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<td>Author(s)</td>
<td>Nishiguchi, Shu; Yamada, Minoru; Fukutani, Naoto; Adachi, Daiki; Tashiro, Yuto; Hotta, Takayuki; Morino, Saori; Aoyama, Tomoki; Tsuboyama, Tadao</td>
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<tr>
<td>Citation</td>
<td>Journal of Clinical Gerontology and Geriatrics (2014), 6(1): 9-14</td>
</tr>
<tr>
<td>Issue Date</td>
<td>2014-10-06</td>
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<td>URL</td>
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Kyoto University
Spot the Difference for Cognitive Decline: A quick memory and attention test for screening cognitive decline

Authors
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Short title: Spot the Difference for Cognitive Decline

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Abstract

Background:
Dementia is currently one of the most common conditions in older adults and early detection of cognitive decline is crucial for identifying dementia. We developed a new type of short-term memory and attention test that uses a spot the difference task: Spot the Difference for Cognitive Decline (SDCD). The purpose of the present study was to examine the accuracy of the SDCD test for the identification of cognitive impairment in community-dwelling older adults.

Methods:
The participants were 443 Japanese community-dwelling older adults. The SDCD test uses two scenery pictures. Participants were instructed to memorize the details of the first picture for 30 seconds, after which they were asked to identify as many differences as possible between the first and second pictures, which were presented sequentially. The number of correct responses comprises the SDCD score (score: 0–10). The Mini-Mental State Examination (MMSE) and Scenery Picture Memory Test (SPMT) were used to measure the participants’ cognitive function. We used a receiver operating characteristic (ROC) analysis to examine the power of the SDCD test and identify the optimal cut-off value of the SDCD score.

Results:
Of the 443 participants, 30 (6.77%) individuals had some cognitive impairment based on the MMSE scores. Participants without cognitive impairment had higher SDCD scores than did those with cognitive impairment (p < 0.001). The SDCD score was significantly associated with the MMSE (r = 0.333) and SPMT (r = 0.402). The ROC curve for the identification of cognitive impairment had a comparatively high area under the curve (0.798) for the SDCD score with the cut-off value of 1/2 (with more than 1 being normal) (sensitivity: 70.5%; specificity: 80.0%).
Conclusions:
The present study found that the SDCD test could be an effective clinical tool for the identification of cognitive impairment in older adults.

Key Words: Short-term memory, attention, cognitive decline, screening test, community-dwelling older adults
1. Introduction

Dementia can drastically influence one’s daily life and is currently one of the most common conditions in older adults. Dementia affects 5–8% of the population over 65 years of age\(^1\) and up to 30% of the people aged 85 years and older\(^2\). Currently, the number of people with dementia is increasing. It has been estimated that approximately 48% of the people with Alzheimer's disease (AD), the most common form of dementia, live in Asia and this percentage is projected to grow to 59% by 2050\(^3\). Dementia and AD have been associated with mortality\(^4\); therefore, the prevention and early detection of cognitive decline is crucial.

The presence of cognitive decline increases the risk of progression to mild cognitive impairment (MCI) and AD\(^5, 6\). It is generally agreed that older adults with early AD, compared to healthy older adults, exhibit a greater decline in memory function\(^7\) and working memory\(^8\) than in other major domains of cognitive function. A central feature of AD is the decline in episodic memory\(^9\). Visual memory, which is included in episodic memory, is an important component of daily life. There are several well-established visual memory tests, such as the Benton Visual Retention Test\(^10\) and the Rey-Osterrieth Complex Figure Test (ROSF)\(^11\), that can be used to assess non-verbal visual memory. However, these tests are not reflective of situations and activities encountered in daily life, are time consuming, and have complex scoring systems.

