Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III): Usefulness in the Early Detection of Alzheimer's Disease

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We examined Alzheimer's disease (AD) patients using a Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition (JWAIS-III) to clarify i) the significance of expansion of the indicated age range, ii) the characteristics of cognitive impairment in AD patients and iii) the efficacy of th neuropsychological assessment for the early detection of AD using the Digit Symbol subtest, which involves attention and episodic memory, and the Pairing supplementary test, which relates to digit symbol-incidental learning. The JWAIS-III was given to 43 AD patients (12 males and 31 females; mean age, 80.9 ± 6.3 years, who fulfilled the diagnostic criteria for AD on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association. Severity of dementia of the patients was classified according to Functional Assessment Staging (F) as follows: 9 patients in F3 (borderline), 15 in F4 (mild AD), 12 in F5 (moderate AD), 7 in F6 (somewhat severe AD) and none in F7 (severe AD). i) Mean intelligence quotients (IQs) were: Full Scale IQ 84.3 ± 14.0, Verbal IQ 84.6 \pm 12.5 and Performance IQ 86.9 \pm 15.5. Comparison of IQs and subtest scores of the patients aged 75 years or older assessed by standard scores for 70 to 74 years of age, which is the upper limit of the indicated age range on the WAIS-R (the previous version of the WAIS-III), with those assessed by the standard scores for the appropriate age revealed that the former were significantly lower in IQ and all subtest scores. ii) Significant differences were noted among the severities of dementia in the scores of 7 subtests for Similarities, Comprehension, Arithmetic, Digit Span, Letter-Number Sequencing, Digit Symbol and Symbol Search. iii) When both the Digit Symbol subtest scores of 7 points or more and the Digit Sumbol-Pairing supplementary test scores exceeding 10% of the cumulative percentile were regarded as normal, 11 of 15 (73.3%) patients in F4 (mild AD) could be detected. These findings suggest that i) expansion of the indicated age range in the WAIS-III allows a more valid assessment of cognitive function in AD patients, ii) a marked decline in abstract thinking and verbal problem-solving ability and relative preservation of Perceptual organization are characteristics of cognitive impairment in AD patients and iii) a combination of the Digit Symbol subtest with the Pairing supplementary test is useful for the early detection of AD.

Key words: Alzheimer's disease; Digit Symbol; Pairing; screening test for dementia; Wechsler Adult Intelligence Scale

Currently one in every 10 persons aged 65 and over has dementia, making it a "common disease" (Urakami et al., 1998; Ishikawa and Ikeda, 2007; Wakutani et al., 2007). In addition, the initial symptoms of dementia such as mild anmesia tend to be overlooked because they are considered an inevitable consequence of aging (Urakami, 2007). Thus, the difficulty of early detection of dementia is a major problem for clinicians involved in dementia.

The Mini-Mental State Examination (MMSE) (Folstein et al., 1975) is frequently used in clinical practice for the neuropsychological assessment of intelligence in Alzheimer's disease (AD) patients. The test mainly assesses recent memory and working memory from a neuropsychological perspective in a short time. However, for a better understanding of the pathophysiology of AD (Meguro and Yamadori, 2000), we need a comprehensive assessment of intelligence including social and behavioral abilities. The most commonly used test for intelligence in clinical use is the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III) (Wechsler, 1997) published in 1997; the current Japanese version (JWAIS-III) (Fujita et al., 2006a) was published in 2006. On the JWAIS-III, some examination items were modified in accordance with Japanese culture, history, education and social background, and its validity has been confirmed, similar to the WAIS-III. On the WAIS-III the upper limit of indicated age range has been expanded from 74 years to 89 years, and new subtests were added to measure the abilities of working memory and of thinking visually and deductively which were not included on the WAIS-Revised (WAIS-R) (Wechsler, 1981; Shinagawa et al., 1990). Several

previous studies have used the WAIS-R to analyze the characteristics of intelligence in AD patients (Fuld, 1984; Utsumi et al., 1995; Nishihagi et al., 2006), but a general consensus has yet to be reached. One study did use the WAIS-III to assess the intelligence of AD patients (Teng et al., 2007), but to our knowledge there are no reports comprehensively studying the characteristics of intelligence in AD patients.

In the present study, we examined AD patients using JWAIS-III to clarify i) the significance of expansion of the indicated age range, ii) the characteristic of cognitive impairment in AD patients and iii) the efficacy of combining the Digit Symbol subtest (Digit Symbol) with the Pairing supplementary test (Pairing) as an indicator of episodic memory for the early detection of AD.

