Clock drawing test to screen for dementia in parkinsonian patients with low educational backgrounds

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Abstract

Objectives: This study was aimed to assess the usefulness of the quantitative assessment of clock drawing test (CDT) combined with the Mini-Mental State Examination (MMSE) compared to that of the Montreal Cognitive Assessment (MoCA) or the MMSE alone for screening of dementia in Parkinson disease (PD) in patients with a low educational level. Methods: A representative sample of 91 PD patients was administered MMSE, MoCA and CDT. The discriminative validity of the MMSE, MoCA, and a MMSE+CDT combination for dementia screening was determined by estimating the sensitivity and specificity of each test and by testing integrated discrimination improvement (IDI). Results: The mean age and educational years were 69.0 (years) and 7.3 in the study population. The best screening cut-off points for the MMSE, MoCA, and MMSE+CDT were 25/26, 21/22 and 41/42. In a group of patients with educational years ≤6, the sensitivity and specificity of the MMSE+CDT were 94.4 and 54.8 with area under the curve (AUC) 0.806 (95% confidence interval, 0.686-0.925), whereas those of the MMSE and MoCA were 94.4 and 45.2 with AUC 0.767 (0.635-0.899), and 83.3 and 35.5 with AUC 0.773 (0.634-0.913), respectively. Compared with the MMSE alone, the IDI of the MMSE+CDT showed a significant improvement in the low-educational level group whereas the IDI of the MoCA did not show such an improvement in this group. Conclusions: In low educational level population, a combination of the quantitative CDT and MMSE is a good screening tool for dementia in PD.

INTRODUCTION

The cumulative prevalence of cognitive impairment in Parkinson disease (PD) has been reported to be 80–90%.1,2 Dementia is associated with psychosis, nursing home admission, and increased mortality risk in PD3,4, and has a major impact on the quality of life of both patients and their caregivers.5 Even though a low educational level is an important risk factor for dementia in PD, an appropriate screening test for dementia in PD patients with a low educational level has not been reported. This is of particular importance in Korea as many Korean elderly were deprived of educational opportunities because of conditions during the colonial rule of Japan and the Korean War. The Mini-Mental State Examination (MMSE)6 primarily assesses memory domain, thus it is inadequate for early detection of dementia in PD patients because cognitive impairment usually begins in frontal and executive functions in PD.7,8 In contrast, the Montreal Cognitive Assessment (MoCA) includes assessments of frontal/executive functions, higher-level language abilities, and complex visuospatial function. Some reports have indicated that the MoCA is a better cognitive screening tool than the MMSE in PD.7,9 However, the usefulness of the MoCA in subjects with a low educational level is questionable because MoCA may be difficult to implement, and its diagnostic value is inferior to that of the MMSE in low educational level elderly populations.7,10 Aneffect of educational level on MoCA score was observed in the Korean MoCA (MoCA-K) validation study.10 The mean educational level in the original MoCA study

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population was 13.3 years\(^7\), whereas that in the MoCA-K study was 8.3 years.\(^{10}\) The difference in optimal cut-off values for dementia screening between these two studies was noticeable (25/26 vs. 22/23, respectively).

The clock drawing test (CDT) can be performed easily and administered quickly, typically taking less than 2 min in an elderly subject.\(^{11,12}\) Moreover, the CDT is reported to be unaffected by cultural differences, environmental backgrounds, and educational level.\(^{11}\) Motor programming, executive function, visuospatial ability, and visual memory can be evaluated by this single test.\(^{13-15}\) Accordingly, if the CDT is combined with the MMSE, it could complement the low specificity of the MMSE in PD patients with low educational backgrounds. Therefore, we assessed the usefulness of the MMSE+CDT combination, compared to that of the MoCA and the MMSE alone, to screen for dementia in PD patients grouped by educational level.

**METHODS**

**Study subjects**

Consecutive 91 PD patients who visited a movement disorders clinic between January 2011 and December 2011 were enrolled in this study. Subjects were enrolled if they were diagnosed with PD\(^{16}\), and had been followed-up for at least six months. Exclusion criteria were subjects with a typical parkinsonism (dementia with Lewy bodies, corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy), secondary parkinsonism, diseases other than PD affecting the brain, medical conditions that could affect cognitive function such as mental illness (depression, schizophrenia), under psychiatric care, structural brain lesions relating to stroke, brain tumors, encephalitis, and serious medical illnesses including thyroid, kidney and liver diseases. To exclude pseudo-dementia such as depression in PD, all subjects were assessed by geriatric depression scale. Clinical data including gender, age, educational level, PD duration, and Hoehn & Yahr (HY) stage were collected for each subject. Four of the 91 subjects did not complete the three screening tests; therefore, data for 87 patients was analyzed. Study protocol was approved by the Institutional Review Board of the SNU Boramae Hospital, and informed consent was obtained from all participating subjects.

