Clinical Neurology and Neurosurgery 186 (2019) 105542

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Reliability, validity and responsiveness of the squares test for manual dexterity in people with Parkinson's disease

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ARTICLE INFO

Keywords:
Parkinson's Disease
Manual dexterity
Squares test
Reliability
Validity
Responsiveness

ABSTRACT

Objective: Impaired manual dexterity is one of the major disorder in people with Parkinson's Disease (PwPD). However, there is limited research examining the measurement properties, especially the validity and responsiveness of the tools used to assess manual dexterity. The aim of this study was to examine reliability, validity, and responsiveness of the Squares Test (ST) in PwPD.

Patients and Methods: Fifty-seven PwPD and 50 healthy people, all of whom were right-handed, were recruited. The ST, Nine-Hole Peg Test, Unified Parkinson's Disease Rating Scale (UPDRS), and Hoehn and Yahr scale were performed in ON state. For responsiveness analysis, the ST and UPDRS motor score (UPDRS-III) were also performed in OFF state.

Results: The ST showed excellent test-retest reliability. The ST was found to correlate significantly with other outcome measures, which indicated good concurrent validity. PwPD demonstrated significantly lower scores of the ST than healthy people, which demonstrated satisfactory known-groups validity. The ST had excellent discriminant validity. The ST scores of 52 for more affected hand and 62 for less affected hand were shown to best discriminate between PwPD and healthy people. The ST is high internal responsiveness based on standardized effect size and standardized response mean (0.79 and 1.88, respectively for more affected hand and 0.85 and 1.83, respectively for less affected hand), and also PwPD had better performance based on the ST in ON state than in OFF state ($p < 0.001$ for both hands). Moderate correlations were found between the change scores of the ST and UPDRS-III, which reflected adequate external responsiveness.

Conclusions: The ST is a reliable, valid and responsive measurement tool for assessing manual dexterity in PwPD.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease, with a prevalence of 9.5% among the elderly [1]. PD is characterized by four major motor signs: resting tremor, bradykinesia, rigidity, and postural instability [2]. These motor symptoms adversely affect hand functionality, even in early stages of the disease [3–6]. Changes in hand such as resting tremor and micrographia occur in approximately 80% of people with PD (PwPD) as the first sign of PD [7].

Manual dexterity, which is defined as the ability to coordinate small movements of the hands and fingers rapidly and accurately [8], is one of the most important components of hand function. Impaired manual dexterity is a commonly reported problem in PD [5,6,9,10]. Reduced movement velocity [11], loss of fine motor control [9], abnormal high grip force in manipulating an object [12], disabilities of hand preshaping [13], impaired reach-to-grasp movement [14], and a lack of performing sequential movements [15] are shown in PD, which could have negative effects on daily living activities such as tying laces, buttoning clothing, using mobile phones and remote controls for TVs [6]. Consequently, deteriorated manual dexterity may reduce quality of life and contribute to the burden of the disease [16].

Identifying and monitoring impaired manual dexterity by using standardized and clinically available measurement tools are important for the optimal assessment and care of PwPD. An appropriate measure should have essential psychometric properties including reliability, validity and responsiveness [17]. However, manual dexterity is commonly assessed using non-standardized methods such as observational

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https://doi.org/10.1016/j.clineuro.2019.105542
Received 24 September 2018; Received in revised form 26 September 2019; Accepted 28 September 2019
Available online 01 October 2019
0303-8467/

