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*Original Article*

# Assessment of finger movement characteristics in dementia patients using a magnetic sensing finger-tap device

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**ABSTRACT**

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**Objective:** Differences in finger movement characteristics during finger-tapping movements among Alzheimer's Disease (AD) patients, Mild Cognitive Impairment (MCI) patients, and healthy elderly individuals were examined using a magnetic sensing finger-tap device (UB-2; Maxell, Tokyo), and relationships with cognitive function were investigated.

**Methods:** Finger-tapping movements were measured and multiple comparisons using mean values of parameters from each group were conducted. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), and Spearman rank-correlation coefficients were used to analyze relationships between these parameters and MMSE scores.

**Results:** Significant differences were observed in total traveling distance, standard deviation (SD) of contact duration, SD of inter-tapping interval, and SD of phase difference between left- and right-hand tapping. MMSE score showed a weak negative correlation with the SD of contact duration of the left hand ($r = -0.28$, $p < 0.05$). Weak positive correlations were observed in total traveling distance of the left hand ($r = 0.3$, $p < 0.05$) and right hand ($r = 0.25$, $p < 0.05$) and the in-phase task for the right hand ($r = 0.28$, $p < 0.05$).

**Conclusion:** These parameters may represent finger movements that are characteristic of AD and MCI.

**Key words:** Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI), finger movement characteristics, finger-tapping

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## Introduction

About 6.3 million individuals in Japan suffer from dementia, due to the aging population and subsequent increase in prevalence of morbidity due to aging, and this figure is expected to reach 7 million by 2025 [1]. The number of dementia patients is expected to continue increasing dramatically, and urgent measures are thus needed.

Dementia can be classified into three major categories: Alzheimer's Disease (AD); cerebrovascular dementia; and Lewy body dementia. AD accounts for 50−70% of all dementia cases and is a disease associated with loss of memory and progressive declines in cognitive function [2]. Due to the importance of early diagnosis, many clinical studies have targeted individuals with Mild Cognitive Impairment (MCI), a borderline state between normal


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aging and dementia proposed by Petersen et al. [3]. Recent research has shown that patients with dementia, including MCI, in the early stages exhibit gait disorders. Early motor impairments may thus assist in the detection of dementia [4].

We have focused on finger movements (finger-tapping movements) as a simple method to evaluate motor impairment in dementia patients. We used a device for measuring motor function of the fingers (UB-1 magnetic sensing finger-tap device; Hitachi Computer Peripherals, Kanagawa) in a preliminary study of finger-tapping movement in dementia patients, and identified parameters that captured the characteristic finger movements of dementia patients [5]. First, in that preliminary study, differences in parameters were compared between an AD/MCI group and a healthy elderly group. Significant differences were observed in three parameters: total traveling distance; standard deviation (SD) of contact duration; and SD of inter-tapping interval. Second, analysis of the associations between these parameters and severity of dementia using the Mini-Mental State Examination (MMSE) revealed a positive correlation with total traveling distance and negative correlations with energy balance, SD of contact duration, SD of inter-tapping interval, and SD of phase difference between left- and right-hand tapping [5].

The first objective of the present study was to use UB-2 (Figure 1), as an improved version of the above-mentioned tapping device, to verify the same characteristic finger movements as UB-1 and confirm the associations with MMSE. Second, as AD and MCI were analyzed as one group for comparisons in the preliminary study, AD and MCI were split and three-group comparisons were performed to determine whether changes in characteristic finger movements can be detected from the MCI stage, since early detection is crucial for MCI.


**Figure 1.** Magnetic sensing finger-tap device (UB-2) Yellow cables are attached to the thumb and index finger of the left hand, and red cables are attached to the thumb and index finger of the right hand. The device itself is connected to a computer. Wave profiles during finger-tapping can be monitored on the computer. The UB-2 is lighter and more portable than the UB-1.

