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Do motor subtypes of Parkinson's disease impact the learning of motor tasks?

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HIGHLIGHTS

- Individuals with postural instability and gait difficulty (PIGD) and tremor-dominant (TD) motor subtypes of Parkinson's Disease can acquire and maintain postural control skills over extended periods;
- The performance during the practice of the PIGD motor subtype in postural control skills is worse than TD motor subtypes, but it does not affect the long-term motor learning process;
- The PD motor subtype does not influence the learning of postural control skills.

ABBREVIATIONS

APAs	Anticipatory postural adjustments
COP	Center of pressure
ES	Effect size
MDS-UPDRS	Unified Scale Evaluation of Parkinson's Disease
MiniBEStest	Mini Balance Evaluation System Test
MoCA	Montreal Cognitive Assessment
PD	Parkinson's disease
PIGD	Postural instability and gait difficulty
TD	Tremor-dominant

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BACKGROUND: Previous studies have demonstrated that people with Parkinson's disease (PD) can acquire postural control skills even with the degeneration of motor areas responsible for consolidation of the representation regarding the learned motor skill in long-term memory. However, these findings have not considered the PD motor subtypes – tremor-dominant (TD), and postural instability and gait difficulty (PIGD). Although there is considerable heterogeneity in motor and non-motor symptoms between TD and PIGD, no study has addressed the effect of the PD subtype on learning postural control skills.
AIM: We investigated the influence of PD motor subtypes on the learning of tasks with different postural control demands.
METHOD: Fourteen individuals with PD (7 TD, 7 PIGD) practiced four motor tasks with high postural and cognitive demands. Participants completed 13 one-hour sessions (2x/week for 7 weeks). We considered the first and last practice sessions, pre-test and post-test, respectively. Also, we conducted one-week and one-month retention tests to assess performance persistence (motor learning). We assessed motor performance through the scores achieved on each motor task.
RESULTS: Both groups demonstrated improvement in performance during the acquisition phase. However, the TD group outperformed the PIGD group in all motor tasks, despite both groups showing improvement in motor performance when comparing the results of pre-test with the post-test, and the improved performance was maintained in retention tests. The performance differences between groups are dissipated during consolidation, and they did not directly affect motor learning.
INTERPRETATION: The TD and PIGD motor subtypes learned postural control tasks with different motor and cognitive demands.

KEYWORDS: Parkinson's disease | Motor subtypes | Postural control | Motor learning

INTRODUCTION

Motor learning is defined as a series of processes associated with practice and/or experience that led to a relatively permanent change in the ability to perform a motor skill [1]. In neurologically healthy individuals, this process depends on subcortical structures, including cerebellum and basal ganglia [2–5]. Specifically, the consolidation of the representation regarding the learned motor skill in long-term memory involves striatum nucleus [6]. In Parkinson's disease (PD) there is degeneration of dopaminergic neurons in the substantia nigra of the basal nuclei [7,8], which could impact motor learning in these individuals. Individuals with Parkinson's disease present cognitive and motor symptoms that can make it challenging to practice motor skills [6], an essential aspect of motor learning9.

Despite having well-defined symptoms, PD is a heterogeneous disease in terms of symptoms that can be classified into PD subtypes: dominant tremor (TD) and postural instability and gait difficulty (PIGD) [10,11]. The TD motor subtype predominates resting tremor, low prevalence of cognitive symptoms, slow progression, and better prognosis. The PIGD motor subtype, on the other hand, presents a predominance of bradykinesia, rigidity and alterations related to posture and gait, higher incidence of dementia, faster progression, and worse prognosis [12].

Classification of motor subtypes is important in the initial phase of PD, as identifying subtypes can help predict the disease clinical course of the disease [13]. Thus, correctly diagnosing subtypes supports predicting how the disease will progress, guiding early treatment options [13]. However, the motor subtype can change across the disease progression, mainly from the TD motor subtype to PIGD [14,15]. An effective method for tracking subtype changes and distinguishing between PIGD and TD motor subtypes is evaluating the standing center of pressure (COP) time series, a crucial aspect of postural control [13].

Postural instability is the most refractory to treatment based on dopaminergic replacement through levodopa and its agonists [16] and, with the evolution of the disease, postural control is affected by both cognitive and motor impairment since it requires the complex interaction of these systems [17], especially among individuals of the PIGD motor subtype [16,17].

