength and weakness of children with ADHD, but also determine whether their cognitive function align with their developmental level,[2,5,6] assisting in differential diagnosis to some extent.

ADHD features a continuous pattern of inattention and/or hyperactivity impulsivity that greatly interferes with the functioning or development of individuals. The combination and number of these symptoms can result in three types of presentation:ADHD-predominantly inattentive (ADHD-I), ADHD-predominantly hyperactive-impulsive (ADHD-HI) and ADHD-combined (ADHD-C).[7] Several researches investigated the performance of various cognitive measures between ADHD subtypes. Some of the researches indicated that different subtypes of ADHD showed more similar than different,[8–11] while other studies indicated the opposite results. Fabio et al suggested that the full intelligence quotient (FIQ) scores in ADHD-I and ADHD-C groups were generally lower than those in the norm group, and ADHD-H presented generally high WISC-III scores.[12] Pinchen Yang et al revealed children with ADHD-I had a greater weakness in processing speed performance of the WISC-IV-Chinese.[13] Parviz Molavi et al found a quantitative differentiation of cognitive abilities among ADHD subtypes with "working memory" as the most compromised cognitive domain. ADHD-I had the poorest cognitive profile while ADHD-H scored highest in all cognitive domains of the WISC-IV.[14] However, there is a consensus that FIQ level of children with ADHD is generally lower than that of typically developing children.[4,15–17] A number of these studies had been performed on English-speaking subjects. Nevertheless, intelligence cannot fully or even meaningfully be understood outside its cultural context.[18] Therefore, it is of particular importance to analyze the presence of such profiles in children whose mother language is not English, in order to understand which intelligence traits of theirs may be universal and culturally specific.[4] Therefore, the present study was aimed at further investigating the intelligence features of school-age children with ADHD, who were Chinese speakers, from the perspective of different subtypes, sexes and ages based on a multicenter and large sample size. The purpose was to better understand the distribution of intelligence structures in school-age children with ADHD and provide some references for clinicians.

Materials and Methods

Participants

772 children aged 6 to 12 years with ADHD were enrolled from the outpatient clinics across five cities in China between March and September 2021. Details on participating centers and the process of subject enrollment are illustrated in Figure 1. The recruitment for this study was conducted at the height of COVID-19 pandemic restrictions. The actual recruitment process took longer than originally planned. To improve efficiency, we had established a dedicated online database for data entry and trained the full-time staff at the sub-centers before officially starting the data entry process. Quality control at the sub-centers was conducted online, with random selection and the original records mailed to us for review.

Inclusion Criteria

The Diagnose of ADHD was made following the criteria of Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) and clinical interview at the first visit by at least two developmental behavioral specialists or psychologists. All children underwent the Chinese Wechsler Intelligence Scale for Children-Third Edition assessment, and their parents completed the Vanderbilt ADHD Parent Diagnostic Scales, and teachers who had contact with the children for more than half a year (usually the homeroom teacher) filled out the Vanderbilt ADHD Teacher Diagnostic

