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Comparison of the digital version B of L-Stroop test (dL-Stroop test B) with MMSE in validity and reliability for screening Mild Cognitive Impairment (MCI)

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1. Introduction

According to the 2019 census conducted by the Japan Labor and Welfare Ministry of Health, it was speculated that by 2025, one in five individuals over the age of 65 in Japan would be diagnosed with senile dementia. This estimation included individuals with MCI, resulting in a population of over ten million affected individuals. Currently, the MoCA-J test is considered more effective than the MMSE or HDS-R for screening MCI. However, all three tests require approximately 10 minutes to complete. This poses a challenge as forgetful elderly individuals are more likely to reject screening tests and not acknowledge their cognitive decline. Thus, there is a need for shorter screening tools that can be used by both general practitioner and non-medical personnel for detecting early-stage of cognitive decline.

A new simple screening test called the L-Stroop test (Lee et al., 2022) was developed, which required to name 30 incongruent Kanji characters on an A4 paper. Digital versions of this test, known as the dL-Stroop A and B tests, were also developed for MCI screening using an iPad, requiring participants to select the name 30 colored Kanji characters with a touch pen (Lee, 2023). These screening methods were inspired by the Stroop effect, which refers to the interference in serial verbal reactions when responding to incongruent stimuli (Stroop, 1935). Stroop reported that naming 100 incongruent words took 74.3% longer (110.3 seconds) than naming congruent colored words (63.3 seconds), reflecting the interference caused by the incongruent stimuli of color and word.

Several studies employing functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and near-infrared spectroscopy (NIRS) have

軽度認知障害（MCI）のスクリーニングテストとして開発したデジタル版 dL-ストループテスト B と MMSE の妥当性と信頼性の検討

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demonstrated an association between the response time delay in the Stroop test and volume loss in the prefrontal cortex, as well as reduced cerebral blood flow in the anterior cingulate cortex (Li et al., 2009; Pardo et al., 1990; Watanabe et al., 2015). Salthouse (2010) demonstrated that memory and speed are strongly associated with age in cognitive functioning during the Stroop test. The research indicated that aging typically involves a decrease in memory, speed, spatial visualization, and reasoning, but not vocabulary knowledge, being preserved in brain reserves unless brain cells and network mechanisms suffer damage. Perianez (2021) reported that naming color words reflects working memory, conflict monitoring, and the speed of visual searches.

Previously, in the L-Stroop test the speed and error rates were hard to compare statistically due to analogue recording process of the test. Fortunately, the results of dL-Stroop test B were automatically recorded in iPad, making it possible to analyze the speed and error rates statically for validating their reliability in screening for cognitive decline. In this study, our aim was to utilize the dL-Stroop test B to evaluate the extent of cognitive function decline in comparison to the MMSE.

2. Materials and Methods

Study participants

All participants classified into the three groups were recruited from the Osaka Lee Clinic, OLC Health Checkup Center, and home-cared patients between February 2021 and May 2022. The study protocol received approval from the Research Ethics Review Committee (N21-002). Participants underwent various neuropsychological cognitive function tests after signing written agreements and digitally approving them on an iPad. A primary care physician, who had completed training in administering and scoring the Montreal Cognitive Assessment (MoCA), evaluated the tests.

The MCI group consisted of 93 participants who were suspected of cognitive decline. The definition of MCI corresponded to previously established criteria (Peterson, 1999). The common factor among these participants was the presence of subjective complaints of gradual memory loss. Some were being treated for common diseases at the outpatient clinic. They visited the clinic regularly for various blood chemistry tests and underwent CT/MRI scans in the case of headache or head injury. Participants with identifiable medical, neurological, or psychiatric explanations for their memory loss were excluded. The grouping criteria, distinguishing them from both the NC and AD groups, were MoCA-J scores between 19-25 points (Yamamoto and Miyake, 2010).

The AD group consisted of 66 participants, with 57% being female. The clinical criteria for AD followed the guidelines of the National Institute on Aging-Alzheimer's Association workgroup and the diagnosis in the fifth edition of DSM-5. Individuals with AD had MoCA-J score of less than 19 points.

The NC group consisted of 72 participants who did not complain of memory loss or cognitive issues, although some were being treated for hypertension, hypercholesteremia, osteoporosis, or other chronic illnesses. Participants with mental disorders were excluded. The grouping criteria for the NC group were a MoCA-J score of more than 26 points. Within the NC group, eighteen participants (25%) scored less than 27 points in MMSE.

