

Four-week trunk-specific exercise program decreases forward trunk flexion in Parkinson's disease: A single-blinded, randomized controlled trial

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ARTICLE INFO ABSTRACT Keywords: Introduction: Pathological forward trunk flexion is a disabling and drug-refractory motor complication of Bent spine syndrome Parkinson's disease (PD) leading to imbalance, pain, and fall-related injuries. Since it might be reversible, early Camptocormia and multidisciplinary management is emphasised. The primary aim was to compare the effects of a four-week Parkinson's disease trunk-specific rehabilitation program on the severity of the forward trunk flexion. The secondary aim was to Postural balance compare the training effects on the motor impairments, dynamic and static balance, pain, falls, and quality of Rehabilitation life Quality of life Methods: 37 patients with PD (H&Y \leq 4) and forward trunk flexion were randomized in the experimental Falls (n = 19) or control group (n = 18). The former consisted of active self-correction exercises with visual and proprioceptive feedback, passive and active trunk stabilization exercises and functional tasks. The latter consisted of joint mobilization, muscle strengthening and stretching, gait and balance exercises. Protocols lasted 4 weeks (60 min/day, 5 days/week). Before, after, and at 1-month follow-up, a blinded examiner evaluated patients using primary and secondary outcomes. The primary outcome was the forward trunk flexion severity (degree). Secondary outcomes were the UPDRS III, dynamic and static balance, pain falls, and quality of life assessment. Results: The experimental group reported a significantly greater reduction in forward trunk flexion than the control group from T0 to both T1 (p = 0.003) and T2 (p = 0.004). The improvements in dynamic and static balance were significantly greater for the experimental group than the control group from T0 to T2 (p = 0.017and 0.004, respectively). Comparable effects were reported on the other outcomes. Pre-treatment forward trunk flexion values were highly correlated to post-treatment trunk deviation changes. Conclusion: The four-week trunk-specific rehabilitation training decreased the forward trunk flexion severity and increased postural control in patients with PD. NCT03741959.

1. Introduction

Pathological forward trunk flexion (FTF) is a drug-refractory complication in patients with Parkinson's disease (PD) leading to imbalance, pain and fall-related injuries. It ultimately affects the quality of life and increases hospitalisation risk [1]. The pathophysiology of FTF in PD is not well understood. The bulk of the literature deriving from animal model and clinical studies suggests two mutually non-exclusive pathophysiologic hypotheses involving central (dystonia, rigidity, proprioceptive disintegration) and peripheral (myopathy, soft tissue changes)

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mechanisms [1–3]. The relative contribution of the different mechanisms might vary between patients and during the disease progression [1,3]. Dystonia might be an early and transient phenomenon followed. as the postural deformity becomes structured, by subsequent musculoskeletal changes [1,3]. Pharmacological treatments are the first-line strategy to improve clinical status in PD. However, pathological FTF in PD is not a levodopa-responsive phenomenon [1–3]. Examination and the evidence that some clinical presentations might be reversibly emphasised the importance of early and multidisciplinary management of this postural complication [1-3]. Rehabilitation is the cornerstone in PD management [1-3]. However, the current efforts are only partially able to resolve postural complications in PD [1,3]. Despite differences in methodologies, the few rehabilitative studies support the overall benefits of trunk rehabilitation in PD with postural complications [4,5]. Basic knowledge on the neurophysiological control of the trunk and spine has demonstrated that it is driven more by automatic and feedforward schemes than voluntary control [6]. Moreover, active movements are more effective than passive positioning in determining to change in the trunk position. In this theoretical framework, rehabilitation of pathological forward trunk flexion should be focused on autocorrection and stabilization to maintain unconsciousness of the self-correction and trunk stabilization during the activities of daily living. The existing rehabilitation approaches on this topic are based on the passive elongation of back muscles associated with gait and balance exercises taken from the usual care rehabilitation in PD [4,5]. The benefit of applying this approach raised by the improvement of trunk automatic and feed-forward postural reactions by using postural perturbations. However, motor and non-motor domains (i.e. dual-task, rigidity, weakness) could interfere with the complicated neural control of the trunk in PD. The knowledge arising from research works to extend rehabilitation in idiopathic spinal deformities would pave the way for specific rehabilitation also approaches in PD [7]. Three main key factors can be identified for effective trunk rehabilitation: active self-correction technique, trunk stabilization exercises and functional tasks to train neuromotor function during the ADLs. To the best of our knowledge, no studies have been performed on this novel approach in patients with PD. Priorities for future research include well-design rehabilitation studies with larger numbers [1,3], the early detection and early rehabilitation to delay the occurrence of irreversible deformities and reduce complications (i.e. pain). The primary aim was to compare the effects of a four-week trunk-specific rehabilitation program on the severity of the FTF in patients with PD. The secondary aim was to compare the training effects on the Unified Parkinson Disease Rating Scale motor subscale (UPDRS III), dynamic and static balance, pain, falls, and quality of life. The hypothesis was that the specific features of the four-week trunk-specific rehabilitation program would allow improving passive and active neuromotor control of the trunk so to stimulate by reflex and self-corrected posture during the ADLs. It would decrease the severity of the FTF in patients with PD significantly more than the usual rehabilitative treatment. The training effects would parallel significant improvements in postural control suggesting the straight influence of postural orientation on postural control.