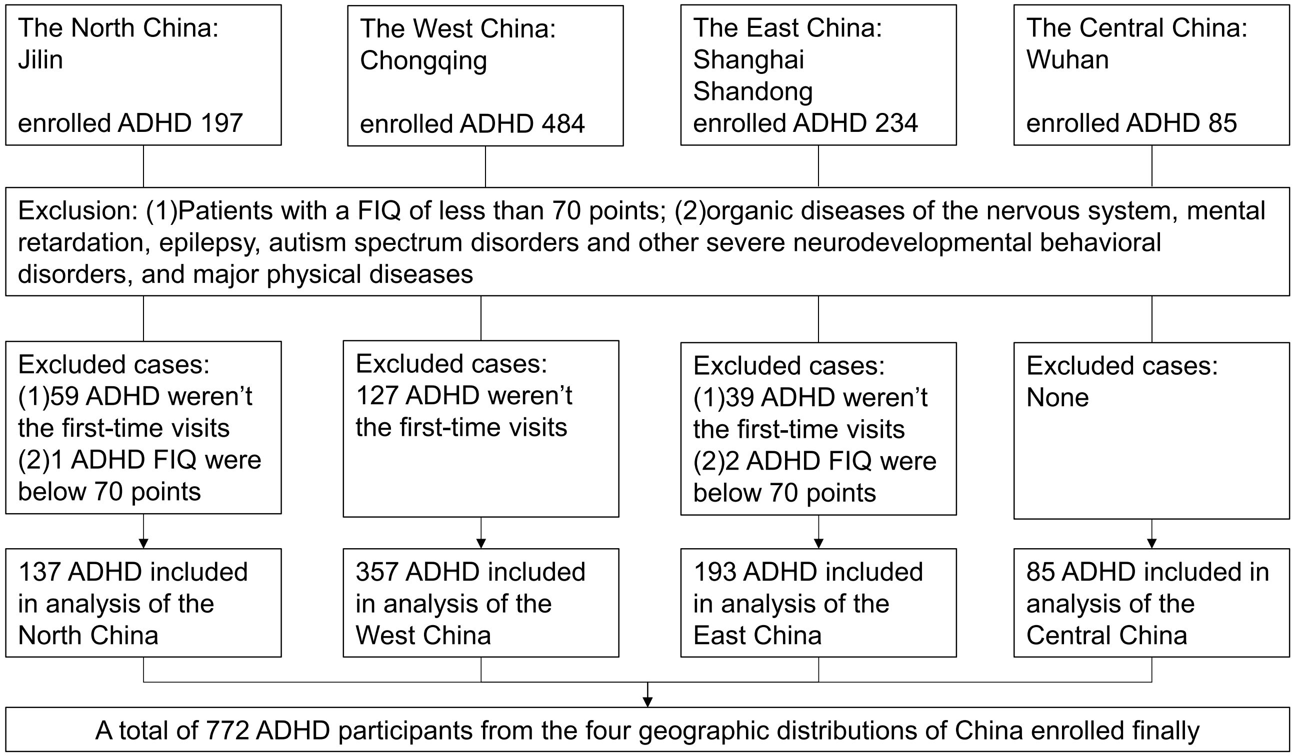

Figure 1 Flowchart of the participant recruitment process in this multi-center study in China.

Scales. All assessments are conducted by professional evaluators. All the primary guardians of children voluntarily participated and signed a written informed consent form.

Exclusion Criteria

Excluding participants with a total intelligence quotient score below 70 or intellectual disability organic neurological disorders, epilepsy, autism spectrum disorders, and other severe neurodevelopmental disorders, as well as those with significant physical illnesses.

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Neuropsychological Assessment

Vanderbilt ADHD Parent/Teacher Diagnostic Scales

These scales were used for assessing the core symptoms, comorbidities and functional impairments of ADHD. Professor Mark, developer of these scales, conducted psychometric analyses in 1998 and 2003, confirming their good reliability and validity.[19,20] The scales have been authorized for use in China by him.

Test of Intelligence Level

The Chinese Wechsler Intelligence Scale for Children-Third Edition (C-WISC-III) was utilized for assessing intelligence levels. The assessment tool is suitable for school-age children between 6 and 16 years old and has good reliability and validity in the Chinese context.[21] The results included three composite IQ sores (FIQ, verbal IQ (VIQ) and performance IQ (PIQ) with M = 100 and standard deviation (SD) = 15), and 11 subtests (information, arithmetic, similarities, vocabulary, comprehension, coding, digit span, picture completion, block design, picture arrangement and object assembly with M = 10 and SD = 3). The initial scores of the whole scale and subscales were transformed into standard scores in light of the norm. IQ ≥ 130, ≥ 120, 110–119, 90–109, 80–89, 70–79 and < 70 were classified as extremely extraordinary intelligence, extraordinary intelligence, high normal intelligence, normal intelligence, low normal intelligence, borderline intelligence and low intelligence, respectively.

Statistical Analyses

Statistical Package for the Social Sciences (SPSS) Statistics 24 of International Business Machines Corporation (IBM) was used to perform statistical analyses. The mean ± SD was adopted to measure the measurement data of normal distribution. Count data were represented by the number of cases and rate (%), and Spearman was used for correlation analysis. Chi-square analysis and analysis of variance were conducted on differences among three groups. ADHD and normative groups were compared using the abstract independent *T*-test. A one-way analysis of variance was used for analyzing the IQ characteristics of the three subtypes. A multivariate analysis of variance was used, with sex and age as independent variables and FIQ, VIQ, PIQ and subtest scores as dependent variables. Participants at the age of 6–12 were recruited. Therefore, the age interval was classified into 6–8 and 9–12. In the current study, the interaction between the two independent variables of sex and age was not significant. Thus, a further multivariate analysis of variance was performed using the selected model, and $P < 0.05$ was considered to show statistical significance.