Deficits in working memory functions (e.g., attention and executive function) caused by AD are thought to contribute to a range of significant problems such as impairments in performing everyday tasks (e.g., keeping track of conversations, walking while talking, and packing a bag). Thus, the attentional function would appear to be important for the early detection of cognitive decline, as the attentional function decreases with the progression of cognitive decline\(^12\).
Thus, we developed a new short-term visual memory and attention test called the Spot the Difference for Cognitive Decline (SDCD) test. The SDCD test is a brief and simple test that uses pictures of familiar-looking scenery. Examinees are asked to find the differences between two scenery pictures. This test can be used in clinical or community-based settings with large populations. In a previous study, it was reported that poor visual memory predicts the onset/progression of dementia\textsuperscript{13}. The spot the difference task has been used as a cognitive test in previous studies\textsuperscript{14-16}, although its usefulness for detecting cognitive impairment had not been described. These spot the difference tasks have often been used in memory function training for older adults with dementia in many countries, including Japan. However, the effects of this training have not been examined empirically. We hypothesized that the SDCD score would be associated with cognitive function, and this test would be able to identify community-dwelling older adults with cognitive impairment. The purpose of the present study, therefore, was to examine the accuracy of the SDCD test for the identification of cognitive impairment in community-dwelling older adults.

2. Methods

2.1. Participants

Participants for this study were recruited through the local press. Four hundred and forty-three Japanese participants aged 65 years and older (mean age, 73.1 ± 5.3 years) responded. We included only community-dwelling older adults who were independent in their activities of daily living. A screening interview was conducted to exclude participants with severe cardiac, pulmonary, or musculoskeletal disorders, as well as those using medications that affect attention (e.g., psychoactive drugs or drugs prescribed for sleep). Written informed consent was obtained from each participant in accordance with the guidelines of the Kyoto University Graduate School.
of Medicine and the Declaration of Helsinki, 1975. The study protocol was approved by the ethics committee of the Kyoto University Graduate School of Medicine.

2.2. SDCD Test Protocol

The SDCD test uses two scenery pictures (Figure 1 and 2) on A4 size paper. Figure 1 is called the “first picture” and Figure 2 is the “second picture.” There are 10 differences between the two pictures: the shape of the chimney smoke, shape of the doorknob, the height of the fountain, the shape of the mountain (seen between the house and fountain), the amount of fruit on the tree, the direction that the dog on the right is facing, the shape of the leftmost flower, the shape of the child’s mouth, the presence of a bird vs. a butterfly, and the presence of the father’s backpack. First, the examinees are instructed to memorize the details of the first picture for 30 seconds. They are also told that there are “some” differences between the first and second pictures. The examiners do not tell the participants that there are 10 differences in total. After showing the first picture, the examiner takes the first picture away and subsequently shows the participant the second picture. The examinees are then asked to name the differences they can find in the second picture, within 1 minute and without any hints. The number of correct answers are then counted to determine the SDCD score. If the examinees’ answers are close but not exactly correct (e.g., a flower type or increase in the fruit), these answers are marked as incorrect and not included in the SDCD score. In a sample of 21 participants, the SDCD had a high test-retest reliability [inter-trial correlation coefficient (ICC) = 0.801; p < 0.001] between the two measurements with a 1-week interval.

2.3. Cognitive Function
Participants’ cognitive function was measured by two neuropsychological tests: the Mini-Mental State Examination (MMSE)\(^{17}\) and the Scenery Picture Memory Test (SPMT)\(^{18}\).

Global cognitive function was assessed using the MMSE, a standard test in cognitive aging research for assessing mental status. Five areas of cognitive function—orientation, registration, attention and calculation, recall, and language—are tested. It has 11 questions in total and a maximum possible score of 30.

The SPMT is a simple memory test that assesses visual memory combined with verbal responses. This test uses a line drawing of a living room in a house on A4-size paper, depicting 23 objects that are commonly observed in daily life. The examinee is instructed to look at the picture for 1 minute and remember the items. After this encoding period, participants are given a distractor task (a brief forward digit-span test). Participants are then asked to recall the objects in the picture without a time limit. The recall of the items usually takes approximately 2 minutes. The number of items recalled is the score on the SPMT. Higher scores indicate better cognitive function.

