

## ORIGINAL ARTICLE

# Retention and impairment of neurocognitive functions in mild cognitive impairment and Alzheimer's disease with a comprehensive neuropsychological test

Lu Yao<sup>1</sup>  | Shinsuke Aoyama<sup>1</sup> | Atushi Ouchi<sup>1</sup> | Yasuji Yamamoto<sup>1,2</sup> | Ichiro Sora<sup>1</sup> 

<sup>1</sup>Department of Psychiatry, Kobe University Graduate School of Medicine, Kobe, Japan

<sup>2</sup>Department of Biosignal Pathophysiology, Kobe University Graduate School of Medicine, Kobe, Japan

**Correspondence**

Ichiro Sora, Professor and Chairperson of Department of Psychiatry, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan.  
Email: [sora@med.kobe-u.ac.jp](mailto:sora@med.kobe-u.ac.jp)

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**Abstract**

**Aim:** MATRICS Consensus Cognitive Battery was developed by the National Institute of Mental Health to establish acceptance criteria for measuring cognitive changes in schizophrenia and can be used to assess cognitive functions in other psychiatric disorders. We used a Japanese version of MATRICS Consensus Cognitive Battery to explore the changes in multiple cognitive functions in patients with mild cognitive impairment and mild Alzheimer's disease.

**Methods:** We administered the Japanese version of MATRICS Consensus Cognitive Battery to 11 patients with mild cognitive impairment (MCI), 11 patients with Alzheimer's disease, and 27 healthy controls. All Japanese versions of MATRICS Consensus Cognitive Battery domain scores were converted to t-scores using sample means and standard deviations and were compared for significant performance differences among healthy control, MCI, and mild Alzheimer's disease groups.

**Results:** Compared with healthy controls, patients with MCI and mild Alzheimer's disease demonstrated the same degree of impairment to processing speed, verbal learning, and visual learning. Reasoning and problem-solving showed significant impairments only in mild Alzheimer's disease. Verbal and visual abilities in working memory showed different performances in the MCI and mild Alzheimer's disease groups, with the Alzheimer's disease group demonstrating significantly more deficits in these domains. No significant difference was found among the groups in attention/vigilance and social cognition.

**Conclusions:** The Japanese version of MATRICS Consensus Cognitive Battery can be used to elucidate the characteristics of cognitive dysfunction of normal aging, MCI, and mild dementia in clinical practice.

**KEYWORDS**

Alzheimer's disease, cognitive retention, MCCB Japanese version, mild cognitive impairment, neurocognitive function

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## 1 | INTRODUCTION

Mild cognitive impairment (MCI) is a clinical condition in which cognitive decline is greater than expected for an individual's age and education but does not interfere with activities of daily living.<sup>1</sup> Boundaries among normal aging, MCI, and mild dementia are difficult to distinguish.<sup>2</sup> Although MCI as a high-risk factor for the progression to dementia has been demonstrated,<sup>3,4</sup> and multiple cognitive domains decline in patients with MCI,<sup>5,6</sup> exact causes remain unknown.

Patients exhibit symptoms of cognitive decline at the MCI stage, but they are still able to perform daily living and social activities. This is a result of the preservation of some cognitive functions in MCI and mild Alzheimer's disease (AD). On the other hand, MCI is a high-risk factor for the development of AD. Therefore, elucidating the characteristics of cognitive impairment in MCI and determining how these characteristics differ from AD is important.