Results

General Information

The characteristics of participants are shown in Table 1, including 643 boys and 129 girls (a male-to-female ratio of 4.98:1) with an age range of 6–12 years old. No statistically significant difference was observed in sex among the three subtypes ($P > 0.05$), and only ADHD-I and ADHD-Cexhibited statistical differences in age ($P < 0.01$).

Distribution of FIQ in School-Age Children with ADHD

School-age children with ADHD showed fluctuations between 70 and 139 points in FIQ, among whom 51.7%, 12% and 36.3% were in the normal level, the high normal level and above, and the low normal level and below, respectively (see Table 2). The distribution of FIQ at different levels of the three subtypes was not statistically significant ($\chi2 = 10.69$, $P > 0.05$).

IQ of Different Subtypes of ADHD and Normative Samples

As shown in Table 3, the FIQ, VIQ and PIQ scores of the total sample were significantly lower than the average FIQ ($t = -8.060$, $P < 0.01$), VIQ ($t = 8.327$, $P < 0.01$) andPIQ ($t = 5.524$, $P < 0.01$) scores of the normal sample group. In the subtests, the scores of children with ADHD in information, vocabulary, arithmetic, coding, digit span, picture completion and picture arrangement were significantly lower than the average of the normal pattern group (see Table 3 for each t and P value). The scores of children with ADHD in block design and object assembly were slightly higher than the average of the normal

Table 1 Participant Characteristics

	ADHD-I n=357	ADHD-HI n=76	ADHD-C n=339	ADHD n=772
Sex, n(%)				
Male	289(81.0%)	65(85.5%)	289(85.3%)	643(83.3%)
Female	68(19.0%)	11(14.5%)	50(14.7)	129(16.7%)
Age(years),mean±SD(range)	8.15±1.49	7.70±1.32	7.71±1.42	7.98±1.45

Abbreviations: ADHD-I, attention deficit hyperactivity disorder, predominantly inattentive; ADHD-HI, attention deficit hyperactivity disorder, predominantly hyperactive-impulsive; ADHD-C, attention deficit hyperactivity disorder-combined; SD, standard deviation.

Table 2 Distribution of FIQ in Different Subtypes of ADHD (Case, Rate)

Level of FIQ	ADHD-I	ADHD-HI	ADHD-C	Total
Extremely extraordinary level	3(0.8)	0(0.0)	4(1.2)	7(0.9)
Extraordinary level	8(2.3)	5(6.6)	8(2.4)	21(2.7)
High normal level	24(6.7)	9(11.8)	32(9.4)	65(8.4)
Normal level	185(51.8)	35(46.1)	179(52.8)	399(51.7)
Low normal	94(26.3)	16(21.0)	80(23.6)	190(24.6)
Borderline level	43(12.1)	11(14.5)	36(10.6)	90(11.7)

Abbreviations: FIQ, full scale intelligence quotient; ADHD-I, attention deficit hyperactivity disorder, predominantly inattentive; ADHD-HI, attention deficit hyperactivity disorder, predominantly hyperactive-impulsive; ADHD-C, attention deficit hyperactivity disorder-combined.

Table 3 C-WISC Test Results in Children with ADHD and Normative Sample (mean±SD)