2.4. Statistical Analysis

We divided the participants into two groups (a normal group and a cognitive impairment group) based on the cut-off score of the MMSE (23/24). The differences between these two groups were statistically analyzed using the unpaired t-test for continuous variables and the \(\chi^2\) test for categorical variables. The differences in the SPMT and SDCD scores were examined using an ANOVA. When a significant effect was found, the Tukey-Kramer post-hoc test was used to examine the differences. In addition, the criterion-related validity was determined by evaluating the correlation between the SDCD score and the two neuropsychological tests using Spearman’s
rank correlation coefficient. Following this, we performed a multiple logistic regression analysis to determine whether the SDCD score was associated with cognitive impairment independently. For this analysis, the two groups (i.e., the normal and cognitive impairment groups), were the dependent variables, and the SDCD score was the independent variable. We controlled for age, gender, body mass index (BMI), medications, and length of education. Furthermore, a receiver operating characteristic (ROC) analysis was used to examine the power of the SDCD score and determine the optimal cut-off value of the SDCD score as a state variable. The area under the curve (AUC), sensitivity, and specificity of the SDCD score were calculated based on the ROC curve. The cut-off value for the SDCD score was determined based on the optimal sensitivity and specificity. Consequently, we performed a univariate logistic regression analysis to determine the correlation between the SDCD and the 5 subtests of the MMSE (orientation, registration, attention and calculation, recall, and language). For this analysis, the groups determined according to the cut-off value of the SDCD were the dependent variables and each subtest of the MMSE was the independent variable.

Data were analyzed using SPSS Statistics for Windows, version 20.0 (SPSS Inc. Chicago, IL, USA). P-values < 0.05 were considered statistically significant.

3. Results

Of the 443 participants, 30 (6.77%) were identified as having cognitive impairment based on an MMSE cut-off score of 23/24. The demographic characteristics of the participants are shown in Table 1. The normal group had a higher SDCD score (2.21 ± 1.38) than did cognitive impairment group (0.77 ± 0.86) (p < 0.001). The normal group also had a higher SPMT score than did the cognitive impairment group (p < 0.001). The education level of the normal group was also higher than that of the
cognitive impairment group \( (p = 0.002) \). There were no significant differences in age, gender, BMI, or the use of medication between the two groups. The participants were reclassified into five groups according to their SDCD scores; the differences between the groups according to the MMSE and SPMT scores are shown in Figures 3 and 4. There were significant differences in the MMSE scores \( (F = 15.7, p < 0.001) \) of the five groups. There were also significant differences between the groups in the SPMT scores \( (F = 22.6, p < 0.001) \). The results of the post-hoc tests are shown in Figures 3 and 4. In addition, the SDCD scores were moderately and positively correlated with those of the MMSE \( (r = 0.333) \) and the SPMT \( (r = 0.402) \) \((p < 0.001)\). These analyses indicated that a higher SDCD score was associated with higher cognitive function. In the logistic regression analysis, the SDCD score was significantly associated with cognitive impairment after adjusting for age, gender, BMI, medications, and length of education \((\text{odds ratio [OR]}: 0.388, 95\% \text{ confidence interval [CI]}: 0.257-0.584, p < 0.001)\).

The ROC curve for the SDCD scores used for the identification of cognitive impairment was based on the MMSE cut-off score \( (23/24) \). The AUC was comparatively high for the SDCD scores \( (0.798, p < 0.001) \), and the cut-off value of the SDCD score was \( 1/2 \) (with more than 1 being considered normal) with a 70.5% sensitivity and 80.0% specificity. A univariate logistic regression analysis showed that there were significant correlations between the SDCD scores and the 4 subtests of the MMSE \( (p < 0.05) \), except for the registration subtest (refer to Table 2).

### 4. Discussion

We examined a new type of short-term memory and attention test, the SDCD, which made use of a spot the difference task to identify cognitive impairment. In the present study, we showed that the SDCD test is a very quick and reliable screening tool for
the identification of cognitive impairment in community-dwelling older adults.

The SDCD test is moderately and positively correlated with global cognitive and memory functions. The SDCD test includes a “memory” phase and a “recall and name the differences” phase. These phases require not just memory functions but also other cognitive functions, such as attention. Some studies in the past have used similar spot the difference tasks as cognitive tests\textsuperscript{14, 15} and only one previous study\textsuperscript{16} has investigated brain activation in a test using a spot the difference task. Although the above-mentioned test did not include a memory phase (like in the SDCD test), the results indicated that there was an activation of brain areas relating to visual information and attention while carrying out the task. Our results indicated that the SDCD was associated with most of the subtests of the MMSE. Thus, the SDCD test appears to be associated not only with attention and memory but also with global cognitive function. We need to minutely assess and investigate other cognitive functions (e.g., executive function and processing speed) and their association with the SDCD test in future studies.