The MATRICS Consensus Cognitive Battery (MCCB), a comprehensive neuropsychological measurement involving multiple cognitive domains, was developed by the National Institute of Mental Health in 2008<sup>7</sup> to establish acceptance criteria for measuring cognitive changes in schizophrenia and to be used in clinical trials of cognitive enhancement therapy for schizophrenia. The MCCB is widely utilized in schizophrenia research,<sup>8-10</sup> and several studies have outlined its standardization in other countries.<sup>11,12</sup> The MCCB is also utilized to assess performance in children, adolescents, and adults,<sup>13</sup> as well as to explore the correlation between cognition and clinical signs.<sup>14</sup> In our previous study, those with chronic schizophrenia were recruited to evaluate the MCCB Japanese version (MCCB-J). The MCCB was significantly correlated with the Brief Assessment of Cognition in Schizophrenia (BACS).<sup>15</sup> The MCCB-J has good validity as a psychometric tool, and it can be used to assess cognitive function in patients with bipolar or eating disorders in Japan.<sup>16,17</sup> Although the basic pathologies of schizophrenia and AD are different, they have similarities in the pattern of regional brain dysfunction, biochemical dysfunction, and symptomatology.<sup>18</sup> In addition, it is well established that impairment in the encoding of new episodic memories is indicative of the earliest stages of AD.<sup>19</sup> Mini-Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale—cognitive subscale (ADAS-cog) are usually used in clinical practice for evaluating the cognition of MCI and AD. Visuospatial, language, concentration, working memory, memory recall, and orientation domains are covered by MMSE.<sup>20</sup> Memory, language, and praxis domains are covered by ADAS-cog.<sup>21</sup> Contrastingly, processing speed, verbal learning, visual learning, working memory, attention/vigilance, reasoning, problem-solving, and social cognition domains are covered by MCCB. Thus, MCCB involves the cognitive domains that MMSE and ADAS-cog do not cover. Hence, MCCB-J may be helpful to explore the changes in broader cognitive domains in MCI and mild AD.

MCI and AD have been the most popular medical jargon among the researchers and are widely used in clinical practice. In 2013, the concept of mild neurocognitive disorders (mild NCD) and major

neurocognitive disorders due to Alzheimer's disease (major NCD due to AD) was defined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5).<sup>22</sup> Diagnostic criteria of mild NCD are largely consistent with the previously proposed nosological entity for MCI,<sup>23</sup> and major NCD is mostly synonymous with dementia.<sup>24</sup> Because of that, the great majority of our understanding of mild NCD and major NCD due to AD based on studies of MCI and AD. In the present study, we aimed to use the MCCB-J to explore and analyze the retention and impairment of these cognitive domains in MCI (mild NCD) and AD (major NCD due to AD). Our study is the first to use the MCCB-J in patients with MCI and AD.

## 2 | METHODS

### 2.1 | Subjects and procedures

Twenty-two native Japanese-speaking outpatients aged >65 years were recruited between April 2017 and December 2019 at the memory clinic of Kobe University Hospital. 11 subjects met the diagnostic criteria for MCI (ie, mild NCD) and 11 subjects met the diagnostic criteria for AD (ie, major NCD due to AD), using the DSM-5.<sup>22</sup> Those with AD met the diagnostic criteria for mild AD (ie, stage 4) using Functional Assessment Staging.<sup>25</sup> None of the patients in the MCI group were receiving medication for cognitive disorder. The mild AD group included 4 on anti-dementia treatment and 7 on non-anti-dementia treatment. The diagnosis was supported by neuropsychological examinations and brain imaging. At least one physician specializing in dementia and one neuropsychologist were present during the diagnosis. Subjects were also assessed by clinical interview to ensure that they had no psychiatric illness (eg, depression, bipolar disorder, brain injury, and alcohol dependence). No recruited subjects were excluded from the analysis based on these criteria or refusal to participate.

Age-matched healthy elderly subjects were recruited from Kobe City, and they were all screened using the MMSE and Geriatric Depression Scale (GDS). Twenty-seven elderly subjects met the criteria of MMSE  $\geq 26$  and GDS  $\leq 6$  and comprised the healthy control group. The exclusion criteria included an intelligence quotient below 80, as assessed using the Japanese version of the National Adult Reading Test (JART).<sup>26</sup>

All participants in the present study were right-handed. Written consent was obtained from all participants, and the study was conducted according to the standards of the Declaration of Helsinki and approved by the Hospital Ethics Committee of Kobe University.