Exclusion criteria included severe color-blindness, speech disorder, and physical disability that hindered the use of an iPad. Three participants were excluded from the total count of 234 for SPSS analysis because they were unable to complete all three cognitive function tests.

Demographic information was summarized in Table 1. A total of 231 patients, aged 43 to 98 (52% female), were divided into three groups: NC (n=72),

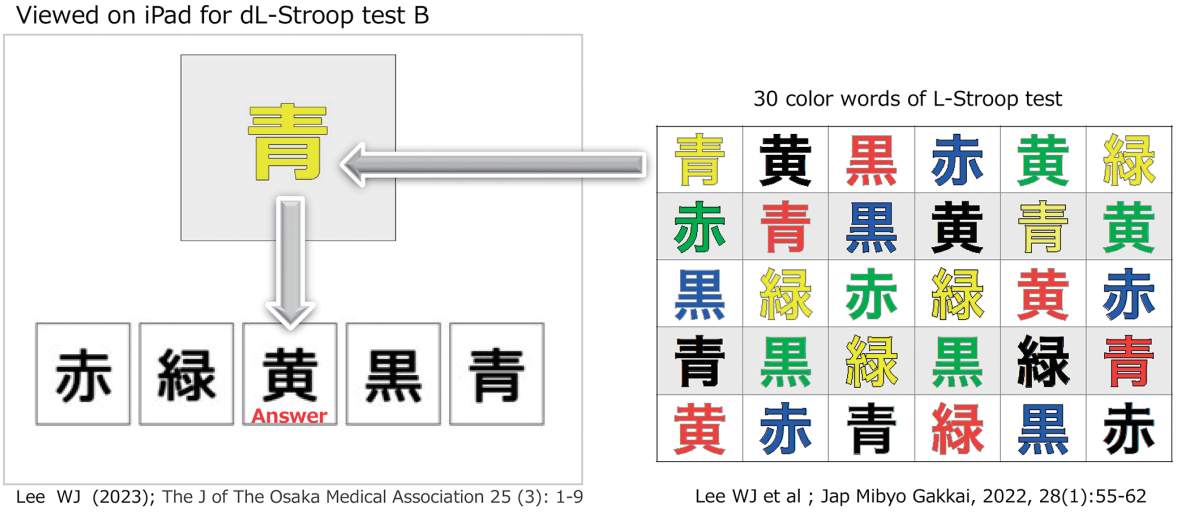
Table 1.　Descriptive analysis

	Sex			Ave. age (yr)		MoCA-J (/30pt)	
	Total	M	F	Mean	SD	Mean	SD
	Count	Count	Count				
NC	72	37	35	64.71	9.14	26.83	1.01
MCI	93	46	47	72.14	9.77	22.28	2.06
AD	66	28	38	80.67	7.33	15.27	3.13
Total	231	111	120	72.26	10.83	21.70	5.00

MCI (n=93), and AD (n=66). The mean age for all groups was 72.26 (SD=10.83) years, with the NC group having a mean age of 64.71 (SD=9.14) years, the MCI group having a mean age of 72.14 (SD=9.77) years, and the AD group having a mean age of 80.67 (SD=7.33) years.

The dL-Stroop test B

The dL-Stroop tests A and B were originally developed by Dr. Lee WJ and programmed by VIZAN Co. In the dL-Stroop test B, participants were asked to select the name of the color of the words with a touch pen. The test included a total of 30 Japanese Kanji characters, which were the same as those used in the L-Stroop test. The colors used were yellow (黄), black (黒), red (赤), blue (青), and green (緑). Figure 1 illustrates the presentation of one Japanese Kanji character at a time on the iPad screen. For example, if the Japanese character for blue (青) was displayed in yellow ink, participants would choose yellow (黄) as the correct answer for the Kanji color instead of blue from the provided options. The time taken to complete all thirty tasks was recorded to three decimal digits, and the error count was also recorded. The Stroop task was conducted up to two times with different data collectors, and the better result was chosen



The dL-Stroop test B, which is the digital version of the L-Stroop test, is conducted by asking participants to select the name of the color of the word by touching the black Kanji character among the five listed below with a touch pen. The time in seconds and the error count are recorded on the PC server.

Figure 1.　dL-Stroop test B protocol

for analysis.

