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Network Analysis of ADHD Symptoms and Cognitive Profiles in Children

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Purpose: Although many studies have reported the cognitive profiles in attention-deficit/hyperactivity disorder (ADHD), the interactions between ADHD symptoms and the patients' cognitive profiles have not been carefully examined through the network analysis. Here, in this study, we systematically analyzed the ADHD patents' symptoms and cognitive profiles, and identified a set of interactions between ADHD symptoms and cognitive domains using the network approach.

Patients and Methods: A total of 146 children with ADHD, 6 to 15 years of age, were included in the study. All participants were assessed by the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) test. The patients' ADHD symptoms were evaluated by the Vanderbilt ADHD parent and teacher rating scales. GraphPad Prism 9.1.1 software was used for descriptive statistics and R 4.2.2 was used for network model construction.

Results: The ADHD children in our sample showed lower scores for full scale intelligence quotient (FSIQ), verbal comprehension index (VCI), processing speed index (PSI) and working memory index (WMI). Among all the ADHD core symptoms and comorbid symptoms, the academic ability, inattention symptoms and mood disorder showed direct interaction with the cognitive domains of WISC-IV. In addition, oppositional defiant of the ADHD comorbid symptoms, and perceptual reasoning of the cognitive domains exhibited the highest strength centrality in the ADHD-Cognition network based on parent ratings. Classroom behaviors of the ADHD functional impairment, and verbal comprehension of the cognitive domains exhibited the highest strength centrality in the network based on teacher ratings.

Conclusion: We highlighted the importance of considering the interactions between the ADHD symptoms and cognitive properties when designing the intervention plans for the ADHD children.

Keywords: attention-deficit/hyperactivity disorder, Wechsler Intelligence Scale for Children-Fourth Edition, network analysis

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in childhood and adolescence, affecting ~5.9% of children worldwide, ~8.4% in USA, ~2.9% in Europe and ~6.3% in China.[1–5] The main characteristics of children with ADHD are age-inappropriate attention distraction, reduced attention span, and excessive activity and emotional impulses regardless of the occasion.[6] Three presentations of ADHD were listed in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V), including predominantly inattentive (ADHD-I), predominantly hyperactive/impulsive (ADHD-H), and combined presentation (ADHD-C).[7–9]ADHD often occurs together with oppositional defiant disorder (ODD), conduct disorder (CD) and mood disorder (MD) and have extensively negative effects on the patient's academic and social life, as well as and other functioning domains such as family functioning and self-concept.

Various studies have shown that the complexity of ADHD is the result of bio-psycho-social interactions.[2,10–14] Although the cause and pathogenesis of the disease are not clear, early detection and personalized treatment can help to

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improve the educational and psychosocial prospective of children with ADHD.[12,15] The evaluation process should take a comprehensive picture of the patient's developmental, behavioral, psychiatric, and cognitive characteristics for outlining appropriate treatment later on.[16,17] Standardized ADHD questionnaires such as Vanderbilt ADHD Rating Scales (VARS) and Weiss Functional Impairment Scale-Parent Form (WFIRS-P) are important auxiliary diagnostic tools.[18] In addition, the American Academy of Child and Adolescent Psychiatry recommended intelligence tests, in order to rule out mental retardation and better understand the cognitive characteristics of children with ADHD.

Intelligence tests such as the Wechsler Intelligence Scale for Children (WISC) are widely used to assess cognitive functions in ADHD children between 6 and 16 years old.[19,20] The 4th edition of WISC (WISC-IV) consists of 10 basic subtests and 4 additional subtests. The results are summarized into a full scale intelligent quotient (FSIQ) and four index scores: verbal comprehension index (VCI), perceptual reasoning index (PRI), working memory index (WMI) and processing speed index (PSI). It has been widely used in China after national standardization in 2006.[21] WISC is considered to be the most appropriate cognitive test for ADHD children at the suitable age.

Children with ADHD tend to have significantly lower overall cognitive abilities than typically developing children, but their FSIQ is mostly in the normal range, with a small number in the borderline range.[22–25] Over the past few decades, studies focusing on the cognitive characteristics of ADHD identified WMI and PSI as the most severely impaired cognitive domains.[26,27] Some studies suggested that WMI was associated with the impulsive symptoms of ADHD while low PSI was associated with inattention.[28] But Fried et al reported that working memory deficits were not universally associated with ADHD.[29,30] Despite the pervasive nature of cognitive impairment associated with ADHD, inconsistent findings in literature could be because the heterogeneity of ADHD was often neglected.[31–33] Identifying different cognitive deficits in children with ADHD can help to tailor educational and rehabilitative intervention programs to the individual.[34] As reported by Posner et al, incorporating neurocognitive and neurobiological measurements could help enrich the psychiatry formulations in clinics. Given the complexity of ADHD presentations, it is essential to incorporate the full dimensions of ADHD core symptoms, comorbid symptoms, cognitive profiles and functional impairment when addressing the relationship between key features of ADHD. Furthermore, to identify the most influential symptom in a given ADHD patient is critical for the personalized treatment strategy.