### 2.2 | Measures

Our neuropsychological assessment was based on the MCCB-J and performed by clinical psychologists who had completed MCCB-J training. The MCCB-J consists of 10 subtests that assess the following seven cognitive domains<sup>27</sup>: trail making test (part A; TMT-A), Brief



Assessment of Cognition in Schizophrenia Symbol Coding (BACS-SC), Category Fluency—Animal Naming test to assess processing speed; Hopkins Verbal Learning Test-Revised (HVLTR) to assess verbal learning; Brief Visuospatial Memory Test-Revised (BVMTR) to assess visual learning (Trials 1, 2, and 3 were selected from the HVLTR and BVMTR, and the total score of the three free recall trials [total recall] was used to evaluate verbal and visual learning separately); Letter-Number Span test (LNS) and Wechsler Memory Scale III-Spatial Span test (WMS III-SS) to assess working memory; Continuous Performance Test—Identical Pairs (CPT-IP) to assess attention/vigilance; Neuropsychological Assessment Battery-Mazes (NAB-Mazes) to assess reasoning and problem-solving; and Mayer-Salovey-Caruso Emotional Intelligence Test's Managing Emotions component (MSCEIT-ME) to assess social cognition (Table 1). Each participant completed the test in approximately 60-90 min.

## 2.3 | Statistical analysis

The sample was classified into three groups by diagnostic category (healthy control, MCI (ie, mild NCD), and mild AD (ie, major NCD due to AD)), and we classified patients with mild AD into 2 groups by drug treatment or non-drug treatment. We used the raw scores of healthy controls and patients from each of the ten MCCB-J tests and the MCCB scoring program to calculate t-scores of the ten MCCB-J tests and seven domains.<sup>27</sup> We used data from the healthy controls as reference data in the statistical analysis.

Kruskal-Wallis test was used to compare the demographic and clinical characteristics. Then, we performed post hoc pairwise multiple comparisons correction for significant differences with the Bonferroni-corrected Mann-Whitney *U* test. To examine the differences in MCCB-J performance among the healthy control, MCI, and mild AD groups, we performed the Kruskal-Wallis test with the seven domain t-scores and ten MCCB-J tests as separate dependent variables and the three groups as subject variables. We then conducted

post hoc pairwise multiple comparison corrections for significant differences using the Bonferroni-corrected Mann-Whitney *U* test to adjust for domains and subtests. Effect size *r* was calculated among healthy control vs MCI, healthy control vs mild AD, and MCI vs mild AD, respectively, for the seven domains and the total score.

Mann-Whitney *U* test was used to compare the performance of mild AD patients between drug treatment and non-drug treatment in the seven domains and ten subtests. Spearman rank correlation analysis was also performed between the total score of MMSE and the total score of MCCB-J.

All statistical analyses were conducted using SPSS (version 11; SPSS Inc, Chicago, IL, USA). Statistical significance was defined as  $P < 0.05$ . To adjust for multiple comparisons (demographic, MCCB-J domains, and subtests) using the Bonferroni correction, the significance level was set at  $P \leq 0.017$ .

## 3 | RESULTS

### 3.1 | Clinical and demographic features

The proportion of females in the healthy control, MCI, and mild AD groups was 55.6%, 72.7%, and 63.6%, respectively. Kruskal-Wallis test revealed significant between-group differences in age ( $P = 0.016$ ), JART ( $P < 0.006$ ), and MMSE ( $P < 0.001$ ). Mann-Whitney *U* test showed that the mild AD group was significantly older than the healthy control group ( $P = 0.004$ ), but the age of the MCI group was not significantly different from that of the healthy control or mild AD groups. The JART score of the mild AD group was significantly lower than that of the healthy controls ( $P = 0.005$ ), but the JART of the MCI group was not significantly different from those of the healthy control and mild AD groups. Compared with the healthy control group, the MMSE Mann-Whitney *U* test for the MMSE showed that the MCI ( $P < 0.001$ ) and mild AD groups ( $P < 0.001$ ) had significantly lower scores, and the mild AD group also had significantly lower

1. Processing Speed TMT-A Category Fluency: Animal Naming BACS-SC	5. Attention/Vigilance CPT-IP
2. Verbal Learning HVLTR	6. Reasoning and Problem-Solving NAB-Mazes
3. Visual Learning BVMTR	
4. Working Memory WMS III-SS LNS	7. Social Cognition MSCEIT-ME

