INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder in school-age children, with a prevalence of 7.2%. However, symptom presentation is not limited to school ages. Based on a national survey in the US, 4.4% of the adult population satisfies the DSM-IV ADHD diagnostic criterion. However, the risk of overdiagnosing ADHD or excessive medication has recently become a substantial issue. Historically, the formulation of the concept of ADHD began with a case report by Sir GF Still in 1902. Still reported 43 cases with “defect of moral control associated with general impairment of intellect,” which represents the hyperactive or impulsive behavioral feature of ADHD in childhood. In 1980, attention deficit disorder (ADD) was included in the DSM-III. ADD subtypes (ADD/H with hyperactivity or ADD/WO without hyperactivity) should be added to the criteria for ADD diagnosis. In the revised text of the DSM-III (DSM-III-R), the first description of ADHD was added, and the recently updated criterion, the DSM-5, has inherited the concept of ADHD. Due to the historical process, the subtypes, such as ADHD-H (primarily hyperactive/impulsive), ADHD-I (primarily inattentive), or ADHD-C (combined), should be identified at ADHD diagnosis. For example, several studies have found more severe and internalized symptoms in children with ADHD-C than those in children with ADHD-I because children with ADHD-I have only impaired attention, whereas children with ADHD-C have impairments in both hyperactivity-im-

Comparative Analysis of the WISC between Two ADHD Subgroups

Yoichiro Kubo1,2, Tetsufumi Kanazawa1,3,4, Yasuo Kawabata1, Koyuki Tanaka1, Tatsushi Okayama1, Miho Fujita1, Atsushi Tsutsumi1, Shingo Yokota2, and Hiroshi Yoneda1

1Department of Neuropsychiatry, Osaka Medical College, Osaka, Japan
2Department of Psychiatry, Han-nan Hospital, Osaka, Japan
3Department of Psychiatry, The University of Melbourne, Melbourne, Australia
4Florey Institute, Oxidation Biology Unit, Melbourne, Australia

Objective The prevalence of attention deficit/hyperactivity disorder (ADHD) in school-age children is 7.2%, and ADHD is divided into clinical subtypes.

Methods The current study explored whether specific cognitive profiles as assessed using the Wechsler Intelligence Scale for Children (WISC)-IV could be obtained for each clinical ADHD subtype (ADHD-Inattentive type and ADHD-Combined type) and investigated the correlation between WISC scores and parental age at their children's birth or birthweight. The enrolled sample comprised 12 ADHD-I and 15 ADHD-C subjects.

Results An impaired Processing Speed Index was found in ADHD-I. The age of the father at the child's birth and birthweight positively correlated with the full scale intelligence quotient (FSIQ) score in the WISC assessment.

Conclusion Inattentiveness within the behaviors of the children with ADHD-I is partly due to the impaired processing speed, therefore effective support for ADHD will be conducted if educator decreases their speaking speed. Since biological basis of ADHD is still largely unknown, future studies using both psychological and biological methods will reveal the etiology of ADHD. These scientific assessments will provide information for more effective approaches in the care of children with ADHD.

Psychiatry Investig 2018;15(2):172-177

Key Words Neurodevelopmental disorder, Child and adolescence psychiatry, Cognitive sciences.
pulsivity and attention. Additionally, practical care is different among the subtypes. As detecting ADHD subtypes is crucial for planning medication, prognostic prediction and improving quality of life, ADHD must be evaluated not only on the basis of symptoms but also with psychological assessments, including cognitive batteries.

In the current retrospective survey, we aimed to identify different features between two ADHD subtypes (ADHD-C and ADHD-I) using the Wechsler Intelligence Scale for Children (WISC) assessment. The WISC is typically administered to children (aged 5 years and older) and adolescents (less than 17 seventeen years old) to evaluate their full scale intelligence quotient (FSIQ), which represents children’s general intellectual ability and cognitive functions. The WISC assessment consists of four factors: the Processing Speed Index (PSI), the Verbal Comprehension Index (VCI), the Perceptual Reasoning Index (PRI), and the Working Memory Index (WMI) (Figure 1).