Several studies have demonstrated that PD does not preclude the learning of motor skills [5,14–21], including postural control skills [18–20]. However, given the heterogeneity of cognitive and motor symptoms between individuals with TD and PIGD, we supposed that the characteristics of each PD motor subtype could influence the learning of postural control tasks. There is a lack in the motor learning scientific literature about the effects of PD motor subtypes on motor learning, even with a current call for new studies to consider the investigation of PD subtypes on motor and cognitive outcomes [21].

Only one study, carried out by Vakil et al [22], included the motor symptoms (predominance of bradykinesia or resting tremor) and procedural memory in PD. The performed task was the stacking of disks in the Tower of Hanoi. There were two outcomes regarding task performance, the execution time and the number of disk movements in three different moments (immediately, 30 minutes later and one week after task practice). The bradykinesia predominance group improved the execution time of the task without improvement in the number of disc movements. The tremor predominance group improved the execution time and the number of disc movements without significant differences to the control group (non-disabled people) [22].

The results of the Vakil et al [22], despite not classifying the groups by motor subtypes but by the predominance of symptoms, we could relate the group with a predominance of bradykinesia with the motor subtype PIGD, and the group with a predominance of tremor with the motor subtype TD. In this study, the TD motor subtype was superior to the PIGD in learning the proposed task.

In this sense, we questioned whether the same behavior would be maintained in tasks with a high demand for postural control since this is the main symptom of the PIGD motor subtype. Only studies in the Motor Control area of study were found in the literature, specifically to postural control tasks. Some studies have demonstrated that the TD subtype performs better than PIGD in balance and gait tasks [23,24] and challenging postural tasks [25]. In this sense, if the PIGD group presents an inferior performance in tasks with high demand for postural control, we hypothesized that this performance could affect the learning of challenging skills with high postural control demands. This study aimed to verify the motor learning process of PD individuals, considering the motor subtypes (TD and PIGD).

METHODS

The study was approved by the Ethics and Research Committee of the School of Physical Education and Sport of the University of São Paulo (CAAE: 44795315.8.1001.5391). This study is part of a larger randomized clinical trial (registration: RBR-27kqv5) that aimed to investigate the effects of a virtual reality intervention in the rehabilitation of individuals with PD [26]. In a complementary study, Freitas et al [27], assessed the performance in the virtual reality intervention using a motor learning experimental design approach (experimental study, with parallel groups (PD x neurologically healthy individuals) including pre, post, and retention tests) to evaluate the motor learning of individuals with PD. In our study, we reanalyzed the Freitas et al [27] to evaluate the impact of PD subtypes on their results [27].

Inclusion and exclusion criteria

Inclusion criteria were individuals diagnosed with idiopathic PD, between stages 1.0 and 3.0 of the Hoehn and Yahr scale [28], motor subtypes TD and PIGD, treated with levodopa and/or its synergists; score < 28 on the Mini Balance Evaluation System Test (MiniBEStest) [29]; who do not have other detectable neurological or orthopedic diseases; who were able to walk with or without the use of aids, with normal or corrected visual acuity; good auditory acuity, these last two criteria being clinically evaluated; without previous experience with the Kinect Adventures!® game and signed the Informed Consent Form for the study.

The exclusion criteria were no other detectable neurological, cardiorespiratory, or orthopedic diseases; no signs of dementia [30] (score of >14/30 on the Montreal Cognitive Assessment (MoCA)) , if they were part of a rehabilitation program within the last six months or if they presented any clinical deficits that made it impossible to perform physical exercises in standing positions, i.e., fall occurrences, freezing observed both at the initial evaluation and during the intervention.

Experimental design

The experimental design was published in Silva [32] and Freitas [27]. Figure 1 displays the distinct phases involved in this design.