2. Materials and methods

2.1. Trial design

This single-blind randomized controlled trial (RCT) compared the effects of a four-week trunk-specific rehabilitation program (experimental group [EG]) versus conventional (control group [CG]) training. One physician with experience in the assessment of PD patients was blinded to group assignment and evaluated study participants.

2.2. Participants

FTF referred to the UOC Neurology B, and the UOC Neurorehabilitation were assessed. Inclusion criteria were: $age \ge 18$ years old: a clinical diagnosis of PD according to current diagnostic criteria [8]: Mini-Mental State Examination score ≥ 24 [9]; at least 5° of forward trunk flexion during standing and walking and completely subside in the recumbent position [10]; Hoehn & Yahr (H&Y) stage ≤ 4 in the "ON" medication phase and on their usual antiparkinsonian treatment [11]. Exclusion Criteria were: severe dyskinesia or "on-off" fluctuations: PD medication modification in the 3 months preceding the enrolment: a history of major spinal surgery or muscle and/or skeletal spine diseases: need for assistive devices to rise from a chair or bed; other neurological (i.e. vertigo, vestibular disorders), orthopaedic or cardiovascular comorbidities that could interfere with postural control. Patients gave their written, informed consent after being informed about the experimental nature of the study. The study was carried out following the Helsinki Declaration, approved by the local Ethics Committee (prog n.2399), and registered at clinical trial (NCT03741959).

2.3. Interventions

One physical therapist was employed for the EG training while another one was involved in the CG training to ensure adherence to their respective rehabilitation programs. Patients received individualized treatment for 60 min/day, 2 days/week for 4 weeks at the physical therapy facility of the Neurorehabilitation Unit (AOUI Verona). The physical therapist provided continuous feedback about patient's performance and increased the task complexity as performance improved. Three sessions were performed as "self-practice" at the patients' home and monitored by phone-calls daily by the treating physiotherapist.

2.4. Experimental group intervention

It consisted of three groups of exercises:1)Active self-correction exercises (20 min) consisted of graded exercises with three levels of difficulty repeated under different sensory conditions: with visual feedback (i.e. mirror), with proprioceptive feedback (i.e. EMG feedback), and without any feedback. Under these three levels of difficulty, the patient had to progressively improve the three-dimensional correction integrating visual and proprioceptive inputs to maintain the best self-corrected posture.2)Trunk stabilization exercises (20 min) consisted of muscle trunk elongation and active graded exercises aimed at strengthening trunk muscles fundamental for the trunk stability and improving the ability of the CNS to coordinate all the muscle actions. According to literature, paraspinal and abdominal wall muscles have been trained as the highest potential for stabilization.3)Functional tasks were used as the element of "distraction" (i.e. dual-task exercises) that engaged the patient's attention and induced them to maintain unconsciousness of the self-correction and trunk stabilization and reduce functional impairment. They were aimed at inducing behavioural changes and automatic mechanisms of posture and movement through automatic motor control feed-forward strategies during ADL activities [6,7,12]. During each treatment session, a total of 10 exercises were repeated several times according to the patient's ability.