## Subjects

### 1. Patient background

The subjects were first-time patients in the Center for Comprehensive Care and Research on Memory Disorders at the authors' hospital, who had been diagnosed with either AD or MCI. The breakdown of the subjects was as follows: AD group, 44 patients with AD (mean age, 74±7 years); MCI group, 20 patients with MCI (mean age, 77±4 years); and Control group, 57 healthy elderly individuals (mean age, 74±7 years). The Control group comprised family members who accompanied the AD and MCI patients to the hospital. Controls led socially independent lives, had no history of attending a memory disorder outpatient clinic and had no problems with cognitive function. MMSE score [6] $\geq$ 28 was the condition for analysis. All subjects were right-handed. Exclusion criteria were as follows: presence of higher brain dysfunction such as impaired consciousness, aphasia, or apraxia; or marked paralysis or finger dexterity impairment due to conditions such as stroke.

### 2. Ethical considerations

All subjects or their family members were given detailed verbal and written descriptions of the present experiment and consent was obtained from each subject prior to enrolment. Approval for the present study was obtained from the Ethics and Conflict of Interest Committee of the National Center for Geriatrics and Gerontology (Approval No. 623-7).

## Methods

### 1. History-taking and assessment

The subjects were asked to complete a medical questionnaire to collect background information. The MMSE was administered to quantify the severity of cognitive function.

### 2. Instrumentation techniques and measuring devices

The UB-2 magnetic sensing finger-tap device (Maxell, Tokyo) was used (Figure 1) as the measuring device. This device is a more portable version of the UB-1. With magnetic sensors attached to the thumb and index finger, finger-tapping movements (repeatedly bringing the tips of the two fingers together and apart) were performed. Finger-tapping movements comprised unimanual tapping movements (dominant hand task and non-dominant hand task), an in-phase task (simultaneous right and left tapping movements), and an anti-phase task (alternating right and left

