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Quantitative assessment of finger tapping characteristics in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease

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Abstract

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Compliance with ethical standards

Ethical standards This study complies with the ethical standards set forth by the AMA. This data is original, has not previously been published, nor is it under consideration for publication elsewhere. All authors listed on this manuscript have significantly contributed to the implementation, analysis and/or drafting of this manuscript.

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Background—Fine motor impairments are common in neurodegenerative disorders, yet standardized, quantitative measurements of motor abilities are uncommonly used in neurological practice. Thus, understanding and comparing fine motor abilities across disorders have been limited.

Objectives—The current study compared differences in finger tapping, inter-tap interval, and variability in Alzheimer's disease (AD), Parkinson's disease (PD), mild cognitive impairment (MCI), and healthy older adults (HOA).

Methods—Finger tapping was measured using a highly sensitive light-diode finger tapper. Total number of finger taps, inter-tap interval, and intra-individual variability (IIV) of finger tapping was measured and compared in AD (n = 131), PD (n = 63), MCI (n = 46), and HOA (n = 62), controlling for age and sex.

Results—All patient groups had fine motor impairments relative to HOA. AD and MCI groups produced fewer taps with longer inter-tap interval and higher IIV compared to HOA. The PD group, however, produced *more* taps with *shorter* inter-tap interval and higher IIV compared to HOA.

Conclusions—Disease-specific changes in fine motor function occur in the most common neurodegenerative diseases. The findings suggest that alterations in finger tapping patterns are common in AD, MCI, and PD. In addition, the present results underscore the importance of motor dysfunction even in neurodegenerative disorders without primary motor symptoms.

Keywords

Alzheimer's disease; Parkinson's disease; Mild cognitive impairment; Finger tapping; Intra-individual variability

Introduction

The economic cost of neurodegenerative disease is enormous and is expected to grow quickly as more people live to older age with more significant physical and cognitive impairments. While many of these disorders have unique characteristics, an emerging evidence indicates that sensory and motor impairments are associated with the onset and progression of many neurological disorders. This includes disorders where motor dysfunction is considered a primary symptom (e.g., Parkinson's disease (PD) [1]) and other disorders, such as Alzheimer's disease (AD), where motor dysfunction is not routinely observed until later in the disease [2]. Clinical assessment of neurodegenerative diseases often involves observation and classification of physical or motor symptoms; however, evaluation of motor abilities across disorders is often heterogeneous, consequently making cross-diagnostic comparisons challenging. For example, for fine motor skills, neuropsychological assessment typically includes use of the finger tapping test (FTT; [3]), while neurological examination often includes a more qualitative assessment of finger-to-thumb tapping. Here, we aimed to quantitatively measure and compare finger tapping in patients with PD, AD, and mild cognitive impairment (MCI), and to compare performance patterns to healthy older adults (HOA).

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While minor sensory motor changes are typical with aging [4], dysfunction of fine motor control is specifically associated with PD [5]. Motor disturbances in PD include tremor at rest, rigidity, bradykinesia, hypokinesia, timing deficits, postural instability, and impaired bilateral coordination [5]. The clinical assessment of fine motor function is typically performed using standardized rating scales, such as the Unified Parkinson's Disease Rating Scale (UPDRS) [6]. These subjective measures of fine motor control can be used successfully to diagnose and delineate individuals suffering from movement disorders. However, subjective scales are often insensitive to subtle decrements in fine motor movements among those with PD [7] and have low reliability [8, 9]. Specifically, bradykinesia in PD includes slowness, a reduction in the amplitude of movement, and is typically accompanied by arrhythmicity, which is difficult to reliably quantify with subjective measurement.

In AD, while cognitive impairments are the most commonly reported symptoms, deficits in motor function have been observed and may be associated with disease progression [10–14], as well as decline in basic and instrumental aspects of activities of daily living (ADLs) [15, 16]. Compared to HOA, patients with AD have slower reaction times that become more apparent with increased task complexity [12]. While this may reflect cognitive slowing associated with the disorder, it may also reflect alterations in motor processing. In fact, dexterity in finger-to-thumb tapping in AD, including time between taps and total distance travelled between the index finger and thumb, is diminished compared HOA [13]. Moreover, individuals with MCI and those early in the course of AD show signs of decreased motor function from basic foot and finger tapping to more complex tasks involving cognitive domains [14, 17]. Patients with MCI and early AD have clinically normal gross motor function, but careful neuropsychological assessment can detect impairments in motor speed, steadiness, and strength, as well as deficits in complex motor tasks such as alternating motor movement handedness and positional tracking with motor movement [18]. However, it remains unclear if these impairments arise in a certain pattern and whether they reflect a specific deficit in motor function or are secondary to dementia-related deficits in attention and memory [19].