2.5. Control group intervention

It consisted of joint mobilization (20 min), muscle strengthening and stretching (20 min), overground gait training and balance exercises (20 min) [4].

2.6. Outcomes

Demographic and clinical data, including Body Mass Index (BMI), age at PD onset, disease duration, Modified H&Y scale, UPDRS [13], Montreal Cognitive Assessment [14], and levodopa equivalent daily

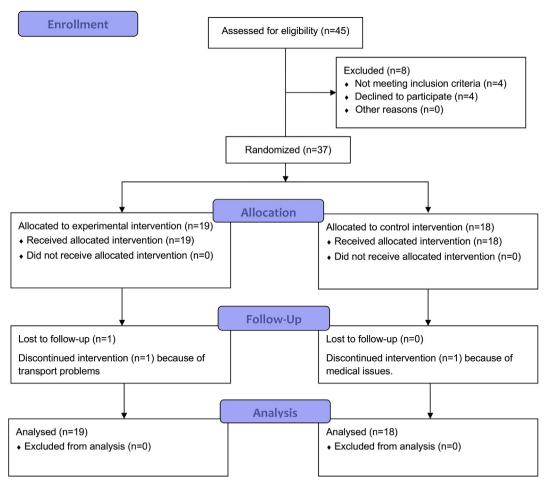


Fig. 1. CONSORT flow diagram.

dose (mg) [15], were collected at T0. The primary and secondary outcomes were measured by the same blinded examiner before (T0), two days after the end of the treatment (T1), and at one-month follow-up after the end of the treatment (T2). The test order was the same across all evaluation sessions as reported below. Patients were tested in the ON state.

The primary outcome was the change in the degrees of FTF between T1 and T0 and between T2 and T0 [16]. Secondary outcomes were changes in the UPDRS III (score range, 0-132 higher = worse symptoms) [13], the Numeric Rating Scale for pain (NRS) (score range, 0-10 higher = worse symptoms), the number of falls in the previous month [17], the Parkinson's Disease Questionnaire-8 (PDQ-8) (score range, 0-32 points; the summed score is divided by the total possible score and given as percentage score out of 100 (higher = worse performance) [18]. Static balance was evaluated using an electronic monoaxial platform (Tecnobody[©], http://www.tecnobody.it). It measures the dislocation of the center of pressure (CoP) while the subject maintains standing position in different sensory conditions. The patient stands barefoot for 30 s on a firm surface with arms alongside the body and feet in a standardized V-shape frame. The main stabilometric parameter was the mean percentage difference of sway (PDS) area (A) (mm²) and length of sway evaluated by the ratio [(RQ-1/(RQ+1) X100)] using the Romberg quotient (RO) (range of ratio, 0-100 higher = worse performance) [19]. Dynamic balance was assessed using the Mini BESTest that identify six different balance control systems (total score: 28 points, higher scores meaning better condition) [20,21].

2.7. Sample size

A sample size of 32 patients (16 per group) was estimated to have 85% power to detect a mean difference in the FTF of -4.5 (SD 5) between the EG and CG on the primary outcome measure (degree) and an alpha (probability of type 1 error) of 5% (10). Assuming a 10% dropout rate, 36 patients were necessary to perform the study (G*Power 3.1) [5].

2.8. Randomization

Eligible patients were assigned to either the EG or the CG by a simple randomization scheme using an automated randomization system (www.randomization.com). Group allocation was kept concealed. The randomization list was locked in a desk drawer accessible only to the principal investigator.

2.9. Blinding

The same blinded examiner measured primary and secondary outcomes at each session. Patients were blinded on the group assignment.

2.10. Statistical analysis

An intention-to-treat analysis (LOCF) was used. Subject characteristics were presented as mean (standard deviation) or median. Nonparametric tests were used because of the non-normally distribution of data. Comparisons between groups were performed using Fisher's exact test for categorical variables, and the Mann-Whitney test for quantitative outcomes. The Mann-Whitney test was applied to assess the homogeneity between the two groups in the demographic and clinical characteristics, and in the primary and secondary outcomes at T0. Difference between T0-T1 performance and between T0-T2 for all outcome measures was computed and compared using the Mann-Whitney test. The Friedman test was applied to investigate withingroup changes in the primary and secondary outcome over time (from T0 to T2). Statistical significance was set at 0.05. If the overall effect from Friedman's was significant, post hoc tests were performed using Wilcoxon signed-rank tests between T0 and T1 and between T0 and T2. Bonferroni's correction was applied for post hoc comparisons $(p \le 0.025)$. The Spearman correlation was carried out to explore the association between forward trunk flexion (primary outcome) and the clinical variables (secondary outcomes). Statistical analysis was performed with SPSS 20.0 (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY, USA).