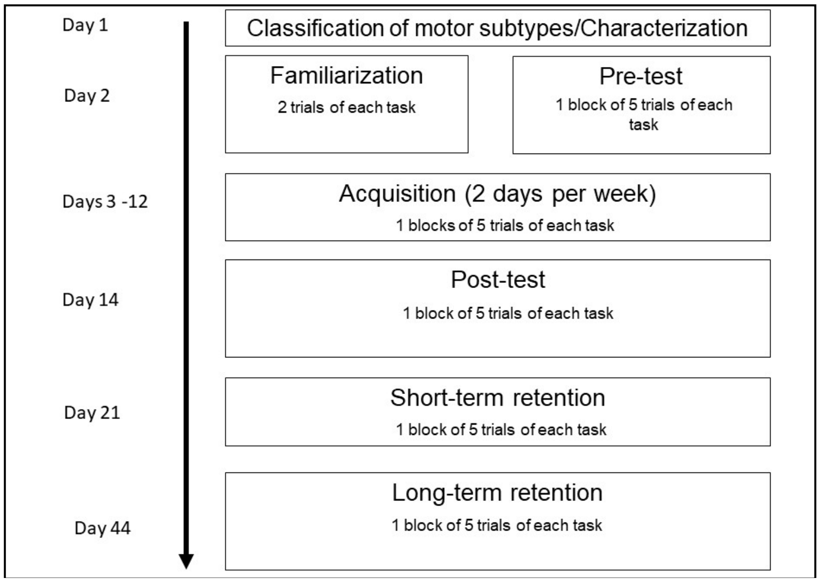

Figure 1. Experimental design.

Initially, the classification of the motor subtypes was determined through Unified Scale Evaluation of Parkinson's Disease (MDS-UPDRS) section III, specifically through items 10 (Gait), 11 (Freezing of gait), 12 (Postural stability), 15 (Postural tremor of the right hands and left), 16 (Kinetic tremor of the right and left hands), 17 (Resting tremor amplitude in the right and left upper limbs, right and left lower limbs, and lip/jaw) and 18 (Persistence of resting tremor) [10]. This classification is an adaptation of the process described by Stebbbins [10].

We collected initial information about the participants in the initial assessment considering age, sex, education, time since diagnosis of PD, medication, motor disease severity assessed with the Hoehn and Yahr Scale [28], the Unified Scale Evaluation of Parkinson's Disease (MDS-UPDRS) section III [33], MiniBESTest and MoCA.

After the initial evaluation, participants participated in 13 training sessions using four Kinect Adventure! games as learning tasks (Xbox 360, Microsoft, Redmond, CA). Whole-body movements were captured with the Kinect camera. Training sessions were conducted individually in a laboratory setting under the supervision of an experienced neurological physical therapist. When needed, participants were offered short rest periods.

The first session consisted of a familiarization period (two trials per task) and a pre-test. A researcher provided detailed instructions about performing the tasks and achieving the goals. The researcher offered movement and posture corrections through manual guidance and verbal commands when needed. During the pre-test, participants performed five trials for each task. The acquisition phase consisted of 11 one-hour sessions offered twice a week. Each session consisted of variable practice in blocks of four tasks, with five trials for each task [34].

The post-test session comprised the same blocks as the acquisition phase but two days after the acquisition phase was finished. If the participant missed a practice session in the acquisition phase, the session was rescheduled for the same week to avoid impacting the practice interval between the experimental sessions.

We administered the short-term retention test one week after the post-test and the long-term retention test one month later. We used the same tasks of the acquisition phase for the retention phase.

The initial assessment and all practice sessions were performed in the ON period of dopaminergic replacement therapy.

Task description

The tasks were selected on the available Kinect Adventure! Games. The selection process was based on a pilot study [36] to ensure: (A) constant displacement of the participant's center of mass through the movement of the upper limbs; (B) weight transfer between lower limbs; (C) squatting; (D) the slopes of the trunk. The cognitive demands established for the selection of games were: (a) visuospatial attention; (B) change of attention; (C) decision making; (D) rapid reaction time; (E) immediate planning and execution. All the components pointed out make the task highly demanding postural control. We selected the following four tasks: 20,000 Leaks; Space Pop; Reflex Ridge and River Rush [32,35].

Specifically, the 20,000 Leaks game involves, as motor demands, lowering, raising, and laterally displacing the center of gravity, taking multidirectional steps; movement of the upper limbs and head; and being able to perform anticipatory postural adjustments. As for cognitive demands, the same game involves focusing attention on several targets, performing a dual task, planning movements, and the reaction time [36] (Table 1).

Space Pop game involves, as motor demands, anteroposterior and lateral displacement of the center of gravity, taking steps in different directions, including backward, abducting, and adducting the upper limbs. As a cognitive demand, the game includes attention to multiple targets; motor dual-task; and movement planning and reaction time [36] (Table 1).

Reflex Ridge game involves, as motor demands, upper limb movements appropriate to the orientation of the spheres, lowering and raising the center of gravity, taking lateral steps to dodge obstacles, and jumping. The game incorporates divided attention into different targets, requiring players to avoid obstacles and reach spheres while planning upper limb movements [36] (Table 1).