Given that motor disruptions arise early in the disease course of PD, AD, and MCI, quantitative motor assessments may useful even in non-motor disorders. Finger tapping is used commonly as a measure of fine motor abilities in PD [1], and becoming more prevalent in AD [13] and MCI [13, 14]. Quantitative procedures for assessing finger tapping include simple lever pressing, digitomotographs [1], sophisticated use of magnets [20], accelerometers [21], optoelectronic motion analysis [22], laser sensors [23], and computerized batteries of physiological function [24]. These quantitative techniques allow for more thorough and accurate assessment of finger tapping with higher precision.

In addition to quantifying the number of taps and the interval over which taps occur, these devices allow for the assessment of intra-individual variability (IIV) of finger tapping. IIV in performance speed increases across adulthood and is a sensitive behavioral indicator of the integrity of the aging brain [17, 25]. Moreover, higher variability in performance speed appears to be maladaptive in HOA; higher variability is associated with poorer cognitive test scores, physical performance, mental health, and reduced functioning on everyday tasks

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[26]. Longitudinal studies of older adults indicate that higher IIV is associated with poorer performance over time, predicts mild cognitive impairment [12, 27], and is associated with increased mortality [28]. Importantly, IIV measures based on moment-to-moment performance speed are more promising and are more directly attributable to abnormalities in brain structure or function than the traditional measures [26]. Here, we assess fine motor tapping, in particular the IIV of finger tapping, in PD, AD, MCI, and HOA using a quantitative light-diode finger tapper. We hypothesized that PD, AD, and MCI individuals would show impairment in finger tapping as compared to HOA and variability of finger tapping would be most affected in PD as compared to AD or MCI.

Methods

Participants

Participants were recruited from the Penn Memory Center (PMC) and Clinical Core of the University of Pennsylvania's Alzheimer's Disease Center (ADCC), the Parkinson's Disease and Movement Disorders Center at the University of Pennsylvania, and the Parkinson's Disease Research, Education and Clinical Center (PADRECC) at the Philadelphia Veterans Affairs Medical Center at the University of Pennsylvania from 2008 to 2015. Diagnostic assessments included medical history, and physical and neurologic examinations conducted by experienced clinicians, including review of neuroimaging, and neuropsychological and laboratory data. Consensus diagnosis was established using standardized clinical criteria [29, 30] on the basis of these data. Healthy older adults (HOA) were recruited and assessed similar to neurological patients [29]. Mild-to-moderate PD patients [Hoehn and Yahr: 2.10 (0.64)] movement disorder neurologists administered the Unified Parkinson Disease Rating Scale Part III Motor Score (UPDRS). A small subset (n = 12) of PD patients were considered to have dementia associated with PD (PDD). A comparison of PD and PDD is provided in the Supplemental Material. The Mini-Mental State Examination (MMSE) was used to screen for cognitive deficits in all individuals. Participant characteristics and performance on screening measures are compared in Table 1. The Institutional Review Board at each participating institution approved the study and written informed consent was obtained.

Light beam finger tapping test

Finger tapping performance was assessed using the Light Beam Finger and Foot Tapper Test (NeuroCognitive Engineering, 1995; Fig. 1). This device consists of two photodiodes sensitive to infrared light. Two light beams, one on each side of the board, project about 1 mm above the board between two raised nodules. Gray lines between the right-side and left-side modules cue respondents where to place their index finger during a test trial. Each downward movement of the index finger through the beam registers the tap. A computer-based software program administers the task and captures raw number of taps and inter-tap interval (e.g., time between consecutive taps). Six-month test–retest reliability in healthy subjects was reported to be high (r= 0.85) [31].

Finger tapping was measured for both dominant and non-dominant hands, with a fixed order of performance being used for all participants. Right-hand performance was tested first,

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followed by the left hand with a 15-s rest period in between each trial. Finger tapping was assessed three times (10-s trials) for each hand and there was a 30-s rest period at the end of each set. Respondents were cued to start tapping by verbal command, and a computer tone cued them to stop tapping. PD patients were testing while on medication.