The ROC curve for the SDCD score indicated that the SDCD test identified cognitive impairment with a high degree of accuracy. Previous studies have reported that some picture-based memory tests can reliably detect dementia\textsuperscript{18-20}. These studies support the results of the present study. Moreover, the SDCD test is able to detect dementia in less time compared to other tests previously studied. Picture-based memory tests have some advantages compared to verbal-based memory tests. First, pictures are remembered better than words, a phenomenon known as the “picture superiority effect”\textsuperscript{21}. Previous studies showed that superiority of memory for pictorial material was often applied as a mnemonic aid for older adults\textsuperscript{22, 23}. Second, picture-based memory tests are not limited by the subject’s level of education. Some verbal-based memory tests cannot be used with a population that has a low level of education\textsuperscript{19}. 
Most verbal-based screening measures have not been validated in samples with low education levels or illiterate individuals\textsuperscript{24, 25}, and it has been shown in previous studies that a low level of education can result in cognitively unimpaired people screening positive for dementia\textsuperscript{24}. Furthermore, the SDCD test takes only approximately 2 minutes to assess short-term memory and attention functioning, in addition to its above-mentioned merits. In the present study, the MMSE took approximately 10 minutes and the SPMT took approximately 5 minutes for participants to complete. The SDCD test appears as an easy game for subjects, because of the simplicity of the differences, but it is actually quite a difficult cognitive task. It is possible that this characteristic makes the SDCD test fun for participants to complete and makes its widespread use possible. Thus, we believe the SDCD test can be used to identify cognitive impairment in older adults in a clinical or community-based setting.

The present study has several limitations. First, although we assessed global cognitive and memory functions with the MMSE and the SPMT, other cognitive functions, such as executive functions and processing speed, were not assessed in this study. We need to assess these cognitive functions and investigate their association with the SDCD test in future studies. Second, participants in the present study were community-dwelling older adults who had not received a diagnosis of dementia or MCI, and we did not confirm the test-retest reliability for older adults with dementia or MCI. In the future, we need to include older adults diagnosed with dementia to ascertain whether the SDCD test can discriminate between normal cognitive function and MCI in older adults.

5. Conclusions
We developed a new type of short-term memory and attention test that uses a spot the difference task for the identification of cognitive impairment. The present study indicates that the SDCD test can be an effective clinical tool for the identification of cognitive impairment in older adults.

Acknowledgements

We would like to thank the volunteers for participating in this study. The authors acknowledge Masahiko Yonemitsu for drawing the pictures used in this study.

Conflict of Interest

The authors declare no conflicts of interest.

References


Figure Legends

1 Figure 1. The first picture used in the Spot the Difference for Cognitive Decline test. The examinees were instructed to memorize the details of the picture, which was presented for 30 seconds.

2 Figure 2. The second picture in the Spot the Difference for Cognitive Decline test. This picture includes 10 differences when compared to the first picture (Figure 1). After studying the first picture for 30 seconds, the examinees were asked to name as many of the differences between the first and second pictures as they could within 1 minute.

3 Figure 3. Comparison of the MMSE scores between the groups formed by the SDCD scores. There were significant differences in the MMSE scores across the five groups (F = 15.7, p < 0.001).

*: Significant difference from Group 0
#: Significant difference from Group 1
$: Significant difference from Group 2

4 Figure 4. Comparison of the SPMT between the groups formed by the SDCD scores. There were significant differences in the MMSE scores across the groups (F = 22.6, p < 0.001).

*: Significant difference from Group 0
#: Significant difference from Group 1
$: Significant difference from Group 2
†: Significant difference from Group 3
Table 1. Characteristics of participants with and without cognitive impairment