	ADHD-I	ADHD-HI	ADHD-C	F	P	Total	Normative	T	P
Subtests									
Information	8.18±3.04	8.87±3.53	8.63±2.86	2.45	0.09	8.60±3.02	10±3	−9.14	0.00
Similarities	10.27±2.79	9.99±3.19	10.04±3.12	0.36	0.70	10.15±3.00	10±3	0.98	0.33
Arithmetic	9.15±3.53	9.81±3.55	8.84±3.73	2.62	0.07	9.09±3.63	10±3	−5.37	0.00
Vocabulary	8.30±2.98	8.68±3.20	8.51±2.96	1.09	0.33	8.44±3.00	10±3	−10.24	0.00
Digit Span	9.12±2.75	9.12±2.71	9.02±2.67	0.06	0.90	9.12±2.71	10±3	−6.05	0.00
Picture Completion	7.59±2.72	8.50±2.66	8.26±2.66	5.37	0.00	8.04±2.70	10±3	−13.50	0.00
Picture Arrangement	8.61±2.93	8.89±2.74	8.70±3.13	0.29	0.75	8.68±3.00	10±3	−8.65	0.00
Block Design	10.27±3.33	10.30±3.94	10.58±3.03	0.70	0.50	10.45±3.26	10±3	2.82	0.00
Object Assembly	10.97±3.26	10.74±3.46	11.14±3.29	0.69	0.50	11.04±3.29	10±3	6.50	0.00
Coding	8.99±2.98	9.36±2.65	9.23±3.14	0.73	0.49	9.14±3.02	10±3	−5.62	0.00
IQs									
VIQ	93.25±13.24	95.73±15.27	93.73±13.96	0.73	0.48	94.01±13.76	100±15	8.18	0.00
PIQ	94.65±13.78	96.38±14.05	96.60±13.53	2.08	0.13	95.92±13.72	100±15	5.58	0.00
FIQ	93.09±12.27	95.52±14.34	94.34±12.81	1.39	0.25	94.35±12.73	100±15	7.98	0.00

Abbreviations: C-WISC, the Chinese version of the Wechsler Intelligence Scale for school-age children, 3rd edition; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient; FIQ, full scale intelligence quotient; ADHD-I, attention deficit hyperactivity disorder, predominantly inattentive; ADHD-HI, attention deficit hyperactivity disorder, predominantly hyperactive-impulsive; ADHD-C, attention deficit hyperactivity disorder-combined.

sample group, and the difference was statistically significant. Only the score of children with ADHD in similarities was not significantly different from that of the constancy sample group. No significant difference was detected in FIQ, VIQ and PIQ among the three subtypes of ADHD. In the subtests, only picture completion was significantly different. In addition, Bonferroni multiple comparisons demonstrated a significant difference between ADHD-I and ADHD-C ($P < 0.01$), but no significant difference in the other two groups ($P > 0.05$).

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Intellectual Characteristics of ADHD by the Sex and Age

According to the multivariate model selection test, both sex and age showed a significant difference (both *P*<0.01). As demonstrated in Supplementary Table 1, significant differences were found in FIQ between sexes (F = 4.974, *P*<0.05). The descriptive statistical results (see Supplementary Table 2) showed that the scores of boys were higher than those of girls. Significant differences were also observed in PIQ, information, vocabulary, block design and coding between sexes (more details in Supplementary Table 1). Boys scored higher than girls in information, vocabulary, block design and PIQ, but lower in coding (see Figures 2 and 3). Significant differences were detected in VIQ, information, similarities, vocabulary, block design and object assembly between ages (more details in Supplementary Table 1). The descriptive statistical results (see Supplementary Table 3) suggested that the senior group (aged 9–12) scored higher in block design and object assembly than the junior one (aged 6–8), but lower in information, similarities, vocabulary and VIQ (see Figures 4 and 5).

Discussion

As mentioned in the introduction, there is no consensus on whether intelligence structures among ADHD subtypes exhibit more similarities or differences. Our study showed no significant differences in FIQ, VIQ, PIQ and most of the subtest scores in children with three subtypes of ADHD (see Table 3). This finding, to some extent, supported the view that there are more similarities among three subtypes. Notably, the inconsistent findings in previous studies[8–14] may be attributed to factors such as the variation in WISC versions and sample sizes. This suggests the need for future studies to

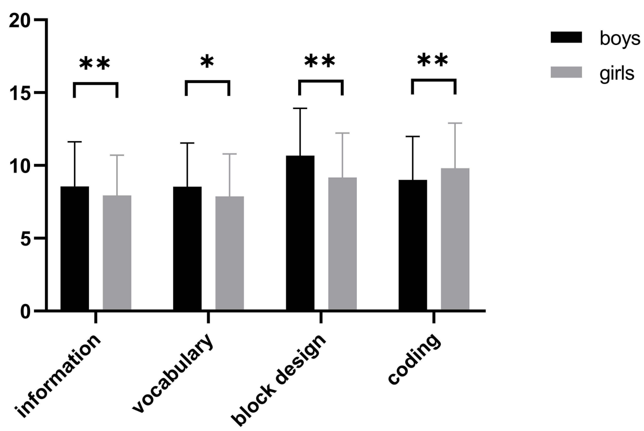

Figure 2 The mean± standard deviation of the subtest scores for different sexes (* means P<0.05, ** means P<0.01).

