INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric conditions of children and adolescents, which has a prevalence of 5% to 8%. Children with ADHD are more frequently to experience learning, communication, and intellectual disabilities, and display tic, oppositional defiant, and conduct disorders. As such, ADHD is related with poor academic performance as well as impaired peer relationships. Because early intervention can mitigate these functional deficits as well as the development of comorbid psychiatric conditions, early diagnosis and treatment of ADHD is crucial.

Although there are no objective diagnostic tests for ADHD, intelligence tests, including the Wechsler Intelligence Scale for Children (WISC), are widely used to evaluate the cognitive function in children with ADHD. Children with ADHD demonstrate lower intellectual ability than typically-developing children (TC). A meta-analysis showed that the average full-scale intelligent quotient (FSIQ) in children with ADHD is 7–10 points below the mean of the comparison group. In addition, FSIQ and four index scores of the WISC can indicate the severity of a variety of impairments in children with ADHD. However, these scores can reflect general cognitive deficits in other conditions, such as intellectual disabilities or borderline intellectual functioning. Thus, the diagnostic value of the WISC in ADHD remains undetermined.

The fourth edition of the WISC (WISC-IV; 2003) incorporates the expanded understanding of development and cognitive neuroscience since the publication of the WISC-III (1991). The subtests and structure of indices substantially differ from the WISC-III to WISC-IV. First, scores of performance and verbal IQ were replaced with scores of four indices: the Verbal comprehension index (VCI), the Perceptual reasoning index (PRI), the Working memory index (WMI), and the Processing speed index (PSI). Second, the subtests and structure of indices substantially differ from the WISC-III to WISC-IV.
(PRI), the Working memory index (WMI), and the Processing speed index (PSI). Although the WISC-IV retains three of the four of verbal IQ subtests from the WISC-III, the PRI has changed substantially and comprises three subtests: two visual reasoning tests with untimed, motor-free manner (Picture concepts and Matrix reasoning), as well as Block design (from the WISC-III). These changes decrease demands on motor/perceptual abilities, providing a more exclusive measure of fluid reasoning. The WMI comprises the Letter-number sequencing subtest, which more effectively measure the ability to focus the attention and maintain the concentration, and the Digit span (forward and backward) subtest. Lastly, the PSI more clearly measures speed of information processing.

Previous study identified 89% of children with ADHD from TC via assessments of Digit span, Information, Vocabulary, and Picture completion using the WISC-III. Another study used Arithmetic, Coding, Symbol search, and Digit span in ‘the Freedom from distractibility index’, in which the four lowest mean subtest scores were observed in children with ADHD. However, a study using ‘the general abilities index’ and ‘cognitive proficiency index’ in the WISC-IV showed low accuracy in discriminating between ADHD children and TC.

To better assess the diagnostic value of the WISC-IV for children with ADHD, we used the Korean version of the WISC-IV (K-WISC-IV), standardized and released in 2011, to compare Korean ADHD children with TC. We also investigated the correlation between indices and scales of the WISC-IV and the scores of the computerized continuous performance test (CPT) to investigate what elements of the WISC-IV reflect core attentional deficits of ADHD.

METHODS

Subjects

Subjects with ADHD were prospectively enrolled from September 2012 to May 2018 on the Department of Pediatric Psychiatry of Asan Medical Center, located in Seoul, South Korea. To include of the study, ADHD subjects had to be from 6 to 12 year-old age and diagnosed ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR), and the Kiddie Schedule Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL), whereas TC subjects had to be from 6 to 12 years of age and not ever meet the criteria for a diagnosis of ADHD. TC subjects were recruited by advertisements on the staff board at Asan Medical Center.

Participants were excluded from this study when they had any of the following exclusion criteria: 1) IQ score lower than 70 according to the K-WISC-IV, 2) any history of schizophrenia, organic mental disorder, and pervasive developmental disorder 3) any history of other neurological disorders including seizure, 4) presence of impairments in any sensorium, and 5) lifetime history of taking stimulants or atomoxetine more than 3 months or history of taking any psychotropic drug within the last 6 months.

The study received ethical approval from the Institutional Review Board in Asan Medical Center (2012-0767). Informed consent was obtained from the parents of all children included in the study, and assent/consent was obtained from all children.