Another aim was to reveal the relationship between parental age at the children’s birth and the subtypes or the subscale scores on the WISC. Recent reports have suggested a higher incidence rate of ADHD (13.1-fold) if the father is more than 45 years old at the child’s birth. Similarly, compared with fathers aged 25–29 years old, fathers less than 20 years old have an increased risk of having children with ADHD (1.5-fold). These inconsistent reports motivated us to determine the association between parental age at ADHD children’s birth and cognitive features in ADHD. In addition, we evaluated the relationship between birthweight and WISC scores, including the FSIQ and four subclassifications.

**METHODS**

During 2014, children meeting the DSM-IV ADHD criteria who visited Han-nan Hospital were analyzed. Han-nan Hospital is located in the west of Japan and has a pediatric psychiatric unit (maximum capacity: 25 children). Each day, an average of 15.1 outpatients visit the pediatric psychiatry hospital, and 1.1 children become new patients.

ADHD patients with a FSIQ (assessed by WISC) less than 70 were omitted from further analysis. Twenty-seven patients (22 boys and 5 girls; average age of 9.7 years) were selected for clinical record collection (Table 1). This retrospective analysis was approved by the Ethical Committee at Han-nan Hospital.

![Figure 1. The components of the four WISC-IV subscales. WISC: Wechsler Intelligence Scale for Children, FSIQ: full scale intelligence quotient.](image)

Table 1. WISC assessment of the participants (N=27)

| Subscale | ADHD-C | ADHD-I | t    |
|----------|--------|--------|------|
| FSIQ     | 96.2 ± 15.3 | 92.6 ± 10.2 | -1.1 |
| Verbal comprehension index | 96.3 ± 12.6 | 97.6 ± 10.6 | 0.5  |
| Perceptual reasoning index | 100.2 ± 19.1 | 94.3 ± 11.9 | -1.5 |
| Block design | 9.7 ± 3.8 | 8.3 ± 2.4 | -2.2* |
| Picture concepts | 10.2 ± 2.8 | 9.1 ± 3.6 | -1.5 |
| Metrics reasoning | 10.3 ± 3.6 | 8.7 ± 2.4 | -2.2* |
| Working memory index | 94.2 ± 14.1 | 92.3 ± 13.0 | -0.6 |
| Digit span | 9.1 ± 3.6 | 8.3 ± 2.4 | -2.2* |
| Letter-number sequencing | 9.1 ± 3.6 | 8.7 ± 2.4 | -2.2* |
| Processing speed index | 94.7 ± 11.6 | 92.3 ± 13.0 | -0.6 |

FSIQ: full scale intelligence quotient, SD: standard deviation

Table 2. Group comparison of WISC assessment (N=27)

| WISC-IV | ADHD-C | ADHD-I | t    |
|---------|--------|--------|------|
| FSIQ    | 99.1 ± 18.3 | 92.6 ± 10.2 | -1.1 |
| Verbal comprehension index | 95.3 ± 14.3 | 97.6 ± 10.6 | 0.5  |
| Perceptual reasoning index | 104.9 ± 22.6 | 94.3 ± 11.9 | -1.5 |
| Working memory index | 95.7 ± 15.2 | 92.3 ± 13.0 | -0.6 |
| Processing speed index | 99.3 ± 11.1 | 89.0 ± 9.7 | -2.5* |
| Coding  | 10.1 ± 2.7 | 7.8 ± 2.4 | -2.2* |
| Symbol search | 10.0 ± 3.4 | 8.3 ± 1.9 | -1.5 |

*p<0.05. WISC: Wechsler Intelligence Scale for Children, ADHD-C: attention deficit/hyperactive disorder (combined type), ADHD-I: attention deficit/hyperactive disorder (inattentive type), FSIQ: full scale intelligence quotient, SD: standard deviation
Statistical procedures included correlation analysis of the relationship between WISC results and parental age or birthweight. Unpaired t-test was used when the two assigned groups (ADHD-I and ADHD-C) were compared in terms of the results from the WISC subscales. Data were analyzed using JMP Pro® statistical software.