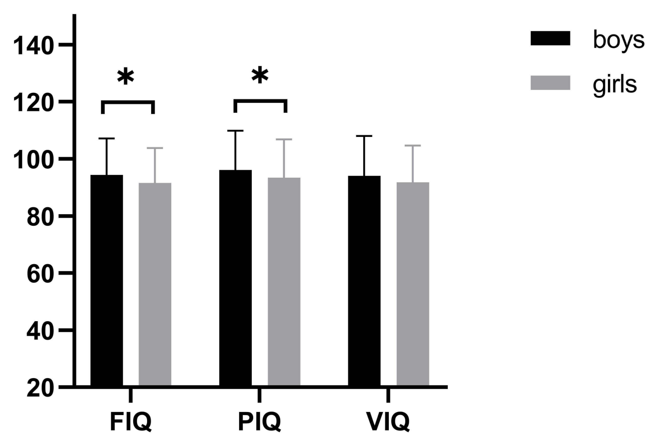

Figure 3 The mean± standard deviation of the FIQ, VIQ and PIQ for different sexes (* means P<0.05).

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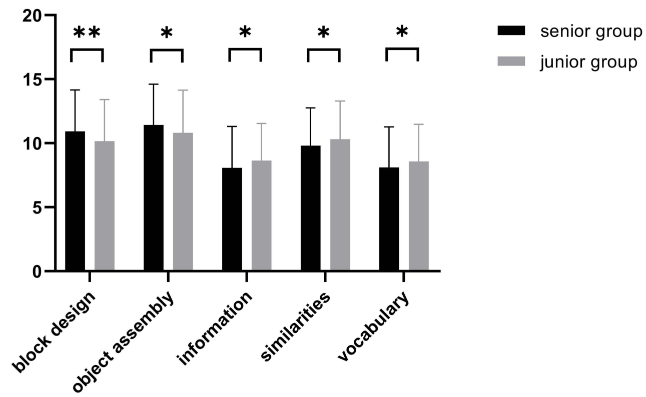

Figure 4 The mean± standard deviation of the subtest scores for different ages (* means P<0.05, ** means P<0.01).

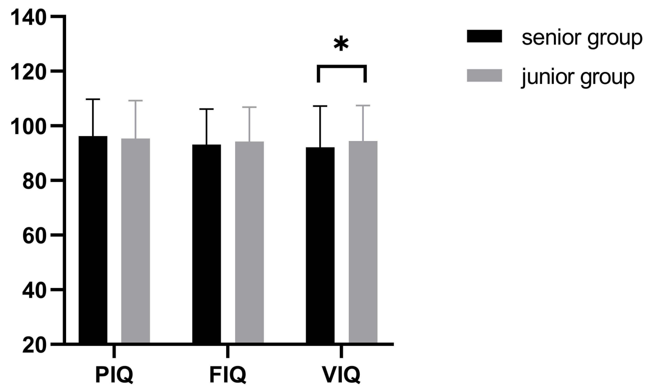

Figure 5 The mean± standard deviation of the FIQ, VIQ and PIQ for different ages (* means P<0.05).

utilize a multimodal cognitive assessment approach to more precisely delineate the cognitive domains where three subtypes exhibit similarities and differences, potentially leading to more targeted interventions and a better understanding of ADHD's heterogeneity.