Assessment and measures

ADHD and other psychiatric comorbidities of both ADHD and TC subjects were diagnosed by certified child and adolescent psychiatrists (H.W.K., H.J.L., and K.J.P.), and psychiatric diagnosis of these conditions were also confirmed by K-SADS-PL, one of the fifth of the K-SADS-PL scores were rated independently by three individuals to ensure consistency in evaluations. Discrepancies were resolved through consensus (kappa coefficients: 0.76 to 0.90).

The K-WISC-IV, standardized by Kwak et al., is an assessment for children and adolescents from 6 years to 16 years 11 months of age and comprises four indices (VCI, PRI, WMI, and PSI). Standardized scores for these indices were used along with FSIQ score, which were transformed from raw scores to scaled scores. The scaled scores were adjusted for age for each variable, including Similarities, Vocabulary, Comprehension, Block design, Picture concepts, Matrix reasoning, Picture completion, Digit span, Digit span forward, Digit span backward, Arithmetic, Coding, and Symbol search.

The Advanced Test of Attention (ATA) is a type of computerized continuous performance test developed and standardized in South Korea, which is used to measure attention and impulsivity. The four major variables recorded are 1) Omission errors (for inattentiveness), 2) Commission errors (for impulsivity), 3) Response time (for task performance speed), and 4) the standard deviations of the response times for correct responses (Response time variability; for the consistency of attention). In addition, the Korean version of the ADHD Rating Scale was used for assessing the severity of ADHD symptoms in children as reported by parents and teachers.

Statistical analysis

Statistical analyses were performed using R (3.5.1) with R studio (1.0.153). The normality of data was assessed by Shapiro-Wilk tests. Results from the ADHD group and TC were compared with chi-square tests, Fisher’s exact tests, Student’s t-tests, and analyses of covariance, adjusted for FSIQ and gender. Partial correlation analyses were used to determine the
relationship among the scores of WISC-IV indices and sub-tests and ATA scores, adjusted for FSIQ and gender.

RESULTS

Subject characteristics
The characteristics of children with ADHD and TC are presented in Table 1. There were no differences between the groups regarding age (p=0.104), but there were more boys in the ADHD group than in the TC group (p<0.001). The majority of children with ADHD were classified as having the inattentive and combined subtypes. Oppositional defiant disorder (p<0.001) and tic disorder (p=0.022) were significantly more frequent in the ADHD than in the TC group. The groups did not differ with regard to other comorbid psychiatric disorders.

Differences in K-WISC-IV and ATA scores between groups
The mean FSIQ was significantly lower in the ADHD than in the TC group (p<0.001) (Table 2). Thus, FSIQ and gender were controlled as covariates in analyses of covariance. Among the index scores of the K-WISC-IV, only WMI (p<0.001) score was significantly lower in the ADHD than in the TC group after adjusting for FSIQ and gender and controlling for multiple comparison. PRI (p=0.030) score was decreased compared to TC, but this difference was disappeared with multiple comparison correction. Among the subtests of these indices, only a score for Digit span (p=0.001) within the WMI were significantly lower in the ADHD group after controlling for FSIQ and gender and adjusting for multiple comparison. Similarities (p=0.043), Picture concepts (p=0.024) and Matrix reasoning (p=0.030) were decreased compared to TC, but this difference was disappeared when adjusted for multiple comparison. For the ATA, after correcting for multiple comparison, only the increase in Omission errors for the auditory task (p<0.001) in the ADHD group remained significant. Response time for the visual task (p=0.031) were also significantly higher in ADHD group than TC, but this significance was disappeared after multiple comparison corrected.

We further dissected the difference between the groups for the Digit span subtest within the WMI of the K-WISC-IV. The mean scores for Digit span forward (p=0.041) and backward (p=0.114) did not differ between the ADHD and TC groups after controlling for FSIQ and gender and correcting for multiple comparisons (Table 3).

Associations among scores of the K-WISC-IV, ATA, and ADHD rating scale
To investigate which factor of the K-WISC-IV would be affected by the attentional abilities of the ADHD group according to the ATA, we performed partial correlation analyses with adjustments for FSIQ and gender. Only WMI showed a meaningful negative correlation (|r|>0.2) with Commission errors on the auditory tasks of the ATA (r=-0.26, p<0.001) (Table 4). Various subtests of K-WISC-IV correlated significantly, but only the Arithmetic subtest (r=-0.25, p<0.001) of the WMI index showed a meaningful negative correlation (Table 5).