Japanese version Montreal of Cognitive Assessment (MoCA-J)

MoCA-J is a cognitive assessment tool that was developed by Nasreddine in 2005, and the Japanese version has been available since 2010. Multiple domains of the brain functions were analyzed with a trail making test, cube, clock, naming, memory, digit span, letter A, serial 7, sentence repetitions, verbal fluency, abstraction, and orientation summing up to a total maximum of 30 points. Visual spatial executive (5 points), naming (3 points), attention (6 points), language (3 points), abstraction (2 points), delayed recall (5 points), orientation (6 points), and an additional one point if the education is below 12 years were considered. The cut-off values of 25/26 for MCI and 18/19 for dementia screening were used (Fujiwara et al., 2010).

Mini-Mental State Examination (MMSE)

MMSE by Folstein MF in 1975 was the most popularly used screening test around the world for dementia. MMSE in Japanese was given with thirty questions. Season, year, month, day and date (5 points), place, prefecture, city, level of the floor, district (5 points), short-term memory of 3 words (3 points), subtraction of 7 from 100 for 5 times (5 points), recall the names of 3 words (3 points), clock and pencil (2 points), repeat sentences (1 point), 3 orders to grab the paper in right, fold in half, and return to the table (3 points), ask to close eyes (1 point), write a sentence (1 point), draw the 2 pentagons in the cross (1 point) which in all sum up to 30 points. The cut-off values 26/27 for screening MCI and 24/25 for AD were used in this study.

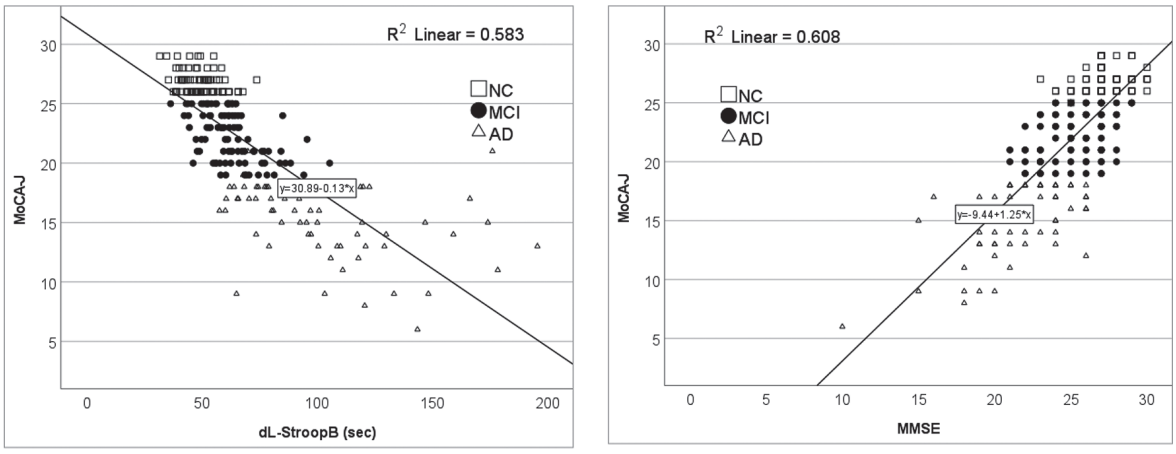
Data Analysis

To evaluate the validity of the dL-Stroop Test B for MCI, several analyses were conducted to assess its relationship with the control group, linearity with the MMSE and MoCA-J scores, and internal consistency reliability. First, scatter plots to MoCA-J were used to examine the linearity for dL-Stroop test B and MMSE. Second, Receiver Operating Characteristic (ROC) curves and the Area Under the Curve (AUC) were used to determine the cut-off values for MCI and AD for the dL-Stroop Test B and MMSE to assess their diagnostic accuracy by the sensitivity, specificity, and positive and negative predictive values. Finally, the speed, error rate, and interference score were determined to assess the dL-Stroop test for the reliability of the color-naming component of the dL-Stroop Test B. ANOVAs followed by a post hoc analysis were performed using SPSS version 28 for Windows.

3. Results

Correlations and scatter graphs of dL-Stroop test B and MMSE with MoCA-J

Scatter graphs of dL-Stroop test B and MMSE against MoCA-J were shown in Figure 2. The Spearman's correlation coefficient between MoCA-J for dL-Stroop test B was 0.815 (95% CI: −0.856～−0.756), and for MMSE was 0.750 (95% CI: 0.685～0.803). The correlation coefficient with confidence intervals between dL-Stroop B and MMSE was −0.674 (95% CI: −0.741～−0.594). Since dL-Stroop test B was inversely related to MoCA-J, the correlation coefficient for the dL-Stroop test B was designated with a negative value whereas for MMSE with a positive value. The distributions of both dL-Stroop test B and MMSE had a similar strength relationship to MoCA-J. The R^2 value for the dL-Stroop test B was 0.593 whereas the R^2 value for MMSE was 0.608. Comparing three groups of NC, MCI, and AD in dL-Stroop test B to MMSE, the linearity found in MMSE with MoCA-J was no longer present after 70 seconds in dL-Stroop test B for AD group due to increased Stroop interference.