Mustafa et al investigated the relationship between symptomatology and the cognitive profiles of the WISC-Fourth Edition (WISC-IV) in ADHD.[22] The WSCI-IV scores of the included subjects were compared with those of the normal sample group. It was found that most scores for subtests were lower in the subject group than in the normal sample group to a great extent, which was roughly the same as the results of our study. FIQ, VIQ and PIQ scores were significantly lower in Children with ADHD group than in the normal group for the following reasons: First, they do have lower intelligence than typical development children. Crosbie J et al showed that the FIQ scores of children with ADHD were about 7 to 12 points lower than the average FIQ scores of typical development children when they were analyzed as a group.[17] Second, the WISC is a standardized intelligence test assessing cognitive ability through a series of tasks over a fixed period, which is known as a static test. Nonetheless, children with ADHD might have difficulty demonstrating their true abilities in this testing environment due to limited self-control and impaired sustained attention. Specifically, they might be distracted by core symptoms like inattention and hyperactivity during the test, which could affect their ability to complete the test and the accuracy of the test results. Third, performance on the WISC is especially affected by executive functions because they include some subtests assessing working memory and processing speed abilities.[4] Moreover, Inhibitory control and working memory have been reported as the most consistently impaired domains in children with ADHD.[23] As a result, assessing the intelligence level of children with ADHD needs to consider the above factors influencing the test results. Dynamic measures of intelligence, which can better measure cognitive modifiability and plasticity, involve presenting subjects with new problem-solving tasks, offering gradual guidance to reveal solutions, and assessing the level of assistance needed for the learner to solve the problem.[12,24,25] Fabio et al[12] found that static and dynamic measurements together could considered a comprehensive examination of intelligence levels in children with ADHD. Therefore, clinically, a more holistic method can be adopted to evaluate the cognitive level of ADHD, like the combination of static and dynamic ways.

It has been well documented that sex differences exist in the prevalence of ADHD. More males develop ADHD in childhood.[26,27] In children and adolescents, males are more commonly diagnosed with ADHD, with a sex ratio of 2:1 to 10:1,[28–32] which was in line with the findings of our study. Significant gender differences were also found in FIQ, information, vocabulary, block design and coding. The scores of boys were higher than that of girls in the first four domains, but lower than that of girls in coding. Females may suffer more general impairments in intellectual functioning, which was mentioned in the expert consensus.[26] This might be reflected in test scores. That is, the test scores of females were mostly lower than that of males. However, it did not mean that females showed lower ability in all cognitive domains. Coding is used to measure hand-eye coordination, attention and memory. This may be because females have less pronounced and lower inattention symptoms[33] than males.[26,34] In summary, clinicians understanding the gender differences in cognitive function can help children with ADHD develop more personalized treatment plans, which is also an important reference in expert guidelines at home and abroad.[35]

The subtests of block design and object assembly belong to the perceptual organization (PO) factor in the C-WISC and are similar to the perceptual reasoning index (PRI) in the WISC-IV. Our data showed that the senior group scored higher than the junior group in block design and object assembly. The total sample also had slightly higher scores in these two subtests compared with the normative one. This indicated that the development speed of PO-related abilities could be gradually improved to close to that of normally developing children with the increase in age, which may be due to the following reasons. As opposed to the verbal comprehension index (VCI) measuring crystallized intelligence, PRI measures fluid intelligence.[36,37] One clear finding of brain research over the past decade, in both imaging research and clinical neuropsychology, has confirmed a connection between activity in the prefrontal cortex (PFC) and performance on fluid reasoning and executive function and working memory tasks.[38] Neuroimaging studies have shown that ADHD causes damage to the frontal cortex, striatum and basal ganglia of children. In particular, the function of the frontal lobe-basal ganglia circuit is abnormal.[37,39,40] Frontal lobe lesions and functional abnormalities can lead to the impairment of executive function.[41,42] Therefore, it is believed that executive function defects in children with ADHD are also related to the dysfunction of the PFC. Recent studies have shown that fluid intelligence can be enhanced by training the working memory skills of people.[43–45] Meanwhile, it has been shown that executive functioning and working memory training improve only fluid intelligence performance and have little or no impact on crystallized abilities or verbal reasoning.[38] Above all, the clinical significance of the WISC lies in not only facilitating diagnosis and differential diagnosis, as mentioned above but also drawing physicians' attention to the distribution of children's intelligence structures. Once the strengths within the intellectual framework are identified, the focus can be put on maximizing related abilities in learning and other domains, which thereby bolsters self-confidence through the accentuation of these strengths. Moreover, recognizing the weaknesses in the intellectual structure calls for a strategic adjustment of learning schedules and expectations. It is essential to explore viable methods for targeted improvement, refine learning techniques and enhance overall efficiency.