Intra-individual variability (IIV)

Trial-by-trial performance values were transformed to their standard equivalents based on the means and standard deviations (SD) of the healthy sample. An index of intra-individual variability (IIV) across trials was calculated for each participant in SD units (see [32]). This index of variability has been used in other studies [32–34], and reflects variation *within a single person* across several trials and is, therefore, an index of an individual's consistency of performance across all trials:

$$\text{Intra}-\text{individual variability} = \sqrt{\sum_{k=1}^{K}\left(\frac{\left(Z_{ik}-A_i\right)^2}{(K-1)}\right)},$$

where Z_{ik} is the kth inter-tap interval for the ith individual and

$$A_i = \sum_{k=1}^{K}\frac{Z_{ik}}{K},$$

is the individual's mean z-transformed inter-tap interval based on all taps.

Statistics

For each hand, finger tapping data were collapsed across all three trials. Total number of finger taps, inter-tap interval (ms), and tapping IIV were entered as dependent measures via ANOVA with diagnosis, age, and sex as predictors. Diagnosis × age and diagnosis × sex interactions were included in the model. When considering IIV, the total number of taps and inter-tap interval were considered as additional covariates as a greater number of taps were associated with lower IIV ($r = -0.47$, $p < 0.001$), and longer inter-tap interval was correlated with more variability ($r = 0.62$, $p < 0.001$). Exploratory analyses investigated both dominant and non-dominant hand response patterns (Supplemental Material). Bonferroni corrected alpha of $p < 0.01$ (0.05/3) was used to determine significance for ANOVAs. Post hoc contrasts were used to examine interactions; Satterthwaite corrections were used when equal variances could not be assumed; corrected degrees of freedom are reported where appropriate. Participant characteristics were compared using ANOVAs and Chi-square tests where appropriate. Pearson correlations were performed between demographic and performance variables.

To assess the "real-world" utility of finger tapping measures to classify subjects with PD- or with AD-type dementia, logistic regression analyses were conducted. The initial analysis included each finger tapping outcome measure as independent predictors of group status. A second analysis assessed the diagnostic utility of all finger tapping measures. A ROC curve,

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which plots true positive rate (sensitivity) against false positive rate (1 – specificity), was generated for each analysis, and the area under the curve (AUC) was computed. AUC provided a quantitative index of each parameter set's ability to distinguish PD or AD (including MCI) individuals from HOA. Receiver-operating characteristic curves with 95% CIs computed with 2000 stratified bootstrap replicates (R package 'pROC' [35]) were created to compare finger taps, ITI, and IIV across diagnoses. Accuracy of the finger tapping metrics was compared using Delong method of comparing two AUCs [36] within the 'proc' R package [37]. *Z*-statistics and the corresponding *p* value were estimated for pairwise AUC comparisons. All statistics were performed in the R Statistical Package (v3.0.3 [38]).

Results

Finger tapping performance

Total tap count—There were significant main effects of diagnosis [$F(3, 290) = 8.48$, $p = 2.03 \times 10^{-5}$], age [$F(1, 290) = 33.38$, $p = 1.95 \times 10^{-8}$], and sex [$F(1, 290) = 11.00$, $p = 1.02 \times 10^{-3}$] for the total number of taps (Fig. 2a). As a group, the HOA participants produced significantly more finger taps than AD ($p = 0.04$), marginally more taps than MCI ($p = 0.07$) and an equivalent number of taps relative to PD ($p = 0.12$). The PD group produced the most taps of any group, but only significantly more than AD ($p = 1.7 \times 10^{-4}$) and MCI ($p = 1.71 \times 10^{-3}$). Finger taps for MCI and AD were similar ($p = 0.88$). On average, older age was associated with fewer taps ($r = -0.33$, $p = 1.65 \times 10^{-9}$) and men produced more taps than women. No interactions were significant. A higher number of taps were significantly associated with better MMSE scores in AD ($r = 0.27$, $p = 0.001$), marginally in MCI ($r = 0.34$, $p = 0.02$), but not in PD ($r = 0.01$, $p > 0.05$) or HOA ($r = -0.06$, $p > 0.05$) subjects. Total taps were not significantly associated with UPDRS Part III ($r = -0.18$, $p = 0.15$) score in PD. A greater number of taps were observed in the dominant than non-dominant hand for all participants (Supplemental Material).