So far, many theoretical models have been proposed to explain the cognitive performance of ADHD through statistical methods such as Pearson's correlation analysis and hierarchical agglomerative cluster analysis, but network analysis has not been used to construct a model of ADHD and cognition.[18,27,35,36] Network analysis is a statistical method that visualizes how specific symptoms interact with each other in a mental disorder.[37] According to the network model theory, symptoms are manifestations of some common underlying factors, and the relationship between symptoms will play a decisive role in the clinical presentation of a disease.[38,39] In the network model, nodes represent variables of symptoms, and links between nodes represent their interconnections. Most importantly, network analysis can identify the central node that interacts with all the other symptom nodes, thereby identifying the effective intervention targets.

In this study, we systematically examined the cognitive profiles of 146 children with ADHD in Hainan Province, south of China. The ADHD children in our study had lower scores for FSIQ, VCI, PSI and WMI when compared to China norm, but they also showed similar capability in the cognitive profile of ADHD with and without comorbid symptoms when assessed by WISC-IV. We then used network analysis to explore the links between ADHD core symptoms, comorbid symptoms, functional impairment and WISC-IV factor structures. Based on the network centrality indices, the oppositional defiant was the most important symptom, and the perceptual reasoning was the key cognitive domain influencing the ADHD children from the parent's perspective. On the other hand, the classroom behavior impairment was the most important symptom, and the verbal comprehension was the key cognitive domain for the impairment of ADHD children from a teacher's perspective. These results highlighted the importance of considering the interactions between the ADHD symptoms and cognitive properties when designing the intervention plans for the ADHD children.

Materials and Methods

Participants

A total of 146 participants aged 6 to 15 years diagnosed with ADHD between July 1, 2020 and November 31, 2022 in the outpatient clinic of Hainan Women and Children's Medical Center were included in the study. The diagnosis of ADHD was based on the DSM-V criteria. The patients went through the following procedures before they received the diagnosis: (1) a clinical interview with the child and at least one parent; (2) clinical observation of the subject's behaviors; (3) Chinese version of Vanderbilt ADHD Diagnostic Parent Ratings Scale (VADPRS), WFIRS-P and Questionnaire-Children with Difficulties (QCD) scales completed by parents; (4) Chinese version of Vanderbilt ADHD Diagnostic Teacher Ratings Scale (VADTRS) completed by teachers who were in contact with the child for at least six months; (5) WISC-IV-Chinese assessment.

Participants were excluded from this study when they met any of the following exclusion criteria: (1) history of taking stimulants or atomoxetine or any psychotropic drug; (2) history of organic mental disorder, autism spectrum disorder and global developmental delay; (3) history of seizures or head trauma; (4) intelligent quotient (IQ) score assessed by WISC-IV lower than 70. A total of 146 ADHD children were included in the analysis.[40] Since our study was a retrospectively cross-sectional study, there was not specific requirement for the sample size. However, for doing network analysis, the number of parameters to estimate grows quickly with the size of the network.[41] For instance, in a ten-node network, at least fifty-five parameters (ten threshold parameters and 10×9/2=45 pairwise association parameters) need to be estimated. The numbers of variables (nodes) in our networks based on parent and teacher ratings are ten and eleven respectively, and our sample size (parameters) is 146. Therefore, the number of samples in our study met the requirement for network analysis.

VADPRS

The VADPRS is reported by the patient's parent. It consists of 55 items, and includes assessment of ADHD symptoms, performance impairment and comorbid symptoms. The symptom assessment includes the eighteen ADHD symptoms: inattention symptoms (IS) and hyperactivity/impulsive symptoms (HIS). There are three comorbidity screening scales: ODD (eight items), CD (fourteen items) and anxiety/depression shown as MD (seven items). They are rated on a four-point scale (0 = never, 1 = occasionally, 2 = often, 3 = very often). The VADPRS includes eight items that assess functional impairment, including academic (overall academic performance, reading, writing and mathematics) and relationship (participation in organized activities and relationships with parents, siblings and peers). These items are rated on a five-point scale (1 = performance is excellent, 2 = above average, 3 = average, 4 = somewhat problematic, 5 = problematic).[16] Cronbach's alpha coefficient was more than 0.90.