RESULTS

Twenty-seven patients were assigned as ADHD-I (n=12) or ADHD-C (n=15) based on the DSM-IV criterion. The average parental age at birth was 31.2 years for fathers and 28.6 years for mothers (n=26, respectively). Unpaired t-tests revealed significant differences between the two groups (ADHD-I and ADHD-C) on the PSI (t=-0.25, p<0.05) but not FSIQ. On the subscale analysis, a significant difference was found only for the Coding scale subtype (t=-2.2, p<0.05) (Table 2).

The correlation analysis comparing parental age at birth and birthweight with the FSIQ and WISC revealed that FSIQ and father’s age at birth were significantly correlated (r=0.50, p=0.0091) (Figure 2). The subscale analysis indicated that both the PRI (r=0.46, p=0.0174) and WMI (r=0.49, p=0.0116) of the WISC correlated with father’s age at the child’s birth. In addition, the birthweight of the 27 patients was significantly correlated with the FSIQ (r=0.40, p=0.0364) (Figure 3) and WMI (p=0.0149) within the subscales. Moreover, if birthweight was analyzed only, including full-term births (n=20, birth between 37 weeks and 41 weeks), the FSIQ, PRI (p<0.01), VCI, WMI, and PSI (p<0.05) were correlated (Table 3).

DISCUSSION

The purpose of the current retrospective survey was to eval-
scores in ADHD-C are consistent with a previous study.11 Thal showed faster speeds on the cognitive tasks. The higher PSI in ADHD subtypes on the WISC, whereas PSI scores were significantly higher in ADHD-C than those in ADHD-I. Processing speed represents how quickly a person can perform simple or automatic cognitive tasks; thus, children with hyperactive behavior will provide information for more appropriate involvement in their care. Treatment strategies are slightly different among ADHD subtypes. For instance, moderate to high doses of methylphenidate (Ritalin) are used for children with ADHD-C, whereas low doses are helpful for most children with ADHD-I.10

The results indicate similar FSIQ scores between the two subtypes on the WISC, whereas PSI scores were significantly higher in ADHD-C than those in ADHD-I. Processing speed represents how quickly a person can perform simple or automatic cognitive tasks; thus, children with hyperactive behavior showed faster speeds on the cognitive tasks. The higher PSI scores in ADHD-C are consistent with a previous study.11 Thaler et al.12 reported that WISC profiles in children with ADHD fit five cluster models in hierarchical cluster analysis. Within the clusters, two clusters (named Reduced PSI and Below Average WMI/PSI) indicated that low WISC-IV PSI was associated with ADHD-I. In other words, children with a lower PSI were recognized as inattentive. A similar trend in the PRI was found, although the difference was not significant. A higher PRI in ADHD-C indicates better outcomes with an educational approach that includes visualization or modeling, especially for children with ADHD-C. By contrast, the VCI is the only subscale in which the scores of ADHD-I exceed those of ADHD-C. This finding potentially suggests that ADHD-I affects verbal and auditory communication.

ADHD-associated inattentiveness is believed to be due to a deficit in the locus coeruleus-norepinephrine system (LC-NE system) because differences in P3 (synonymous name: P300, Event Related Potential) amplitudes has been frequently found in people with inattentiveness.14-16 However, concluding that inattentiveness in ADHD is directly related to altered P3 amplitudes is difficult because deficits in P3 amplitudes are observed not only in ADHD-I patients but also in boys with disinhibitory disorders, such as conduct disorder, antisocial personality disorder, alcoholism, or nicotine dependence.17 The locus coeruleus (ceruleus) is located in the pons and is involved in physiological responses to stress or damage. Through the release of norepinephrine, the LC-NE system regulates many brain functions involved in attention, memory, emotions, and behavioral flexibility.18,19 Similar findings have also been obtained with electroencephalogram (EEG) measurements. Previous research has shown that alpha wave patterns in individuals with ADHD are different from those inagematched controls.20 Furthermore, increased theta and slower alpha waves, which are associated with inefficient brain processing or disturbed awareness, have been repeatedly found in subjects with ADHD; however, this feature is not unique to ADHD.21 People with obsessive compulsive disorders, learning disorders, or some types of dementia tend to show similar EEG patterns. Inattention is one of the domains regulated by the LC-NE system; therefore, the specific etiology of inattentiveness in ADHD patients should be studied more intensively with an electrophysiological approach.