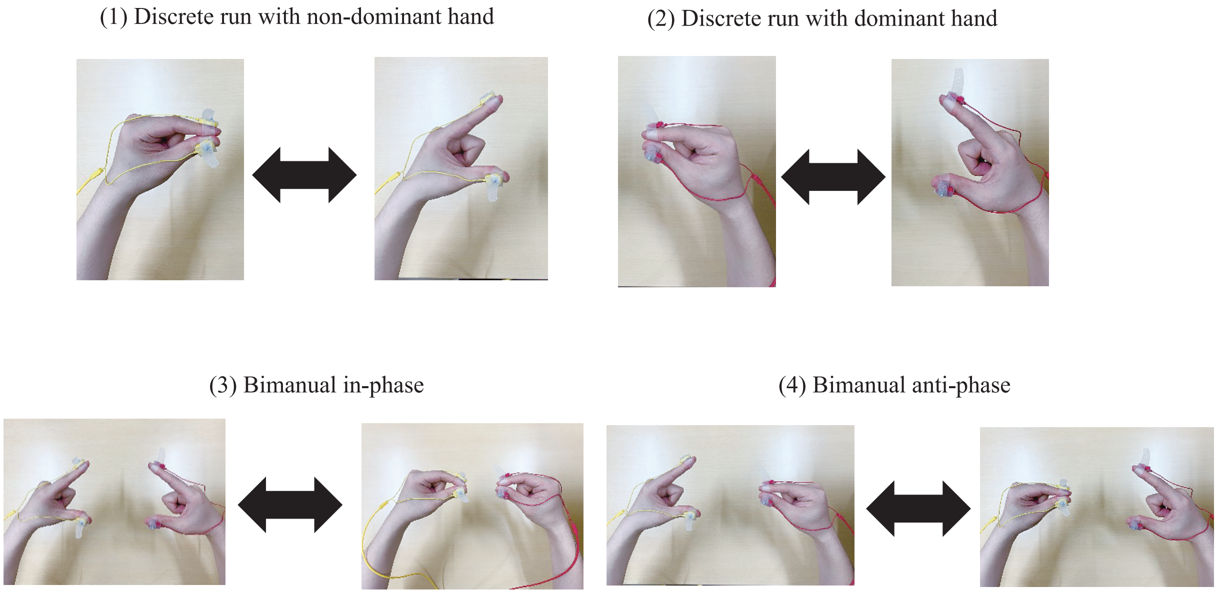


**Figure 2.** Finger-tapping (bringing the tips of the thumb and index finger together and apart).
(1) Non-dominant hand movement: Finger-tapping as fast as possible with the left thumb and index finger. (2) Dominant hand movement: Finger-tapping as fast as possible with the right thumb and index finger. (3) In-phase movement: Simultaneous finger-tapping as fast as possible with both hands. (4) Anti-phase movement: Alternating finger-tapping between the right and left hands as fast as possible. The distance between the two fingers is kept at about 3−4 cm apart when conducting Steps (1) to (4), and the task is performed for 15 s.

tapping movements) (Figure 2). Before measuring each movement, we asked the subject to tap "as fast as possible" for an approximately 5-s practice run to test whether the subject understood the tapping movements. After this practice, the subjects were asked to perform each of the task movements in the following order: non-dominant hand task, dominant hand task, in-phase task, and anti-phase task. Measurements were taken for 15 s. After measuring and recording the distance between the fingers at 10-ms intervals of tapping movements, the magnetic sensing finger-tap device used in this study also calculated 44 parameters.

In the preliminary study, parameters such as total traveling distance, SD of contact duration, SD of inter-tapping interval, energy balance, and SD of phase difference between left- and right-hand tapping appeared to represent useful characteristic finger-tapping movements of dementia patients [5]. The present study therefore also analyzed total traveling distance, energy balance, SD of contact duration, SD of inter-tapping interval, and SD of phase difference between left- and right-hand tapping. Total traveling distance was the sum of the distance traveled during movement of the two fingers, regardless of whether the fingertips came into contact. This value represents the total amount of exercise. Energy balance is the ratio of the integrated sum of squares of positive speeds to the integrated sum of squares of negative speeds, representing the balance of speeds between finger movements apart and back together. SD of contact duration is the dispersion of time while the fingers are together. SD of inter-tapping interval is the dispersion of inter-tapping interval (time difference between the minimum points of two adjacent taps). When one inter-tapping interval is considered as 360°, the SD of the phase difference between left- and right-hand tapping was taken as the dispersion of angular representation showing the time lag between left and right hands. The SD of phase difference between the left- and right-hand tapping is a parameter calculated only for the in-phase and anti-phase tasks.

### 3. Data analysis

The following parameters were extracted from measured data as finger movement characteristics: total traveling distance, energy balance, SD of contact duration, SD of inter-tapping interval, and SD of phase difference between left- and right-hand tapping. The Tukey-Kramer test was used to conduct multiple comparisons of differences between mean parameter values of the three groups (AD, MCI, and Control groups). The Spearman rank correlation was used to determine associations between finger movement characteristics and cognitive function (MMSE). The level of statistical significance was set at $p < 0.05$ and SPSS Statistics version 25.0 statistical analysis software (IBM Japan, Tokyo) was used.

## Results

### 1. Comparison of parameters among the three groups

Table 1 compares the parameters among each group. Except for the anti-phase task, total traveling distance