VADTRS

This scale consists of 43 items and is rated by the teacher on the child's performance over the last six months. The VADTRS includes the same eighteen ADHD symptoms, and combines ten items screening for ODD and CD, and seven items for MD (anxiety or depression). A four-point response scale from never (0) to very often (3) is used. In addition, VADTRS rates eight items of functional impairment: academic (reading, mathematics and written expression) and CBI (peer relations, following directions, disrupting class, assignment completion and organizational skills). Ratings for performance range from problematic (1) to above average (5).[42] Cronbach's alpha coefficient was 0.89 ~ 0. 96.

WISC-IV

WISC-IV was developed in 2003 to test individual cognitive abilities of children aged between 6 and 16 years. The WISC-IV consists of ten core subtests and four additional subtests. In addition to the FSIQ, the results of the ten core tests were combined to form four index scores, including VCI (Similarities, Vocabulary, Comprehension, Information/ additional subtest, and Word Reasoning/additional subtest), PRI (Block Design, Picture Concepts, Matrix Reasoning, and Picture Completion/additional subtest), WMI (Digit Span, Letter-Number Sequencing, and Arithmetic/additional subtest) and PSI (Coding, Symbol Search, and Cancellation/additional subtest). WISC-IV was standardized in China since 2006, and received the appraisal by the Psychometric Professional Committee of the Chinese Psychological Society in March 2008.[20,43] The mean for all index scores is 100 and standard deviation is 15, while the mean of standard scores obtained for each subtest is 10 and standard deviation is 3.

Statistical Analysis of Data

Statistical analyses were performed using GraphPad Prism (Version 9.1.1). Kolmogorov–Smirnov/Shapiro–Wilk test was used to check the normal distribution of variables. The continuous variables were presented as mean ± standard deviation (SD), and categorical variables were presented as percentages.[35] One-sample Wilcoxon signed rank test was used to compare the WISC-IV scores of ADHD children in our study with the reliability norms of Chinese children, and dependent sample *t*-test was used to compare differences in the WISC-IV index scores of our samples. In addition, Mann–Whitney *U* test was used to assess the difference in the WISC-IV scores between the ADHD groups with and without comorbid symptoms. A *P* value of <0.05 was considered statistically significant.

Network Model Construction

Two networks of ADHD symptoms and cognitive profiles were constructed. One was based on VADPRS reported by parents (n = 146), while the other one was based on VADTRS reported by teachers (n = 136).[44] The data of VADTRS was missing in 10 patients (6.8%), and the missing data was processed by pairing deletion of both VADTRS items and the WISC-IV scores. Network models were constructed by R Version 4.2.2 (R Core Team, 2021), and operated in RStudio Version 2022.12.0+353.[45] The *glasso* function in the *qgraph* package was used to estimate a Gaussian graphical model (GGM) of the network composed by ADHD symptoms and cognitive profiles.[46,47] Least absolute shrinkage and selection operator (LASSO) regularization and the extended Bayesian information criterion (EBIC) were used to analyze the network and calculate the optimal degree of shrinkage.[48] The tuning parameter of the EBIC was set to 0.5.

As suggested by the code developer, one should use Spearman correlation for the network construction of small samples. The nodes in networks represented subscales from the VADPRS or VADTRS (higher scores indicating a poorer outcome) and four indexes of the WISC-IV (higher scores indicating better cognitive functioning). The edges represented regularized partial correlations between nodes. Blue edges indicate positive associations, and red edges indicate negative associations. The thicker the edge is, the higher the correlation.

Centrality Indices Estimation

The centralityPlot function in *qgraph* was used to calculate three centrality indices in order to quantify the features of the nodes: strength, betweenness and closeness. The strength indicates the most impactive symptom for the network overall by quantifying how well a node is directly connected to other nodes. The closeness quantifies how well a node is indirectly connected to other nodes.[45] The betweenness quantifies how important a node is in the average path between two other nodes.

Network Accuracy and Stability Estimation

The network accuracy and stability were estimated by the R package *bootnet*.[45,49] First, the accuracy of the edge was evaluated through the 95% confidence interval (CI) of the bootstrap edge weight. Narrower CIs suggested a more precise estimation of the edge. Second, the stability of the centrality was tested by case-dropping bootstrapping, and the centrality stability coefficient (CS-coefficient) was calculated.[41,49] It was suggested that CS-coefficient should be at least above 0.25, but preferably above 0.50. In the ADHD-Cognition network based on the parent ratings, the strength of CS-coefficient was 0.28. And in the ADHD-Cognition network based on the teacher ratings, the strength of CS-coefficient was 0.36. Therefore, the strength centrality in our study was acceptable.