3. Results

In all 45 patients were consecutively assessed. Four patients were excluded because they did not meet inclusion criteria and 4 patients declined to participate. A total of 37 patients were randomly assigned to either the EG (n = 19) or the CG (n = 18). Two patients in the EG and 1 in the CG discontinued interventions (Fig. 1). No significant betweengroup differences in demographics and clinical data (Table 1) or in primary and secondary outcome measures were measured at T0 except for the percentage of women significantly lower in the CG, and the PDS area and the PDQ-8 significantly higher (worse) in the EG than the CG (p = 0.045 and p = 0.004, respectively). No adverse events or safety concerns arose during the conduction of study.

3.1. Primary outcome

The reduction in FTF was significantly greater for the EG than the CG from T0 to both T1 (p = 0.003) and T2 (p = 0.004) (Table 2). The

Table 1

Baseline demographic and clinical characteristics.

EG training produced a mean reduction at T1 of 9,73° (-20,79%) and T2 of 8,84° (-18,89%) in the FTF. In contrast, the CG training produced a mean reduction at T1 of 1,62° (-3,52%) and T2 of 0,95° (-2%). An example of the effects of the experimental training protocol is reported in Fig. 2. Overall, a significant reduction in FTF from T0 to T2 in either the EG (p < 0.001) or CG (p = 0.001) were measured. Post hoc comparisons are reported in Table 2.

3.2. Secondary outcomes

The improvement in the dynamic balance by the Mini BESTest was significantly greater for the EG than the CG only from T0 to T2 (p = 0.017). No significant differences between the two groups were measured from T0 and T1 (p = 0.06). Similarly, the improvements in the static balance assessed using the PDS Area was significantly greater for the EG than the CG from T0 to T2 (p = 0.004). No significant differences between the two groups were measured from T0 and T1 (p = 0.16). No significant differences between the EG and the CG were measured in the UPDRS III and the PDS length of Sway from T0 to both T1 and T2. Overall, in both groups a significant improvement in the UPDRS III [EG:p = 0.001; CG:p = 0.01] and Mini BESTest performance [EG:p < 0.001; CG:p = 0.01] from T0 to T2 were measured. Post hoc comparisons are reported in Table 2. In both groups, no significant overall effects on PDS Area and PDS length of sway were measured. Although, no significant differences in the quality of life perceived between the two groups were measured from T0 and T1 (p = 0.59), the EG reported a significantly higher quality of life than the CG from T0 to T2 (p = 0.02). Overall, the EG reported a higher quality of life perceived from T0 to T2, albeit not significant (p = 0.06). An opposite trend consisting of a reduction in the quality of life was observed in the CG, albeit not significant (p = 0.06). No significant differences between the two groups were measured on pain from T0 and T1 (p = 0.87) and from T0 and T2 (p = 0.25). Overall, in both groups a significant reduction of pain was measured from T0 to T2 [EG:p = 0.001; CG: p < 0.001]. No significant differences between the two groups were