The Spearman's correlation coefficient between dL-Stroop test B and MMSE was -0.674 (95% CI -0.741~-0.594)
P < 0.001

Figure 2.　Scatter plots for dL-Stroop test B and MMSE against MoCA-J

Differentiation for NC/MCI and MCI/AD with ROC curves AUC.

ROC curves for dL-Stroop test B and MMSE were generated and the AUC for its 95% CI were shown in Figure 3 and 4.　In NC/MCI differentiation, AUC for the dL-Stroop test B was 0.888（95% CI：0.846-0.930）, and for MMSE was 0.842（95% CI：0.792-0.992）.　While for MCI/AD differentiation, AUC for the dL-Stroop test B was 0.941（95% CI：0.912-0.970）and for MMSE was 0.911（95% CI：0.874-0.948）.

As shown in Table 2, the dL-Stroop test B had a cut-off value of 59.27 seconds to differentiate between MCI and NC.　The test exhibited a sensitivity of 76.73%, specificity of 90.14%, positive predictive value（PPV）of 94.57%, and negative predictive value（NPV）of 63.75%, as determined from the ROC curves.　Meanwhile, the MMSE had a cut-off value of 26/27 points, with a sensitivity of 66.04%, specificity of 88.89%, PPV of 92.92%, and NPV of 54.24%.　Moreover, to distinguish AD from MCI, the dL-Stroop test B had a cut-off value of 70.02 seconds, with a sensitivity of 87.30%, specificity of 88.10%, PPV of 73.33%, and NPV of 94.87%.　Similarly, the MMSE had a cut-off value of