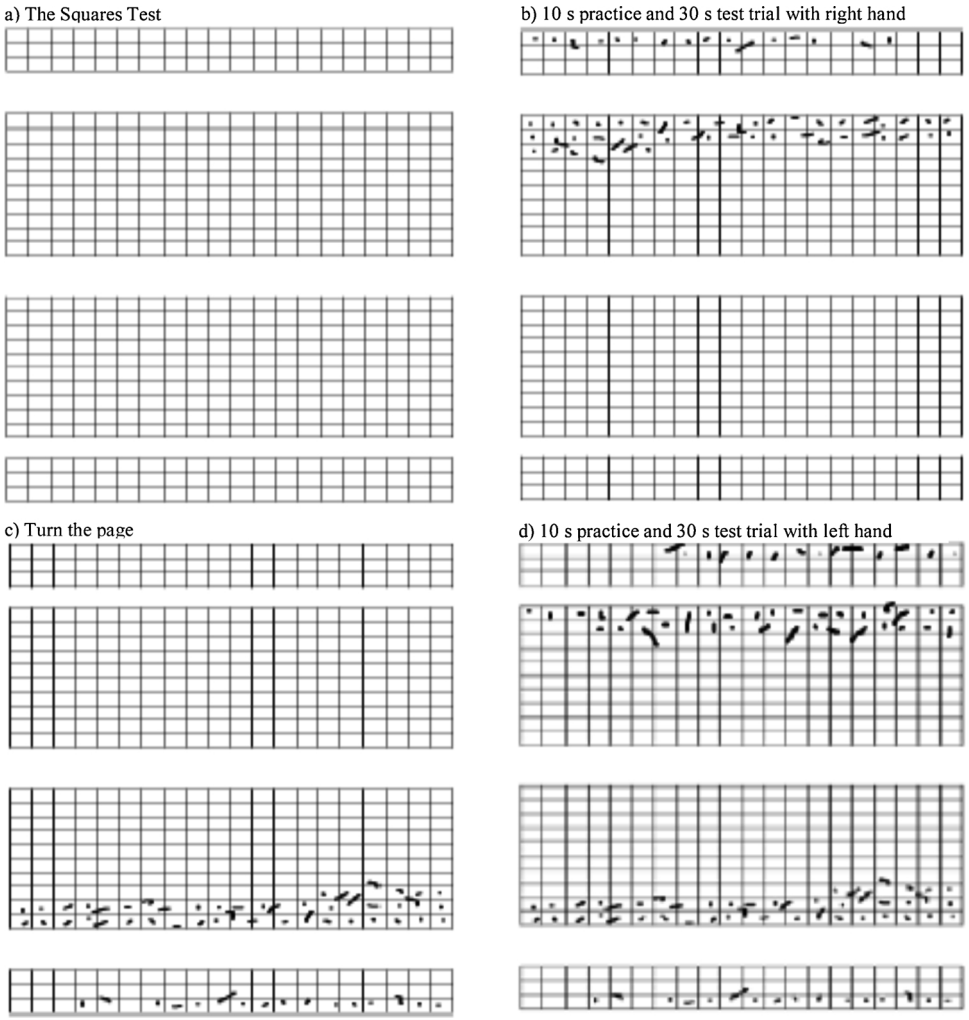

Fig. 1. The Squares Test. Individuals have one practice and test trial for each hand. (a) The Squares test, (b) placed in 34 squares with the right hand during 30 s test trial, (c) turn the page for use left hand, (d) placed in 23 squares with the left hand during 30 s test trial.

analysis and non-standardized timed tasks in PD [18]. Standardized tests such as the Nine-Hole Peg Test (9-HPT) [19], Purdue Pegboard Test [20,21], and Jebsen Taylor Hand Function Test [22] are reliable and valid measurement tools that are used in research and clinical practice for PwPD. However, they are time-consuming and have special test materials. In addition, clinicians and researchers do not have suitable assessment tools which support the measurement properties, especially the validity and responsiveness [23–25].

The squares test (ST) is originally developed to determine handedness. It is easily administrated, inexpensive, not time-consuming, and uses simple equipment including paper and pencil [26]. The ST assesses hand functionality such as manual dexterity and finger dexterity based on the total number of dots placed accurately in squares. It is a reliable and valid measurement tool for assessing manual dexterity in people with multiple sclerosis [27]. To date, however, no study has used the ST to examine the manual dexterity of PwPD.

There is clearly a need for a reliable, valid and responsive test that reflects manual dexterity. Thus, the aim of our study was to examine reliability, validity and responsiveness of the ST in PD.

2. Materials and methods

2.1. Participants

We included 57 people with idiopathic PD (35 men, 22 women) and 50 healthy people (34 men, 16 women). All the PwPD were selected consecutively on the basis of the inclusion criteria: at least 40 years of age, neurologist-diagnosed idiopathic PD (using UK Brain Bank criteria) [28], Hoehn and Yahr (H&Y) stage between 1 and 4 [29], and living in the community. We excluded individuals with other major diseases (e.g., stroke, dementia, and severe rheumatoid arthritis), diagnosis of atypical Parkinsonism, H&Y stage 5, or previous surgical management of PD. Healthy people were recruited as control subjects from community centers through poster advertising if they were 40 years or older and did not use any medications with dopaminergic or anticholinergic properties.