**Cognitive screening tests**

Blinded trained research staff (HYJ and TJK) administered three cognitive screening tests to each subject. The Korean MMSE (K-MMSE), the CDT, and the MoCA-K were sequentially administered using previously reported protocols.\(^{6,10,17,18}\) In the MoCA-K, the phonemic fluency task was replaced with a semantic fluency task, because phonemic fluency is more influenced by educational level than semantic fluency.\(^{19}\) The CDT method consists of the “command” and “copy” conditions. In the command condition, subjects draw a clock face, add all numbers to the face, and set the hands for 10 past 11. After subjects finished the command condition, the copy condition was administered. In the copy condition, subjects were instructed to copy, as accurately as possible, a clock face from a model in which the hands were set for 10 past 11. In this study, scoring of the CDT results followed the rating criteria proposed by Rouleau et al.\(^{20}\) That quantitative rating method has a 10-point scoring system for each condition.\(^{20}\) Errors in the CDT are separately identified in both command and copy conditions for each of six error categories: 1) clock size, 2) graphic difficulties, 3) stimulus-bound response, 4) conceptual deficit, 5) spatial and/or planning deficit, and 6) perseveration. Spatial and/or planning deficit errors were further evaluated by assessing five aspects: 1) neglect of the left hemisphere, 2) deficit in planning, 3) deficit in spatial layout of numbers, 4) numbers written outside the clock face, and 5) numbers written counterclockwise.

Three screening tests are iterative tasks (e.g. orientation in the K-MMSE and in the MoCA-K, CDT command condition in the MoCA-K). Thus, to minimize the putative learning effects of each test and with consideration of possible cognitive fluctuation, the K-MMSE+CDT and the MoCA-K were performed at the same time of different days within a month. Results of the CDT were independently analyzed by two different neurologists who were blind to the patient’s diagnosis and the score assigned by the other neurologist. The CDT command and copy conditions in the quantitative analysis were each given 10 points, resulting in a total score for the K-MMSE+CDT combination range of 0 to 50 points.

**Defining the presence of dementia**

The neurologists who did not know about the results of the cognitive tests, classified whether the subjects had dementia or not.
The presence of dementia in our subjects was defined according to the diagnostic criteria for probable PD dementia. Briefly, subjects who had core features (PD and a dementia syndrome with insidious onset and slow progression) and cognitive deficits in at least two of the four cognitive domains (i.e., attention, executive function, visuo-spatial function, and memory), which can affect daily living activities, were diagnosed as having PD dementia. The presence of dementia was determined by neurologists who were unaware of the score of each screening tests. The CDT score was not used for defining the presence of dementia.

Data analysis

Intergroup comparisons were undertaken by using a Pearson χ² test and a Fisher’s exact test for categorical variables, or an independent-sample t-test and Mann-Whitney test for continuous variables. The reliability between two raters was assessed using intraclass correlation coefficient (ICC).

The sensitivity and specificity of the three tests (K-MMSE, MoCA-K and K-MMSE+CDT) were estimated. Receiver operating characteristics (ROC) along with area under the curve (AUC, 95% confidence interval) were plotted, and the positive predictive value (PPV) and negative predictive value (NPV) were derived for each test. The optimal screening cut-off point was defined as the lowest value that achieved >80% sensitivity and >80% NPV, whereas the optimal diagnostic cut-off point was defined as the highest value that achieved >80% specificity and >80% PPV.

Subgroup analysis was used to assess the effectiveness of the screening tests according to the subgroup’s educational level: a low-educational level group (LOW, ≤6 years of education) and high-educational level group (HIGH, >6 years of education). Based on the previously derived optimal screening cut-off point, the sensitivity, specificity, PPV, and NPV of the K-MMSE, MoCA-K, and K-MMSE+CDT tests were determined for each subgroup. ROC curve with AUC was obtained for each subgroup, and the effects of improved prediction of dementia were assessed using the integrated discrimination improvement (IDI). Finally, errors in the subject’s CDT results were compared between each subgroup. All statistical analyses were performed by using SPSS 21.0 version for Windows (SPSS Inc., Chicago, IL, USA), and R version 3.2.1 (http://www.r-project.org), and a p < 0.05 was considered significant.