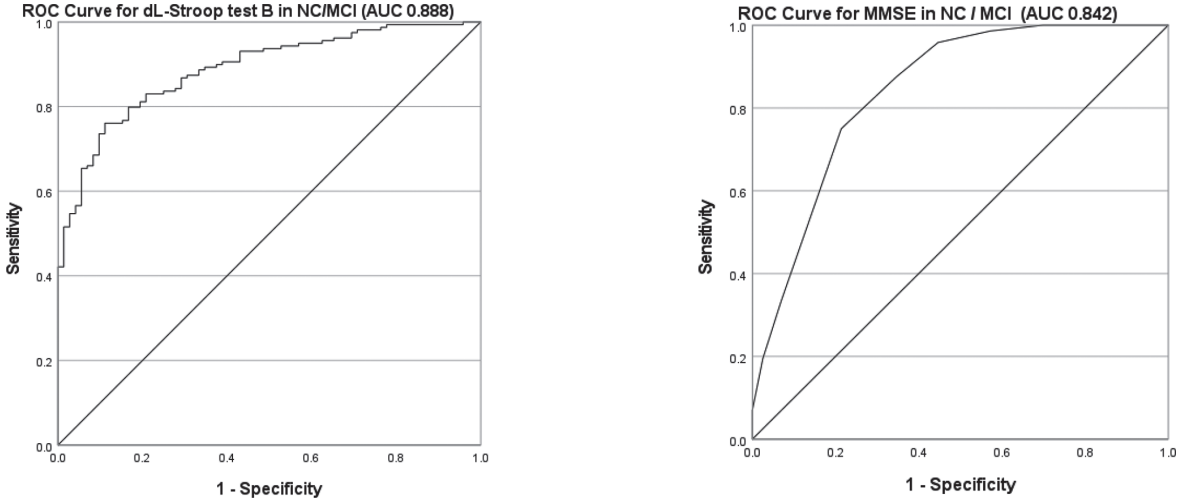


Figure 3.　ROC curves and AUCs for dL-Stroop B and MMSE　in NC/MCI differentiation

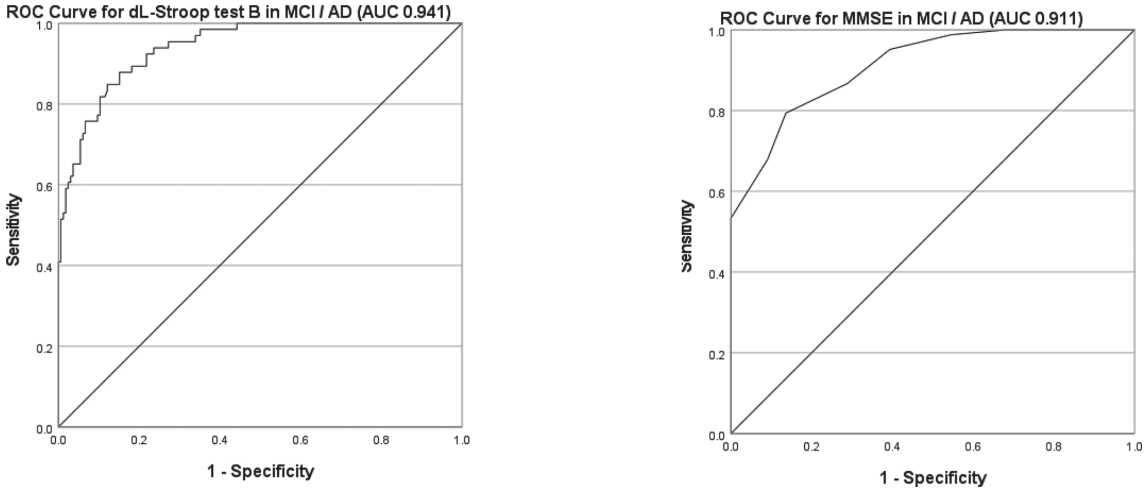


Figure 4. ROC curves and AUCs for dL-Stroop B and MMSE in MCI/AD differentiation

Table 2. Cut-off values of dL-Stroop B and MMSE with sensitivity, specificity, PPV, and NPV

MCI	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
dL-Stroop B	59.27 sec	76.73	90.14	94.57	62.75
MMSE	26/27 pt	66.04	88.89	92.92	54.24
AD	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
dL-Stroop B	70.02 sec	87.30	88.10	73.33	94.87
MMSE	24/25 pt	85.71	77.98	54.41	93.57

24/25 points for discriminating AD from MCI, with a sensitivity of 85.71%, specificity of 77.98%, PPV of 54.41%, and NPV of 93.57%.

The Stroop interference scores of dL-Stroop test B

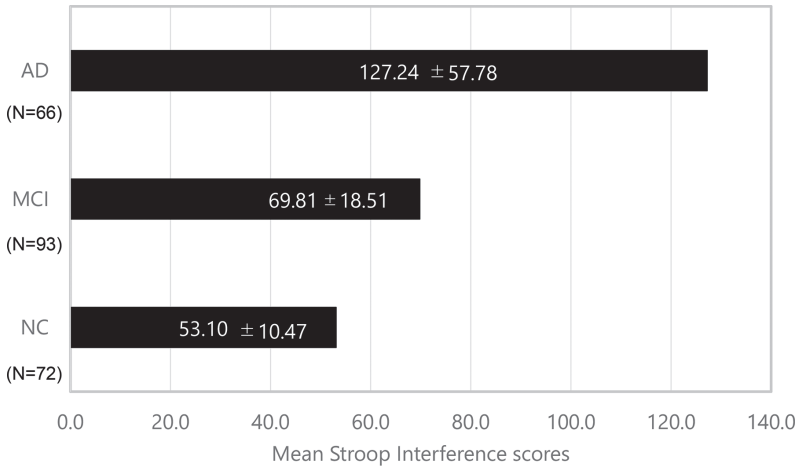
As shown in Figure 5, the interference score proposed for Stroop test in Perianez et al. (2021) was applied to the dL-Stroop test B.

Interference score = total time (sec) + ((2 × mean time per word) × number of errors)

The interference scores were calculated as 53.10 ± 10.50 for NC, 69.81 ± 18.51 for MCI, and 127.24 ± 57.78 for AD. A significant increase in interference scores was observed from MCI to AD, compared to the rise from NC to MCI. The ANOVAs confirmed that the differences in interference scores between the NC, MCI, and AD groups in the dL-Stroop test B were highly significant (p <0.001). Furthermore, post hoc tests including Tukey, Scheffe, and Bonferroni also indicated significant differences (p<0.05).