Results

Sociodemographic Data

Among the 146 ADHD children aged between 6 and 15 years old (8.82 ± 2.03, mean ± SD), 26.7% (39) were diagnosed with ADHD-I, 5.5% (8) were ADHD-H and 67.8% (99) were ADHD-C. In addition, participants were screened for comorbid diseases by VADRS: ODD (55.5%), CD (0.7%) and MD (18.5%), and multiple comorbidities (11.6%). The total IQ of children with ADHD in the study was 94.53 ± 12.52 (mean ± SD). Majority of the participants (46.6%) had IQs in the normal range (90–109) and a small number (13.7%) showed IQs in the borderline range (70–79). The characteristics of children with ADHD in the study are presented in Table 1.

Cognitive Profiles in Children with ADHD

We first compared the WISC-IV index scores of 146 ADHD children with the average of the normative sample in China. VCI, WMI, PSI and FSIQ of children with ADHD were significantly lower than the normative sample, while PRI was significantly higher (for VCI, PSI and FSIQ, $P<0.001$; for WMI and PRI, $P<0.05$; one-sample Wilcoxon signed rank test). In addition, the VCI mean score in our sample was significantly lower than the mean scores of PRI, WMI, PSI and FSIQ ($P<0.001$, dependent *t*-test), indicating that VCI was the worst cognitive domain for ADHD children. On the contrary, the PRI mean score was significantly higher than the mean scores of VCI, PSI and FSIQ ($P<0.001$, dependent *t*-test), suggesting that the ADHD children showed strength in the cognitive domain of perceptual reasoning. When WISC-IV test scores of the ADHD children were compared with the corresponding values of the norm group, most of them were significantly lower ($P<0.001$, one-sample Wilcoxon signed rank test), except for Picture concepts, Digit span, Symbol search (Table 2), suggesting that the ADHD children had their own cognitive characteristics.

Cognitive Profiles in ADHD with and without Comorbid Symptoms

We next analyzed the WISC-IV index scores of ADHD with and without comorbid symptoms. The index scores of both groups ranged from 87 to 104, and were not significantly different between the two groups ($P>0.05$, Mann–Whitney *U* test). The lowest index score of ADHD with comorbid symptoms was VCI, similar to the ADHD children without comorbidities ($P<0.05$, Mann–Whitney *U* test). The results are presented in Figure 1.

Table 1 Demographic and Clinical Characteristics of ADHD

	Mean ± SD; N (%)
Age	8.82 ± 2.03
Sex	
• Girls	19 (13.0)
• Boys	127 (87.0)
ADHD subtype	
• ADHD-I	39 (26.7)
• ADHD-H	8 (5.5)
• ADHD-C	99 (67.8)
Comorbid symptoms	
• Without comorbidity	55 (37.7)
• Oppositional defiant disorder	81 (55.5)
• Conduct disorder	1 (0.7)
• Mood disorder	27 (18.5)
FSIQ	94.53 ± 12.52
• 129≥FSIQ≥120	5 (3.4)
• 119≥FSIQ≥110	14 (9.6)
• 109≥FSIQ≥90	68 (46.6)
• 89≥FSIQ≥80	39 (26.7)
• 79≥FSIQ≥70	20 (13.7)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ADHD-I, ADHD predominantly inattentive; ADHD-H, ADHD predominantly hyperactive/impulsive; ADHD-C, ADHD combined type; FSIQ, full scale intelligent quotient; Mood disorder includes anxiety/depression.

Table 2 WISC-IV Subtest and Index Scores in 146 Children with ADHD

Assessment	Mean (SD)	Standardized Scores (Mean)	*P* value*
Index			
Verbal comprehension	88.36 ± 13.63	100 ± 15	*P*<0.001
Perceptual reasoning	102.60 ± 13.73	100 ± 15	*P*=0.031
Working memory	97.97 ± 11.89	100 ± 15	*P*=0.038
Processing speed	95.73 ± 13.59	100 ± 15	*P*<0.001
Full scale intelligent quotient	94.53 ± 12.52	100 ± 15	*P*<0.001
Subtest			
Similarities	8.99 ± 2.94	10 ± 3	*P*<0.001
Vocabulary	6.39 ± 2.82	10 ± 3	*P*<0.001
Comprehension	8.24 ± 2.56	10 ± 3	*P*<0.001
Block design	10.94 ± 2.92	10 ± 3	*P*<0.001
Picture concepts	9.75 ± 2.73	10 ± 3	*P*=0.177
Matrix reasoning	10.68 ± 2.72	10 ± 3	*P*=0.006
Digit span	9.92 ± 2.36	10 ± 3	*P*=0.742
Letter-number sequencing	8.56 ± 2.36	10 ± 3	*P*<0.001
Coding	8.33 ± 3.09	10 ± 3	*P*<0.001
Symbol search	10.25 ± 2.69	10 ± 3	*P*=0.611

Notes: *One-sample Wilcoxon signed rank test.