TABLE 1 MCCB-J consists of 10 subtests assessing seven cognitive domains

Abbreviations: BACS-SC, Brief Assessment of Cognition in Schizophrenia—Symbol Coding test; BVMTR, Brief Visuospatial Memory Test—Revised; CPT-IP, Continuous Performance Test—Identical Pairs; HVLTR, Hopkins Verbal Learning Test—Revised; LNS, Letter-Number Span test; MCCB-J, MATRICS Consensus Cognitive Battery, Japanese version; MSCEIT-ME, Mayer-Salovey-Caruso Emotional Intelligence Test's Managing Emotions component; NAB, Neuropsychological Assessment Battery—Mazes (NAB); TMT-A, trail making test, part A; WMS III-SS, Wechsler Memory Scale III Spatial Span test.



scores than the MCI group ( $P = 0.001$ ). No significant difference was found in education level among the three groups (Table 2).

### 3.2 | Performance between drug treatment and non-drug treatment in mild AD

The mild AD group was further classified based on treatment as follows: anti-dementia treatment group ( $n = 7$ ) and non-anti-dementia treatment group ( $n = 4$ ). The Mann-Whitney  $U$  test results of the MCCB-J domain and subtest scores revealed between anti-dementia treatment group and non-anti-dementia treatment group. Because the performance of the anti-dementia treatment group and non-anti-dementia treatment group did not show a significant difference, they were combined as one group for further analysis.

### 3.3 | MCCB-J neurocognitive function scores and Correlation between total score of MMSE and total score of MCCB-J

Kruskal-Wallis test of MCCB-J domain scores revealed between-group differences in processing speed ( $P < 0.001$ ), verbal learning ( $P < 0.001$ ), visual learning ( $P < 0.001$ ), working memory ( $P < 0.001$ ), and reasoning and problem-solving ( $P = 0.004$ ). Mann-Whitney  $U$  test and effect size showed that compared with healthy controls, the MCI and mild AD groups demonstrated significantly worse performance and large or medium effect size in processing speed ( $P < 0.001$   $r = 0.65$ ,  $P < 0.001$   $r = 0.57$ ), verbal learning ( $P < 0.001$   $r = 0.53$ ,  $P < 0.001$   $r = 0.64$ ), and visual learning ( $P = 0.006$   $r = 0.39$ ,  $P < 0.001$   $r = 0.61$ ); the mild AD group had significantly worse performance and large effect size on the working memory domain ( $P < 0.001$   $r = 0.61$ ), but the MCI group was not significantly different, with a medium effect size of  $r = 0.39$ ; the mild AD group had significantly worse performance and medium effect size in the reasoning and problem-solving domains ( $P = 0.004$   $r = 0.41$ ), but the MCI group showed no significant difference and medium effect size ( $r = 0.34$ ). Attention/vigilance and social cognition domains showed no significant difference and small effect size among the three groups (Figure 1, Table S1).

Kruskal-Wallis test of MCCB-J subtest scores revealed between-group differences on the TMT-A ( $P < 0.001$ ), BACS-SC ( $P < 0.001$ ), category fluency—animal naming ( $P < 0.001$ ), HVLTR ( $P < 0.001$ ), BVMT-R ( $P < 0.001$ ), LNS ( $P < 0.001$ ), WMS III-SS ( $P = 0.001$ ), and NAB Maze ( $P = 0.004$ ). Mann-Whitney  $U$  test showed, that compared with healthy controls, the MCI and mild AD groups demonstrated significantly worse performance on the TMT-A ( $P < 0.001$ ,  $P = 0.005$ , respectively), BACS-SC (both  $P < 0.001$ ), category fluency—animal naming (both  $P < 0.001$ ), HVLTR (both  $P < 0.001$ ), and BVMT-R (both  $P < 0.001$ ); the mild AD group demonstrated significantly worse performance on the WMS III-SS ( $P < 0.001$ ) and NAB Maze ( $P = 0.004$ ), but the MCI group showed no significant difference compared with healthy controls. A significant difference

was found among the three groups on the LNS (healthy control  $>$ MCI,  $P = 0.007$ ; healthy control  $>$ mild AD,  $P < 0.001$ ; MCI  $>$ mild AD,  $P = 0.004$ ). CPT-IP and MSCEIT-ME subtests showed no significant difference among the three groups (Figure 2, Table S2).