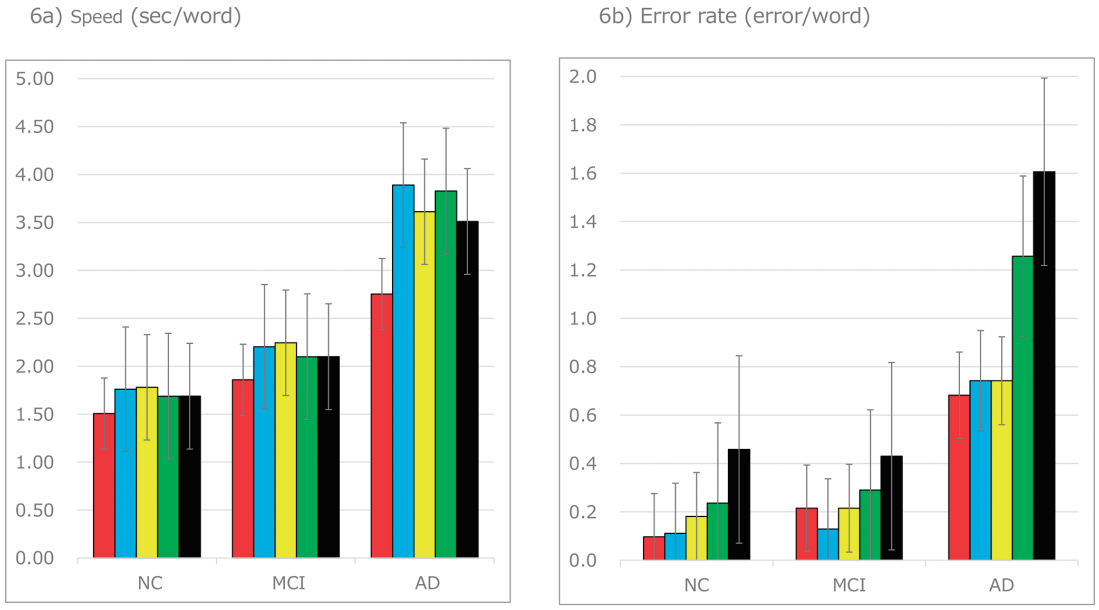
The speed and error rates in the dL-Stroop test B

The speed and error rate of naming colored Kanji characters were shown in Figure 6. In Figure 6a, the red was the fastest in naming color words in NC (1.507±0.34 sec), MCI (1.859±0.50 sec), and AD (2.753±1.02 sec) when compared to other colors. The slowest in naming color words was yellow for NC (1.78±0.41 sec) and MCI (2.24±0.55 sec), while for AD was blue (3.89±1.66 sec), followed by green (3.83±1.82 sec) and yellow (3.61±1.23). The speed of naming the color of Kanji characters between the NC, MCI, and AD was highly significant for all 5 color words between the groups by ANOVA analysis (p < 0.001), and the multiple comparisons in post hoc tests by Tukey and Bonferroni demonstrated good signifi-



The Stroop interference score is calculated by
total time (sec) x mean time per word) x number of errors (Stroop 1935)
ANOVAs (p <0.001)
post hoc tests by Tukey Scheffe,and Bonferroni (p <0.05)

Figure 5. Stroop Interference scores for dL-Stroop test B



ANOVAs (p <0.001)
post hoc tests by Tukey, Bonferroni (p<0.05)

ANOVAs (p <0.05)
post hoc tests by Tukey, Bonferroni (p<0.1)

Figure 6. Speed and Error rate of naming color words in dL-Stroop test B

cance (p <0.05).

The error rate of naming colored Kanji characters were shown in Figure 6b. The most frequent color error in all 3 groups of NC, MCI and AD was black in NC (0.458±0.08), MCI (0.430±0.09), and AD (1.606±0.13) followed by green in NC (0.236±0.24), MCI (0.290±0.33) and AD (1.257±0.83). The least error rate found in NC and AD was red in NC (0.097±0.04) and AD (0.682 ± 0.09), while in MCI was blue (0.129±0.04). The error rate for 5 colors were statistically significant between the NC, MCI, and AD with ANOVAs (p<0.05). However, post hoc tests by Tukey and Bonferroni were not significant due to small numbers of error in both NC and MCI.

4. Discussion

In summary, the dL-Stroop test B showed a higher correlation coefficient with the MoCA-J compared to the MMSE. In the ROC and AUC evaluations for NC/MCI differentiation, the dL-Stroop test B demonstrated higher sensitivity, specificity, PPV, and NPV than MMSE. In MCI/AD differentiation, the dL-Stroop test B showed higher specificity and PPV than MMSE. The diagnostic criteria in MMSE for MCI（24/25）and AD（26/27）were higher than MMSE-J（Sugiura M, 2018）. The dL-Stroop test B could be used to diagnose MCI and AD（Table 3）.