River Rush game involves, as motor demands, latero-lateral displacement of the center of gravity, lateral steps, and jumps. As cognitive demands, selective attention to the different paths with a greater number of balls, in addition to attention to reaching targets, motor planning to move the boat in the best direction [36] (Table 1).

Table 1. Rasks description. Adapted by Freitas et al[27] and Mendes et al[36].

Task	Motor demands	Cognitive demands
20,000 Leaks 	Lowering, raising, and laterally displacing the center of gravity, taking multidirectional steps; movement of the upper limbs and head; and being able to perform anticipatory postural adjustments	Focusing attention on several targets, performing a dual task, planning movements, and the reaction time
Space Pop 	Anteroposterior and lateral displacement of the center of gravity, taking steps in different directions, including backward, abducting, and adducting the upper limbs	Attention to multiple targets; motor dual-task; and movement planning and reaction time
Reflex Ridge 	Upper limb movements appropriate to the orientation of the spheres, lowering and raising the center of gravity, taking lateral steps to dodge obstacles, and jumping	Divided attention into different targets, some to be avoided (obstacles) and others to be reached (spheres), planning upper limb movements
River Rush 	Latero-lateral displacement of the center of gravity, lateral steps and jumps	Selective attention to the different paths with a greater number of balls, in addition to attention to reaching targets, motor planning to move the boat in the best direction

Data analysis

For all tasks, the final score was used as the dependent variable. Normality tests and homogeneity of variance were performed using the Kolmogorov-Smirnov and Levene tests, respectively. Inferential analyses of the pre-test, post-test, and short-term and long-term retention times were performed using the Multiple Comparison Analysis of Variance (4x2). We performed a calculation of the p-value and effect size (ES). The alpha of 0.05 was used as statistical significance.

RESULTS

Fourteen PD individuals (7 TD and 7 PIGD) participated in this study (Table 2). The groups did not differ in the co-variable measures, except for postural control assessments. No participant missed a session during the acquisition phase. However, one participant from the EG did not complete the study due to clinical instability and he was excluded from the study however an intention-to-tret-analysis was performed with the data (Figure 2).

Table 2. Characterization of study participants (Tremor dominant group - TDG, n=7; Postural instability and gait difficulty Group - PIGDG, n=6).

	TDG	PIGDG	*p*
Sex (F/M)	3/4	1/6	_____
Age mean (sd)	68.71 (5.64)	62.5 (6.83)	0.24
Education mean (sd)	12.57 (4.54)	8.5 (3.83)	0.11
MoCA mean (sd)	25.85 (1.57)	20.5 (4.41)	0.08
MiniBESTest mean (sd)	23.28 (5.49)	18 (7.53)	0.17
MDS-UPDRS mean (sd)	15.85 (7.64)	25.34 (7.99)	0.05*
H&Y (number of participants)	1.0: 2 1.5: 2 2.0: 0 2.5: 1 3.0: 2	1.0: 1 1.5: 0 2.0: 1 2.5: 2 3.0: 2	______

TDG: Dominant Tremor group; PIGDG: Postural instability and gait difficulty group; H&Y: Modified Hoehn & Yahr Scale; MoCA: Montreal Cognitive Assessment; MiniBESTest: Mini Balance Evaluation System Test F: female; M: male; sd: standard deviation; *: $p \leq 0.05$.

