

**Title: Home calligraphic exercises as manual dexterity training in patients with Parkinson's disease: a pilot feasibility study**

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## **Abstract**

**Purpose:** To assess the feasibility and effects on manual dexterity and the quality of life (QoL) of a 12-week home calligraphic training program in patients with Parkinson's disease (PD).

**Methods:** A pilot study with participants recruited from the Movement Disorders consultation at the Hospital 12 de Octubre (Madrid). The main outcome, manual dexterity, was assessed using the Purdue Pegboard Test (PPT). Secondary outcomes included clinical rating scales that contemplate aspects related to manual dexterity (DextQ-24, UPDRSII, UPDRSIII), and QoL (PDQ-39 and EuroQoL-5D).

**Results:** Thirty PD patients (57% males) with a mean age of 66.11 (9.76) years and 93% adherence rate. The PPT scores improved significantly ( $p < 0.0001$ ) from T0 (start of the study) to T1 (after 24 weeks). No statistically significant change was found in DextQ-24, UPDRS-II and UPDRS-III, but a clearly improvement was observed in the QoL measurement: EuroQoL-5D ( $p < 0.0001$ ), PDQ-39 ( $p < 0.0001$ ) and modified PDQ-39 ( $p = 0.022$ ).

**Conclusions:** This is the first study to demonstrate the feasibility and improvement in hand dexterity assessed by the PPT for patients diagnosed with PD after a 12-week home calligraphic training program. A significant improvement was noted in the QoL measurements, such as the PDQ-39, modified PDQ-39, and EuroQoL-5D.

**Key words:** Parkinson's disease; calligraphic exercises; manual dexterity; quality of life; disability

## **Introduction:**

Most patients with Parkinson's disease (PD) suffer from impaired manual dexterity, making it difficult to perform activities of daily living (ADL) such as eating, buttoning, or shaving. This difficulty can appear in the early stages of the disease decreasing the quality of life (QoL) of these patients [1]. Handwriting problems are especially relevant since it is a complex automated activity that encompasses both fine dexterity skills and a set of cognitive, sensory, and perceptual-motor components [2][3]. Although micrographia is not formally included in the diagnostic criteria for PD, it is usually one of the initial symptoms that leads the patient to consult a neurologist. Its pathophysiology is uncertain, but it is believed to be caused by the loss of automaticity due to dysfunction of the basal ganglia [4].

In recent years, there have been several studies on manual dexterity and writing in patients with PD [5][6][7]. Some of them have proposed writing as a biomarker of PD [5], while other studies show improvement in these aspects after a rehabilitation program [6][7]. In 2016, Nackaerts et al. carried out the first randomized study applying writing programs in the intervention group, with improvement in certain calligraphic aspects such as amplitude [8]. In 2017, Vanbellinghen et al. conducted a clinical trial on manual dexterity by applying a home program to an intervention group that included manual dexterity and coordination tasks (HOMEDEXT), showing an improvement compared to the control group [7].

To our knowledge, no studies have comprehensively addressed the feasibility and potential efficacy of manual dexterity training based solely on home calligraphic exercises in subjects diagnosed with PD. Performing calligraphic exercises at home is easy and

inexpensive. Therefore, this pilot study aimed to evaluate the feasibility and effects of a 12-week home calligraphic training program on manual dexterity and QoL.

## **Methods:**

### - Subjects:

A sample of 30 participants diagnosed PD was recruited from the Movement Disorders consultation at the Hospital 12 de Octubre in Madrid. Participants were eligible if they were between the ages of 40 to 80 years and had a clinical diagnosis of PD defined by the United Kingdom Parkinson's Disease Society Brain Bank Criteria [9] with Hoehn and Yahr stages I to IV [10]. They had to be in the medication ON phase (90 minutes after levodopa intake) and the medication had to remain stable 28 days before and during the intervention. The exclusion criteria were as follows: dementia defined as a score of <21 score in the Montreal Cognitive Assessment (MoCA) test [11]; physical comorbidities in the upper extremities not related to PD that could interfere with exercise performance as arthritis, recent fractures, sequelae of stroke or neuropathy; presence of severe tremor or dyskinesias in the dominant hand, being defined severe tremor as a punctuation of  $\geq 3$  in any of the items 20 or 22 of the Unified Parkinson's Disease Rating Scale (UPDRS)-part III, and of  $\geq 2$  point in the item number 33 of UPDRS-IV for severe dyskinesias [12]. Ethical approval for the study was obtained from the Hospital 12 de Octubre Ethics Committee and written informed consent was obtained from all the participants.