Inter-tap interval—Significant main effects of diagnosis [$F(3, 290) = 4.97$, $p = 2.23 \times 10^{-3}$], age [$F(1, 290) = 20.86$, $p = 7.32 \times 10^{-6}$], and sex [$F(1, 290) = 8.96$, $p = 2.99 \times 10^{-3}$] were found for inter-tap interval (Fig. 2b). As a group, HOA had shorter inter-tap intervals than AD ($p = 0.04$) and MCI ($p = 0.04$), but were equivalent to PD ($p = 0.68$). The PD group had shorter inter-tap intervals than AD ($p = 0.02$) or MCI ($p = 0.03$) groups. Inter-tap intervals were similar for MCI and AD groups ($p = 0.68$). Older age was associated with higher inter-tap interval ($r = 0.28$, $p = 1.18 \times 10^{-6}$), and men had shorter inter-tap intervals than women. No interactions were significant. Longer inter-tap interval was associated with poorer MMSE scores in AD ($r = -0.22$, $p = 0.01$) and MCI ($r = -0.29$, $p = 0.05$), but not in PD ($r = -0.01$, $p > 0.05$) or HOA ($r = 0.04$, $p > 0.05$). Inter-tap interval was not associated with UPDRS ($r = 0.22$, $p = 0.09$) score in PD patients. Inter-tap interval was similar for dominant and non-dominant hands (Supplemental Material).

Tapping IIV—The main effects of diagnosis [$F(3, 288) = 58.50$, $p = 2.00 \times 10^{-16}$], age [$F(1, 288) = 6.12$, $p = 0.01$], and sex [$F(1, 288) = 40.62$, $p = 7.31 \times 10^{-10}$] were significant for tapping IIV, even after accounting for total number of taps and inter-tap interval. HOA were the most consistent tappers (Fig. 2c). IIV in HOA was lower than in AD ($p = 3.40 \times 10^{-4}$),

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MCI ($p = 0.01$), and PD ($p = 2.00 \times 10^{-14}$). As a group, PD was the most variable in finger tapping, and significantly more variable than AD ($p=2.30\times10^{-8}$) or MCI ($p= 1.20 \times 10^{-6}$). Older age was associated with greater tap IIV ($r= 0.62$, $p= 2.20 \times 10^{-16}$), and women were more variable than men. IIV was greater for the dominant as compared to non-dominant hand (Supplemental Material).

As shown in Fig. 3, greater finger tapping IIV in HOA, AD, and MCI groups was associated with fewer overall number of taps and longer tapping latencies. Yet, in PD, this pattern was reversed; greater finger tapping IIV was associated with more taps and faster tapping. Higher finger tap IIV was associated with poorer MMSE scores in AD ($r= -0.18$, $p< 0.04$), MCI ($r= -0.31$, $p< 0.04$), and HOA ($r = -0.30$, $p < 0.02$), but not PD ($r = -0.08$, $p > 0.05$). Tap IIV was associated with duration of illness $r= -0.70$, $p < 1.19 \times 10^{-10}$, but not UPDRS score in PD patients.

Inclusion of duration of illness or medication dosage [e.g., levodopa equivalent doses (LEDD)] as additional factors did not alter the results presented above.

Classification sensitivity and specificity of finger tapping measures

For PD patients, logistical regression analysis of finger tapping IIV yielded an area under the curve (AUC) of 0.89 (0.83–0.97), which was significantly greater than total taps (AUC = 0.59; $Z = 4.55$, $p = 5.25 \times 10^{-6}$) or ITI (0.57; $Z= 4.67$, $p= 2.98 \times 10^{-6}$). As illustrated (Fig. 4), with classification accuracy greater than 80%, IIV of finger tapping could discriminate patients with PD from HOA with 88% sensitivity and 76% specificity. Finger tapping IIV was marginally better than total taps ($p= 0.08$) in differentiating AD from HOA (Supplemental Material). Finger tapping IIV (AUC = 0.78) was also better at differentiating PD from AD than total number of taps (AUC = 0.68; $Z = 1.91$, $p = 0.05$) and marginally better than ITI (AUC = 0.67; $p= 0.07$) with a sensitivity of 64% and specificity of 79%.

Discussion

In the current study, HOA and individuals with MCI, AD, and PD were tested using a sophisticated light-diode finger tapper. Tapping frequency, inter-tap interval, and intra-individual variability were measured, and the general pattern of finger tapping performance was determined in each neurodegenerative condition. To our knowledge, this is the first study to investigate simple finger tapping across these three conditions using a sophisticated, but simple to use, light-diode finger tapper. Overall, we find that patients with MCI, AD, and PD all have abnormalities in finger tapping as compared to HOA and that variability in finger tapping is an important feature to measure.

Tapping performance: frequency and inter-tap intervals

The traditional finger tapping performance results demonstrate a differential pattern of tapping frequency and inter-tap intervals in older adults with AD, MCI, and PD. During a repeated ten-second response window, patients with AD and MCI produced the fewest number of finger taps, while patients with PD produced the most—even more than cognitively healthy older adults. In addition, AD and MCI individuals had the longest ITIs, while the PD patients had the shortest—similar to cognitively healthy older adults.