Additional studies using functional neuroimaging approaches, such as SPECT, PET and fMRI, have repeatedly detected associations between ADHD and abnormalities in the fronto-striatal circuitry, including the dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), dorsal anterior cingulate cortex (dACC), and striatum.22 Although the apparent deficit in fronto-striatal circuitry may be downstream of the initially impaired brain regions, ADHD pathology is at least related to this circuitry. Beyond the fronto-striatal model, newer approaches with Diffusion Tensor Image (DTI) of the default mode network have shown deficits in many other brain regions, such as visual networks. For in-

| Subscales in WISC test                  | Average score (N=27) | SD  | Father’s age at child’s birth | Mother’s age at child’s birth | Birthweight (N=27) | Birthweight (full-term birth N=20) |
|----------------------------------------|----------------------|-----|------------------------------|-------------------------------|--------------------|-----------------------------------|
| FSIQ                                   | 96.2 ±15.3           |     | r=0.50**                     | r=0.15                        | r=0.40*            | r=0.67**                          |
| Verbal comprehension index             | 96.3 ±12.6           |     | r=0.32                       | r=0.24                        | r=0.22             | r=0.52*                           |
| Perceptual reasoning index             | 100.2 ±19.1          | r=0.46* |                            | r=0.05                        | r=0.34             | r=0.60**                          |
| Block design                           | 9.7 ±3.8             |     | r=0.45*                      |                               |                    |                                   |
| Picture concepts                       | 10.2 ±2.8            |     | r=0.35                       |                               |                    |                                   |
| Metrics reasoning                      | 10.3 ±3.6            |     | r=0.38                       |                               |                    |                                   |
| Working memory index                   | 94.2 ±14.1           | r=0.49* |                            | r=0.33                        | r=0.46*            | r=0.56*                           |
| Digit span                             | 8.7 ±2.4             | r=0.44* |                            |                               | r=0.45*            |                                   |
| Letter-number sequencing               | 9.1 ±3.6             | r=0.29 |                            | r=0.28                        |                    |                                   |
| Processing speed index                 | 94.7 ±11.6           | r=0.34 |                            | r=0.21                        | r=0.32             | r=0.46*                           |

*p<0.05, **p<0.01. WISC: Wechsler Intelligence Scale for Children, FSIQ: full scale intelligence quotient, SD: standard deviation.
stance, a 33-year follow-up study of ADHD children detected decreased cortical thickness in the medial occipital cortex.\textsuperscript{22} Although abnormalities in the medial occipital cortex (BA18, BA19) have been repeatedly shown in earlier neuroimaging studies,\textsuperscript{23,24} sufficient attention has not been given to this region. High-resolution MRI has indicated reduced gray matter volume in the bilateral occipital cortex\textsuperscript{25} in people with ADHD (n=31) compared with healthy controls (n=31); therefore, the reduced PSI could be partly explained by impaired visual function in individuals with ADHD.

Inattentiveness in ADHD-I is characterized by a “sluggish cognitive tempo” (SCT).\textsuperscript{26-28} SCT items on the DSM-IV Field Trial for ADHD were discarded due to insufficient predictive power to distinguish ADHD subtypes\textsuperscript{29}; however, SCT has been re-evaluated because SCT is consistent with the features of sluggishness, drowsiness, spaciousness, lethargy, and hypomania in children with ADHD-I.\textsuperscript{10} Additionally, SCT refers to frequently observed conditions such as daydreaming, having difficulty staying awake in certain situations, and becoming easily bored, easily confused or more lethargic than others. A difficulty staying awake in certain situations, and becoming more frequently observed conditions such as daydreaming, have trouble concentrating or sitting still in classrooms. Therefore, future studies should expand the recruitment duration to include more psychological analysis data. Another limitation is the lack of data from ADHD-H (primarily hyperactive/impulsive). Most previous studies have focused on the difference between ADHD-C and ADHD-I because cases with pure ADHD-H phenotypes are rarely seen in school-age children.\textsuperscript{1}