Network Analysis

Model 1: ADHD-Cognition Network Based on Parent Ratings

The ADHD-Cognition network based on the parent ratings is displayed in Figure 2A. The estimated network had 27 out of 55 possible edges, with the edge weighting from −0.16 to 0.38, and an overall network density of 0.49.[41] The accuracy of edge weights stability in the network was confirmed by the narrow bootstrapped 95% confidence interval (Supplementary Figure 1). In this network, there were six edges between ADHD items and cognition items, and all of them were negative, indicating that the more severe the ADHD symptoms were, the lower the WISC-IV index scores. The four items related to the academic ability in VADPRS were significantly correlated with the WISC-IV index scores: AI-VCI (edge weight = −0.08), AI-PRI (edge weight = −0.12), AI-WMI (edge weight = −0.16), AI-PSI (edge weight = −0.07). And inattention, the core symptom of ADHD was negatively correlated with the PSI of WISC-IV (IS-PSI, edge weight = −0.10). In addition, the comorbid symptom MD was negatively correlated with the VCI of WISC-IV (MD-VCI, edge weight = −0.02). Detailed information about the network structure was in Supplementary Table 1.

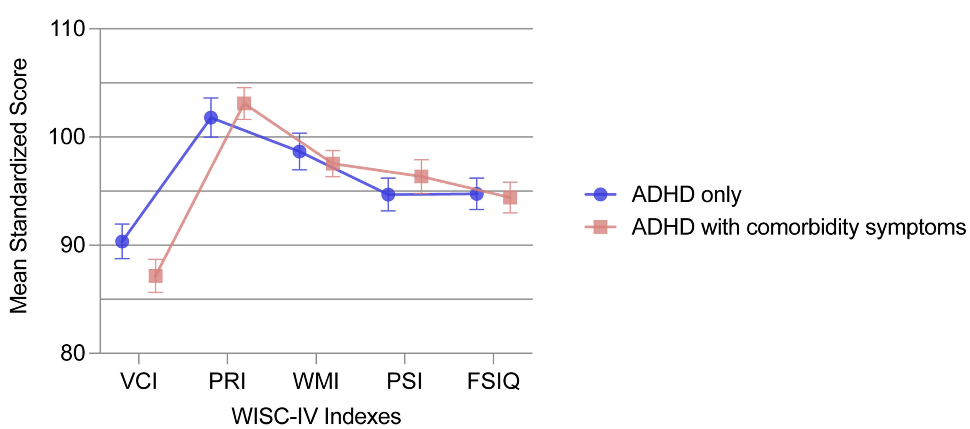

Figure 1 The cognitive profiles in ADHD with and without comorbid symptoms. Estimated mean scores of WISC-IV indexes for children with ADHD alone (n = 55) and with comorbid symptoms (n = 91). Error bars represent standard errors.

Abbreviations: WISC-IV, Wechsler intelligence scale-fourth edition; VCI, verbal comprehension index; PRI, perceptual reasoning index; WMI, working memory index; PSI, processing speed index; FSIQ, full scale intelligence quotient.