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Fewer taps and higher inter-tap interval in AD and MCI corroborate several previous studies that show fine motor impairment in MCI and early AD, including during finger tapping [18] and coordinated hand movements, such as writing [16]. In addition, individuals with AD and MCI individuals are less accurate and perform more slowly during cognitive testing [12, 19, 39]. As finger tapping deficits were evident in MCI, it is likely that simple fine motor functioning declines even prior to the onset of dementia. However, our findings disagree with two other studies, which find a similar number of finger taps in very mild AD [40] and similar motor response time in amnestic MCI [12] as compared to HOA. However, there are notable differences between these studies and ours. In the former study [40], finger tapping was measured during both restrained and unrestrained conditions, which could systematically affect performance, whereas, in the current study, finger tapping was only performed in an unrestrained condition. In the latter study [12], response time was measured in a complex motor task requiring target detection via finger taps, whereas we measured simple finger tapping. In fact, in Gorus et al. [12], total response time and decision response time were both slowed in MCI as compared to HOA, which argues that some aspects of the motor response are clearly impaired. Yet, it is likely that the motor dysfunction observed interacts with cognitive decline as reported in the previous studies. We find total taps and inter-tap interval to be significantly associated with MMSE performance in AD and MCI individuals, but not in HOA or PD individuals, which further suggests that basic motor dysfunction and cognitive decline are connected. Clearly, an additional work is necessary to determine if fine motor dysfunction is directly related to central motor dysfunction or secondary to the cognitive dysfunction associated with dementia. Nonetheless, we provide evidence of the deterioration of fine motor control in AD and MCI.

Abnormal finger tapping in PD was an expected result and our findings corroborate several previous studies in PD using both traditional [7, 22, 41–47] and advanced methodology to capture finger and upper limb movement [1, 20, 48]. PD patients, in the current study, however, produced the most number of finger taps at rate similar to healthy older adults. Hastened tapping may seem paradoxical as motor responses are typically slowed in PD. However, hastened tapping is observed in PD [47] particularly during synchronous responses. It is possible that intrinsic oscillations of the central nervous system, known to be disrupted in PD [49], lead to asynchronization of finger tapping and more speeded responses. Moreover, festination of gait, speech, and finger tapping are common in PD [50, 51], and thus, this involuntary acceleration of movement may explain higher number of taps in PD. Alternatively, it is probable that the combination of hypokinesia, which reduces the overall magnitude of each finger tap, or tremor superimposed on voluntary finger movements, would result in more taps in some patients with PD. In fact, a recent investigation of finger tapping in PD patients finger tapping speed and amplitude (sequence effect) is progressively reduced in PD [52]. Unfortunately, we are unable to differentiate these two possibilities in the current study as the magnitude of finger movement during tapping was not captured. Nevertheless, this pattern of responding likely reflects extrapyramidal motor dysfunction associated with nigro-striatal pathway degeneration in PD [53].

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IIV of finger tapping

One of the unique aspects of this study was the ability to measure the IIV of finger tapping. Variability of finger tapping performance results demonstrated a similar pattern—more variability—in older adults with AD, MCI, and PD as compared to cognitively healthy older adults. PD patients were the most variable responders followed by AD and MCI, while HOA were the most consistent. PD patients showed more variability in finger tapping in their dominant hand (Supplemental Material). Finally, finger tapping IIV was more effective at differentiating between PD and HOA as well as PD and AD individuals than other tapping outcome measures. In general, IIV was more discriminative than either the total number of finger taps or inter-tap interval.

Higher IIV is common in AD [54, 55], MCI [27, 56–58], and PD [58, 59]; however, in the majority of these studies, an in AD, in particular, the focus on variability, was during cognitive testing (i.e., response time). IIV within the basic motor system has received far less attention. In a recent study of continuous tapping, AD patients had greater finger tapping variability as compared to older and younger adults [10]. Another study of both AD and MCI individuals found a higher standard deviation of finger-to-thumb tapping as compared to HOA when using magnetized sensors [13]. Other studies of gait and more complex cognitive/motor tasks suggest that IIV can be informative in AD and MCI [12, 60–64]. Given that finger tapping measurements are not typical in the study of AD, a few other studies report differences or changes in IIV of finger tapping in AD or MCI. However, in PD, there are several reports of elevated motoric IIV and its potential utility in diagnostic approaches [1, 65, 66].