### - Procedures

The participants performed a dynamic program of home calligraphic exercises for 12 weeks. There were three phases, each lasting for a period of one month. At the beginning of each phase, participants were instructed by a neurologist and a graphic art specialist in a

face-to-face session at Hospital 12 de Octubre, and a calligraphic exercise workbook was provided. During the following month, the participants performed the calligraphic exercises at home, in 45-minute sessions per day, three times a week. The calligraphic exercises were designed by two graphic arts specialists with the aim of working both the dominant and non-dominant hands, through a series of specific movements and strokes (Figure 1). The workbooks were delivered at the end of each month for follow-up. Participants were evaluated at the start of the study (T0) and after 24 weeks (T1).

#### - Outcome measures

The participant's affiliation data were collected at the baseline visit: age, sex, education (years and level), marital status, dominant hand, time of evolution of the disease and Hoehn and Yahr stage. Then a MoCA test was done to rule out dementia. The same trained neurologist in the group performed all outcome evaluations at T0 and T1 on each participant at Hospital 12 de Octubre.

Manual dexterity, as the main effect, was assessed using the Purdue Pegboard Test (PPT). This is a standardised and well-validated instrument for measuring dexterity in patients with PD [13][14]. It consists of four subtests: dominant hand, non-dominant hand, bimanual, and assembly task. First, patients put as many pegs as possible in the holes on the board within 30 seconds with the dominant hand, then with non-dominant hand and bimanual. The fourth subtest is the assembly task, where patient have to manipulate pegs, collars and washers on the board in 60 seconds. The final score is the number of pegs and pieces placed on the board.

Clinical rating scales that contemplate aspects related to manual dexterity were applied as secondary outcomes: Dexterity Questionnaire-24 (DextQ-24) which is a reliable and valid questionnaire to evaluate dexterity in patients with PD in almost all stages of the disease

(H&Y I-IV) [15], UPDRS-II [12] that was used to evaluate dexterity-related ADL in patients with PD, and the UPDRS-III was used for assessing the motor skills.

To measure the QoL we used the 39-item Parkinson's Disease Questionnaire (PDQ-39), which is a questionnaire specifically designed to assess the QoL in PD [16], and European Quality of Life-5(EuroQoL-5D) [17]. The EuroQoL-5D consists of two parts: a visual analogue scale similar to a thermometer and a descriptive part that embraces six domains of health status. In addition, within the PDQ39, we analysed the subgroup of items 11 to 16 more specific to the basic ADL that require fine motor skills: personal cleanliness, dress, button-up, writing, cutting food, and holding a glass.

- Statistical analyses:

All statistical analyses were performed using Stata Statistical Software (16, StataCorp LLC, College Station, TX, USA) for Windows. Prior to the main statistical analyses, the Shapiro-Wilk test was performed to assess the normality of the continuous variables. Descriptive data were presented as mean and standard deviation (SD) for normal continuous variables and as median and interquartile range (IQR) for non-normal continuous variables. Categorical variables were expressed as absolute or relative frequencies. Normally distributed variables were compared using paired t-tests. Non-normally distributed variables were compared using Wilcoxon test, with a level of significance of 0.05. Bonferroni correction was also applied.

We applied the formula " $MDD\% = z * SEM * \sqrt{2}$ ", where SEM is the standard error of measurement, to calculate the minimum detectable difference (MDD). In this calculation, the SD was used for all tests. MMD corresponds to the minimum amount of change that is detectable beyond the threshold error [18].

**Results:**

Thirty PD patients (57% males) with a mean age of 66.11 (9.76) years, and 70% of which had elementary school certification, participated in this study. Sociodemographic and clinical characteristics are shown in Table 1.

Twenty-eight of the 30 participants completed the home calligraphic exercises, indicating a 93% adherence rate. No significant differences were found between participants who completed or did not completed the calligraphic program ( $p > 0.05$ ).

Table 2 shows the pre- and post-intervention PPT scores. The dominant hand scores improved significantly from T0 to T1: -1.35 (SD: 0.68) (95% CI, -1.61-1.08,  $p < 0.0001$ ). Also, scores on the non-dominant hand, bimanual and assembly task were significantly ( $p$ -values  $< 0.05$ ) better from T0 to T1: - 0.98 (SD: 0.81) (- 1.29 - -0.66), - 0.71 (SD: 0.53) (- 0.92- -0.51) and -1.86 (SD: 2.92) (-2.99- -0.73) respectively.