The ethics committee of the university approved the study protocols. It was performed in accordance with the guidelines of the Declaration of Helsinki. All eligible participants were informed about the objectives and procedures of the study. Written informed consent was obtained from all individual participants included in the study.

2.2. Procedures

Participants' dominant hand is determined based on the preference of one hand to perform skillful and unimanual tasks such as writing [30,31]. All PwPD were assessed in ON state with the ST, 9-HPT, Unified Parkinson's Disease Rating Scale (UPDRS), and H&Y scale. Healthy people only completed the ST. Test-retest reliability was assessed in a subgroup of PwPD (n = 30) who repeated the ST after 1 week. Fourty-five PwPD were re-assessed with the ST and UPDRS motor score (UPDRS-III) in their OFF state to examine responsiveness while 12

PwPD were not re-assessed due to not having OFF state and motor deterioration according to UPDRS-III.

2.3. Outcome measures

The ST was modified from its original design in this study. To perform the ST, a sheet of white paper is needed on which four grids are printed. Two grids are 20 squares across by 3 squares at the top and bottom of the paper for practice trials and two grids are 20 squares by 10 squares at the middle of the paper for test trials. The edge length of the square is 6 mm. Individuals place a dot inside as many squares as possible during 10 s for practice trial and 30 s for test trial. They start in the upper row of the grid and complete each row from left to right for their right hand and right to left for their left hand. The paper 180° is turned by the examiner after testing the right hand so that the unused grids are at the top of the paper. For each hand, the score was calculated the total number of dots marked in the squares during test trial. Higher dot scores indicate better manual dexterity [26,27]. An example of the ST can be seen in Fig. 1.

The 9-HPT is one of the most commonly used tests and a clinically appropriate measurement tool for assessing manual dexterity in PD [19]. A square board with nine holes and a container with nine wooden pegs are used. Participants pick up the pegs from the container one by one and then return them to the container as quickly as possible. If a peg is dropped, the examiner quickly retrieves it or replaces it with a spare peg. The 9-HPT is a time-monitored test, where the examiner starts timing when an individual touches the first peg and stops when the last is placed in the container. This test procedure has been standardized. Lower times indicate better manual dexterity [32]. Each hand was tested twice.

UPDRS is used to assess disease severity in PD. It consists of four parts including: (1) mentation, behaviour, and mood, (2) activities of daily living, (3) motor examination, and (4) complications of treatment. Higher scores reflect higher disease severity [33].

H&Y scale is used to describe how the symptoms of PD progress. This scale ranges from 1 to 5 and higher stages indicate more severe disease [29].

2.4. Statistical analysis

Descriptive statistics were used to summarize the demographic characteristics of the subjects. The normality of data was assessed using the Kolmogorov-Smirnov Test. The chi-square and independent *t-tests* were used to make comparisons between characteristics of PwPD and healthy people.

Test-retest reliability was assessed using intraclass correlation coefficients (ICC). The ICC was classified as: excellent (> 0.75), moderate to good (0.50-0.75), and fair (< 0.50) [34]. Bland Altman plots were constructed to visualize the level of agreement between two measures for the ST [35].

Concurrent validity, known-groups validity, and discriminant validity were performed to assess validity. Concurrent validity was assessed using Pearson´s correlation coefficient (r) or Spearman correlation coefficient (r_s) with the 9-HPT, UPDRS total, UPDRS activities of daily living (UPDRS-II), UPDRS-III, and H&Y stage [34]. Known-groups validity of the ST was assessed by comparing scores on the ST between PwPD and healthy people using independent *t-tests*. Discriminant validity was assessed by the receiver operating characteristic (ROC) curves. ROC analysis was used to determine the best ST cutoff score. ROC curves were plotted to determine the area under the curve (AUC), which represents the ability of the ST to discriminate between PwPD and healthy people [34]. A general guideline of the AUC suggested AUC ≥ 0.70 for acceptable discrimination and ≥0.80 for excellent discrimination [36].