RESULTS

Subject characteristics

The characteristics of the 87 subjects are summarized in Table 1. One third (n = 29) of the subjects met the diagnostic criteria for probable PD dementia. Seven (8.0%) subjects had already on anti-dementia medication. The dementia group was significantly older than the non-dementia group; however, PD duration, HY stage, and education years were not significantly different between the two groups. Patients’ age, duration of PD, and HY stages were not different between the HIGH and LOW groups. The ICC for the reliability of the CDT scoring was 0.994 (p < 0.001) for the command condition and 0.981 (p < 0.001) for the copy condition.

Sensitivity and specificity of cognitive tests

The neuropsychometric properties of the study population screened for the detection of dementia are shown in Table 2. Regarding the K-MMSE results, the optimal screening cut-off point for probable PD dementia was 25/26. The optimal diagnostic cut-off point could not be calculated because no value achieved a >80% PPV. The MoCA-K results indicated an optimal screening cut-off point of 21/22 and an optimal diagnostic cut-off point of 13/14. The K-MMSE+CDT combination produced optimal screening and diagnostic cut-off points of 41/42 and 30/31, respectively (Table 2). In the total study population, the ROC AUC (95% confidence interval) were 0.790 (0.690–0.891) for the K-MMSE, and 0.814 (0.723–0.905) for the MoCA-K, and 0.808 (0.711–0.904) for the K-MMSE+CDT results.

Subgroup analysis according to the educational level

The educational level subgroup analyses were based on the obtained optimal screening cut-off points for the three screening tests. In the LOW group, the overall discriminative validity was highest for the K-MMSE+CDT compared with the MoCA-K and MMSE (Table 3). When we analyzed the IDI, the IDI of the K-MMSE+CDT combination showed a significant improvement than that of the K-MMSE in the LOW group (p = 0.040) whereas the IDI of the K-MoCA were not different from that of the K-MMSE in this group.

On the contrary, in the HIGH group, the overall best discriminative validity was seen for the
Table 1: Characteristics of the subjects included in the analysis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients n=87</th>
<th>Nondemented n=58 (66.7%)</th>
<th>Demented n=29 (33.3%)</th>
<th>P-value</th>
<th>LOW n=49 (56.3%)</th>
<th>HIGH n=38 (43.7%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, (range)</td>
<td>69.0 (41-84)</td>
<td>67.2 (41-84)</td>
<td>72.6 (57-84)</td>
<td>0.002</td>
<td>70.3 (54-84)</td>
<td>67.4 (41-84)</td>
<td>0.112</td>
</tr>
<tr>
<td>Sex, n, (% male)</td>
<td>42 (48.3%)</td>
<td>26 (44.8%)</td>
<td>16 (55.1%)</td>
<td>0.363</td>
<td>15 (30.6%)</td>
<td>27 (71.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education, y, (range)</td>
<td>7.3 (0-16)</td>
<td>7.6 (0-16)</td>
<td>6.7 (0-16)</td>
<td>0.463</td>
<td>3.7 (0-6)</td>
<td>12.0 (9-16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PD duration, y, (range)</td>
<td>4.2 (1-15)</td>
<td>4.0 (1-15)</td>
<td>4.7 (1-15)</td>
<td>0.166</td>
<td>4.0 (1-14)</td>
<td>4.5 (1-15)</td>
<td>0.445</td>
</tr>
<tr>
<td>Dementia, n, (% demented)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>18 (36.7%)</td>
<td>11 (28.9%)</td>
<td>0.445</td>
</tr>
<tr>
<td>HY stage, n, (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11 (12.6%)</td>
<td>7 (12.1%)</td>
<td>4 (13.8%)</td>
<td></td>
<td>4 (8.2%)</td>
<td>7 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>8 (9.2%)</td>
<td>4 (6.9%)</td>
<td>4 (13.8%)</td>
<td></td>
<td>7 (14.3%)</td>
<td>1 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>40 (46.0%)</td>
<td>26 (44.8%)</td>
<td>14 (48.3%)</td>
<td>0.246</td>
<td>23 (46.9%)</td>
<td>17 (44.7%)</td>
<td>0.235</td>
</tr>
<tr>
<td>2.5</td>
<td>9 (10.3%)</td>
<td>4 (6.9%)</td>
<td>5 (17.2%)</td>
<td></td>
<td>6 (12.2%)</td>
<td>3 (7.9%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14 (16.1%)</td>
<td>12 (20.7%)</td>
<td>2 (6.9%)</td>
<td></td>
<td>7 (14.3%)</td>
<td>7 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4 (4.6%)</td>
<td>4 (6.9%)</td>
<td>-</td>
<td></td>
<td>1 (2.0%)</td>
<td>3 (7.9%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1 (1.1%)</td>
<td>1 (1.7%)</td>
<td>-</td>
<td></td>
<td>1 (2.0%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>K-MMSE score, (range)</td>
<td>24.2 (14-30)</td>
<td>25.5 (15-30)</td>
<td>21.6 (14-29)</td>
<td>&lt;0.001</td>
<td>23.2 (14-29)</td>
<td>25.6 (17-30)</td>
<td>0.003</td>
</tr>
<tr>
<td>MoCA-K score, (range)</td>
<td>19.4 (7-30)</td>
<td>21.7 (7-30)</td>
<td>14.9 (7-23)</td>
<td>&lt;0.001</td>
<td>17.6 (7-30)</td>
<td>21.7 (8-29)</td>
<td>0.001</td>
</tr>
<tr>
<td>CDT-command score (range)</td>
<td>7.5 (0-10)</td>
<td>8.3 (0-10)</td>
<td>6.1 (0-10)</td>
<td>&lt;0.001</td>
<td>6.8 (0-10)</td>
<td>8.5 (4-10)</td>
<td>0.003</td>
</tr>
<tr>
<td>CDT-copy score (range)</td>
<td>7.8 (0-10)</td>
<td>8.7 (1-10)</td>
<td>6.2 (0-10)</td>
<td>&lt;0.001</td>
<td>7.1 (0-10)</td>
<td>8.7 (3-10)</td>
<td>0.003</td>
</tr>
<tr>
<td>K-MMSE+CDT score (range)</td>
<td>39.6 (14-50)</td>
<td>42.5 (16-50)</td>
<td>33.9 (14-48)</td>
<td>&lt;0.001</td>
<td>37.1 (14-49)</td>
<td>42.8 (24-50)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Mann-Whitney test, †independent-sample t-test, ‡Pearson χ² test, ††Fisher’s exact test
LOW = low-educational level group; HIGH = high-educational level group; PD = Parkinson disease; HY = Hoehn & Yahr; K-MMSE = Korean Mini-Mental State Examination; MoCA-K = Korean version of Montreal Cognitive Assessment; CDT = clock drawing test
Table 2: Discriminant validity of the K-MMSE, MoCA-K and K-MMSE+CDT for dementia screening in Parkinson disease patients