In a clinical setting, the MMSE is administered by a medical professional to assess brain functions such as orientation, attention, memory, language, and visuospatial skills. It typically takes about 10 minutes and produces scores ranging from 0 to 30 points. On the other hand, the dL-Stroop test B, conducted on an iPad, requires less than 2 minutes to complete. This test evaluates the ability to inhibit automatic cognitive processes in favor of focusing on the color of the ink rather than reading the word itself. As the test is performed and scored using iPad algorithms, it can be conducted by non-medical staff. The dL-Stroop test B assesses executive functions and cognitive control, which are crucial for everyday tasks such as decision-making, planning, and problem-solving.

The Stroop effect is an effective measure of memory loss, as the Stroop interference increases with time. The speed of naming incongruent colored Kanji characters tends to decrease with age, and this decline is further amplified in individuals with memory loss due to executive function impairments in color-to-word recognition in dementia patients. The Stroop interference measured in the dL-Stroop test B（Figure 5）showed a smaller increase from NC to MCI compared to MCI to AD groups. Dementia patients were more likely to make errors when naming color words in an incongruent manner, whereas MCI patients tended to make fewer mistakes. As a result, both the decrease in speed and increase in error rate were more noticeable in AD compared to MCI and NC groups. Unlike the MMSE and MoCA-J, which rely on the cumulative scores of separate brain domains reflecting functional deficits up to 30 points, the dL-Stroop test B focuses on the speed of conflict monitoring, working memory, and visual search of preserved vocabulary as measures of cognitive function decline.

It is interesting to observe the Stroop effects of colors in the dL-Stroop test. Firstly, the quickest color to be named in all three groups of NC, MCI, and AD was red. This could be due to its evolutionary significance. Red, often associated with danger, urgency, and key events across many cultures due to its connection with fire and blood, may stand out and hence be recognized more quickly. Additionally, the primary colors we perceive from a very young age are red, green, and blue. Furthermore, since the Tokyo Mainichi Shinbun newspaper published an article on March 13, 1930, identifying traffic light “green” as

Table 3. Diagnostic criteria of dL-Stroop test B for NC, MCI and AD

	NC	MCI	AD
dL-Stroop test B（sec）	≦60	60-69	≧70
Mean ±SD	49.42±8.43	62.59±12.66	102.17±32.70
95% CI for mean	47.44～51.42	59.98～65.12	94.13～110.21
median	48.78	61.49	97.73
MMSE（pt）	≧27	25-26	≦24
MOCA-J（pt）	≧26	19-25	≦18

"blue," our brains have been conditioned to perceive traffic light as red, yellow, and blue accordingly. As cognitive function declines in AD, the slowest color recognition was for blue, followed by green, while in NC and MCI it was yellow.

Secondly, the most errors in naming-colored words were observed with black in all three groups of NC, MCI, and AD. A possible interpretation is that there is a higher likelihood of misnaming when reading and naming the color word "black" as compared to other colors. Given that most of the text we encounter is in black, we automatically read the text printed in black. Consequently, we tend to name the word "black" even when it is colored differently. As cognitive function declines, we are more likely to misname the word "black". Furthermore, less education in elderly females may also contribute to an increased Stroop interference. Thus, colors themselves impose various stimuli on our sensory receptors, affecting speed and accuracy as we age, whether we are experiencing cognitive decline.

This paper thoroughly reviewed previous studies related to dementia, color evaluation, and other related papers to ensure the validity of the content. It is considered that face validity was secured as the naming color words in speed was found to be faster in the order of NC, MCI, and AD for all colors with Cronbach alpha between 0.590 to 0.834 as shown in Table 4. And through factor analysis on the naming color speed of the five colors, it was confirmed that they were composed of ensuring convergent validity. The results showed that the extracted factor accounted for 76.38% of the variance, and the factor loadings in the component matrix also showed high values of 0.8 or more (data not shown). Therefore, the dL-Stroop test had secured content validity, face validity, and convergent validity.

The limitation in this study was that not all participants were classified with CT/MRI and biomarkers for diagnosis. Although it may be useful for screening dementia, it cannot provide a diagnosis of the specific type of the disease.

Several pitfalls exist in the dL-Stroop test B. Firstly, its simplicity and quick speed can lead to overdiagnosis, particularly in individuals experiencing extreme stress or sleep deprivation, resulting in decreased concentration rather than true cognitive impairment. Secondly, the touch panel technique might cause mismatches in the iPad's response, especially for AD participants who lack experience and press the screen for too long. Finally, the repeated tests in the dL-Stroop test B can vary more than 10 seconds, compared to 3 seconds in the L-Stroop test.