	All sample (n = 37) 71.59 (6.46) 24/13 24 38 (3 60)	Experimental Group	Control Group	Р
		(n = 19)	(n = 18)	
Age (years) mean (SD) ^a	71.59 (6.46)	72.42 (6.40)	70.72 (6.60)	0.64
Gender (Male/Female) b	24/13	9/10	15/3	0.038*
BMI ^a	24.38 (3.60)	23.74 (2.79)	25.01 (4.29)	0.46
Age at disease onset (years) mean (SD) ^a	64.29 (8.65)	64.42 (9.20)	64.16 (8.29)	0.94
Disease duration (years) mean (SD) ^a	7.31 (5.16)	8.01 (5.90)	6.57 (4.29)	0.46
LEDD ^a	715.81 (430.13)	803.31 (405.81)	623.44 (447.38)	0.2
Ongoing Pharmacological Therapy n (%) ^b				0.86
L-Dopa monotherapy	11 (30.6%)	5 (27.8%)	6 (33.3%)	
DA monotherapy	3 (8.3%)	1 (5.6%)	2 (11.1%)	
L-Dopa + DAs	12 (33.3%)	7 (38.9%)	5 (27.8%)	
L-Dopa + Das + other antiparkinsonian drugs	10 (27.8%)	5 (27.8%)	5 (27.8%)	
H&Y median [Q25; Q75] ^a	2.5 [1.5; 3]	3 [1.5; 3]	2 [1.37; 3]	0.19
UPDRS total ^a	62.43 (24.59)	62.15 (25.74)	62.72 (24.07)	0.88
MoCA score ^a	23.87 (3.49)	23.68 (3.48)	23.93 (3.63)	0.77
Camptocormia n (%) ^b	25 (67.5%)	12 (63.15%)	13 (72.2%)	0.72
Isolated forward trunk flexion	28 (75.7%)	12 (63.2%)	16 (88,9%)	
Forward trunk flexion combined with lateral deviation	9 (24.3%)	7 (36.8%)	2 (11,1%)	

Legend: BMI, Body Mass Index; LEDD, Levodopa equivalent daily dose; L-Dopa = L-dopa + carbidopa, L-dopa + carbidopa extended release, L-dopa + benserazide, L-dopa + benserazide extended release, melevodopa + carbidopa. DA = pramipexole, pramipexole extended release, ropinirole, ropinirole extended release, rotigotine, pergolide, cabergoline, apomorphine. Other antiparkinsonian drugs = anticholinergics, MAO-B inhibitors, amantadine, tolcapone; H&Y, Hohen & Yahr, Modified Hoehn and Yahr Scale; UPDRS, Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; SD, standard deviation; *, p-value < 0.05.

^a Mann-Whitney Test.

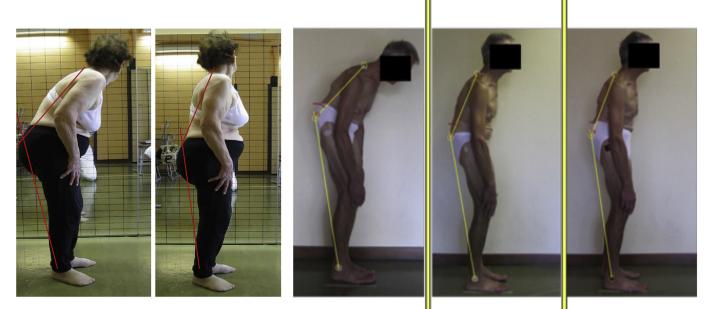
^b Fisher's exact test.

 Table 2

 Descriptive and Inferential Statistics for the primary and secondary outcomes.

		то	T1	T2	Mann-W	hitney test		Friedman Test	Wilcoxon signed rank test	
					Т0	ΔT0-T1	ΔT0-T2	T0-T2	T0-T1	T0-T2
		Mean (SD)	Mean (SD)	Mean (SD)	Р	Р	Р	Р	Р	Р
Trunk forward flexion	EG	46.78 (11.75)	37.05 (8.40)	37.94 (8.87)	0.60	0.003*	0.004*	< 0.001*	0.001 [§]	$0.002^{\$}$
	CG	46.00 (8.68)	44.38 (8.57)	45.05 (7.95)	0.68			0.001*	0.007 [§]	$0.02^{\$}$
UPDRS III	EG	34.36 (13.84)	29.47 (11.42)	29.42 (11.64)	0.88	0.79	'9 0.84	0.001*	0.001 [§]	$0.01^{\$}$
	CG	33.94 (13.9)	29.5 (13.55)	30.38 (11.45)				0.01*	0.01 [§]	0.01 [§]
MINI Best	EG	15.10 (5.95)	20.21 (5.49)	20.26 (5.49)		0.06	0.017*	< 0.001*	$< 0.001^{\$}$	$< 0.001^{\$}$
	CG	18.83 (5.93)	21.44 (5.18)	21.16 (5.39)	0.07			0.01*	0.01 [§]	0.03
PDS Area	EG	28.98 (22.36)	24.57 (28.12)	2.42 (37.51)	0.01*	0.16	0.004*	0.13	0.68	0.01
	CG	11.26 (28.81)	21.87 (31.40)	23.86 (28.08)				0.49	0.21	0.18
PDS Length of Sway	EG	15.62 (13.5)	16.11 (13.64)	11.45 (17.3)	0.45	0.96	0.72	0.38	0.009	0.11
	CG	12.18 (10.84)	10.98 (19)	10.35 (12.26)				0.46	0.55	0.52