<table>
<thead>
<tr>
<th></th>
<th>K-MMSE</th>
<th>MoCA-K</th>
<th>K-MMSE+CDT (all)</th>
<th>K-MMSE+CDT (command)</th>
<th>K-MMSE+CDT (copy)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cut-off</strong></td>
<td>18/19</td>
<td>13/14</td>
<td>30/31</td>
<td>24/25</td>
<td>24/25</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>17.2</td>
<td>44.8</td>
<td>27.6</td>
<td>27.6</td>
<td>27.6</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>96.6</td>
<td>94.8</td>
<td>96.6</td>
<td>94.8</td>
<td>96.6</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>71.4</td>
<td>81.3</td>
<td>77.5</td>
<td>72.7</td>
<td>72.7</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>70.0</td>
<td>81.3</td>
<td>80.0</td>
<td>72.4</td>
<td>72.7</td>
</tr>
<tr>
<td><strong>AUC (95% CI)</strong></td>
<td>0.790 (0.690-0.891)</td>
<td>0.814 (0.723-0.905)</td>
<td>0.808 (0.711-0.904)</td>
<td>0.797 (0.696-0.899)</td>
<td>0.822 (0.729-0.914)</td>
</tr>
</tbody>
</table>

*aPoint of maximum combined sensitivity and specificity.
bOptimal screening cut-off point.
cOptimal diagnostic cut-off point.

PPV = positive predictive value; NPV = negative predictive value; AUC = area under the curve; CI = confidence interval.
The results of this study reveal that the K-MMSE+CDT combination has good overall discriminant validity for PD dementia screening in a low educated Korean population. It has been raised that the CDT can supplement the MMSE for dementia screening in poorly educated non-English speakers.\textsuperscript{12,24} The present study has an advantage over previous studies in that three brief screening tests were simultaneously compared according to educational level in Asian PD population.

Patients’ age, severity of PD, and frequency of dementia were not different significantly between the HIGH and LOW groups. However, in our LOW group patients, the MoCA-K tended to show better performance compared with the other two screening tests (Table 3). The IDI of the MoCA-K was significantly higher than that of the K-MMSE in the HIGH group (\( p = 0.017 \)).