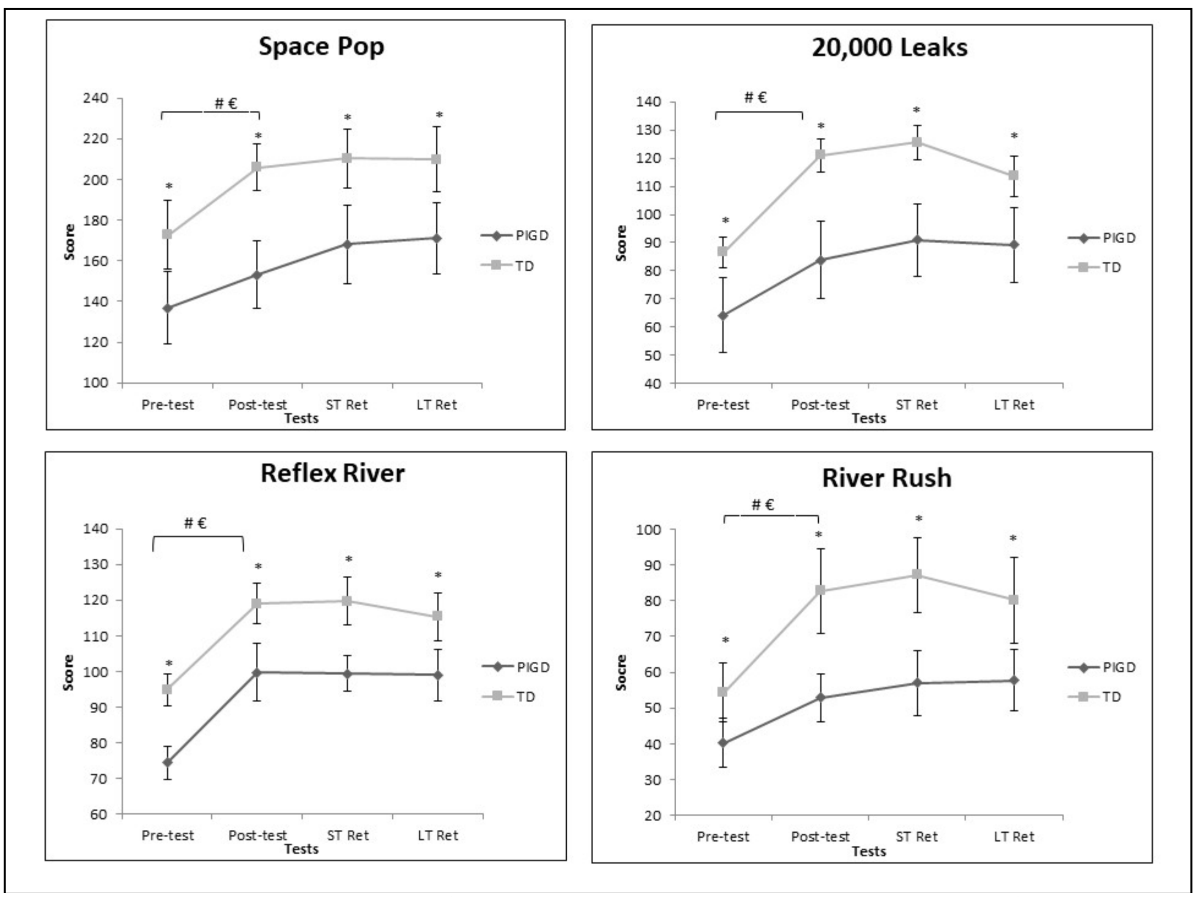

Figure 2. Measures of learning in the practiced games (Tremor dominant Group - n=7; Postural instability and gait Group - n=7). ST Ret CP: Short-term Retention, LT Ret: Long-term Retention, TDG: Tremor dominant group; PIGDG: Postural instability and gait difficulty group, * intergroup difference, #: intragroup difference in TDG, €: intragroup difference in PIGDG. p≤0.05.

Both groups demonstrated improvement in performance during the acquisition phase, but the PIGDG scored worse than the TDG for all tasks (20,000 Leaks: $p<0.00$; ES =1.000; Space Pop: $p<0.00$; ES =0.980; Reflex Ridge: $p <0.00$; ES =1.000; River Rush: $p<0.00$ ES =1.000) There was no interaction effect between the moment and group factors.

Despite the lower performance of PIGDG compared to TDG, in intragroup analysis, there was a significant increase in the performance between the pre-test and post-test in both groups for all tasks (20,000 Leaks: $p<0.00$; ES =1.000; Space Pop: $p=0.04$; ES=0.550; Reflex Ridge: $p<0.00$; ES=1.000; River Rush: $p=0.01$; ES=0968), and the post-test performance was maintained for the short and long-term retention tests in all tasks.

DISCUSSION

The present study aimed to verify the motor learning process of individuals with PD, considering the motor subtypes (TD and PIGD) in tasks with high demand for postural control, and the initial hypothesis was that the inferior performance presented by the PIGD motor subtype could affect the learning of these tasks. The results did not support the hypothesis that the motor subtype would impact the motor learning of postural skills control. The participants of both groups learned the tasks despite the inferior performance of the participants of the PIGD motor subtype.