Responsiveness is classified as internal responsiveness and external responsiveness. Internal responsiveness is defined as the ability of a measure to detect change over a specific time period. Internal responsiveness of the ST was calculated using the standardized effect size (SES) and the standardized response mean (SRM) and paired *t-test* between ON and OFF state. The SES and SRM were derived from the following formula [37,38]:

SES = (post-test mean – pre-test mean) / SD baseline,

SRM = (post-test mean – pre-test mean) / SD changes

An effect size ≥0.80 is indicative of large responsiveness, an effect size of 0.50-0.79 is indicative of moderate responsiveness, and an effect size < 0.50 is indicative of small responsiveness [37]. External responsiveness is defined as the ability of a measure to detect change over a specific time period with reference to the changes determined by an external criterion. External responsiveness was evaluated by examining the r_s between the change scores of the ST and the UPDRS-III [37]. A moderate correlation is considered to be adequate for external responsiveness.

Values of all correlation coefficients were classified as poor (0–0.25), fair (0.25–0.50), moderate (0.50–0.75), and strong (0.75–1) [34]. All analyses were performed with the use of SPSS Statistics 15 software (SPSS Inc., USA). All reported p values were two-tailed. The level of significance was set at $p < 0.05$.

3. Results

Fifty-seven PwPD (35 men [61.4%], 22 women [38.6%]) with a mean age of 67.5 ± 9.4 years and a mean time since PD of 8.4 ± 6.0 years were recruited. Another 50 healthy people (34 men [68.0%], 16 women [32.0%]) with a mean age of 67.1 ± 9.5 years were recruited. The group characteristics of participants are summarized in Table 1.

Table 2 showed excellent test-retest reliability for more affected and less affected hand (ICC = 0.955 and ICC = 0.934, respectively). The Bland–Altman plots showed that 28 out of 30 data points of the ST scores for more affected hand and 29 out of 30 data points of the ST scores for less affected hand were within the 95% limits of agreement (± 1.96 standard deviations) (Fig. 2.A and B, respectively).

Table 3 showed correlations between the ST and other outcome measures. For more affected hand, the ST has a strong negative correlation with the 9-HPT ($r = -0.789$, $p < 0.001$), moderate negative correlations with the UPDRS total, UPDRS-II, UPDRS-III, and H&Y stage ($r = -0.713$, $p < 0.001$; $r = -0.715$, $p < 0.001$; $r = -0.690$,

Table 1
Group's characteristics.

Characteristic	People with Parkinson´s Disease (n = 57)	Healthy People (n = 50)	p
Age (years)	67.5 ± 9.4	67.1 ± 9.5	0.901
Gender (n)			
Male	35	34	0.477
Female	22	16	
Dominant Side (n)			
Right	57	50	1.000
Left	0	0	
Disease duration (years)	8.4 ± 6.0	–	
H&Y Stage (n)			
1	4		
2	25	–	
3	22		
4	6		
UPDRS-total	41.9 ± 18.4	–	
UPDRS-II	10.7 ± 6.4	–	
UPDRS-III	26.1 ± 10.4	–	

Abbreviations: H&Y: Hoehn and Yahr, UPDRS: Unified Parkinson's Disease Rating Scale, UPDRS-II: Unified Parkinson's Disease Rating Scale Activities of Daily Living, UPDRS-III: Unified Parkinson's Disease Rating Scale Motor Score.

Table 2
Test-retest reliability of the Squares Test in people with Parkinson´s Disease.

Variable	Testing Hand	ICC (95% CI)
Test-retest reliability	More affected hand	0.955 (0.905–0.978)
	Less affected hand	0.934 (0.861–0.968)

Abbreviations: CI: confidence interval, ICC: intraclass correlation coefficient.

$p < 0.001$; $r_s = -0.648$, $p < 0.001$, respectively). For less affected hand, the ST has a strong negative correlation with the 9-HPT ($r = -0.810$, $p < 0.001$), moderate negative correlations with the UPDRS total, UPDRS-II, UPDRS-III, and H&Y stage ($r = -0.594$, $p < 0.001$; $r = -0.628$, $p < 0.001$; $r = -0.592$, $p < 0.001$; $r_s = -0.510$, $p < 0.001$, respectively).