Mechanistically, there are several potential sources of higher variability in neurological conditions. The loss of tactile input is diminished in normal aging [67], and may be further disrupted in AD, MCI, or PD [68]. Older age is associated with the lengthening of the two phases of the finger tapping cycle—onset to offset and offset to onset [24], and thus, it is possible that in these conditions, there is an acceleration of this age-related loss of tactile sensory feedback, which contributes to inconsistent tapping performance [24]. It is also possible that timing mechanisms become disrupted, which is evident in directed finger tapping tests. Spontaneous and synchronized self-paced finger tapping, including speeded tapping, requires an individual to tap at a self-determined rate, which may diminish with age. For example, AD patients tapped more frequently and were more variable when asked to tap along with a tone and to maintain that tap rhythm when the tone was removed [10]. While this type of tapping test differs from the simple finger tapping test used in the current study, higher IIV in AD patients indicates some loss of motor fidelity.

It is also possible that the loss of central processing ability leads to a loss of tapping consistency. We show that within the HOA, AD and MCI groups' finger tapping variability is negatively associated with MMSE score, which corroborates the previous work [13]. One reason for this relationship may be that attention is necessary to maintain precision of fine motor movements and disruption of attention leads to more variable responding [69]. Since AD, MCI, and PD all affect neurocognitive functioning, including attention, this too may be contributor to higher IIV. Moreover, longer and more variable finger tapping onset, but not the offset, is associated with lower attentional ability, poorer short-term memory, and with a

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diagnosis of dementia [17]. Finally, higher variability could reflect a loss of efficiency or organization of the neurobiological substrate for motor function [70] and thus result in behavioral deficits. Whether one of these mechanisms is more prevalent in AD or PD remains unclear. While it is likely that interactions between cognitive and sensory systems are impacting IIV in AD and MCI more than PD, future studies should aim to specifically elucidate these mechanisms.

Limitations

We acknowledge that our study has several limitations. First, finger tapping and MMSE were the only tasks acquired for all subjects. No other measures of speeded cognitive processing or motor function were systematically assessed, thus limiting our ability to determine the specificity of tapping deficits. Future studies should consider capturing performance variability across the motoric and cognitive spectrum. Second, there was no significant association between UPDRS ratings and our light-diode finger tapping measures in PD. While this is surprising, other studies have shown that the UPDRS captures more aspects of finger tapping amplitude than speed [71]. Here, we did not measure amplitude, but rather frequency, inter-tap interval, and variability, which may explain this lack of association. Third, our tests were done once on individuals with well-established clinical diagnoses, so that we could not determine whether these findings are present early in the course of these diseases or whether they change over time. While the groups were similar in age, there were more men with PD and more women in the AD, MCI, and HOA groups. This could systematically bias the PD results as men tap at higher rates and are faster. We attempted to address this limitation in our statistical model; however, it may still have had an effect on the results. Finally, it is worth noting that the underlying pathology of the reported deficits is uncertain and that future molecular imaging work will be crucial in determining the specificity of these effects. It is also plausible that other contributing, but unmeasured, factors (e.g. cardiovascular disease) could contribute the reported effects.

Conclusions

Altogether, our results indicate that on a group level, AD, MCI, and PD exhibit significantly impaired finger tapping. In addition, the pattern of dysfunction was relatively unique for each disorder. As compared to healthy older adults, the group with AD produced a finger tapping pattern that was lower in frequency with slower, more variable inter-tap interval. The AD group, but not those with MCI, showed more variability in dominant hand finger tapping. The pattern in the PD group consisted of high frequency, short inter-tap interval, and highly variable finger tapping. Further studies are needed to determine if these whether these differences are present early in the disease course, in particular in AD-type dementia, to be useful in disease diagnosis and whether these patterns change over time, so that they could be useful as a marker of disease progression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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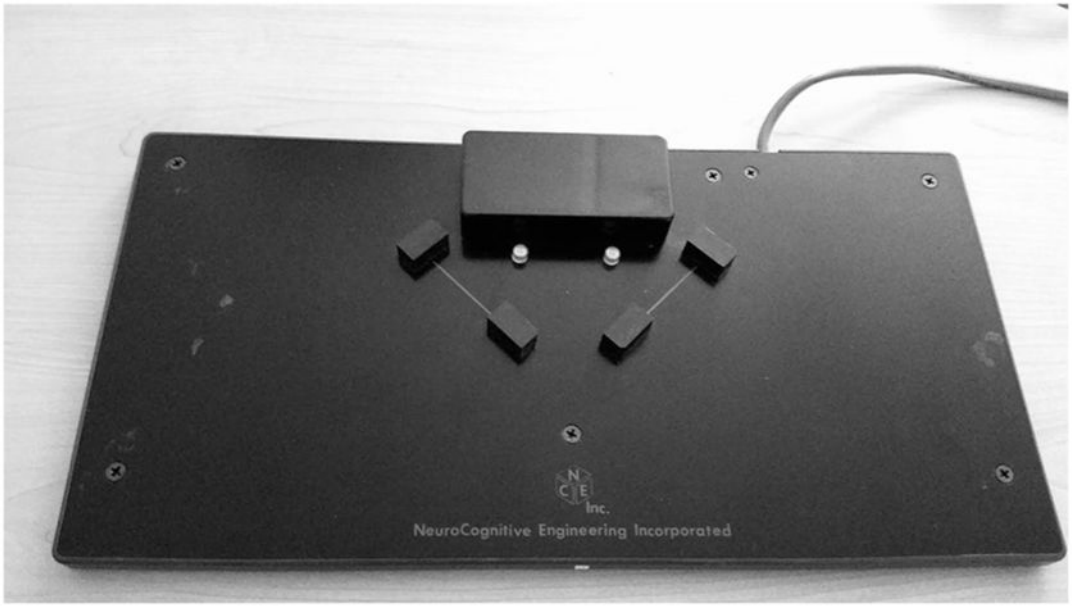