**Table 1.** Comparison of parameters among the three groups.

| Parameters | Task | Measured value ± SD | | | *p*-Value | |
|---|---|---|---|---|---|---|
| | | AD | MCI | Control | AD vs. control | MCI vs. control |
| Total traveling distance | Non-dominant hand | 4.515±1.755 | 4.963±1.595 | 5.545±1.793 | 0.013 | 0.411 |
| | Dominant hand | 4.799±1.878 | 5.347±2.061 | 6.157±1.515 | 0.001 | 0.180 |
| | In-phase | | | | | |
| | Left | 4.684±1.888 | 4.851±1.673 | 4.851±1.673 | 0.002 | 0.057 |
| | Right | 4.692±1.683 | 5.570±1.983 | 5.846±1.589 | 0.003 | 0.805 |
| | Anti-phase | | | | | |
| | Left | 4.221±1.723 | 4.119±1.297 | 4.981±1.620 | 0.057 | 0.103 |
| | Right | 4.472±1.904 | 4.879±1.765 | 5.200±1.775 | 0.126 | 0.777 |
| Energy balance | Non-dominant hand | 0.803±0.149 | 0.808±0.122 | 0.848±0.129 | 0.248 | 0.498 |
| | Dominant hand | 0.837±0.165 | 0.832±0.132 | 0.823±0.135 | 0.882 | 0.967 |
| | In-phase | | | | | |
| | Left | 0.769±0.141 | 0.808±0.145 | 0.826±0.154 | 0.141 | 0.879 |
| | Right | 0.801±0.178 | 0.828±0.105 | 0.819±0.140 | 0.827 | 0.972 |
| | Anti-phase | | | | | |
| | Left | 0.638±0.157 | 0.679±0.193 | 0.672±0.160 | 0.576 | 0.984 |
| | Right | 0.598±0.199 | 0.610±0.172 | 0.585±0.134 | 0.917 | 0.827 |
| SD of contact duration | Non-dominant hand | 0.034±0.023 | 0.030±0.012 | 0.023±0.009 | 0.004 | 0.203 |
| | Dominant hand | 0.026±0.015 | 0.027±0.016 | 0.019±0.008 | 0.014 | 0.018 |
| | In-phase | | | | | |
| | Left | 0.029±0.015 | 0.030±0.011 | 0.021±0.008 | 0.005 | 0.020 |
| | Right | 0.025±0.017 | 0.022±0.007 | 0.018±0.006 | 0.020 | 0.387 |
| | Anti-phase | | | | | |
| | Left | 0.058±0.033 | 0.062±0.036 | 0.047±0.043 | 0.329 | 0.304 |
| | Right | 0.065±0.053 | 0.063±0.054 | 0.044±0.033 | 0.063 | 0.245 |
| SD of inter-tapping interval | Non-dominant hand | 0.082±0.206 | 0.046±0.018 | 0.033±0.015 | 0.128 | 0.919 |
| | Dominant hand | 0.049±0.089 | 0.034±0.016 | 0.024±0.012 | 0.066 | 0.766 |
| | In-phase | | | | | |
| | Left | 0.044±0.037 | 0.042±0.028 | 0.029±0.012 | 0.014 | 0.137 |
| | Right | 0.042±0.046 | 0.031±0.019 | 0.024±0.011 | 0.009 | 0.658 |
| | Anti-phase | | | | | |
| | Left | 0.099±0.069 | 0.102±0.056 | 0.087±0.149 | 0.866 | 0.863 |
| | Right | 0.090±0.058 | 0.103±0.090 | 0.066±0.046 | 0.114 | 0.051 |
| SD of phase difference between the left hand and right hand tapping | In-phase | 62.052±80.884 | 36.112±23.004 | 35.490±23.022 | 0.033 | 0.999 |
| | Anti-phase | 73.957±39.360 | 87.929±112.469 | 60.704±30.718 | 0.470 | 0.146 |

In comparisons between the AD and Control groups, total traveling distance except for the anti-phase task was significantly smaller and the SD of contact duration was significantly larger in the AD group.
In addition, the in-phase task differed significantly for SD of inter-tapping interval and SD of phase difference between left- and right-hand tapping.
The MCI and Control groups showed significant differences in SD of contact duration between the dominant hand task and in-phase task for the left hand.
Values of $p < 0.05$ are shown in red.

was significantly smaller for the AD group than for the Control group, and the SD of contact duration was significantly larger in the AD group than in the Control group. A significant difference in SD was seen for inter-tapping interval during the in-phase task (right and left), indicating rhythm irregularities. A significant difference in the SD of phase difference was seen between left- and right-hand tapping during the in-phase task, indicating a large dispersion of time lag between the two hands.