Significant differences in the ST scores were found between PwPD and healthy people for more affected/non-dominant and less affected/dominant hand ($p < 0.001$ and $p < 0.001$, respectively) (Table 4).

The ST showed excellent discriminant validity between PwPD and healthy people for more affected/non-dominant and less affected/dominant hand. The cutoff scores were 52 dots for more affected/non-dominant hand (area under the curve [AUC], 0.935; sensitivity, 86.0%; specificity; 90.0%) and 62 dots for less affected/dominant hand (area under the curve [AUC], 0.923; sensitivity, 94.7%; specificity; 82.0%), which were found to best discriminate healthy people from those with PwPD. Fig. 3 showed the results of the ROC analysis.

Table 5 showed the results of the responsiveness indices of the ST. The values of the SES and SRM in the ST score were 0.79 and 1.88, respectively for more affected hand and 0.85 and 1.83, respectively for less affected hand. The results of the paired t tests indicated that the score changes of the ST were statistically significant for both hands ($p < 0.001$). Table 5 also showed moderate negative correlations between the changes of the ST and those of the UPDRS-III for more affected and less affected hand ($r_s = -0.696$, $p < 0.001$ and $r_s = -0.717$, $p < 0.001$, respectively).

4. Discussion

This has been the first systematic study investigating the test-retest reliability, validity, and responsiveness of the ST in PD.

The test-retest reliability of the ST was excellent for both hands. In addition, excellent test-retest reliability of the ST is also represented by the excellent agreement in Bland-Altman plots.

The ST score had moderate to strong negative correlations with the 9-HPT, UPDRS total, UPDRS-II, UPDRS-III, and H&Y stage for both hands, which indicated good concurrent validity.

The ST scores showed strong negative correlations with the 9-HPT, which could result from the fact that the ST is very similar to the 9-HPT in several features such as manipulating object, velocity, timing, aiming, and movement of wrist.

Table 3
Correlation between the Squares Test and other outcome measures.

Variable	The ST score of more affected hand	p	The ST score of less affected hand	p
9-HPT	$r = -0.789$	< 0.001*	$r = -0.810$	< 0.001*
UPDRS total	$r = -0.713$	< 0.001*	$r = -0.594$	< 0.001*
UPDRS-II	$r = -0.715$	< 0.001*	$r = -0.628$	< 0.001*
UPDRS-III	$r = -0.690$	< 0.001*	$r = -0.592$	< 0.001*
H&Y stage	$r_s = -0.648$	< 0.001*	$r_s = -0.510$	< 0.001*

Abbrevations: 9-HPT: Nine-Hole Peg Test, H&Y: Hoehn and Yahr, PD: Parkinson's Disease, ST: Squares Test, UPDRS: Unified Parkinson's Disease Rating Scale, UPDRS-II: Unified Parkinson's Disease Rating Scale Activities of Daily Living, UPDRS-III: Unified Parkinson's Disease Rating Scale Motor Score. r: Pearson´s Correlation Coefficient, r_s: Spearman´s Correlation Coefficient.

Moderate negative correlations were found between the ST scores and other measures of PD-specific impairments. Our results are in agreement with those of Proud et al. [20] who found moderate negative correlation between manual dexterity with UPDRS-III and UPDRS-total ($r = -0.61$, $p = 0.001$ and $r = 0.65$, $p = 0.003$, respectively), and Vanbellingen et al. [16] who found a moderate negative correlation between manual dexterity and H&Y stage ($r = -0.60$, $p < 0.01$). These correlations were resulted from several items of the UPDRS, especially UPDRS-III, such as bradykinesia, rigidity, finger tapping, hand movements, pronation-supination movements, postural tremor of hands, kinetic tremor and resting tremor. Additionally, activities of daily living such as handwriting, cutting food and handling utensils, dressing, hygiene in UPDRS-II require manual dexterity.

As expected, the results showed that the ST score was able to seperate PwPD with different abilities of manual dexterity (ie, known-groups validity) as indicated by the significant difference in scores between PwPD and healhty people for both hands. Previous studies [6,20,22,39] reported similar findings in spite of different measurement tools, which showed that PwPD had a worse manual dexterity performance when compared to healthy people. Impaired manual dexterity could probably be due to PD-specific impairments including manual dexterity, finger dexterity, finger-tapping speed, steadiness and movement planning [40].