Based on the results of the study, however, healthy control, MCI, and mild AD groups did not show any correlation between the MMSE and MCCB-J total scores.

## 4 | DISCUSSION

We used comprehensive neuropsychological tests that are rarely used in memory clinics to assess cognitive characteristics and changes in patients with MCI and mild AD by utilizing the MCCB-J. We found that, compared with the healthy control group, the patient groups scored significantly lower and had a large or medium effect size in processing speed, verbal learning, and visual learning. The mild AD group scored significantly lower in reasoning and problem-solving than healthy control. Verbal and visual abilities in working memory showed different performances between the MCI and mild AD groups. In addition, there was no significant difference and a small effect size among the three groups in attention/vigilance and social cognition domains.

### 4.1 | Cognitive impairment in the MCI and mild AD groups

#### 4.1.1 | Processing speed, verbal learning, and visual learning

Lower performance in processing speed, verbal learning, and visual learning compared with healthy control was observed in the MCI and mild AD groups. Processing speed is the ability to identify, discriminate, integrate, and decide about information. It is a measure of the time required to respond to and/or process information in one's environment.<sup>28,29</sup> A previous study found that processing speed mediates age-related memory effects but not dementia-related memory effects.<sup>30</sup> A decline in processing speed may occur in the early stages of dementia, before the onset of any other clinical symptoms.<sup>31</sup> No statistically significant difference was found in age between healthy control and MCI groups in our current study, but a decline in processing speed was observed in the MCI group. This may indicate that compared with the age-matched group, impairment of processing speed is not caused by age-related memory effect in the MCI stage. Processing speed is significantly impaired as early as the MCI stage, rather than just in the initial stages of AD. Thus, the assessment of MCI should not only focus on episodic memory but also processing speed as this can be used as a risk factor to assess MCI.

As mentioned previously, trials 1, 2, and 3 were selected from the HVLTR<sup>32</sup> and BVMT-R,<sup>33</sup> and the total score of the three free recall trials (total recall) was used to evaluate verbal and visual learning

TABLE 2 Demographic and clinical characteristics

	HC n = 27 (M = 12, M/n = 44.4%)  Mean ± SD	MCI n = 11 (M = 3, M/n = 27.3%)	Mild AD n = 11 (M = 4, M/n = 36.4%)	P-value	Post hoc comparisons
Age (range)	75.78 ± 4.66 (66–85 years old)	78.27 ± 5.24 (71–85 years old)	81.09 ± 5.26 <sup>a</sup> (68–87 years old)	0.016	HC = MCI (P = 0.225) HC > mild AD (P = 0.004) MCI = mild AD (P = 0.21)
Education (years)	13.78 ± 2.40	13.00 ± 3.19	12.09 ± 2.55	0.193	n.s
MMSE	29 ± 1.24	25.91 ± 1.92 <sup>b</sup>	22.27 ± 2.37 <sup>a,c</sup>	<0.001	HC > MCI (P < 0.001) HC > mild AD (P < 0.001) MCI > AD (P = 0.001)
FIQ-JART	108.96 ± 8.065	103.64 ± 11.138	97.82 ± 10.515 <sup>a</sup>	<0.006	HC = MCI (P = 0.260) HC > mild AD (P = 0.005) MCI = mild AD (P = 0.321)

Abbreviations: AD, Alzheimer's disease; FIQ, Full scale of IQ; HC, healthy controls; JART, Japanese Adult Reading Test; M, Males; MCCB-J, MATRICS Consensus Cognitive Battery, Japanese version; MCI, mild cognitive impairment; n.s., not significant.

<sup>a</sup>Significant pairwise differences between healthy control and mild AD (P < 0.017).