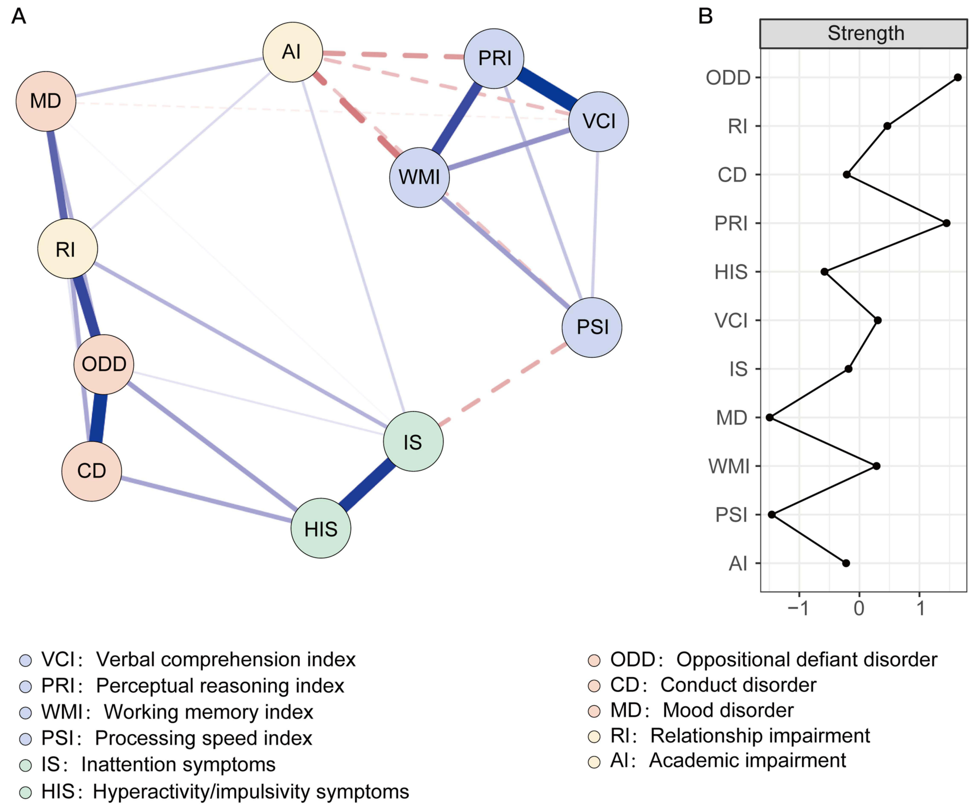

Figure 2 The ADHD-Cognition network based on the parent ratings and the corresponding strength centrality indices. (**A**) The ADHD-Cognition network based on the parent ratings of the children with ADHD. The nodes in the network represent ADHD symptoms and cognitive profiles, and the edges represent strength of association between nodes. Blue edges and red edges represent positive and negative correlations, respectively, and thicker edges represent higher correlations. (**B**) The strength centrality of each node in the ADHD-Cognition network based on the parent ratings. Nodes are depicted on the y-axis and Values shown on the x-axis are standardized z-scores. Node strength signifies to the number and strength of the direct associations of a node with other nodes in the network.

We next applied three measures of centrality, including betweenness, closeness and strength.[41] Based on the stability analyses, only strength centrality (CS-coefficient = 0.28) was interpretable for the estimated network (Supplementary Figure 2).[50] ODD (strength = 1.64) and PRI (strength = 1.45) had a higher index of centrality (Figure 2B), suggesting that they were more central in the network and more closely linked to other symptoms when compared to other nodes. Taken together, the academic impairment of ADHD children was most strongly connected to cognition, according to the parent ratings. Inattention, the core symptom of ADHD was directly related with the cognitive domain of processing speed. In addition, ADHD comorbid MD was closely related with the cognitive domain of verbal comprehension. Notably, based on the network centrality indices, the oppositional defiant was the most important symptom, and the perceptual reasoning was the key cognitive domain influencing the ADHD children from the parent's perspective.

Model 2: ADHD-Cognition Network Based on Teacher Ratings

In the ADHD-Cognition network based on the teacher ratings (Figure 3A), there were in total 45 possible edges, while only 27 edges were present in the network. The edge weight was ranging from −0.15 to 0.47, with an overall network density of 0.60. There were four negative edges between the academic impairment and WISC index scores: AI-VCI (edge weight = −0.13), AI-PRI (edge weight = −0.06), AI-WMI (edge weight = −0.08), AI-PSI (edge weight = −0.12). In addition, there were five negative edges between ADHD items and cognition indices: MD-VCI (edge weight = −0.16), MD-PRI (edge weight = −0.04), CBI-VCI (edge weight = −0.03), IS-VCI (edge weight = −0.03), IS-PSI (edge weight = −0.02), indicating that the severity of ADHD symptoms could affect the cognitive performance. Interestingly, HIS of ADHD was positively correlated with PRI (edge weight = 0.06), suggesting that the core symptoms of hyperactivity/impulsiveness might have a positive impact on the cognitive domain of perceptual reasoning. Notably, the stability of