Non-statistically significant change was found for DextQ-24 ( $p=0.99$ ), UPDRS-II ( $p=0.94$ ) and UPDRS-III ( $p=0.23$ ). Regarding the QoL measurements, the visual analogue scale part of the EuroQoL-5D, PDQ-39 and modified PDQ-39 showed a significant improvement ( $p$ -values  $< 0.05$ ) from pre- to post-intervention. No significant differences were found in the descriptive part of the EuroQoL-5D ( $p=0.07$ ) (Table 3).

## **Discussion:**

To the best of our knowledge, this is the first study to demonstrate the feasibility and the improvement in hand dexterity assessed by the PPT in patients diagnosed with PD after a 12-week home calligraphic training program. A significant improvement was noted in QoL measurements, such as the PDQ-39, modified PDQ-39, and EuroQoL-5D.

The high adherence rate (93%) supports the feasibility of this home calligraphic program. This training has no adverse effects, and the home-based approach is cost-effective, as the supervision of a therapist is not required. In addition, after the covid-19 pandemic, those therapies that can be developed individually at home have acquired importance and value.

A significant improvement in hand dexterity was observed across the four PPT subtest. This test is considered an adequate tool for measuring hand dexterity with available test-retest and inter-rater reliability studies in subjects diagnosed with PD. Furthermore, the PPT appears to be a more reliable measure of dexterity loss in people with PD as compared to other similar tests, such as the 9-hole plug test (9HPT) [14]. However, there are no reference values for PPT in patients with Parkinson's disease. Although our results showed a significant improvement in the scores of all PPT subtests after the intervention, it would be interesting to assess whether this difference is clinically significant. For this reason, we calculated the MMD, which corresponds to the minimum amount of change that is detectable beyond the threshold error [18]. For the dominant hand, non-dominant hand, and bimanual task, the mean change obtained was higher than the MMD, indicating that our results could be considered clinically significant (Table 2).

Previous studies have shown that writing-based training programs improve certain aspects of writing, such as size and speed, suggesting that consolidation of motor learning is possible in PD [8][19][6]. Vorassot et al. carried out a randomised controlled trial to assess the efficacy of a 4-week handwriting exercise in PD participants. The handwriting practice book consisted of 44 Thai alphabets and each page contained 30 copies of the identical letter of the alphabet. An improvement in writing speed and motor function of the hands, as measured by UPDRS-III, was observed [20]. As suggested by Vanbellinggen, we believe that the UPDRS-III is not specific for the study of dexterity, with other tests such as the 9HPT or PPT being more suitable [7]. Vanbellinggen et al. were the first to conduct a

randomised clinical trial to analyse manual dexterity measured with the 9HPT after manual exercise-based home training (HOMEDEXT), excluding writing. A significant difference was observed, in favour of the HOMEDEXT group as compared to the Thera-band group (control), in the 9-HPT scores and dexterity-related-ADL [7]. Previously, Mateos-Toset et al. showed that a single hand-exercise session (15-minute exercise focused on hand training using therapeutic putty) improved manual dexterity and strength in PD participants [21].

The underlying mechanism by which an improvement in manual dexterity is achieved after writing exercises is unknown. Some authors have proposed consolidation in motor learning and neuroplasticity as possible mechanisms [6][20].

In this study, no improvement was observed in other scales that consider aspects related to general dexterity such as the UPDRS-II, nor in the motor aspects included in the UPDRS-III, probably due to lack of specificity in the function of manual dexterity. A slight but no significant improvement was observed in the DEXTQ-24, which was developed and validated to specifically cover different dexterity-related-ADL in PD [15].

Our results show a clear improvement in the QoL of these PD patients as measured by the PDQ-39, which is a questionnaire specifically designed to assess the QoL in PD. This improvement is still significant in its modified version, which includes the items (from 11 to 16) that are related to fine motor skills. None of the previous studies based on training involving writing have analysed this item. Other studies, such as that by Ferrazoli et al., which analysed a multidisciplinary, aerobic, motor-cognitive and intensive rehabilitation treatment [22], or one by Vanbellingen et al., based on the HOMEDETEX program, showed a clear improvement in the PDQ-39 [7]. EuroQoL-5D results also support an improvement in the QoL.

The main limitation of this pilot study was that there was no control group for comparison. Second, as mentioned above, since there are no normalised PPT values in patients with PD, it is difficult to establish what would be a clinically significant improvement. This preliminary study suggests evidence of its feasibility and the beneficial effect on manual dexterity and the QoL after 12-weeks calligraphic exercises at home. These encouraging results prompted us to develop a randomised controlled trial to confirm these positive results. We consider it an easy-to-perform and low-cost therapy that can have significant benefits for the patient.

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