Subjects and Methods

Subjects

The subjects were 43 AD patients, 12 males and 31 females, who were outpatients in the Clinic of Neurology, Shinsei Hospital, Kurayoshi City, Japan. Their ages ranged from 56 to 93 years, with a mean of 80.9 ± 6.3 years. The patients were diagnosed as AD based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (American Psychiatric Association, 1994) and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984). Functional Assessment Staging (F), a behavioral and functional assessment scale (Reisberg et al., 1982, 1984), was

Table 1. Intelligence factors and their subtests on the JWAIS-III

	Verbal Comprehension	Working Memory	Perceptual Organization	Processing Speed
Subtest	Vocabulary	Arithmetic	Picture Completion	Digit Symbol
	Similarities	Digit Span	Block Design	Symbol Search*
	Information	Letter-Number Sequencing*	Matrix Reasoning*	
	Comprehension		Picture Arrangement	

JWAIS-III, Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition.

^{*} Newly added subtests.

used as an indicator of the severity of dementia as follows: F1, normal; F2, appropriate for age; F3, borderline; F4, mild AD; F5, moderate AD; F6, somewhat severe AD and F7, severe AD. In the present study, 9 patients were in F3, 15 in F4, 12 in F5, 7 in F6 and none in F7.

Tests administered

JWAIS-III

The Object Assembly subtest was excluded from the present analysis because this subtest has a lower reliability coefficient than all of the other subtests (Fujita et al., 2006b). Therefore, in this study a total of 13 subtests were administered, consisting of 7 subtests for the Verbal scale and 6 for the Performance scale. On the JWAIS-III, 4 intelligence factors have been used based on the results of factor analysis for standardized data (Fujita et al., 2006b). The intelligence factors and their subtests are shown in Table 1. On the WAIS-III, the upper limit of the indicated age range was expanded from 74 to 89 years in light of the increased aging of society. Three new subtests, Letter-Number Sequencing, Matrix Reasoning and Symbol Search, were added to assess cognitive functions from many angles. Furthermore, the Pairing supplementary test (Pairing) was also added to assess Digit Symbol-incidental learning, which made it possible to assess both episodic memory and sustained attention at the same time. On the Digit Span subtest (Digit Span) standard values for the numbers of digit spans recited correctly forward and backward, and for differences in the numbers of digit spans between the two have been reported, which makes it possible to assess cognitive function qualitatively.

Explanation and procedure of Digit Symbol and Pairing

Digit Symbol is a task of writing the symbols paired with each digit. Examinees write those symbols paired with each digit to blanks from indicated models. Pairing is a recall task of the symbols paired with each digit used the subtest. Imme-

diately after finished Digit Symbol, the examinees are required to write the symbols to blanks under the digits by episodic memory.

Japanese version of the Mini-Mental State Examination (JMMSE)

The JMMSE (Mori et al., 1985) was given at about the same time as the JWAIS-III. The MMSE (Folstein et al., 1975; Mori et al., 1985) is a simple intelligence test for the multifaceted assessment of cognitive functions through the administration of 11 subtests: time orientation, place orientation, immediate memory, recent memory, calculation, naming, recitation, behavior in response to verbal directions, reading comprehension, writing letters and copying patterns. A perfect score on the MMSE is 30 points and the cutoff for dementia/ non-dementia is 23/24 points.

Methods of tests administered

Taking into consideration the examinee's fatigue, the two tests were administered in 2 or 3 sessions, each of which took 1 h a day. These tests were performed within a month and no changes in clinical symptoms were noted during that period. Calculation of scaled scores for the 3 patients whose ages exceeded 89 years, the indicated age limit in WAIS-III, was done using the standard scores for subjects aged 85 to 89 years.

Ethical considerations

The purpose of this study was explained to all subjects and their families, and written consent for test participation was obtained.

Statistical analysis

SPSS Ver. 15, Windows version (SPSS, Tokyo, Japan) was used for statistical analysis. A P value less than 0.05 (P < 0.05) was considered significant, and that of 0.05 or more but less than 0.10 (0.05 $\leq P < 0.10$) was considered to have a tendency towards significance.