Children with ADHD-C adapt more easily to education with visualized methods (e.g., graphs, figures, and behavioral modeling); children with ADHD-I have a harder time adapting because of their limited PRI. Similar results will be obtained if educators choose verbal communication, although educators should decrease their speaking speed because we found worse PSI in children with ADHD-I on the current WISC assessment. A recent meta-analysis aimed at accurately estimating the prevalence of ADHD concluded that the prevalence is 7.2% and 6.6–7.8% at 95% CI.\textsuperscript{1} ADHD prevalence varies among schools, cultures, and countries. Children with ADHD have trouble concentrating or sitting still in classrooms. Therefore, effective involvement in the care of children with ADHD is needed, and the current psychological assessment findings could be helpful for developing support for these children.

REFERENCES

1. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics 2015;135:e994-e1001.
2. Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 2006;163:716-723.
3. Bonati M, Reale L, Reducing overdiagnosis and disease mongering in ADHD in Lombardy. BMJ 2013;347:f7474.
4. Still G. Some abnormal psychical conditions in children: the Goulstonian lectures. Lancet 1902;12:58.
5. Barkley RA, DuPaul GJ, McMurray MB. Comprehensive evaluation of attention deficit disorder with and without hyperactivity as defined by research criteria. J Consult Clin Psychol 1990;58:775-789.
6. Gross-Tsur V, Goldzweig G, Landau YE, Berger I, Shmueli D, Shalev RS. The impact of sex and subtypes on cognitive and psychosocial aspects of ADHD. Dev Med Child Neurol 2006;48:901-905.
7. Solanto MV, Gilbert SN, Raj A, Zhu J, Pope-Boyd S, Stepak B, et al. Neurocognitive functioning in AD/HD, predominantly inattentive
and combined subtypes. J Abnorm Child Psychol 2007;35:729-744.
8. D’Onofrio BM, Rickert ME, Frans E, Kuja-Halkola R, Almqvist C, Sjölander A, et al. Paternal age at childbearing and offspring psychiatric and academic morbidity. JAMA Psychiatry 2014;71:432-438.
9. McGrath JJ, Petersen L, Agerbo E, Mors O, Mortensen PB, Pedersen CB. A comprehensive assessment of parental age and psychiatric disorders. JAMA Psychiatry 2014;71:301-309.
10. Diamond A. Attention-deficit disorder (attention-deficit/hyperactivity disorder) without hyperactivity: a neurobiologically and behaviorally distinct disorder from attention-deficit/hyperactivity disorder (with hyperactivity). Dev Psychopathol 2005;17:807-825.
11. Fenollar-Cortés J, Navarro-Soria I, González-Gómez C, García-Sevilla J. Cognitive Profile for Children with ADHD by Using WISC-IV: Subtype Differences. Rev Psicodidáctica 2015;20:157-176.
12. Thaler NS, Bello DT, Etcoff LM. WISC-IV profiles are associated with differences in symptomatology and outcome in children with ADHD. J Atten Disord 2013;17:291-301.
13. Sroubek A, Kelly M, Li X. Inattentiveness in attention-deficit/hyperactivity disorder. Neurosci Bull 2013;29:103-110.
14. Holcomb PJ, Ackerman PT, Dykman RA. Auditory event-related potentials in attention and reading disabled boys. Int J Psychophysiol 1986;3:263-273.
15. Howells FM, Stein DJ, Russell VA. Synergistic tonic and phasic activity of the locus coeruleus norepinephrine (LC-NE) arousal system is required for optimal attentional performance. Metab Brain Dis 2012;27:267-274.
16. Kratz O, Studer P, Malcherk S, Erbe K, Moll GH, Heinrich H. Attentional processes in children with ADHD: an event-related potential study using the attention network test. Int J Psychophysiol 2011;81:82-90.
17. Iacono WG, Carlson SR, Malone SM, McGue M. P3 event-related potential amplitude and the risk for disinhibitory disorders in adolescent boys. Arch Gen Psychiatry 2002;59:750-757.