When the MCI and Control groups were compared, a significant difference was observed only in the SD of contact duration during the dominant hand task and the in-phase task (left hand). Similarly, a significant difference was seen when these comparisons were made between the AD and Control groups. No significant differences were apparent in any of the parameters for anti-phase tasks. No significant differences were seen in any of the parameters when the AD and MCI groups were compared.

**2. Relationship between finger-tapping movement and MMSE**

A weak negative correlation ($r = -0.28$, $p < 0.05$) was observed in the non-dominant hand task of the SD for contact duration. A weak positive correlation was

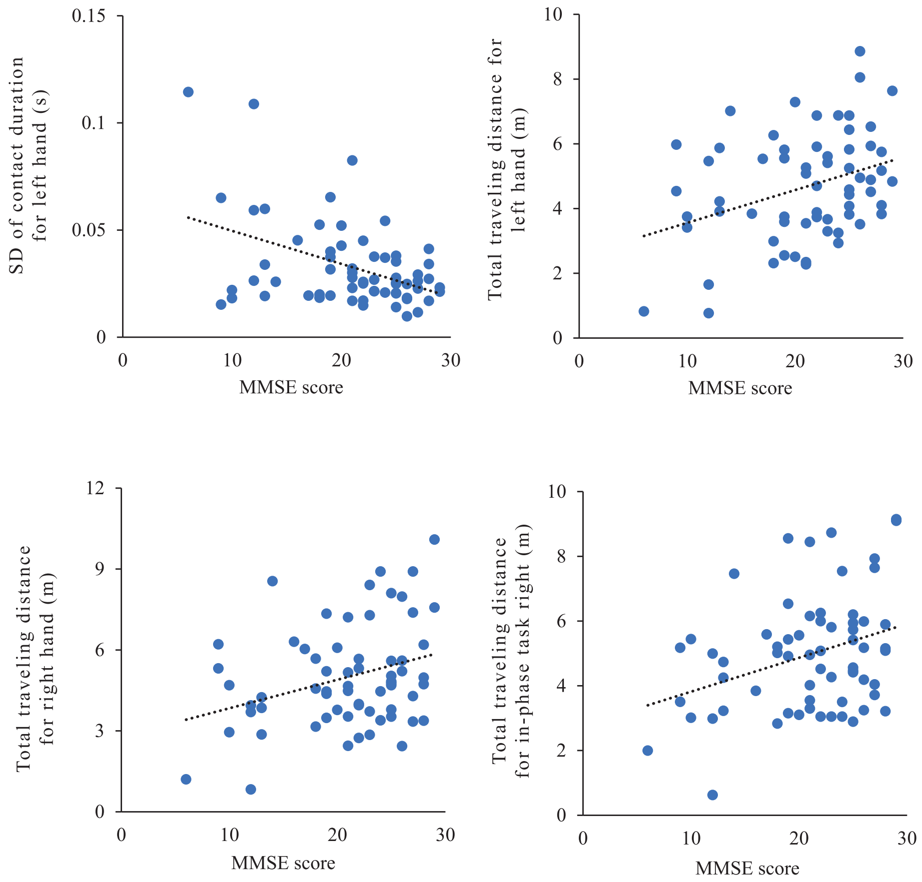


**Figure 3.** Associations between parameters and MMSE score.
A weak negative correlation ($r = -0.28$, $p < 0.05$) is observed in the non-dominant hand task for the SD of contact duration. A weak positive correlation is observed in the left hand ($r = 0.3$, $p < 0.05$) and right hand ($r = 0.25$, $p < 0.05$) of total traveling distance as well as in the right hand in the in-phase movement task ($r = 0.28$, $p < 0.05$).

observed for the left hand ($r = 0.3$, $p < 0.05$), right hand ($r = 0.25$, $p < 0.05$), and right hand of the in-phase task ($r = 0.28$, $p < 0.05$) and total traveling distance (Figure 3). No correlations with other parameters were identified.