Table 2. IQ scores (mean \pm SD) by JWAIS-III and JMMSE scores in each severity of dementia in 43 AD patients

	Overall mean	F3 [9]	F4 [15]	F5 [12]	F6 [7]
JWAIS-III					
Full Scale IQ	84.3 ± 14.0	92.6 ± 14.5	90.9 ± 11.9	76.8 ± 8.9	72.4 ± 11.3
Verbal IQ	84.6 ± 12.5	93.0 ± 12.6	90.9 ± 9.3	76.2 ± 7.4	74.6 ± 10.6
Performance IQ	86.9 ± 15.5	93.6 ± 15.7	92.7 ± 14.8	81.9 ± 12.4	74.3 ± 12.8
JMMSE*	20.2 ± 4.6	25.2 ± 2.2	22.4 ± 2.2	17.8 ± 2.9	13.4 ± 1.7

AD, Alzheimer's disease; F, Functional assessment staging: F3, borderline; F4, mild AD; F5, moderate AD; F6, somewhat severe AD; IQ, intelligence quotient; JMMSE, Japanese version of the Mini-Mental State Examination; JWAIS-III, Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition.

Table 3. Scaled scores (mean \pm SD) on the JWAIS-III subtests for each severity of dementia in 43 AD patients

AD patients					
Subtest	Overall mean	F3 [9]	F4 [15]	F5 [12]	F6 [7]
Verbal Scale					
Vocabulary	8.0 ± 2.1	8.8 ± 2.0	8.8 ± 2.5	7.2 ± 1.4	6.9 ± 1.7
Similarities	6.5 ± 3.1	8.4 ± 2.7	7.7 ± 2.2	4.8 ± 2.6	4.0 ± 3.1
Information	7.3 ± 1.8	8.3 ± 2.7	7.4 ± 1.2	6.8 ± 1.2	6.6 ± 2.1
Comprehension	6.7 ± 2.7	7.9 ± 3.0	7.7 ± 2.9	5.8 ± 1.8	4.7 ± 1.8
Arithmetic	8.3 ± 2.8	10.0 ± 3.4	9.3 ± 2.8	6.9 ± 1.6	6.4 ± 1.1
Digit Span	8.9 ± 2.7	9.9 ± 3.9	10.3 ± 2.0	6.8 ± 1.6	8.3 ± 1.4
Letter-Number Sequencing	7.5 ± 3.2	10.7 ± 3.7	7.6 ± 2.7	7.1 ± 1.0	4.0 ± 1.9
Performance Scale					
Picture Completion	7.8 ± 3.2	9.0 ± 2.9	9.0 ± 3.2	6.2 ± 2.9	6.7 ± 2.9
Block Design	8.1 ± 2.7	9.1 ± 2.3	8.8 ± 2.3	7.5 ± 2.5	6.1 ± 3.4
Matrix Reasoning	9.0 ± 3.0	9.2 ± 2.8	9.7 ± 3.2	9.1 ± 2.7	6.7 ± 2.4
Picture Arrangement	8.3 ± 2.7	9.9 ± 2.6	9.0 ± 3.0	7.2 ± 2.3	7.0 ± 1.6
Digit Symbol	7.5 ± 2.7	8.6 ± 3.0	8.5 ± 2.4	7.2 ± 2.5	4.6 ± 1.3
Symbol Search	7.2 ± 3.0	9.1 ± 3.9	7.9 ± 2.1	6.4 ± 2.0	4.3 ± 2.8

F, Functional assessment staging: F3, borderline; F4, mild Alzheimer's disease (AD); F5, moderate AD; F6, somewhat severe AD.

Results

IQ scores by the JWAIS-III and JMMSE scores

The overall mean intelligence quotient (IQ) scores by the JWAIS-III and JMMSE scores in the 43 AD patients are shown in Table 2, as well as those for each severity of dementia. Full Scale IQ was 84.3 ± 14.0 , Verbal IQ was 84.6 ± 12.5 , and Per-

formance IQ was 86.9 ± 15.5 . The mean JMMSE score was 20.2 ± 4.6 points. A significant correlation, moderate in degree, was noted between IQs and JMMSE scores. Scores for Spearman's correlation coefficient were r = 0.690 (P < 0.01) between Full Scale IQ and JMMSE, r = 0.683 (P < 0.01) between Verbal IQ and JMMSE, r = 0.595 (P < 0.01) between Performance IQ and JMMSE. Table 3 shows scaled scores (mean \pm SD) on each subtest of the JWAIS-III.

^{[],} number of patients.

^{*} A perfect score 30, cutoff point for dementia/non-dementia 23/24.

^{[],} number of patients.