The subtests of information, similarities and vocabulary belong to the VC factor in the C-WISC and are similar to the VCI in the WISC-IV. Growing evidence shows that children with ADHD are more likely to have language difficulties compared with typically developing ones.[27] Language disorder is a common disorder of ADHD as well. Most concerning of all, the co-occurrence of language problems may exacerbate academic impairments in children with ADHD.[46] The first possible reason is the interaction between language problems and ADHD symptoms. Early attentional deficits may exert a negative influence on the reading outcomes of school-age children by compromising the acquisition of language skills, which in turn, imperils subsequent reading achievement.[47] Second, a multinational and multidisciplinary consensus study of language development problems[48] mentioned that children starting school with oral language problems were at risk of reading problems and poor academic attainment, with little evidence showing that the language gap closes over time. Third, VC measures crystallized intelligence, and executive functioning and working memory training have little or no impact on crystallized abilities or verbal reasoning, as mentioned above. All of these might explain the current findings. The scores of the senior group were still below those of the normative group with the increase of age. As a subset of reading disorder that involves difficulties with word recognition and decoding, dyslexia is highly comorbid with ADHD, with a co-occurrence rate of 25 to 40%.[49] The senior group in this study was categorized into 9–12 years old, and usually studied in the third grade or above of primary schools in China. After the third grade, learning tasks become more onerous, and higher requirements are put forward for the learning skills of children, such as reading, spelling and logical thinking skills. Given this, clinicians need to pay special attention to the language development of ADHD children, and actively screen for and identify specific learning disorders like dyslexia co-existing with ADHD in the treatment and management of such children. Through early identification and intervention, these children can be helped to better cope with academic challenges, raise learning efficiency and self-confidence, and promote overall academic and social development.

Limitations

The findings of this study should be explained in the context of some limitations. Firstly, this was a cross-sectional study that adopted a relatively limited and non-dynamic method to evaluate the intellectual structures of children with ADHD. Besides, it was impossible to dynamically follow the intellectual development of ADHD with multiple dimensions from childhood to adulthood. In the future, the multi-modal assessments of the intelligence characteristics of ADHD, including combining the WISC, executive function tests, near infrared reflectance spectroscopy, brain magnetic resonance imaging, etc. may be used to longitudinally track the cognitive function of ADHD. Secondly, children with intellectual disabilities, who were defined to have an FIQ score of below 69, and children with ADHD comorbid with other neurodevelopmental disorders were excluded from this study. Further comparisons between ADHD and ADHD comorbid disorders like specific learning disorders and autism spectrum disorder can be made in the future. Although a control group was not set up, the comparison with the normal sample of the C-WISC made up for this deficiency to some extent. Lastly, the confounding effects of other factors like parental education and socioeconomic status were not taken into consideration.

Conclusion

In summary, the present study supports that different subtypes of ADHD share more similarities in intelligence structures. From the perspective of the sex, the scores of boys with ADHD were higher than those of girls with ADHD in PIQ, information, vocabulary and block design, but lower in the coding. This indicates that clinicians should consider the gender differences and the distribution of intellectual strengths and weaknesses of children with ADHD. By capitalizing on strengths to bolster specific abilities and tailoring learning strategies to mitigate weaknesses, clinicians can provide primary caregivers with guidance and empower these children to enhance their learning capabilities and overall efficiency. From the perspective of the age, the senior group scored higher in block design and object assembly than the junior one, but lower in VIQ and VC factor. This indicates that focusing on developing children's language development and proactively screening for related comorbidities, including specific learning disabilities, are important in the management and treatment of school-age children with ADHD.

Data Sharing Statement

We are committed to share the data mentioned in this study, but since the data sources are multi-centric and include intellectual assessment results, please apply by contacting the corresponding author via Email (chenli@cqmu.edu.cn) for access, and this offer is valid indefinitely.

Ethical Approval and Informed Consent Statements

This study was conducted in accordance with the Declaration of Helsinki. Approval was granted on May 2018. The Institutional Review Board (IRB) at the Children's Hospital of Chongqing Medical University acted as the central IRB, whose review was accepted by all participating institutions' IRBs (Ref. No.79, 2018). The central IRB determined that this research involved minimal risk and approved a waiver for informed consent.

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Disclosure

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