MCI is a crucial stage of cognitive decline and represents a high-risk state for progression to AD. Previous studies have utilized the Stroop and Reverse-Stroop tests (Watanabe, 2013, 2015) in clinical assessments of attentional functions, but these were not feasible for MCI screening. Recent advancements introduce AI techniques through free conversation (Horigome et al., 2022) and with multiple drawing tasks (Kobayashi et al., 2022) for early detection of

Table 4. Reliability for Speed of naming color words in dL-Stroop test B

Color	NC				MCI				AD			
	mean	scale variance	total corre coefficient	Cronbach alpha	mean	scale variance	total corre coefficient	Cronbach alpha	mean	scale variance	total corre coefficient	Cronbach alpha
Red	6.916	1.774	0.453	0.716	8.648	4.264	0.568	0.746	14.841	26.557	0.628	0.832
Green	6.736	1.227	0.737	0.590	8.408	3.734	0.590	0.731	13.767	19.834	0.683	0.815
Yellow	6.643	1.564	0.557	0.677	8.262	4.151	0.549	0.747	13.982	23.944	0.726	0.804
Black	6.735	1.708	0.360	0.748	8.407	3.281	0.538	0.767	14.084	23.081	0.591	0.834
Blue	6.663	1.578	0.449	0.718	8.303	3.747	0.625	0.720	13.704	20.261	0.747	0.790

In addition, the extracted factor of the variance was 76.38% ; the factor loadings in the component matrix was 0.8 or more

cognitive decline. Cognitive function decline encompasses a broad spectrum, starting with subjective cognitive impairment, progressing to MCI, and eventually leads to Alzheimer's disease. This process can be influenced by multiple factors, and may potentially reverse through various aspects of lifestyles (Hashimoto et al, 2022). Future studies should aim to refine the mechanical techniques and protocols of the dL-Stroop test B to enhance its potential for early detection of AD.

5. Conclusions

For the first time, the dL-Stroop test B has been statistically validated in comparison with MMSE. The dL-Stroop test B is significantly more sensitive than MMSE in detecting MCI and early dementia. It is evaluated on a time-second scale rather than 30-point scale, covering a broad spectrum from 60-69 seconds, compared to a 25-26 points range for MCI in MMSE. Unlike other tests, the dL-Stroop Test B does not require a complex 10-minute administration process for naming colored words. Finally, the test can be administered by anyone interested in assessing cognitive decline. Thus, the dL-Stroop test B serves as a simple, stand-alone, easy, and quick screening tool for the early detection of MCI and AD.

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Comparison of the digital version B of L-Stroop test（dL-Stroop test B）with MMSE in validity and reliability for screening Mild Cognitive Impairment（MCI）

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OBJECTIVES : This study aimed to compare a 2-minute dL-Stroop test B with the MMSE for screening MCI.

DESIGN : Validation study.

SETTINGS : A community clinic.

PARTICIPANTS : Ninety-three patients who met MCI clinical criteria supported by MoCA-J were compared with 66 patients with Alzheimer's disease（AD）and 72 healthy normal controls（NC）.

MEASUREMENTS : The MoCA-J, dL-Stroop test B, and MMSE were conducted to participants to determine sensitivity and specificity for MCI and AD.

RESULTS : A negative correlation of −0.674 was found between the dL-Stroop test B and MMSE by the Spearman's Law. The cut-off value of MCI for dL-Stroop test B was 59.27 seconds, with a sensitivity of 76.73%, specificity of 90.14%. For the MMSE, the cut-off value was 26/27 points, with a sensitivity of 66.04%, specificity of 88.89%. Regarding AD, the cut-off value for the dL-Stroop test B was 70.02 seconds, with a sensitivity of 87.30%, specificity of 88.10%. The MMSE cut-off value was 24/25 points, with a sensitivity of 85.71%, specificity of 77.98%.

CONCLUSION : The range of MCI detection using the dL-Stroop test B was 60-69 seconds, while for the MMSE was 25-26 points. The dL-Stroop test B is a quick and simple screening tool better than the MMSE for detecting MCI and AD.

Keywords : L-Stroop test, The digital version B of L-Stroop test（dL-Stroop test B）, Mild Cognitive Impairment（MCI）, Alzheimer's disease（AD）

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