## Discussion

Studies on finger functions in elderly individuals have identified declines in finger dexterity and muscle strength with aging [7, 8], and finger-tapping movements show fewer taps and delayed tapping response times [9]. Moreover, studies on finger function in dementia patients have shown deteriorations in fine motor control [10], and have also reported longer intervals between finger-tapping and fewer taps in AD and MCI patients compared to healthy elderly individuals [11].

In line with the preliminary study, a comparison between the AD and Control groups in the present study showed significant differences in parameters such as total traveling distance, SD of contact duration, and SD of inter-tapping interval. Unlike the preliminary study, this investigation also showed a significant difference in parameters such as the SD of phase difference between left- and right-hand tapping. The newly identified difference may have been due to the fact that AD and MCI were split, and comparisons were made among the three groups. In AD patients, delayed contact duration during finger-tapping, reduced amount of exercise, irregular rhythm, and time lag between the two hands may represent characteristics of finger movements.

Subjects in a previous, tablet-based study were given the task of touching markers that appeared on the tablet screen following a certain rhythm, and the results showed that the contact duration in the group of patients with AD and MCI was significantly longer than that in healthy elderly individuals [12]. In the present study, a significant difference in the SD of contact duration of the dominant hand task and the in-phase task was seen for the MCI group compared to the Control group. A significant difference in comparisons between the AD and Control groups was also apparent. The delay in contact duration during finger-tapping is considered to be a clinical finger movement characteristic, but might actually be a characteristic pattern observed from the MCI stage, as an earlier stage. In the present study, no significant differences between the MCI and Control groups were found with parameters other than the SD of contact duration. This may be due to the large variability in sample size between the MCI and Control groups. Furthermore, in comparisons between the AD and Control groups, significant differences were only absent for anti-phase tasks. Executing the anti-phase task may have also been difficult for healthy elderly individuals and fatigue may have had some effect, as it was the last task in order of performance. No significant differences were identified in any of the parameters when the AD and MCI groups were compared. This may have been affected by the severity of AD. Subjects were first-time patients in the Center for Comprehensive Care and Research on Memory Disorders at the authors' hospital and the AD group may have included subjects that were relatively closer to the MCI level.

When the association between finger function and cognitive function was examined, a negative correlation was found between the non-dominant hand task of the SD of contact duration and MMSE score. As mentioned previously, delayed contact duration is highly likely to represent an early stage characteristic observed from the MCI stage. Furthermore, MMSE score correlated positively with left hand, right hand, and right hand in-phase tasks of the total traveling distance. Total traveling distance as a parameter is affected by speed and the number of taps. Previous studies have reported a decline in finger-tapping speed [13] and a reduced number of finger taps [11] among AD patients, and the present results were in line with those of previous studies. Parameters related to the SD of contact duration and total traveling distance may likely be factors contributing to finger functions when the severity of cognitive function worsens.

While finger movements are intricately linked to various regions and locations in the brain, much remains unknown. Bimanual coordination involves the corpus callosum [14] and the basal ganglia [15], while rhythmic tapping involves the motor cortex, supplementary motor area, basal ganglia, thalamus, and cerebellum [16]. Corpus callosum atrophy and microscopic changes in the brain have been reported as early changes in AD [17, 18]. Some form of minor motor impairment is thus highly likely to be present prior to the onset of dementia or perhaps during the MCI stage, which is an early stage of dementia.

When Perri et al. [19] conducted a study targeting MCI subjects, they reported a 21.4% annual conversion rate to dementia. According to Davis et al. [20], the annual conversion rate to MCI due to AD was in the range of 4−10%. Various studies have examined conversion rates not limited to these, and while no consensus has yet been reached, early detection of the MCI condition is clinically significant.