A vast literature points have demonstrated that individuals with PD can learn different motor skills [5,18,20,37–40], including postural control skills [18–20]. However, these studies have limited participant characteristics to individuals with mild to moderate stages of the disease and without a predominant motor or cognitive symptom. Despite Parkinson's disease being a progressive and heterogeneous condition regarding motor and cognitive symptoms, the participants were grouped and compared to neurologically healthy individuals.

Some specific impairments have been identified in the pathophysiology of the motor subtypes. The TD motor subtype presents degeneration in the medial substantia nigra, ventral internal globus pallidus, thalamus and midbrain and a smaller distribution of Lewy bodies [12]. The PIGD motor subtype presents degeneration in the ventrolateral substantia nigra [12], significantly wider distribution of Lewy bodies [12] and increased density in the regions of the substantia nigra and frontal lobe. In addition, they present increased gray matter atrophy in the supplementary motor area, postcentral gyrus, precentral gyrus, medial frontal gyrus; caudate nucleus and cerebellum [41,42]. According to Marinelli [43,] in the initial stages of motor learning, there is a predominance of involvement of the "visuo-cognitive loop" (involving dorsolateral prefrontal cortex – inferior parietal cortex – anterior part of the striate nucleus), which is followed by a gradual reduction in favor of activating the "motor loop" (involving motor, pre-motor, somatosensory area and supplementary motor area – posterior part of the striate nucleus).

In this regard, we can speculate that the various motor subtypes might impact different phases of motor learning due to their distinct pathophysiology involving other areas. Specifically, the PIGD motor subtype, characterized by degeneration in the ventrolateral substantia nigra, may face more significant challenges in automating learned motor actions, particularly in the consolidation phase. However, our study did not identify any significant difference between the post-test and retention intervals in short- and long-term retention. Therefore, it is unclear if the motor subtypes have varying effects on the retention of postural control skills.

The performance of the PIGD motor subtype participants was inferior to the TD participants in all analyzed phases and all proposed tasks. Our study did not aim to investigate the effect of PD subtypes on performance during practice. Nevertheless, the results are consistent with previous studies on motor control, which have demonstrated inferior motor performance in PIGD participants compared to TD participants in postural control tasks. Pelicioni et al [24] reported that PIGD motor subtype individuals exhibit poorer performance in a sit-to-walk task than TD motor subtype individuals. The sit-to-walk task is a highly challenging postural task, similar to the tasks proposed in our study. Pelicioni et al [24] also showed inferior performance in the timed-up-and-go in individuals of the PIDG motor subtype in relation to non-PIGD, with a higher frequency of falls for PIDG [44].

The statistically significant difference found in the MDS-UPDRS [45] between the groups could explain the significant difference in performance. However, both groups were similar in the MiniBEStest, a specific postural control test. MiniBESTest assesses four postural control systems: anticipatory postural adjustments (APAs), postural responses, sensory orientation, and gait stability. MiniBESTest evaluates, among other items, the base of support, the alignment of the center of pressure, strength, and range of motion of the ankle, sitting and standing, functional reach, balance in single-leg stance, gait and performance in the stand-up and walk test in a simple task and dual task [46]. Therefore, we believe MDS-UPDRS differences in baseline can not explain the differences in motor learning between the groups.

Understanding the mechanisms of motor learning in different subtypes of PD is crucial for clinical decision-making [47]. Studies on motor learning have been used to guide clinical interventions for neurorehabilitation [48]. The success of these interventions depends on how well several factors, such as the quality of practice, feedback, attention, and instruction, are aligned to the characteristics of each clinical population. It is crucial to consider the individual differences of patients with the same neuro disease, as they may respond differently to specific interventions. Our study highlights that individuals with PGID may require more postural control and balance training than TD individuals during rehabilitation due to their lower responsiveness. This information must be considered when designing neurorehabilitation programs for PD patients. Our study has some limitations. It is a sub-analysis of the study by Freitas et al [27]. Thus, the number of participants was determined based on the sample calculation of the original study; then, future studies with a larger sample size are needed to validate our findings.

Secondly, our findings are restricted to postural control tasks. It is important to investigate tasks with varying demands to determine how they affect motor learning in individuals with PGID and TD. For instance, PD motor subtypes may affect performance and learning of manipulative tasks differently than postural control tasks.

CONCLUSION

Individuals with Parkinson's disease classified as postural instability and gait difficulty (PIGD) or tremor-dominant (TD), can learn postural control skills. They can retain these skills in both the short and long-term, even though the PIGD motor subtype exhibits inferior performance compared to the TD motor subtype.

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