18. Malenka RC, Nestler EJ, Hyman, SE, Sydor A, Brown RY. Molecular Neuropharmacology: A Foundation for Clinical Neuroscience. NY: McGraw-Hill Medical; 2009.
19. Benarroch EE. The locus ceruleus norepinephrine system: functional organization and potential clinical significance. Neurology 2009;73:1699-1704.
20. Nazari MA, Wallois F, Aarabi A, Berquin P. Dynamic changes in quantitative electroencephalogram during continuous performance test in children with attention-deficit/hyperactivity disorder. Int J Psychophysiol 2011;81:230-236.
21. Bush G, Valera EM, Seidman LJ. Functional neuroimaging of attention-deficit/hyperactivity disorder: a review and suggested future directions. Biol Psychiatry 2005;57:1273-1284.
22. Proal E, Reiss PT, Klein RG, Mannuzzo S, Gotimer K, Ramos-Olaza-gasti MA, et al. Brain gray matter deficits at 33-year follow-up in adults with attention-deficit/hyperactivity disorder established in childhood. Arch Gen Psychiatry 2011;68:1122-1134.
23. Dickstein SG, Bannon K, Castellanos FX, Milham MP. The neural correlates of attention deficit hyperactivity disorder: an ALE meta-analysis. J Child Psychol Psychiatry 2006;47:1051-1062.
24. Vance A, Silk TJ, Casey M, Rinehart NJ, Bradshaw J, Bellgrove MA, et al. Right parietal dysfunction in children with attention deficit hyperactivity disorder, combined type: a functional MRI study. Mol Psychiatry 2007;12:826-832, 793.
25. Ahrendts J, Rüschi N, Wilke M, Philipson A, Eickhoff SB, Glauche V, et al. Visual cortex abnormalities in adults with ADHD: a structural MRI study. World J Biol Psychiatry 2011;12:260-270.
26. Carlson CL, Mann M. Sluggish cognitive tempo predicts a different pattern of impairment in the attention deficit hyperactivity disorder, predominantly inattentive type. J Clin Child Adolesc Psychol 2002;31:123-129.
27. Carlson CL, Mann M. Attention-deficit/hyperactivity disorder, predominantly inattentive subtype. Child Adolesc Psychiatr Clin N Am 2000; 9:499-510, vi.
28. McBurnett K, Pfiffner LJ, Frick PJ. Symptom properties as a function of ADHD type: an argument for continued study of sluggish cognitive tempo. J Abnorm Child Psychol 2001;29:207-213.
29. Frick PJ, Lahey BB, Applegate B, Kerdyck L, Ollendick T, Hynd GW, et al. DSM-IV field trials for the disruptive behavior disorders: symptom utility estimates. J Am Acad Child Adolesc Psychiatry 1994;33:529-539.
30. Mueller AK, Tucha L, Koerts J, Groen Y, Lange KW, Tucha O. Sluggish cognitive tempo and its neurocognitive, social and emotive correlates: a systematic review of the current literature. J Mol Psychiatry 2014;2:5.
31. Lahey BB, Schaugency EA, Hynd GW, Carlson CL, Nieves N. Attention deficit disorder with and without hyperactivity: comparison of behavioral characteristics of clinic-referred children. J Am Acad Child Adolesc Psychiatry 1987;26:718-723.
32. Desman C, Petermann F, Hampel P. Deficit in response inhibition in children with attention deficit disorder with and without hyperactivity: comparison of symptom dimensions: neuropsychological and psychosocial correlates. J Abnorm Child Psychol 2014;42:483-503.
33. Bauermeister JJ, Barkley RA, Bauermeister JA, Martinez IV, McBurnett K. Validity of the sluggish cognitive tempo, inattention, and hyperactivity symptom dimensions: neuropsychological and psychosocial correlates. Am J Abnorm Child Psychol 2012;40:683-697.
34. D’Onofrio BM, Lichtenstein P. The Age Gauge: Older Fathers Having Children. In Cerebrum: the Dana forum on brain science. Dana Foundation, 2014, July.
35. Malaspina D, Reichenberg A, Weiser M, Fennig S, Davidson M, Harlap S, et al. Paternal age and intelligence: implications for age-related genomic changes in male germ cells. Psychiatr Genet 2005;15:117-125.