The ST had excellent discriminant validity for both hands. The cutoff scores were 52 dots for more affected/non-dominant hand (area under the curve [AUC], 0.935; sensitivity, 86.0%; specificity; 90.0%) and 62 dots for less affected/dominant hand (area under the curve [AUC], 0.923; sensitivity, 94.7%; specificity; 82.0%), which reflected

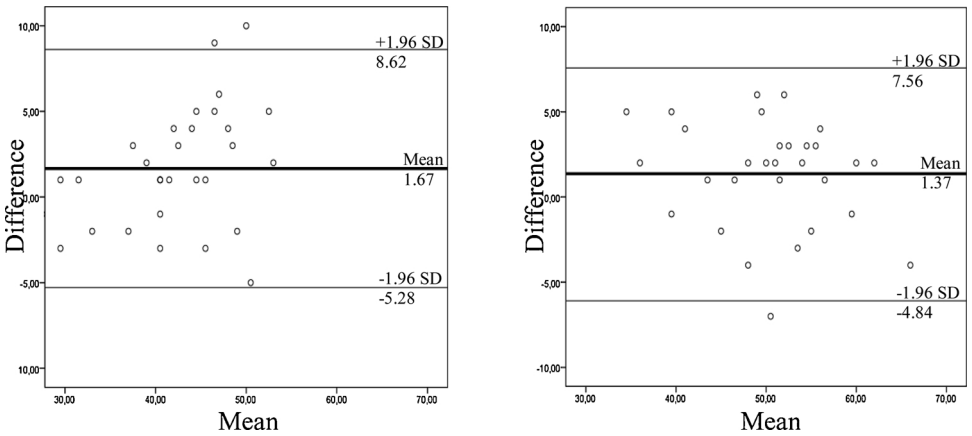

Fig. 2. A) Bland–Altman plot of the ST scores for more affected hand, B) Bland–Altman plot of the ST scores for less affected hand. The thick dash lines represent the mean difference between the initial test and retest. The thin dash lines represent the 95% limits of agreement (± 1.96 standard deviations).

Table 4
Known-groups validity of the Squares Test.

The ST Score	People with Parkinson´s Disease (n = 57)	Healthy People (n = 50)	p
More affected/non-dominant hand	41.05 ± 10.01	61.70 ± 9.17	< 0.001*
Less affected/dominant hand	48.56 ± 10.29	68.10 ± 9.83	< 0.001*

Abbrevation: ST: Squares Test.