Table 4. JWAIS-III IQ scores for the 38 AD patients exceeding 75 years of age obtained by raw score-scaled score conversion tables

IQ	Conversion table for the age group 70–74 years	Conversion table for the appropriate age group*	Difference	Probability
Full Scale IQ	75.50	84.00	8.50	< 0.05
Verbal IQ	78.71	84.66	5.95	< 0.05
Performance IQ	76.08	86.18	10.10	< 0.05

AD, Alzheimer's disease; IQ, intelligence quotient; JWAIS-III, Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition.

Table 5. Scaled scores on the subtests of the JWAIS-III obtained by raw score-scaled score conversion tables

Subtest	Conversion table for the age group 70–74 years	Conversion table for the appropriate age group	Difference	Probability
Verbal Scale				
Vocabulary	7.26	8.24	0.98	< 0.05
Similarities	5.47	6.45	0.98	< 0.05
Information	6.84	7.34	0.50	< 0.05
Comprehension	5.89	6.84	0.95	< 0.05
Arithmetic	6.79	8.03	1.24	< 0.05
Digit Span	8.00	8.95	0.95	< 0.05
Letter-Number Sequencing	5.55	7.42	1.87	< 0.05
erformance Scale				
Picture Completion	5.89	7.79	1.90	< 0.05
Block Design	6.74	7.89	1.15	< 0.05
Matrix Reasoning	7.61	8.89	1.28	< 0.05
Picture Arrangement	6.32	8.16	1.84	< 0.05
Digit Symbol	5.63	7.47	1.84	< 0.05
Symbol Search	5.66	6.92	1.26	< 0.05

JWAIS-III, Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition.

IQs and scaled subtest scores obtained by the indicated age range for raw scorescaled score conversion tables

On the WAIS-R, the upper limit of the indicated age range was 74 years. Among the 38 patients aged 75 years and older in our study, we analyzed IQs and scaled scores obtained by a raw scorescaled score conversion table for patients aged 70 to 74 years and those obtained by a conversion table for the appropriate age group using *t*-tests.

Table 4 shows the mean IQ scores obtained

by scaled scores for the JWAIS-III, showing significant differences in Full Scale-, Verbal- and Performance-IQ scores. When the conversion table for patients aged 70 to 74 years was used, all IQ scores, particularly the Performance-IQ score, were low.

Table 5 shows the mean scaled scores for the subtests, showing significant differences in each subtest. When a conversion table for patients aged 70 to 74 years was used, scaled scores were low in all subtests. Relatively marked differences were noted in scores of Arithmetic and Letter-Number Sequencing on the verbal scale. These

^{*} IQs for the 3 patients exceeding 89 years of age were obtained using the standard scores of subjects for 85–89 years.

Table 6. Correlations of JWAIS-III subtest scores with severities of dementia

Subtest	Subtest Effect of severity		Multiple comparisons			
Verbal Scale						
Vocabulary	NS					
Similarities	*	F3 > F5, F3 > F6, F4 > F5, F4 > F6	(Bonferroni's procedure)	6.64		
Information	NS		_			
Comprehension	**	F3 > F6, F4 > F6	(Bonferroni's procedure)	6.19		
Arithmetic	*/**	F3 > F5, F3 > F6/F4 > F5, F4 > F6	(Bonferroni's procedure)	6.15		
Digit Span	*	F4 > F5	(Tamhane's procedure)	5.47		
Letter-Number Sequence	ing *	F3 > F6, F4 > F6, F5 > F6	(Tamhane's procedure)	6.22		
Performance Scale						
Picture Completion	NS					
Block Design	NS					
Matrix Reasoning	NS					
Picture Arrangement	*	No significant combination	(Bonferroni's procedure)	6.57		
Digit Symbol	*	F3 > F6, F4 > F6	(Bonferroni's procedure)	5.78		
Symbol Search	*	F3 > F6, F4 > F6	(Bonferroni's procedure)	7.03		

^{*}P < 0.05

are the subtests for measuring working memory. All subtests for the performance scale showed differences of more than 1 point.

Comparison of scores among subtests and among severities of dementia

One-way analysis of variance (ANOVA) revealed significant differences in scores among the subtests [F(12, 546) = 3.30]. Multiple comparisons using Tamhane's procedure revealed significant differences in scores between the Similarities subtest (Similarities) and Digit Span, Similarities and Matrix Reasoning, Comprehension and Digit Span and Comprehension and Matrix Reasoning (inter-group square sum/degrees of freedom = 7.71). Scores for Similarities and Comprehension were significantly lower than those for Digit Span and Matrix Reasoning. Differences between other subtests were not significant.