DISCUSSION

In our study, children with ADHD showed lower scores for the FSIQ, WMI, and Digit span subtests of the K-WISC-IV. In addition, the WMI score and Arithmetic subtest score of the WISC-IV correlated negatively with Commission errors on the auditory task of the ATA. In our previous retrospective chart review, we reported that children with ADHD showed low average scores in WMI and PSI which were clinically correlated with ATA scores and hypothesized that WISC-IV profile, especially the WMI could play an important role in diagnosing ADHD. This prospective comparison of children with ADHD and TC confirmed our hypothesis and suggest that the WISC-IV can be used to measure attention deficits in children with ADHD. Our results are consistent with several previous findings.
showing that children\textsuperscript{11,23-30} and adults\textsuperscript{31} with ADHD consistently have lower FSIQ scores, which moderately correlate not only with ADHD symptoms\textsuperscript{32-34} but also with functional outcomes.\textsuperscript{35,36} We and other researchers have found that lower FSIQ scores of WISC-III and WISC-IV in children with ADHD are attributable to deficits in PSI and WMI rather than in VCI and PRI.\textsuperscript{22,37,38} Here, we show that WMI scores are significantly lower in ADHD children when adjusting for FSIQ and gender, demonstrating that the WMI as well as FSIQ can be used as measures of ADHD. Lower WMI scores in children with ADHD are associated with decreased behavioral function.\textsuperscript{35,39} Indeed, a working memory impairment is a core neuropsychological deficit in subjects with ADHD and is proposed as an endophenotype of ADHD.\textsuperscript{40-42} Working memory deficits involve "cool" executive function, comprising motor response inhibition, sustained attention, response variability, and cognitive switching as well as working memory, and are consistently reported in clinical and cognitive neuroscience studies.

Table 2. The K-WISC-IV and ATA scores of ADHD and TC subjects

| Assessment                  | ADHD          | TC            | t or χ² | p-value | Adjusted p-value* |
|-----------------------------|---------------|---------------|---------|---------|-------------------|
| N                           | Mean (SD)     | N             | Mean (SD) |         |                   |
| FSIQ                        | 95.4 (15.0)   | 106.0 (13.6)  | 7.04    | <0.001  | -                 |
| VCI                         | 98.4 (12.9)   | 103.7 (15.0)  | 3.65    | <0.001  | 0.121             |
| Similarities                | 218 9.4 (2.0) | 152 10.6 (2.7)| 3.86    | <0.001  | 0.043             |
| Vocabulary                  | 218 10.6 (2.7)| 152 11.2 (3.2)| 1.97    | 0.05    | 0.113             |
| Comprehension               | 218 9.0 (2.6) | 152 9.9 (2.9) | 3.06    | 0.001   | 0.856             |
| PRI                         | 99.9 (16.2)   | 107.9 (15.9)  | 4.78    | <0.001  | 0.012             |
| Block design                | 218 10.5 (3.0)| 152 115. (3.1)| 3.08    | 0.008   | 0.556             |
| Picture concepts            | 176 9.4 (3.2) | 151 10.5 (3.2)| 3.22    | 0.003   | 0.024             |
| Matrix reasoning            | 217 9.8 (3.0) | 152 11.3 (2.9)| 4.75    | <0.001  | 0.030             |
| Picture completion          | 146 9.3 (2.6) | 78 10.3 (2.6) | 2.53    | <0.001  | 0.057             |
| WMI                         | 96.1 (16.5)   | 107.8 (13.6)  | 7.2     | <0.001  | <0.001            |
| Digit span                  | 218 9.5 (3.5) | 152 11.8 (2.8)| 6.65    | 0.003   | 0.001             |
| Arithmetic                  | 164 9.1 (3.1) | 120 11.1 (2.9)| 5.55    | <0.001  | 0.114             |
| PSI                         | 91.3 (14.7)   | 99.2 (14.3)   | 5.14    | <0.001  | 0.111             |
| Coding                      | 218 8.3 (3.2) | 152 9.5 (2.9) | 3.44    | <0.001  | 0.496             |
| Symbol search               | 218 8.7 (2.8) | 152 10.2 (2.9)| 5.02    | <0.001  | 0.729             |
| ATA visual                  |               |               |         |         |                   |
| Omission errors             | 29.1 (44.0)   | 13.2 (41.0)   | -3.57   | <0.001  | 0.255             |
| Commission errors           | 29.6 (38.9)   | 11.9 (24.4)   | -4.96   | <0.001  | 0.883             |
| Response time               | 7.8 (15.3)    | 6.1 (11.0)    | -1.33   | 0.64    | 0.031             |
| Response time variability   | 19.9 (27.5)   | 8.0 (25.7)    | -4.32   | <0.001  | 0.359             |
| ATA auditory                |               |               |         |         |                   |
| Omission errors             | 12.8 (24.7)   | 7.7 (22.0)    | -2.07   | <0.001  | 0.001             |
| Commission errors           | 14.7 (24.8)   | 5.6 (17.6)    | -3.93   | <0.001  | 0.080             |
| Response time               | -3.2 (12.5)   | 0.4 (8.0)     | 3.08    | 0.034   | 0.543             |
| Response time variability   | 0.04 (11.1)   | -3.2 (9.0)    | 2.93    | 0.005   | 0.149             |