<sup>b</sup>Significant pairwise differences between healthy control and MCI (P < 0.017).

<sup>c</sup>Significant pairwise differences between MCI and mild AD (P < 0.017).

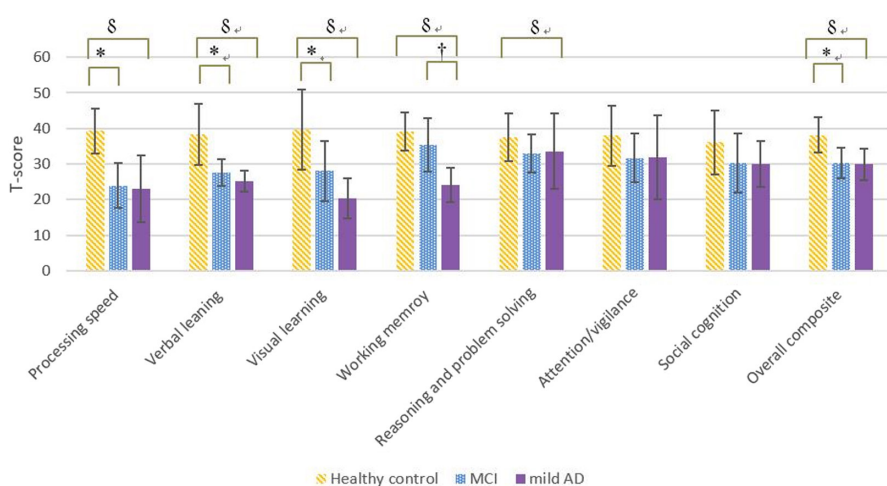


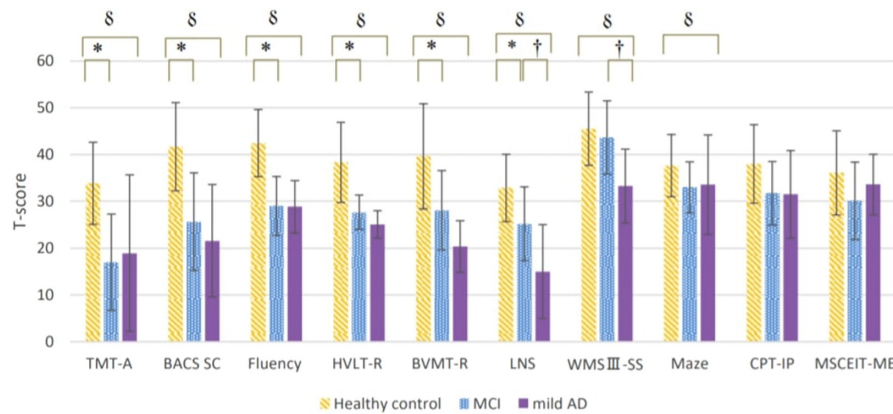
FIGURE 1 Kruskal-Wallis test for all MCCB-J domains and overall cognitive composite t-scores. Error bars show standard deviation. MCI: mild cognitive impairment; AD: Alzheimer's disease; MCCB-J: MATRICS Consensus Cognitive Battery, Japanese version. § Significant pairwise differences between healthy control and mild AD groups (P < 0.017); \* Significant pairwise differences between healthy control and MCI groups (P < 0.017); † Significant pairwise differences between MCI and mild AD groups (P < 0.017)

separately. Total recall from the HVLT-R can discriminate between patients with AD and controls<sup>34,35</sup> but has previously demonstrated a relatively low discrimination capacity for distinguishing MCI from healthy control.<sup>35</sup> Research involving the HVLT-R and BVMT-R combined with blood-based biomarkers of AD and a brief neuropsychological test revealed that, as an early prediction of risk for developing MCI or AD, global cognitive function, episodic memory, language fluency, and serum  $A\beta_{1-42}/A\beta_{1-40}$  ratio achieved an excellent accuracy of 91%, but the sensitivity and specificity of verbal learning and visual learning with blood-based biomarkers was not apparent.<sup>36</sup> Verbal and visual learning declined to the same degree in MCI and mild AD stages. Hence, whether verbal learning and visual

learning can be used as routine clinical examinations for distinguishing healthy controls and MCI needs further examination.