Fig. 1.

Light beam finger tapper (NeuroCognitive Engineering). The apparatus consists of two light beams, one on each side of the board, which project about 1 mm above the board between two raised nodules. Gray lines between the right-side and left-side modules cue respondents where to place their index finger during a test trial. Lowering an index finger through the beam registers the tap. A computer-based software program administers the task and captures the number of finger taps and inter-tap intervals during a 10-s trial of finger tapping

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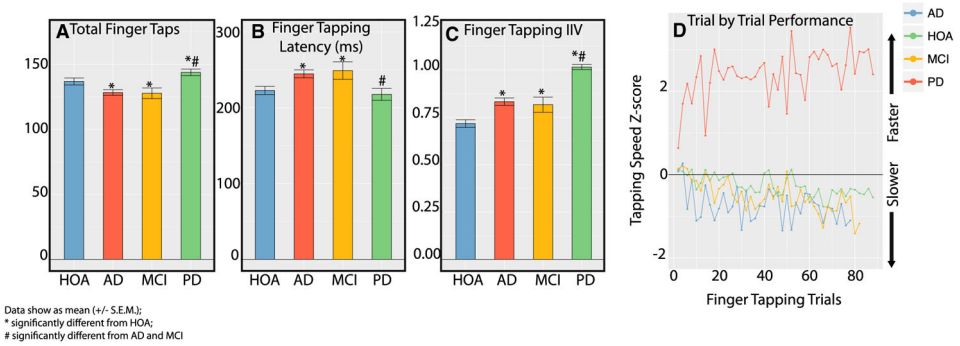

Fig. 2.

Finger tapping patterns using a light-diode finger tapper. **a** Healthy older adults tapped more than AD and MCI individuals. PD individuals produced the most number of taps. **b** Healthy older adults had a shorter inter-tap interval than AD and MCI, but not PD individuals. **c** Healthy older adults were the more consistent than AD, MCI, and PD. PD individuals were the most variable. **d** Example tapping patterns. Normalized (*z*-transformed) tapping patterns for one HOA, AD, MCI, and PD participant. Each individual's performance was normalized to the average of HOA. The healthy older adult (green) tapped more times, with less time between taps and was more consistent than the MCI (yellow) or AD (red) individual. The PD (red) individual tapped a similar number of times as the HOA individual, but had more taps than all other individuals shown. In addition, the PD individual showed the largest intra-individual variability (IIV) in finger tapping

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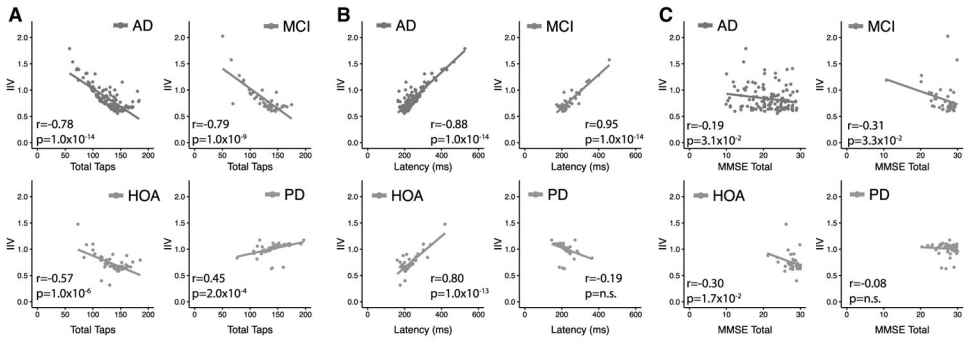

Fig. 3.