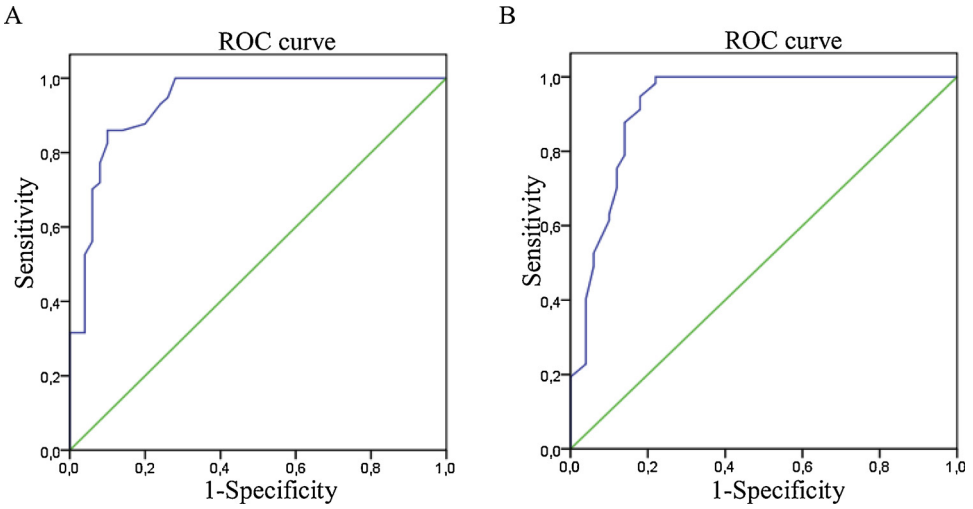

Fig. 3. ROC curves. A) ROC curves for the ST scores for more affected/non-dominant hand, showing discrimination between healthy people and PwPD (AUC, 0.935; sensitivity, 86.0%; specificity, 90.0%). B) ROC curves for the ST scores for less affected/dominant hand, showing discrimination between healthy people and PwPD (AUC, 0.923; sensitivity, 94.7%; specificity, 82.0%).
Abbreviations: AUCarea under the curve, PwPDPeople with Parkinson´s Disease, ROCReceiver operating characteristic, STSquares Test.

Table 5
Responsiveness indices of the the Squares Test.

			Internal Responsiveness			External Responsiveness
The ST score	ON state	OFF state	SES	SRM	p	Change in UPDRS-III
More affected hand	40.38 ± 10.61	32.09 ± 8.86	0.79	1.88	p < 0.001*	$r_s = -0.696$
Less affected hand	47.11 ± 10.34	38.31 ± 9.61	0.85	1.83	p < 0.001*	$r_s = -0.717$

Abbreviation: SES: Standardized Effect Size, SRM: Standardized Response Mean, ST: Squares Test.
r_s: Spearman´s Correlation Coefficient.

that the ST scores could discriminate the performance of healthy people from that of PwPD. These results are consistent with those of Gielen et al. [27] who reported excellent discriminant validity (AUC = 0.9145) for the ST in people with multiple sclerosis. In particular, we selected the ST due to resembling handwriting since a routine writing task such as writing one's full name could be used to discriminate PwPD from healthy subjects and reliable clinical assessment tool in PD [41]. Haaxma et al. [39], reported that writing time and space of a predetermined sentence had acceptable discriminant validity (AUC = 0.71 and AUC = 0.73, respectively). Higher discriminant ability of the ST was due to its characteristics such as placing a dot in a square without drawing the square's side lines, lifting the hand continuously, and performing wrist flexion and extension movement consecutively.

For internal responsiveness, we found moderate and large value of the SES of the ST for more affected and less affected hand, respectively while large values of the SRM of the ST for both hands. The score changes of the ST were statistically significant, which was similar to those of Gebhardt et al. [6] and Foki et al. [42] showing that the performance of manual dexterity was significantly better in ON state than in OFF state. These results in internal responsiveness suggested that the ST could be useful to assess recovery or deterioration of manual dexterity for PwPD. We used to the UPDRS-III as the reference instrument to examine external responsiveness. Changes in the ST scores had moderate negative correlations with changes in the UPDRS-III scores for both hands. That is, decrease in scores of the ST reflected sufficient changes in motor symptoms as measured by the UPDRS-III. Overall, these results suggested high internal and adequate external responsiveness for the ST.

This study has several limitations. First, all participants' dominant hand was their right hand, the participants in the PD group were community-dwelling, there are only 4 PwPD in H&Y stage 1 and 6 in H &Y stage 4, which may have limited the generalization of our findings. Further research is needed to validate the ST in PwPD whose dominant hand is left, PwPD should be institutionalized and categorized into subgroups based on H&Y stage. Second, there are no healthy people in the responsiveness analysis, which limits the comparison of results of responsiveness between PwPD and healthy people. Third, since the same examiner performed the ST and the UPDRS-III in ON and OFF state, the convergence of measurements may be high. Future studies with different examiners performing the measures are needed to determine the responsiveness of the ST.

5. Conclusion

The ST is a reliable, valid, and responsive measurement tool for the assessment of manual dexterity in PwPD. The ST scores of PwPD were significantly lower than those of healthy people, indicating there were deficits in the manual dexterity. The cutoff scores of 52 dots and 62 dots were found to discriminate well between healthy people and PwPD for performing more affected and less affected hand, respectively. Moreover, the ST may be useful for detecting motor deterioration over

time due to its responsiveness to changes in UPDRS-III. The ST is a simple, easy to manage, and clinically available assessment tool, which could be used in clinical and research assessment of manual dexterity of PwPD.

Funding

None.

Declaration of Competing Interest

None.

Acknowledgement

The authors thank the participants who participated in this study.

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