

# Improvement in Gait Performance after Training Based on Declarative Memory Cues in Patients with Parkinson's Disease: A Randomized Clinical Trial

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## Introduction

Among the motor alterations in PD patients, gait is particularly

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DMCS while the control group ful lled the gait training without the support of any kind of cues or cognitive strategies. To verify retention a er the training, participants were assessed and re-assessed as a follow up 2 and 60 days a er the end of their training.

Both trainings consisted of 8 individual training sessions, twice a week, for four weeks. A er the training sessions, no instruction was o ered to patients for training at home.

## **Experimental training**

e ET consisted of 3 phases, the rst one (Phase 1) was done only in the rst session of training, and the other two (Phase 2 and 3) were repeated at each of the 8 sessions.

**Phase 1:** Initially, in order to better understand the strategy, patients received a short and simple explanation about the de ciency in automatic movement resulting from PD. Following the explanation, the patients memorized a sequence of declarative cues (Figure 2).

e patients would then move on to the next stage only a er having successfully memorized the cue sequence.

Phase 2: Patients organized a sequence of cues using cards

illustrating the subcomponent movements (key movement) involved in taking steps. e sole purpose of this approach was to further consolidate the memorization of cues. e patients would then move on to stage 3 only upon completion of 5 consecutive successful attempts.

**Phase 3:** Gait motor training guided by the cues. In this stage, the patients had to train using declarative cues as a gait performance support through 8 sets following the instruction "Walk in your ordinary speed. Use the key movements to guide your steps saying each of them while you do them". Each set was performed following di erent four trajectories with 80 meters of extension. Markers on the ground delimited the straight and crooked trajectories. e declarative cues had to be evoked verbally by the patients themselves, during gait, triggering the corresponding movement. Whenever patients proved unable to use the cues properly, e.g. they were not able to coordinate the retrieval of cues together with the respective movement, they returned to phase 2.

## **Control training**

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appropriate [48].

e UPDRS has been considered by the Movement Disorders

**Phase 1:** Patients received a short and simple explanation about the de ciency in automatic movement resulting from PD.

**Phase 2**: Patients received a general verbal attentional instruction of "pay attention to your steps and try to walk as well as you can", before starting the walk.

**Phase 3**: Motor training of gait, where the patient had to perform 8 sets, following the instruction "Walk in your ordinary speed, paying attention to your steps" in the identical four trajectories of ET. Additional instructions or cues were not provided by the physiotherapist.

#### **Outcome measures and test procedure**

e three assessments were performed in individual sessions by an independent blinded examiner, before (A1) and two (A2) and sixty days (A3) a er the end of training.

All patients were tested at between 40 and 120 minutes a er their last L-dopa dose, whereby each patient was tested at same time of the day.

**Primary outcome:** e primary outcome was the gait performance in terms of speed and stride length. Patients were asked to walk in a straight trajectory of 20 meters following the sole instruction "upon the go signal, walk as fast as possible to the line and stop". e speed was calculated based on the time to walk 20 meters timed using a digital chronometer. e stride length was calculated based on the number of steps measured using a pedometer.

**Secondary outcome:** e secondary outcome was independence in activities of ADL, assessed by Section II of the Uni ed Parkinson Disease Rating Scale (UPDRS-II). is section includes 12 questions (items 5 to 16) on patient's performance in ADL. Among these questions, two of them investigate gait performance [frequency of falls due to freezing (14); inability to walk (15)], with scores ranging from zero (normal) e application followed the procedure recommended by Goetz to 4 et al. [44]: (1) Reading to the patient the introductory statement for each item of the UPDRS-II. (2) A er the introduction, the interviewer asked the patient: "With all these considerations in mind, do you have any problems in this activity?" (3) If the initial answer was "No" (likely rating is "Code 0"), the rater probed for "Code 1" to verify that this response is not more appropriate. (4) If the initial answer was "Yes,' the interviewer probed for the moderate option, using "Code 2" as an anchor. (5) Depending on subsequent answers to this probed regarding "Code 2," the interviewer should move up or down the scale (to more or less severe options) to nd the most appropriate item response. (6) When the best item response code was determined, the interviewer veri ed this by reviewing those response codes immediately above and the patient should con rm that these other response codes were not

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### Results

Demographic and clinical characteristics of patients in the two groups at baseline are presented in Table 1. Forty four patients presenting mean disease duration of 6.5 years (SD 2.28), mean age of 70.38 years (SD 5.34), comprising 18 women and 26 men, 24 had stage 2, and 20 stage 3, disease evolution according to the Hoehn and Yahr classi cation. ere were no signi cant di erences between the two groups (unpaired t-test; p > 0.05). All participants completed the training without any adverse e ects.

For gait speed (Figure 3), signi cant e ects were observed for training type [F(1,58)=40.23, p<.01, ES=.90], and assessments [F(2,116)=142.31, p<.01, ES=.90] and their interaction [F(2,116)=113.29, p<.001, ES=.95]. e interaction demonstrated that gait speed increased for ET, but not for CT. Post-hoc intra-group comparisons using the Tukey HSD test showed signi cant improvement between A1xA2, and A1xA3 for ET, but not for CT. Inter-group comparison showed non-signi cant di erences in gait speed in A1, but signi cant di erences in A2 and A3 between EG and CG.