Among severities, differences in scores for each subtest were analyzed with ANOVA using the *F* scale as an inter-examinee factor. Multiple comparison analysis was also conducted with subtests where severity of dementia had a main effect which

was noted in 8 of the 13 subtests: Similarities, Comprehension, Arithmetic, Digit Span, Letter-Number Sequencing, Picture Arrangement, Digit Symbol and Symbol Search [F(3, 39) = 6.72, 3.62, 4.85, 5.70, 9.55, 2.90, 5.04 and 5.11, respectively]. In the 8 subtests, there were significant differences in scores among severities of dementia as shown in Table 6.

Correlation of Pairing with Delayed recall of 3 words

We analyzed the correlation of scores for the Pairing, a newly added supplementary test for the Digit Symbol of the WAIS-III, with those of the Delayed recall of 3 words on the JMMSE. We divided the scores for each test into "good" and "poor" according to the standard data for the Pairing (Fujita et al., 2006c): the scores showing a cumulative percentage of 11% or more were classified as "good" and those less than 11%, as "poor" (Table 7). In the Delayed recall of 3 words in the JMMSE, a correct recall of 2 or 3 words was classified as "good" and that of 1 or none, as "poor". In both tests, 8 patients were rated as good and 24 patients, poor. Five patients were good in the Pairing but poor in the Delayed recall

^{**}P < 0.10, indicating a tendency towards significance.

F, Functional Assessment Staging: F3, borderline; F4, mild Alzheimer's disease (AD); F5, moderate AD; F6, somewhat severe AD; JWAIS-III, Japanese version of the Wechsler Adult Intelligence Scale, 3rd Edition; MSe, inter-group square sum/degrees of freedom; NS, not significant.

Table 7. Classification of scores for Digit Symbol and Pairing

Digit 5	mboi and Pairing
Good	
Score:	7 points or more in the Digit Symbol subtest
Cumula	ative percentage: 11% or more in the Pairing supplementary test
Poor	
Score:	less than 7 points in the Digit Symbol subtest

Cumulative percentage: less than 11% in

the Pairing supplementary test

Table 8. Number of patients in each severity of dementia based on the scores for Digit Symbol and Pairing

Classification of scores		F4	F5	F6	Total
Good in both Digit Symbol and Pairing	6	4	0	0	10
Good in Digit Symbol and poor in Pairing	1	7	8	1	17
Poor in Digit Symbol and good in Pairing	1	1	1	1	4
Poor in both Digit Symbol and Pairing	1	3	3	5	12
Total	9	15	12	7	43

F, Functional assessment staging: F3, borderline; F4, mild Alzheimer's disease (AD); F5, moderate AD; F6, somewhat severe AD.

of 3 words. Six patients were poor in the Pairing but good in the Delayed recall of 3 words. Analysis with Fisher's exact test revealed a significant correlation between the Pairing and the Delayed recall of 3 words.

Scores for the Digit Symbol and Pairing in each severity of dementia

Based on the scores for Digit Symbol and Pairing, the patients were divided into good and poor groups. On the Digit Symbol, scores of 7 points or more (-1 SD of the standard scaled score) were called good, and those less than 7 points were called poor. On the Pairing, cumulative percentages (Fujita et al., 2006c) of 11% or more were called good, and those less than 11% were called poor. As shown in Table 8, when both a Digit Symbol score of 7 points or more and scores on the Digit Symbol-Pairing supplementary test 11% and more of the cumulative percentile were regarded as normal, 3 of 9 (33.3%) F3 patients (borderline), 11 of 15 (73.3%) F4 patients (mild AD), 12 of 12 (100 %) F5 patients (moderate AD) and 7 of 7 (100 %) F6 patients (somewhat severe AD) could be detected.

Difference between the longest digit span forward and the longest digit span backward on the Digit Span test

The difference between the longest digit span forward and the longest digit span backward was 1.22 digits in F3 patients, 1.60 in F4, 0.92 in F5 and 1.43 in F6, with an overall mean of 1.30 digits. Stan-

dard data have 1.45 ± 1.28 digits (minimum: 1.10, maximum: 1.79) as an overall mean (Fujita et al., 2006c). Compared to the standard data there was no difference in span in each severity of dementia group for AD patients. There was also no correlation among severities of dementia in AD patients.