Associations between finger tapping IIV, total taps, inter-tap interval, and MMSE scores. **a** Higher IIV was associated with fewer finger taps in AD, MCI and HOA; however, PD patients showed the opposite pattern. **b** Higher IIV was associated with longer response inter-tap interval for AD, MCI, and HOA; however, PD patients showed the opposite pattern. **c** Higher IIV was associated with lower MMSE scores in AD, MCI, and HOA, but not PD

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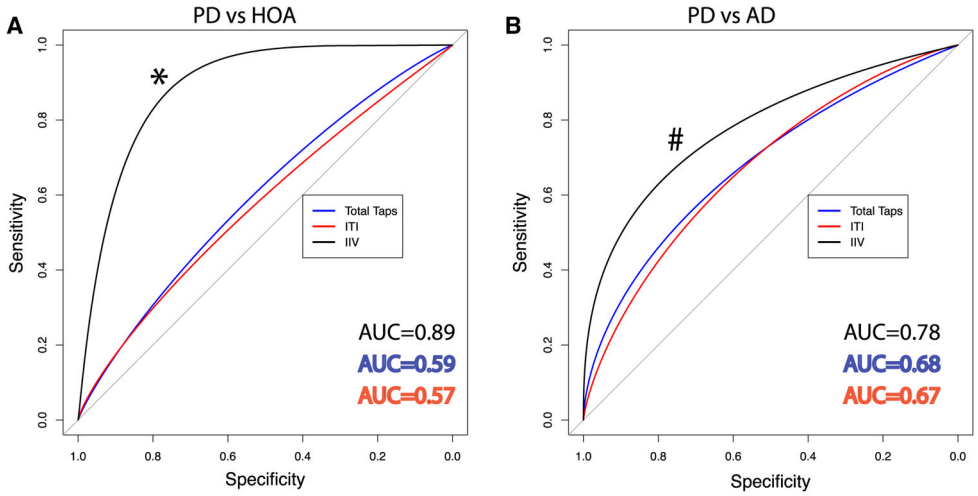

Fig. 4.

Receiver-operating characteristic curves for diagnostic classification using finger tapping outcome measures. **a** Intra-individual variability (IIV) of finger tapping better discriminated between PD and HOA than either the total number of taps or inter-tap interval (ITI). **b** IIV of finger tapping discriminated PD from AD better than total taps, and marginally better than ITI. $^{*}p < 0.05$; $^{\#}p = 0.05$

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Table 1

Participant characteristics and clinical scores

	HOA	AD	MCI	PD
N	62	131	46	63
Age, mean (SD)	71.37 (9.47)	75.85 *,#,+ (7.86)	72.3 (9.03)	71.63 (6.83)
Education, mean (SD)	14.64 (4.29)	13.66 + (4.24)	13.41 (4.79)	15.96 ^ (2.44)
Sex (M/F)	19/43	53/78 +	19/27	40/23 ^,‡
Hand (A/L/R)	1/5/56	5/14/112	1/2/43	3/8/52
Dominant hand (A/L/R)	1/4/56	1/10/120	0/2/44	3/8/52
Race (% Caucasian)	59.68	73.28	63.04	96.82
Duration of illness (years)	–	3.86 (3.33)	3.79 (3.98)	10.41 (18.69)
MMSE, mean (SD)	28.77 (1.82)	21.39 *,#,+ (4.93)	26.45 † (3.46)	27.49 ‡ (2.31)
CERAD NP Score, total (SD)	82.6 (9.43)	47.73 *,# (14.85)	64.8 † (13.59)	–
CDR, mean (SD)	0.049 (0.145)	0.826 *,# (0.43)	0.454 † (0.145)	–
UPDRS motor score, mean (SD)	–	–	–	19.81 (9.48)
DRS, mean (SD)	–	–	–	136.96 (6.4)
LEDD				587 (337)

Results of pairwise *t* tests between groups

MMSE Mini-Mental State Examination, *CERAD NP Score* Consortium to Establish A Registry for Alzheimer's Disease Neuropsychological Test Score, *CDR* Clinical Dementia Rating Scale, *UPDRS* Unified Parkinson's disease rating scale, *LEDD* levodopa equivalent doses

* AD significantly different than MCI

+ AD significantly different than PD

AD significantly different than HOA

^ PD significantly different than MCI

‡ PD significantly different than HOA

† MCI significantly different than HOA. All significant values $p < 0.05$; hand (*A* ambidextrous, *L* left, *R* right)