For step length (Figure 4), signi cant e ects were observed for training type [F(1,58)=47.66, p<.01, ES=.90], and assessments [F(2,116)=181.10, p<.001, ES=.95] and their interaction [F(2,116)=177.24, p<.001, ES=.99]. e interaction demonstrated that step length increased for ET, but not for CT. Post-hoc intra-group comparisons using the Tukey HSD test showed signi cant improvement between A1 X A2, and A1xA3 for ET, but not for CT. Inter-group comparison showed nonsigni cant di erences in step length in A1, but signi cant di erences in A2, and A3 between EG and CG.

For independence in ADL (Figure 5), signi cant e ects were observed for assessments [F (2,116) = 358.35, p<.01, ES=.80] and their interaction with training type [F (2,116) =118.35, p<.01, ES=.85]. e interaction demonstrated that punctuation decrease for ET, but not for CT. Post-hoc intra-group comparisons using the Tukey HSD test showed signi cant improvement between A1 X A2, and A1 X A2 for ET, but not for CT.

Figure 3:

ere was a signi cant correlation between the improvements in the gait parameters and independence in ADL in A2 (SLPI X ADLPI, R=.46; GSPI X ADLPI, R=.70) and A3 (SLPI X ADLPI, R=.49; GSPI X ADLPI, R=.75), indicated that the e ects of DMCS were generalized to gait-related ADLs.

To summarize, there was a signi cant improvement in gait speed, step length and independence in ADL a er ET, which remained 60 days a er training.

#### Discussion

e present study aimed at investigating the e ects of the gait

training based on declarative memory cue strategy on gait performance in patients with PD.

Two key ndings emerged from this study. e rst of these was that DMCS was e ective for improving gait speed and stride length in patients with PD and, the most important, the training e ects remained a er 60 days without any additional training. Few studies have shown long-term results a er cue training. Some studies reported retention of the gait improvements a er 4 weeks without training [4,10]. е most complete studies that investigated the largest number of patients showed that the e ects of the intervention on the gait in absence of cues reduced signi cantly a er 3 and 6 weeks without training [17,18]. Several factors may have contributed to maintenance of the gait improvement in the current study: (1) the support of the declarative system, (2) easy management of cues and, (3) the detailed explanation on the de ciency in automatic control provided to the patients before the training in order to emphasize the need of implementation of the new strategy to minimize the gait disturbance resulting from PD. In comparison with previous studies, these factors may have facilitated the continuous use of the declarative memory cues by patients a er the training, increasing the retention of the training e ects [51-53].

e second key nding was that the positive e ect was transferable to gait-related ADL, considering the improvements in the independence in ADL. ese results suggest that, a er training, DMCS can be used by patients at home. e tool used to assess the e ect on ADL (section II of the UPDRS) has been widely validated and assesses the perception of the patients themselves regarding their performance in ADLs, over the preceding two weeks [49]. e analysis of the longitudinal metric attributes of the UPDRS showed that the independence in ADL is a valid measure for follow-up of PD patients, being more precise than other scales [54]. Additionally, the minimal clinically important change in reference to the status before treatment for the UPDRS-ADL score is two points for Hoehn and Yahr stages 1-2 and three points for Hoehn and Yahr stage 2-3 [55]. erefore, the mean change found in the current study of 3 points (17.93  $\pm$  4.44 to 14.83  $\pm$ 4.13), can be considered clinically important. is represents a further considerable contribution to gait treatment in the light of a systematic review on e ects of external cues on gait, which concluded that, despite reliable results in laboratory tests, the evidence of generalization of improvement to gait-related ADLs are limited [56].

Taken together, these ndings indicate that the DMCS constitutes an important alternative to treatment of gait dysfunction in PD. One of the mechanisms that might be involved in this strategy could be the attention to movement. Undoubtedly, the increase in attention on gait is an important mechanism activated in this strategy, given the need to retrieve the cues from declarative memory and to manage them during is process most likely depends on working memory and it is well gait. known that this memory module is closely associated with attention. Some studies have indicated that working memory is hampered in PD [57,58] but, even considering that patients in the current study might have had undetected working memory de cits, this would not impair their ability to use the declarative cues. Moreover, it is important to point out that the CT in this study also involved increased attention on gait, and yet positive e ects have not been found. us, there are two possible alternative explanations behind the di erences observed between results obtained from the two strategies: the DMCS allows best engagement of attention, or attention is not the most important factor in improving gait. Further studies are necessary to elucidate possible di erences in the demand of attention between the strategies, since this goes beyond the scope of this study. Considering the second possibility, we believe that declarative cues were a key factor impacting the results. A er memorization and training, the cues not only engage the patient's attention to their foot movements, but also facilitate the movement chunking involved in the gait, triggering the next movement into a previously memorized sequence. It may compensate the de ciency in automatic control on gait associated to the lack in the movement chunking [40,41]. is evidence sustains the possibility of compensation from declarative memory for implicit de ciency,

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