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Cognitive impairment</th>
<th>p-value</th>
</tr>
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<tr>
<td></td>
<td>(n = 413, MMSE ≥ 24, 27.4 ± 2.0)</td>
<td>(n = 30, MMSE &lt; 24, 22.4 ± 1.1)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>72.9 ± 5.3</td>
<td>74.4 ± 5.3</td>
<td>0.160</td>
</tr>
<tr>
<td>Female (n (%))</td>
<td>269 (65.3%)</td>
<td>20 (66.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.7 ± 3.1</td>
<td>22.2 ± 2.8</td>
<td>0.384</td>
</tr>
<tr>
<td>Number of medications taken (n)</td>
<td>2.53 ± 2.59</td>
<td>2.48 ± 2.46</td>
<td>0.237</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>0.002**</td>
</tr>
<tr>
<td>Less than 6 years (n (%))</td>
<td>3 (0.7%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6–9 years (n (%))</td>
<td>98 (23.7%)</td>
<td>17 (56.7%)</td>
<td></td>
</tr>
<tr>
<td>10–12 years (n (%))</td>
<td>212 (51.3%)</td>
<td>10 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>More than 12 years (n (%))</td>
<td>100 (24.2%)</td>
<td>3 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>SDCD</td>
<td>2.21 ± 1.38</td>
<td>0.77 ± 0.86</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SPMT</td>
<td>13.8 ± 3.5</td>
<td>10.1 ± 2.8</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

Note:

Normal and cognitive impairment groups were defined according to the MMSE cut-off score of 23/24.

MMSE = Mini-Mental State Examination; BMI = body mass index; SDCD = Spot the Difference for Cognitive Decline; SPMT = Scenery Picture Memory Test

* p < 0.05.  ** p < 0.01
Table 2. Correlation between SDCD score and subtests of MMSE

<table>
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<tr>
<th>Subtests (Total score)</th>
<th>Subtests score</th>
<th>SDCD score &lt; 2 (n = 146)</th>
<th>OR [95%CI]</th>
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</thead>
<tbody>
<tr>
<td>Orientation (10)</td>
<td>8 or less</td>
<td>20 (13.7%)</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>30 (20.5%)</td>
<td>0.26 [0.11-0.62]**</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>96 (65.8%)</td>
<td>0.21 [0.10-0.46]**</td>
</tr>
<tr>
<td>Registration (3)</td>
<td>2 or less</td>
<td>4 (2.7%)</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>142 (97.3%)</td>
<td>0.61 [0.16-2.30]</td>
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<tr>
<td>Attention and calculation (5)</td>
<td>2 or less</td>
<td>69 (47.3%)</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10 (6.8%)</td>
<td>1.10 [0.47-2.59]</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>18 (12.3%)</td>
<td>1.19 [0.61-2.34]</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>49 (33.6%)</td>
<td>0.57 [0.36-0.88]*</td>
</tr>
<tr>
<td>Recall (3)</td>
<td>1 or less</td>
<td>22 (15.1%)</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>51 (34.9%)</td>
<td>0.21 [0.09-0.50]**</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>73 (50.0%)</td>
<td>0.13 [0.06-0.31]**</td>
</tr>
<tr>
<td>Language (9)</td>
<td>7 or less</td>
<td>14 (9.6%)</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>38 (26.0%)</td>
<td>0.18 [0.06-0.59]**</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>94 (64.4%)</td>
<td>0.12 [0.04-0.36]**</td>
</tr>
</tbody>
</table>

Note:

For each univariate logistic regression analysis, SDCD scores < 2 or ≥2 were the dependent variables and each subtest of the MMSE was the independent variable.

* p < 0.05.  ** p < 0.01
Figure 1. The first picture used in the Spot the Difference for Cognitive Decline test. The examinees were instructed to memorize the details of the picture, which was presented for 30 seconds.
Figure 2. The second picture in the Spot the Difference for Cognitive Decline test. This picture has 10 differences compared to the first picture (Figure 1). After studying the first picture for 30 seconds, the examinees were asked to name as many of the differences between the first and second pictures as possible within 1 minute.
Figure 3. Comparison of the MMSE scores between the groups formed by the SDCD scores. There were significant differences in the MMSE scores across the five groups ($F = 15.7, p < 0.001$).

*: Significant difference from Group 0

#: Significant difference from Group 1

$: Significant difference from Group 2
Figure 4. Comparison of SPMT between the groups formed by the SDCD scores. There were significant differences in the MMSE scores across the groups ($F = 22.6$, $p < 0.001$).

*: Significant difference from Group 0
#
#: Significant difference from Group 1
$: Significant difference from Group 2
†: Significant difference from Group 3