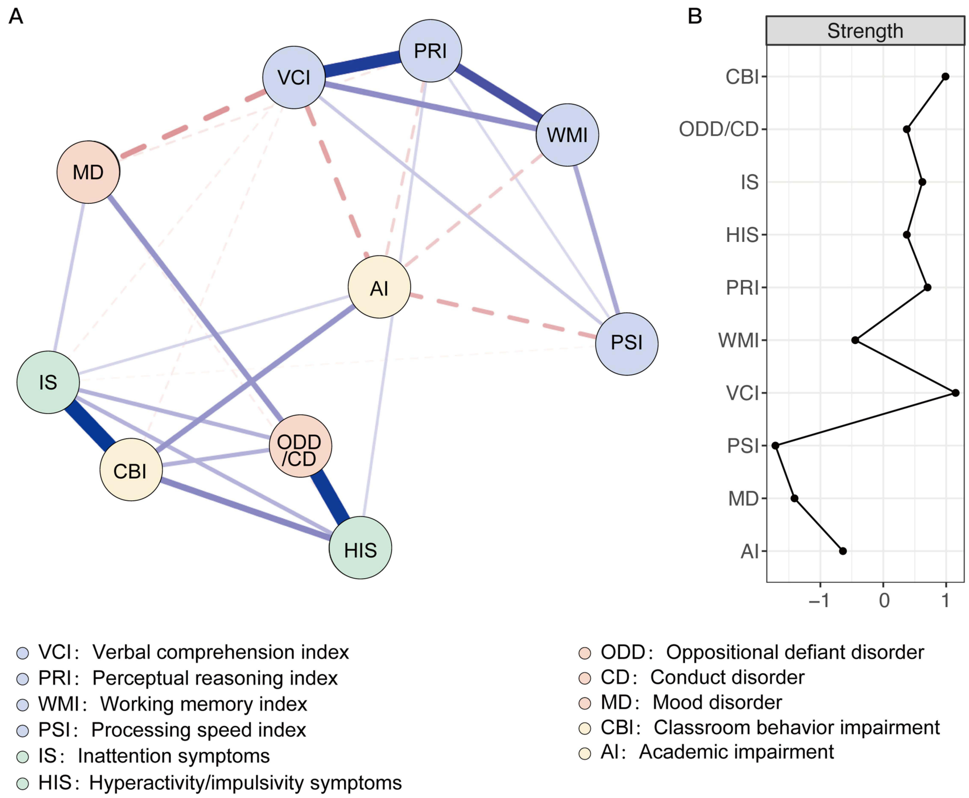

Figure 3 The ADHD-Cognition network based on the teacher ratings and the corresponding strength centrality indices. (**A**) The ADHD-Cognition network based on the teacher ratings of the children with ADHD. The nodes in the network represent ADHD symptoms and cognitive profiles, and the edges represent strength of association between nodes. Blue edges and red edges represent positive and negative correlations, respectively, and thicker edges represent higher correlations. (**B**) The strength centrality of each node in the ADHD-Cognition network based on the teacher ratings. Nodes are depicted on the y-axis and Values shown on the x-axis are standardized z-scores. Node strength signifies to the number and strength of the direct associations of a node with other nodes in the network.

edge weights in this network was acceptable, with moderate bootstrapped 95% confidence intervals (Supplemental Figure 3). More detailed information about the network structure are provided in Supplementary Table 2.

We next calculate the strength centrality and its stability (CS-coefficient = 0.36, Supplementary Figure 4). We found that VCI (Strength = 1.15) and CBI (Strength =0.98) exhibited the highest strength centrality in the network based on the teacher ratings (Figure 3B). Therefore, the classroom behavior impairment was the most important symptom, and the verbal comprehension was the key cognitive domain affecting ADHD children, from a teacher's perspective.

Discussion

In this study, we analyzed the cognitive profiles of ADHD children with WISC-IV, and found that they showed distinctive characteristics. Although the ADHD children had lower scores for FSIQ, VCI, PSI and WMI when compared to China norm, they also showed better capability in PRI. In addition, the WISC-IV index scores between ADHD with and without comorbid symptoms were not statistically significant. Interestingly, the ADHD-Cognition network based on parent and teacher ratings revealed eighteen pathways through which different ADHD symptoms and various cognitive domains could potentially interact. Importantly, the oppositional defiant was the most important symptom, and the perceptual reasoning was the key cognitive domain influencing the ADHD children from the parent's perspective. In addition, the classroom behavior was the most important symptom, and the verbal comprehension was the key cognitive domain impairment affecting ADHD children from a teacher's perspective. To our knowledge, this is the first study using network analysis to examine the ADHD symptoms and cognitive domains, and our results provide a better understanding of ADHD symptoms in order to design personalized treatment strategy.

Our data showed that ADHD children had worse performance in VCI, PSI and WMI, while VCI had the lowest WISC-IV index score in our samples. This was similar with the cognitive profiles of ADHD children in Taiwan.[51–54] However, the studies based on ADHD children in USA, Germany and Spain showed higher VCI and PRI scores than other cognitive indexes.[43] VCI were influenced by the subjects' cultural and language background, level of education, and ability to learn and absorb knowledge. The reason for the discrepancy in these studies could be related to the difference in language properties. While Chinese is uniquely based on characters and other languages such as English, German and Spanish are mostly based on alphabetical symbols system.[51,55,56] This system comes in a fixed order that is similar to every child, and the requirement of attention to perform these subtests might be different with Chinese. Therefore, the attention deficit might produce various degree of impact on to the cognitive performance.[35,53] Interestingly, we found that the PRI scores of children with ADHD were better than the Chinese norm, which was consistent with the study of Walg et al, in contrary to the study of Dinçer et al. Notably, our study and the study of Walg et al were based on boys and girls, and the study of Dinçer et al was only based on boys, suggesting the impact of gender difference onto the cognition. As opposed to VCI which measures crystallized intelligence, PRI measures the fluid. A higher score in PRI suggested that the ADHD children might possess cognitive strengths in perceptual reasoning.[57] Previous studies reported a relationship between PRI and mathematic ability in typically developing children. Thus, mathematics could be an entry point to improve the academic performance of ADHD children and thereafter increase their self-esteem. Taken together, our results provided a better understanding of the ADHD children's intellectual functioning, which may be useful to help ADHD children in schooling and academic achievement.