#### 4.1.2 | Working memory

Working memory is the ability to maintain and manipulate information for a brief period.<sup>37</sup> It coordinates information in two independent domain-specific storage components for verbal and visuospatial codes.<sup>38,39</sup> Because of the separability of spatial and verbal working memory,<sup>40</sup> the LNS and WMS III-SS, which are tasks for verbal and visuospatial ability in working memory, respectively, did not perform



**FIGURE 2** Kruskal-Wallis test for all MCCB-J domains and overall cognitive composite t-scores. Error bars show standard deviation. Abbreviations: TMT-A: trail making test, Part A; BACS-SC: Brief Assessment of Cognition in Schizophrenia—Symbol Coding test; HVLT-R: Hopkins Verbal Learning Test—Revised; BVMT-R: Brief Visuospatial Memory Test—Revised; LNS: Letter–Number Span test; WMS-SS: Wechsler Memory Scale III Spatial Span test; CPT-IP: Continuous Performance Test—Identical Pairs; NAB: Neuropsychological Assessment Battery—Mazes (NAB); MSCEIT-ME: Mayer-Salovey-Caruso Emotional Intelligence Test's Managing Emotions component; MCI: mild cognitive impairment; AD: Alzheimer's disease; MCCB-J: MATRICS Consensus Cognitive Battery, Japanese language version. ≈ Significant pairwise differences between healthy control and mild AD groups ( $P < 0.017$ ); \* Significant pairwise differences between healthy control and MCI groups ( $P < 0.017$ ); † Significant pairwise differences between MCI and mild AD groups ( $P < 0.017$ )

consistently in patients with MCI and mild AD. The visuospatial ability of working memory depends principally on the right parietal areas.<sup>41</sup> In patients with MCI, the parietal area has not demonstrated accelerated brain volume changes compared with that in healthy controls,<sup>42</sup> but this was observed in the early stages of AD.<sup>43</sup> Hence, this might explain why the impaired performance of visuospatial ability will appear in mild AD but not MCI. Contrastingly, we found that the LNS was the singular subtest that showed a group difference, suggesting that it might distinguish MCI from mild AD. Our current results also demonstrated that verbal impairment could be observed earlier than visual impairment in working memory in patients with MCI. In addition, in a meta-analysis, Reger et al selected studies that included AD-only data and showed that visuospatial skills may be the most helpful in identifying at-risk drivers.<sup>44</sup> This suggests that working memory can be used not only as a clinical neuropsychological test to distinguish healthy aging, MCI, and mild AD but also as a basis for assessing driving fitness in the elderly.

## 4.2 | Cognitive retention in MCI and cognitive impairment in mild AD

### 4.2.1 | Reasoning and problem-solving

NAB Mazes were selected to evaluate reasoning and problem-solving function through the maze-tracing task, which is sensitive to frontal lobe lesions.<sup>45</sup> The maze task also involves inductive reasoning, which is often used to generate a prediction or to make forecasts. It is one of the most important and ubiquitous of all problem-solving activities.<sup>46,47</sup> Baghel et al determined that the integration of multiple relations between mental representations is critical for higher-level cognition. Relational integration may be a

basic common factor that connects various abilities that depend on prefrontal function, including problem-solving, for which an intact prefrontal cortex is essential.<sup>48</sup> The present study indicates that the integrity of the frontal lobe is relatively preserved in MCI but not in mild AD as a lower performance was observed only in the mild AD group. This suggests that obvious frontal lobe damage would not be observed and inductive reasoning/problem-solving is preserved in the MCI stage.