In recent years, early detection of AD has been conducted using cerebrospinal fluid biomarkers such as Aβ, total tau, and phosphorylated tau [21, 22] and tests such as magnetic resonance imaging [23], single photon emission computed tomography [24], and positron emission tomography [25]. These measurements need to be taken at a medical facility, placing limitations on the measurement setting, imposing financial and physical burdens on subjects, and requiring more time for measurement and analysis. However, the measurement device used in the present study imposes little burden on the subjects, is unaffected by the setting, and is easy to use.

In the present study, differences among the AD, MCI, and Control groups were examined using a magnetic sensing finger-tap device, with the analysis focused on items such as total traveling distance, energy balance, SD of contact duration, SD of inter-tapping interval, and SD of phase difference between left- and right-hand tapping. Significant differences were observed in the comparison of these parameters between the AD and Control groups. A significant difference was also found in the SD of contact duration between the MCI and Control groups. This suggests that these parameters may be used as one method of evaluation for capturing characteristic finger movements in AD and MCI.

Various limitations of the present study also need to be considered. First, the sample size for the MCI group was small and variability in sample sizes was evident among groups. Second, while the severity of dementia can be assessed using methods such as the Clinical Dementia Rating [26], the present study did not conduct any investigations according to the degree of severity. Third, no detailed examinations according to the type of MCI were performed. Fourth, declines in attention and performance functions have been reported with dementia [27], but these were not investigated in the present study. Fifth, brain functions during finger-tapping were not analyzed in detail. Sixth, the effects of fatigue or muscular endurance on each of the individual subjects were not considered. When the MCI and Control groups were compared, $p$-values of 0.1 were observed for the dominant hand and left hand for the anti-phase task of total traveling distance, and the left hand for the in-phase task and right hand for the anti-phase task of the SD of inter-tapping interval. When sample size analyses of these parameters were conducted, we found that the following sample sizes were required: 66 subjects each for the dominant hand of the total traveling distance; 43 subjects each for the left hand in the anti-phase task of the total traveling distance; 45 subjects each for the left hand in the in-phase task of the SD of inter-tapping interval; and 60 subjects each for the right hand in the anti-phase task of the SD of inter-tapping interval.

In future studies, we intend to increase the number of subjects, identify parameters with high ability to detect identifying finger movement impairments in dementia patients, and examine their use as early diagnostic tools for dementia and MCI.