Discussion

In previous studies using the WAIS-R, cognitive function in individuals aged 75 years and over was frequently assessed using reference values for the 70 to 74 year age group. The present analysis of 38 patients with AD revealed that both scaled scores in the subtests and IQs obtained by reference values for the appropriate age group were significantly higher than those obtained by reference values for the 70- to 74-year age group. The difference was more prominent in Arithmetic and Letter-Number Sequencing subtests for working memory and in all subtests of the performance scale which are related to fluid intelligence. Thus, it was suggested that the expansion of the indicated age range in the WAIS-III allowed valid assessment of cognitive function in AD patients aged 75 years and over.

Several previous studies evaluating intelligence of AD patients using the WAIS-R have shared the views that in healthy adult performance intelligence decreases with age while verbal intelligence is relatively preserved and that AD patients have a marked decrease in performance intelligence (Fleischmann, 1994; Utsumi et al., 1995). However, there is another view that a decline in

crystallized intelligence, in which verbal intelligence is a major component, is characteristic of AD patients (Larrabee et al., 1985; Matsuda, 1998).

The 4 subtests included in verbal comprehension nearly correspond to crystallized intelligence reported by Horn et al. (1985). The term, verbal comprehension indicates whole language ability including being able to speak, think logically, reason, and express one's self, in addition to the ability to understand language. It is generally believed that crystallized intelligence, which is constructed through education and learning, is little affected by aging compared with fluid intelligence, the ability to adapt to new situations (Horn, 1985; Kaufman, 1990; Fleischmann, 1994). The subtests for Vocabulary and Information involve semantic memory. In the present study, there was no obvious difference in the scores for each severity of dementia between the two subtests, suggesting that this type of memory is relatively preserved even in the F6 patients. In contrast, the scores for the subtests Similarities and Comprehension decreased with the progress of dementia. These results were similar to those of Matsuda (1998) and Nishihagi et al. (2006). These findings suggest that a decrease in the abilities to think logically and categorically (Kita, 1998) as measured by the subtest for Similarities, and those to understand matters related to everyday life and to solve problems using past experiences (Kobayashi and Fukunaga, 1995) as measured by the subtest for Comprehension, is characteristic of intellectual impairment in AD.

In Arithmetic, there were significant differences in the scores between borderline (F3) and moderate (F5) or more severe (F6) AD patients, showing that the score for the subtest decreased rapidly at the stage of moderate dementia. The subtest for Digit Span consists of two tasks: digit span forward and digit span backward. While the former involves immediate memory, the latter requires parallel processing (the figures are rearranged in reverse order while the indicated stimuli are maintained), which is a task supported by working memory. Thus, in the test for digit span backward the information processing load increases, which restricts the number of digit spans

correctly recited. Kaplan et al. (1991) reported that attention impairment is quite likely when there is a marked difference in the number of digit spans correctly recited forward and backward. Attention described here means sustained and divided attentiveness during task performance, which Lezak called mental tracking (Kashima et al., 2005). Perry and Hodges (1999) reported the impairment of divided attention in AD. They stated that divided attention and aspects of selective attention are particularly vulnerable while sustained attention is relatively preserved in the early stages of AD. In the present study, the number of digit spans correctly recited forward and backward was almost the same as that in healthy individuals, and the scaled score calculated as the sum of the digit span forward and the digit span backward was also relatively high, and there was no difference in scores in each severity of dementia. Besides, the scores for Digit Span remained higher than those of other subtests for working memory. From these results, we may conclude that the test for digit span is a rather simple task and does not directly reflect the divided and/ or selected attention, and we think the validity of Digit Span as a test to measure attention must be reexamined further. Letter-Number Sequencing was thought up as a new subtest for working memory. In this study, there were no significant differences between borderline and moderate AD cases, but markedly decreased in F6 patients (somewhat severe AD).

Perceptual organization is an intelligence factor on the Performance scale, and indicates the ability to recognize interactions between stimulus elements and to construct these elements into a unified form (Kita, 1998). One study has described that visual and spatial cognitive impairments appear in the relatively early stages of AD (Sato et al., 2001). In the present study, however, we found no significant differences in the scores of the subtests for perceptual organization among severities of dementia, suggesting that the ability to recognize and process information about visual stimuli, which includes visual and spatial cognitive functions and visual spatial construction, is preserved at least up to F5 (moderate AD). In particular, deductive rea-

soning ability measured by Matrix Reasoning was preserved in F6 (somewhat severe AD) patients, suggesting that this ability is highly resistant in AD.