The clinical manifestations of ADHD are not restricted in settings. On the one hand, childhood adversity in the family can contribute to both ADHD and cognitive impairment. On the other hand, interactions between ADHD children and the school settings can affect the patient's educational achievement.[58,59] Therefore, it is necessary to observe ADHD children both in the family and at the school. Our network analysis revealed that there was a negative correlation between PSI (WISC-IV) and IS (VADRS) in both the ADHD-Cognition network based on parent and teacher ratings.[60] It indicates that the inattention symptom can affect children's performance in the processing speed, as suggested by other studies. PSI is related to writing speed and visual mental speed.[61,62] It measures the speed with which individuals execute cognitive tasks, and the cortical-striatal circuit is conceptualized as a physiologic basis for processing speed. Recent studies suggested that slower processing speed could explain much of the deficit in working memory and inhibitory control performance in ADHD children.[63–65] Moreover, PSI could provide considerably predictive value with a child's functioning in educational settings. Therefore, a lower processing speed of ADHD children should be taken into account when helping them in school.[66] For instance, the school can make reasonable time adjustments of the lectures for ADHD children.[62] In addition, processing speed training can enhance performance on untrained speeded tasks.

In our study, we identified a potential disease pathway between the comorbidity of MD and the cognitive domain of VCI in ADHD.[67] Mood disorders were a common comorbidity of ADHD, with up to 35% of children with ADHD experiencing anxiety or depression. However, the literature about the relationship between verbal comprehension and mood disorders in ADHD was limited.[68] One study reported a close association between developmental language disorders and negative emotions.[69] And another study reported that the cognitive decline in verbal reasoning was associated with emotional dysregulation in females with mild behavioral impairment. Although more studies are required to solidate our finding, our results provide valuable information for psychiatrists, psychologists, and therapists to look at ADHD patients from a more comprehensive point of view.

The network models suggested that ODD and CBI were the central nodes among the core and comorbid symptoms of ADHD, indicating that they have the greatest influence on the overall network.[70,71] Social domain impairment was a common functional impairment in ADHD and multiple regression analysis demonstrated that oppositional defiant symptoms were the most important predictor of difficulties in the interpersonal domain of functioning. Our study and others together suggested that doctors should carefully evaluate the comorbidities such as ODD in addition to the core symptoms of ADHD. Moreover, interventions for the individual with ADHD should give sufficient emphasis onto targeting the comorbidities for the best outcome of alleviating the functional impairment.

Our study has important research and clinical implications. Here, we used network analysis to portray the interaction between ADHD symptoms which were previously unexplored. Our study would provide researchers some hints for exploring the neuronal mechanisms behind ADHD symptoms.[72] Interestingly, a study using MRI demonstrated that striatal and thalamic functional connectivity was associated with the therapeutic effects of lisdexamfetamine in ADHD.[9,73,74] Moreover, the striatal and thalamic circuitry have been indicated in the habit formation and goal-directed learning which could be the neural basis for ADHD symptoms such as executive cognitive problems and working memory capacity. Thus, our work could help clinicians to view the ADHD children from a more systematic perspective. Particularly, we have highlighted the significance of treating the comorbidity, social predicaments and school difficulties of ADHD, in addition to the core symptoms.

Strengths and Limitations

It is a strength of our study that the patients included in our study had never been treated with medications such as methylphenidate and atomoxetine, which reflected the real-world situation of ADHD without pharmaceutical interventions. For each child, we analyzed the evaluations of both parent and teacher at the same time, which mitigated the effects of variability in observational perspectives. But there are still some limitations in the study. Firstly, we do not have a control group since these are field data. Secondly, our study was a single-center study and has a relatively small sample size.[40] Thirdly, we are unable to further determine the causal relationships between nodes in the network model because this is a cross-sectional study but not a longitudinal study.

Conclusion

We found both VCI, PSI and WMI index were among the weakness domains in ADHD children. PSI was associated with higher ratings of inattentive symptoms. ODD and CBI were the most influential ADHD symptoms among all the comorbid symptoms and functional impairment symptoms, while perceptual reasoning and verbal comprehension were two cognitive domains connected to other symptom nodes of ADHD children most strongly. This study provides valuable information for further understanding the importance of comorbidity and functional impairment in ADHD, as well as for designing treatment strategies.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Hainan Women and Children's Medical Center (No: HNWCMC-2022-158) and due to anonymous data selection from hospital record informed consent from the participants was not required.

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Disclosure

The authors report no conflicts of interest in this work.

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