## 4.3 | Cognitive retention in the MCI and mild AD

### 4.3.1 | Attention/vigilance and social cognition

Compared with the healthy control group, worse performance of attention/vigilance and social cognition domains was not observed in MCI and mild AD groups in our current study. The attention/vigilance domain was assessed using the CPT-IP, which measures sustained attention. Sustained attention refers to the ability to maintain or focus attention over a period of time,<sup>49</sup> and it is typically assessed in a vigilance task.<sup>50</sup> Our results indicate that even patients with mild AD have a sustained attention capacity. This is likely because individuals with AD have increased activity in the prefrontal regions during cognitive tasks compared with that seen in age-matched healthy controls, compensating for losses attributable to the degenerative disease process in mild AD.<sup>51</sup> Overall, sustained attention is relatively preserved in the early stages of AD, which has been validated in a previous study.<sup>52</sup>

The manner in which we interpret, analyze, and remember information about the social environment is a characteristic of social cognition.<sup>53</sup> The study of information processing in a social setting is referred to as social cognition, and it enables individuals to take advantage of being part of a social group.<sup>54</sup> Managing



emotions was selected from the MSCEIT to measure an individual's action in controlling emotions that are troublesome and negatively affect relationships.<sup>55</sup> A previous study demonstrated that compared with the performance of social cognitive dysfunction in frontotemporal dementia, the degree of impairment in AD was minimal.<sup>56</sup> Although with the severity of social cognition, long-term disease progression can be tracked, AD progression cannot be predicted at the early stage using social cognition; this may account for the relative independence between social and general cognition.<sup>57</sup> Retention of cognitive function in attention/vigilance and social cognition may explain why patients with MCI and mild AD are still able to perform social activities despite the general cognitive decline.

## 5 | LIMITATIONS

The present study has several limitations. First, the sample size was small. Refusal to participate was common because the MCCB-J takes 60-90 min to complete. Some subjects discontinued the test due to physical exhaustion, making the test results unusable. We did not observe much difference between those who completed the test and those who did not complete the test (unpublished data). Further studies may reveal detailed differences between those who have completed the test and those who have not completed the test. Second, because of the small sample size, the correlation between MMSE and MCCB-J total scores could not be observed among the healthy control, MCI and mild AD groups. Third, whether the poor performance in mild AD was correlated with age was not evaluated. Although the data showed that MCI and mild AD have a larger proportion of females, we did not assess the impact of sex on the results. A larger sample size is necessary for future studies. More detailed classification and comparison should be conducted, and the relationships and differences among different groups should be elucidated.

## 6 | CONCLUSIONS

Our findings demonstrate the retention and impairment of neuropsychological functions in MCI and mild AD using the MCCB-J, suggesting that processing speed can be used as a risk factor for assessing MCI. Whether verbal and visual learning can be used as routine clinical examinations for distinguishing between healthy controls and MCI requires further study. Working memory can be used not only as a clinical neuropsychological test to distinguish MCI from AD but also as a basis for assessing the driving fitness of the elderly. Notably, reasoning and problem-solving were preserved in MCI. Attention/vigilance and social cognition did not demonstrate obvious impairment in the MCI and mild AD groups, suggesting their importance in maintaining social activity. In clinical practice, physicians will be able to use the MCCB-J to regularly evaluate preserved and impaired cognitive functions and record behavioral changes.

## APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

The study protocol has been approved by the suitably constituted Research Ethical Committee of the Kobe University Graduate School of Medicine (No.1610), and it conforms to the provisions of the Declaration of Helsinki.

## ANIMAL STUDY

N/A.

## INFORMED CONSENT

All participants provided written consent to the study after a full explanation of the study procedures.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

Lu Yao and Ichiro Sora designed the study. Lu Yao, Shinsuke Aoyama, Yasuji Yamamoto, and Ichiro Sora collected the data. Atushi Ouchi administered the psychological test. Lu Yao and Atushi Ouchi analyzed the data. Lu Yao wrote the draft. Lu Yao, Shinsuke Aoyama, Yasuji Yamamoto, and Ichiro Sora wrote the final manuscript. All authors approved the final manuscript.

## DATA AVAILABILITY STATEMENT

Research data are not shared. This is because the participants did not consent to open data sharing.

## ORCID

Lu Yao  <https://orcid.org/0000-0001-6465-2209>

Ichiro Sora  <https://orcid.org/0000-0003-0741-8373>

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