There were significant differences in the scores on the subtests for Digit Symbol and Symbol Search among the severities of dementia, suggesting that the speed of processing, which is supported by not only sustained attention, but divided and selected attention, decreases with progression of dementia.

There are two ways to use the WAIS- III for the detection of AD: one is to determine the presence or absence of dementia and its severity based on quantitative assessment of specific subtests, and the other is to detect AD based on the characteristic patterns of the scores in the subtests. In the quantitative assessment of specific subtests, it is important that intelligence levels of AD patients are closely related to their pre-morbid levels. In patients with a high pre-morbid intelligence level, dementia might be overlooked in the early stages. In the present study there were no subtests showing an obvious decrease of scaled scores in both borderline (F3) and mild dementia (F4) cases. Thus it was difficult to detect AD based on the scaled scores of the subtests alone.

There are some studies (Fuld, 1984; Utsumi et al., 1995; Nishihagi et al., 2006), using subtest profiles from the WAIS-R for the detection of AD. In the WAIS-III, however, the upper limit of the indicated age was expanded from 74 to 89 years old, and new subtests were added. Therefore, the scaled scores from the WAIS-R cannot simply be applied to the WAIS-III.

In AD, impairment of recent and episodic memory appears in the early stages, and impairment of remote (distant) memory becomes obvious with the progression of dementia. Immediate memory is quite likely to be preserved even at advanced stages (Furuta and Mimura, 2006). In studies using the JMMSE, it has been reported that impairment of recent memory measured by the delayed recall of 3 words is most useful for the early detection of AD (Furuta and Mimura, 2006). Kaplan et al. (1991) have reported that processing

functions such as coordinated movement, memory, visual sensory perception, writing speed, and writing precision influence the Digit Symbol scores. In light of this finding, Incidental Memory and Copy supplementary tests were added to the WAIS-III in order to measure memory and writing speed, respectively. The Pairing is a part of Incidental Memory and is administered after the Digit Symbol is completed. Based on memory on the Digit Symbol, examinees have to recall and write the digit symbol corresponding to the figures shown in the subtest. In the present study, scores for the Pairing correlate significantly with the Delayed recall of 3 word scores in the JMMSE, suggesting that the Pairing test is useful in screening for dementia in AD. Furthermore, when the subjects were divided into the "good" and "poor" groups, according to the performances in the Digit Symbol and the Pairing, we could detect 73.3% of the patients in F4 (mild dementia of AD). These results are equivalent to the specificity of 84% and more according to the norm of the WAIS-III (Fujita et al., 2006b, 2006c), and indicate that combining the Digit Symbol and the Pairing tests is useful for the early detection of AD.

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References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV. Washinton DC: American Psychiatric Association; 1994.
- 2 Fleischmann UM. Cognition in humans and the borderline to dementia. Life Sci 1994;55:2051–2056.
- 3 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975:12:189–198.
- 4 Fujita K, Maekawa H, Dairoku K, Yamanaka K. [A Japanese version of the WAIS-III.] Tokyo: Nihon Bunka Kagakusha; 2006a (in Japanese).
- 5 Fujita K, Maekawa H, Dairoku K, Yamanaka K. [A Japanese version of the WAIS-III: theoretical manual.] Tokyo: Nihon Bunka Kagakusha; 2006b. p. 30–39, p. 57–67 (in Japanese).