Multiple comparison corrected significance level p<0.002. *adjusted for FSIQ and gender. Different number of subtests of K-WISC-IV due to children’s developmental stages. ATA: Advanced Test of Attention, K-WISC-IV: Korean–Wechsler Intelligence Scale for Children, Fourth Edition, TC: typically-developing children, FSIQ: full-scale intelligent quotient, VCI: verbal comprehension index, PRI: perceptual reasoning index, WMI: working memory index, PSI: processing speed index, TC: typically-developing children.
of children with ADHD. Working memory utilizes the inferior frontal-striatal circuit in the brain and is described as a limited-capacity system to manipulate cognitive representations from stimuli, to search for similar or same stimuli in previous experiences, and also to maintain responses. Thus, working memory deficits reflect the core attention deficit of ADHD children and, as demonstrated here, can be assessed via the WMI of the WISC-IV.

We also found that WMI scores negatively correlated with scores of Commission errors on the auditory ATA but not with Omission errors. Although both types of errors are associated with inattention, hyperactivity, and impulsivity, Commission errors is considered to measure response inhibition whereas Omission errors measure selective attention. However, the relationship between response inhibition and working memory is complex. Our results are consistent with Raiker et al.’s study which reported that working memory is associated with ADHD-related impulsivity. By contrast, Chhabildas et al. did not observe a response inhibition deficit in individuals who have the hyperactive-impulsive subtype of ADHD and suggested that inattentive symptoms, rather than hyperactivity/impulsivity symptoms, are a core neuro-psychological impairment of ADHD. Nevertheless, a meta-analysis indicated that response inhibition is one of the strongest and most consistent factors contributing to executive function in ADHD regardless of subtype. Thus, further study is needed to determine the association between working memory and response inhibition in children with ADHD.

Among the subtests included in the WMI, the score for the Digit span subtest was decreased in children with ADHD compared with TC, consistent with a previous study, but the score for the Arithmetic subtest was not. Digit span and Arithmetic subtests, along with the Coding and Symbol search subtest of the WISC-III, were used to measure working memory in a study by Fried et al. as Freedom from distractibility factor scores, which are more decreased for children with ADHD than for TC. Rosenthal et al. also reported lower Digit span scores for individuals with ADHD than for TC, but the difference was not significant after controlling for general cognitive ability. Scores for the Digit span backward, a measure of central executive system in the putative working memory model, are lower for children with ADHD than in TC, particularly in those with an inattentive type of ADHD, but this

| Table 4. Partial correlation analyses among four indexes of K-WISC-IV and ATA, adjusted for FSIQ and gender |
| Assessment | VCI | PRI | WMI | PSI |
| ATA visual | Omission errors | 0.09 | 0.02 | -0.11* | -0.02 |
| Commission errors | 0.07 | -0.65 | -0.04 | 0.02 |
| Response time | 0.10 | 0.06 | 0.03 | -0.20*** |
| Response time variability | 0.11* | -0.04 | <0.01 | -0.09 |
| ATA auditory | Omission errors | <0.001 | 0.75 | -0.12* | <0.01 |
| Commission errors | 0.17** | -0.01 | -0.26*** | 0.03 |
| Response time | -0.10 | 0.58 | 0.14** | -0.07 |
| Response time variability | 0.03 | 0.04 | -0.10 | 0.02 |