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## References

1. Cabinet Office. See the 2016 White Paper on Aging Society (whole version). Available from https://www8.cao.go.jp/kourei/whitepaper/w-2016/html/zenbun/s1_2_3.html (cited Jan 15, 2020).
2. Giri M, Zhang M, Lü Y. Genes associated with Alzheimer's disease: an overview and current status. Clin Interv Aging 2016; 11: 665−81.
3. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999; 56: 303−8.
4. Dodge HH, Mattek NC, Austin D, Hayes TL, Kaye JA. In-home walking speeds and variability trajectories associated with mild cognitive impairment. Neurology 2012; 78: 1946−52.
5. Suzumura S, Osawa A, Nagahama T, Kondo I, Sano Y, Kandori A. Assessment of finger motor skills in individuals with mild cognitive impairment and patients with Alzheimer's disease: relationship between finger-to-thumb tapping and cognitive function. Jpn J Compr Rehabil Sci 2016; 7: 19−28.
6. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12: 189−98.
7. Dayanidhi S, Valero-Cuevas FJ. Dexterous manipulation is poorer at older ages and is dissociated from decline of hand strength. J Gerontol A Biol Sci Med Sci 2014; 69: 1139−45.
8. Martin JA, Ramsay J, Hughes C, Peters DM, Edwards MG. Age and grip strength predict hand dexterity in adults. PLoS One 2015; 10: e0117598.
9. Cousins MS, Corrow C, Finn M, Salamone JD. Temporal measures of human finger tapping: effects of age. Pharmacol Biochem Behav 1998; 59: 445−9.
10. Yan JH, Dick MB. Practice effects on motor control in healthy seniors and patients with mild cognitive impairment and Alzheimer's disease. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2006; 13: 385−410.
11. Roalf DR, Rupert P, Mechanic-Hamilton D, Brennan L, Duda JE, Weintraub D, et al. Quantitative assessment of finger tapping characteristics in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease. J Neurol 2018; 265: 1365−75.
12. Suzumura S, Osawa A, Maeda N, Sano Y, Kandori A, Mizuguchi T, et al. Differences among patients with Alzheimer's disease, older adults with mild cognitive impairment and healthy older adults in finger dexterity. Geriatr Gerontol Int 2018; 18: 907−14.
13. Camicioli R, Howieson D, Oken B, Sexton G, Kaye J. Motor slowing precedes cognitive impairment in the oldest old. Neurology 1998; 50: 1496−8.
14. Kennerley SW, Diedrichsen J, Hazeltine E, Semjen A, Ivry RB. Callosotomy patients exhibit temporal uncoupling during continuous bimanual movements. Nat Neurosci 2002; 5: 376−81.
15. Mink JW. The basal ganglia: focused selection and inhibition of competing motor programs. Prog Neurobiol 1996; 50: 381−425.
16. Dhamala M, Pagnoni G, Wiesenfeld K, Zink CF, Martin M, Berns GS. Neural correlates of the complexity of rhythmic finger tapping. Neuroimage 2003; 20: 918−26.
17. Anandh KR, Sujatha CM, Ramakrishnan S. Segmentation and analysis of corpus callosum in alzheimer MR images using total variation based diffusion filter and level set method. Biomed Sci Instrum 2015; 51: 355−61.
18. Kara F, Hofling C, Robner S, Schliebs R, Van der Linden A, Groot HJ. et al. In vivo longitudinal monitoring of changes in the corpus callosum integrity during disease progression in a mouse model of Alzheimer's disease. Curr Alzheimer Res 2015; 12: 941−50.
19. Perri R, Serra L, Carlesimo GA, Caltagirone C. Preclinical dementia: an Italian multicentre study on amnestic mild cognitive impairment. Dement Geriatr Cogn Disord 2007; 23: 289−300.
20. Davis M, O'Connell T, Johnson S, Cline S, Merikle E, Martenyi F, et al. Estimating Alzheimer's disease progression rates from normal cognition through mild cognitive impairment and stages of dementia. Curr Alzheimer Res 2018; 15: 777−88.
21. Agarwal R, Tripathi CB. Diagnostic utility of CSF tau and A$\beta$(42) in dementia: a meta-analysis. Int J Alzheimers Dis 2011; 2011: 503293.
22. Ahmed RM, Paterson RW, Warren JD, Zetterberg H, O'Brien JT, Fox NC, et al. Biomarkers in dementia: clinical utility and new directions. J Neurol Neurosurg Psychiatry 2014; 85: 1426−34.
23. Frisoni GB, Fox NC, Jack CR Jr, Scheltens P, Thompson PM. The clinical use of structural MRI in Alzheimer disease. Nat Rev Neurol 2010; 6: 67−77.
24. Yeo JM, Lim X, Khan Z, Pal S. Systematic review of the diagnostic utility of SPECT imaging in dementia. Eur Arch Psychiatry Clin Neurosci 2013; 263: 539−52.
25. Pike KE, Ellis KA, Villemagne VL, Good N, Chételat G, Ames D, et al. Cognition and beta-amyloid in preclinical Alzheimer's disease: data from the AIBL study. Neuropsychologia 2011; 49: 2384−90.
26. Berg L. Clinical Dementia Rating (CDR). Psychopharmacol Bull 1988; 24: 637−9.
27. Sobol NA, Hoffmann K, Vogel A, Lolk A, Gottrup H, Høgh P, et al. Associations between physical function, dual-task performance and cognition in patients with mild Alzheimer's disease. Aging Ment Health 2016; 20: 1139−46.