- 6 Fujita K, Maekawa H, Dairoku K, Yamanaka K. [A Japanese version of the WAIS-III: Manual for test administration and scoring.] Tokyo: Nihon Bunka Kagakusha; 2006c. p. 208, p. 210. (in Japanese).
- 7 Fuld PA. Test profile of cholinergic dysfunction and of Alzheimer-type dementia. J Clin Neuropsychol 1984;6:380–392.
- 8 Furuta N, Mimura M. [Cognitive impairment of early-stage Alzheimer's disease.] Nippon Ronen Seishin Igakkai Zasshi 2006;17:385–392 (in Japanese).
- 9 Horn JL. Remodeling old models of intelligence. In: Wolman BB, ed. Handbook of intelligence. Wiley: New York; 1985. p. 267–300.
- 10 Ishikawa T, Ikeda M. Mild cognitive impairment in a population-based study. Psychogeriatrics 2007;7: 104–108
- 11 Kaplan E, Fein D, Morris R, Delis DC. WAIS-R as a neuropsychological instrument. In: Fujita K, ed. [A Japanese version of the WAIS-III: theoretical manual.] Tokyo: Nihon Bunka Kagakusha; 2006. p. 74–75 (in Japanese). Fujita K, translator. San Antonio: The Psychological Corporation; 1991.
- 12 Kashima K, Mimura M, Muramatsu T. [A collection of Lezak's neuropsychological tests.] Tokyo: Sozo-Publishing; 2005. p. 193–197 (in Japanese).
- 13 Kaufman AS. Assessing adolescent and adult intelligence. Boston: Allyn and Bacon; 1990. p. 222–231.
- 14 Kita Y. [A glossary. Theory and clinical use of a Japanese version of the WAIS-R.] Tokyo: Nihon Bunka Kagakusha; 1998. p. 341–359 (in Japanese).
- 15 Kobayashi T, Fukunaga T. [Psychology and handling of the demented elderly.] Tokyo: World Planning; 1995. p. 153–206 (in Japanese).
- 16 Larrabee G, Largen JW, Levin HS. Sensitivity of age-decline resistant ("hold") WAIS subtests to Alzheimer's disease. J Clin Exp Neuropsychol 1985;7: 497–504.
- 17 Matsuda O. Comparative study of mental function in normal elderly and elderly with mild dementia of the Alzheimer's type via WAIS-R profiles. Tokyo Gakugei Daigaku Kiyo. Dai Ihci Bumon. Kyoiku Kagaku 1998;49:103–110 (in Japanese with English abstract).
- 18 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices on department of health and human services task force on Alzheimer's disease. Neurology 1984;34:939–944.
- 19 Meguro K, Yamadori A. [Alzheimer's disease: "cognitive impairment".] Tokyo: Nakayama Shoten; 2000. p. 86–101 (in Japanese) (Rinsho Seishin Igaku Koza, Vol S9).
- 20 Mori E, Mitani Y, Yamadori A. Usefulness of a Japanese version of the Mini-Mental State Test in neu-

- rological patients. Shinkei Shinrigaku 1985;1:82–90 (in Japanese with English abstract).
- 21 Nishihagi M, Kondo M, Hashimoto T, Nakagawa M. Comparison of mild cognitive impairment and Alzheimer-type dementia using the WAIS-R profile. Ninchi Shinkei Kagaku 2006;8:61–66 (in Japanese with English abstract).
- 22 Perry RJ, Hodges JR. Attention and executive deficits in Alzheimer's disease. A clinical review. Brain 1999;122:383–404.
- 23 Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry 1982;139: 1136–1139.
- 24 Reisberg B, Ferris SH, Anand R, Leon MJ, Schneck MK, Buttinger C, et al. Functional staging of dementia of the Alzheimer type. Ann N Y Acad Sci 1984;435:481–483.
- 25 Sato M, Meguro K, Ishizaki J, Ishii H, Yamadori A. Early detection of patients with Alzheimer's disease with the Benton Visual Form Discrimination Test. Shinkei Shinrigaku 2001;17:62–68 (in Japanese with English abstract).
- 26 Shinagawa F, Kobayashi S, Fujita K, Maekawa H. [A Japanese version of the WAIS-R.] Tokyo: Nihon Bunka Kagakusha; 1990 (in Japanese).
- 27 Teng E, Lu PH, Cummings JL. Neuropsychiatric symptoms are associated with progression from mild cognitive impairment to Alzheimer's disease. Dement Geriatr Cogn Disord 2007;24:253–259.
- 28 Urakami K, Adachi Y, Wakutani Y, Isoe K, Ji Y, Takahashi K, et al. Epidemiologic and genetic studies of dementia of the Alzheimer type in Japan. Dement Geriatr Cogn Disord 1998;9:294–298.
- 29 Urakami K. Prevention of dementia. Psychogeriatrics 2007;7:93–97.
- 30 Utsumi K, Fukatsu R, Fujii M, Nakano N, Midorikawa Y, Takahata N. Characteristics of the WAIS profile in patients with Alzheimer's disease. Rinsho Seishin Igaku 1995;24:229–238 (in Japanese with English abstract).
- 31 Wakutani Y, Kusumi M, Wada K, Kawashima M, Ishizaki K, Mori M, et al. Longitudinal changes in the prevalence of dementia in a Japanese rural area. Psychogeriatrics 2007;7:150–154.
- 33 Wechsler D. Wechsler Adult Intelligence Scale-Revised. San Antonio: The Psychological Corporation; 1981.
- 32 Wechsler D. Wechsler Adult Intelligence Scale— Third Edition. San Antonio: The Psychological Corporation; 1997.

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