*p<0.05, **p<0.01, ***p<0.001. ATA: Advanced Test of Attention, K-WISC-IV: Korean–Wechsler Intelligence Scale for Children, Fourth Edition, VCI: verbal comprehension index, PRI: perceptual reasoning index, WMI: working memory index, PSI: processing speed index, FSIQ: full-scale intelligent quotient

| Table 5. Partial correlation analyses among 14 subtests of K-WISC-IV and ATA adjusted for FSIQ and gender |
| K-WISC-IV subtests | ATA visual | ATA auditory |
| Omission errors | Commission errors | Response time | Response time variability | Omission errors | Commission errors | Response time | Response time variability |
| Similarities | 0.04 | -0.02 | 0.12* | 0.02 | 0.05 | 0.03 | 0.02 | 0.03 |
| Vocabulary | 0.11* | 0.11* | 0.05 | 0.12* | -0.44 | 0.11* | -0.08 | 0.03 |
| Comprehension | 0.002 | 0.03 | 0.03 | 0.06 | 0.01 | 0.16** | -0.13 | 0.01 |
| Block design | 0.09 | 0.04 | 0.04 | 0.001 | 0.07 | 0.005 | -0.02 | 0.10 |
| Picture concepts | -0.02 | -0.06 | 0.08 | -0.01 | 0.01 | 0.006 | 0.06 | 0.10 |
| Matrix reasoning | -0.09 | -0.13* | -0.04 | -0.10 | 0.07 | -0.09 | 0.11* | -0.15** |
| Picture completion | 0.001 | 0.003 | -0.04 | 0.06 | -0.12 | 0.08 | -0.04 | -0.05 |
| Digit span | -0.06 | -0.02 | 0.02 | -0.02 | -0.09 | -0.14** | 0.10 | -0.07 |
| Arithmetic | -0.11 | 0.02 | 0.03 | 0.07 | -0.09 | -0.25*** | 0.08 | -0.38 |
| Coding | -0.02 | 0.07 | -0.15** | -0.04 | 0.003 | 0.004 | -0.09 | 0.06 |
| Symbol search | -0.02 | -0.06 | -0.18*** | -0.11* | 0.001 | 0.005 | -0.01 | -0.02 |

*p<0.05, **p<0.01, ***p<0.001. ADHD: attention deficit/hyperactivity disorder, ATA: Advanced Test of Attention, K-WISC-IV: Korean–Wechsler Intelligence Scale for Children, Fourth Edition, FSIQ: full-scale intelligent quotient
is not consistently reported across the subtypes of ADHD.\textsuperscript{51,55} We previously found that scores for the Digit span backward and auditory tasks of the ATA are correlated in children with ADHD.\textsuperscript{52} But this correlation was not observed in the present study using TC as a control group. In addition, another study performed in South Korea showed decreased Digit span score compared to verbal IQ index measured by K-WISC-III.\textsuperscript{57} Overall, the Digit span subtest of the WMI predicts the attention ability of children with ADHD, but more studies are needed to investigate whether Digit span forward and backward scores represent attention abilities in children with ADHD.

Several limitations should be considered when interpreting our results. First, ADHD is more prevalent in boys, and a gender difference was expected and can be a marker of a reliable and representative cohort.\textsuperscript{59} Second, this study focused mainly on the relationship between the WISC-IV and ATA; thus, the functional abilities of ADHD children were not included. Furthermore, this study was carried out in a hospital setting and thus may not generalize to other populations. Finally, the data presented here show associations and not causal relationships. Despite these limitations, there were strengths in this study. First, the number of subjects enrolled in this study were sufficient to detect an effect of tasks. Second, diagnosis of ADHD and comorbid psychiatric disorders are based on the K-SADS-PL which is a semi-structured interview conducted by experienced pediatric psychiatrist. Third, the tasks used to measure cognitive function and attention were comprehensive and could complement each other. Fourth, this was a prospective case-control study comparing ADHD children with TC. Finally, all study participants were not taking any psychotropic medication. Because stimulant is known to improve FSIQ and all indexes of WISC-IV, including only drug-naïve subject is important to assessing WISC-IV profile of ADHD. About 70% of children newly diagnosed ADHD take stimulants in South Korea, and children with ADHD who receive stimulants showed increased FSIQ and all of indexes of WISC-IV.\textsuperscript{59-62}

In summary, we investigated the demographic and cognitive characteristics of children with ADHD using the K-WISC-IV, ADHD Rating Scale, and ATA. The results of this study show that working memory is impaired in children with ADHD and can be assessed with the WMI of the WISC-IV.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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