### DISCUSSION

The results of this study reveal that the K-MMSE+CDT combination has good overall discriminant validity for PD dementia screening in a low educated Korean population. It has been raised that the CDT can supplement the MMSE for dementia screening in poorly educated non-English speakers.\textsuperscript{12,24} The present study has an advantage over previous studies in that three brief screening tests were simultaneously compared according to educational level in Asian PD population.

In our study, we detected significant correlations between CDT scores and all items (except orientation) in the MoCA-K (correlation coefficients ranging from 0.4 to 0.65) and observed a complementary effect of the K-MMSE+CDT combination in the LOW group. Unlike the K-MMSE+CDT, the MoCA-K did not show such a complementary effect in the LOW group. However, in the HIGH group, the discriminative validity of the MoCA-K was superior to that of the K-MMSE, which was similar to the previous reports.\textsuperscript{19} Patients’ age, severity of PD, and frequency of dementia were not different significantly between the HIGH and LOW groups. However, in our LOW group patients, the MoCA-K tended to show better performance.
over estimate cognitive impairment. The optimal cut-off point of the MoCA-K in the present study was 21/22, similar to that reported in a previous MoCA-K validation study.10 Our cut-off was 5 points lower than the original MoCA cut-off of 26/27.18 The mean educational years in the present and the original MoCA study were 7.3 and 13.3, respectively. As the MoCA requires completion of
complex executive tasks, the cognitive function evaluated in the MoCA has been correlated with the subject’s educational level.25,26 The usefulness of the K-MMSE+CDT combination compared with the MoCA-K in the LOW group may be due to complexity of the MoCA-K test.

Our analysis of CDT errors indicates that such an analysis can detect spatial and/or planning deficits in PD patients. This result is consistent with previous reports indicating that, compared to Alzheimer’s disease (AD) patients, PD patients can make more planning errors, although the global scores of the two patient groups are not significantly different.27 Though other types of errors showed a tendency to decrease in copy condition, spatial and/or planning deficit errors were still higher in both the command and copy condition in our study. A high prevalence of planning errors was also detected in vascular dementia (VD)14, dementia with Lewy bodies, and Huntington’s disease (HD) patients20, which suggests more subcortical involvement than cortical involvement in these disorders. Another longitudinal study of CDT and MMSE reported that, at every follow-up evaluation, spatial and/or planning deficits were the most frequent errors in PD dementia, whereas conceptual deficits were most frequent in AD.28 In addition, impairment of clock-face drawing, specifically the production of postmeridian digits, has been shown to appear earlier in relation to cognitive status in PD than in AD patients, suggesting a disturbance of cognitive switching and impairment inattentional set shifting.29 Graphic difficulty was common in our PD patients regardless of educational level and dementia status, thus suggesting that this difficulty is more likely related to a parkinsonian motor symptom than a cognitive symptom. In summary, the types and frequencies of CDT errors observed in our PD patients are similar to those reported in HD and VD patients, suggesting that frontal/executive and visuospatial impairments have a role in the poor clock drawing results in PD patients.

There were no differences in the type or frequency of CDT errors detected between the dementia group and non-dementia groups, and it seemed that the non-demented subjects made more mistakes under the certain conditions. This might be a result from a small sample size of our study. However, more likely because the CDT error was counted as ‘absent’ in this study when the subjects could not draw the clock, there could be a bias in the qualitative CDT in the dementia group. The qualitative CDT analysis without quantitative CDT score may be insufficient to detect dementia in PD patients.

The CDT is reported to be sufficiently sensitive to detect mild cognitive impairment (MCI) in PD patients with >6 years of education.30,31 However, whether CDT errors have discriminative validity in detecting MCI in PD subjects with a low educational background, needs to be investigated further because the current study was only designed to compare the validities of three brief screening test approaches to dementia screening.

The present study results should be interpreted with caution. The results may not be generalizable because the enrolled patients were limited to ethnic Koreans, and all were recruited from a single movement disorders clinic. The majority of patients had mild to moderate PD; thus, there were few subjects displaying severe motor disabilities. Additionally, we did not have a matched non-PD control group; thus, we were unable to examine whether the CDT errors were specific to PD or were common in a low educational level population. In addition, the sample size was rather small; however this was expected as the study subjects were recruited as a representative sample of low educational level Koreans with PD. To confirm the usefulness of a MMSE+CDT combination, and to reveal the clinical significance of CDT errors in PD, further studies involving a larger number of subjects and incorporating detailed neuropsychological evaluations are warranted.

DISCLOSURE

Conflict of interest: none

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