Legend: T0, pre-treatment; T1, post-treatment; T2, 1-month follow-up; SD, standard deviation; P, p-value; EG, experimental group; CG, control group; PDS, percentage difference of sway; n.s., not significant; *, $p \le 0.05$; ${}^{\$}$, $p \le 0.025$.



Active Self-correction exercise with visual feedback (mirror)

Forward trunk flexion T0: 52°

Forward trunk flexion T1: 32°

Forward trunk flexion T2: 29°

Fig. 2. Experimental training protocol exercises and effects.

Left side: The patient has to actively improve her trunk alignment by visual feedback (mirror). Right side: Measurement of forward trunk flexion before, after rehabilitation and at follow-up.

measured on the number of falls per month from T0 and T1 (p = 0.49) and T0 and T2 (p = 0.29). However, only the EG reported an overall reduction in the number of falls per months from T0 to T2 (p = 0.004). Post hoc comparisons are reported in Table 3. Correlation analysis showed a good negative correlation between the forward trunk flexion at T0 and the amount of changes in the trunk forward flexion between T1 and T0 (r = -0.7, p < 0.001) and between T2 and T1 (r = -0.67, p = 0.002) were measured. In the CG, there was a significant correlation between the forward trunk flexion and the amount of changes in the trunk flexion and the amount of changes in the trunk flexion and the amount of changes in the trunk flexion and the amount of changes in the trunk flexion only between T2 and T0 (r = -0.53, p = 0.02)

(Supplementary Fig. 1).

4. Discussion

The main findings of the present study are that the four-week trunkspecific exercise program reduced the degrees of FTF in patients with PD more than the conventional treatment, and the training effects were maintained at one-month post-treatment. These positive training effects were associated with improvements in dynamic balance and central integration of sensory input processes, as assessed by the Mini BESTest
 Table 3

 Descriptive and Inferential Statistics for pain, quality of life and number of falls.

		Т0	T1	T2	Mann-W	nn-Whitney test		Friedman test	Wilcoxon signed rank test	
					TO	ΔT0-T1	ΔТ0-Т2		T0-T1	T0-T2
		Mean (SD)	Mean (SD)	Mean (SD)	р	р	р	р	р	
NRS	EG	7.26 (7.75)	3.78 (5.08)	3.36 (4.64)	0.86	0.07	07 0.05	0.001*	0.007 [§]	$0.012^{\$}$
	CG	6.16 (6.1)	3.77 (6.05) 2.88 (6.25)	2.88 (6.25)	0.80	0.87	0.25	< 0.001*	0.002 [§]	0.003 [§]
PDQ-8	EG	25.49 (11.84)	21.54 (10.04)	23.02 (12.59)	0.04*	0.59 (0.02*	0.06	0.009 [§]	0.11
	CG	18.74 (10.82)	15.27 (8.56)	21 (8.82)	0.04*			0.06	0.18	0.28
Falls (n/month)	EG	1.63 (2.6)	0.63 (1.11)	0.42 (0.69)	0.27		0.29	0.004*	0.04	0.01 [§]
	CG	0.66 (1.08)	0.27 (0.95)	0.22 (0.73)		0.49		0.06	0.10	0.04

Legend: T0, pre-treatment; T1, post-treatment; T2, 1-month follow-up; SD, standard deviation; p, p-value; EG, experimental group; CG, control group; NRS, Numeric Rating Scale; PDQ-8, Parkinson's Disease Questionnaire -8; n, number; *, $p \le 0.05$; 8 , $p \le 0.025$.

and the stabilometric assessment respectively. The good correlation between the degrees of forward trunk flexion at T0 and the improvements obtained at T1 and T2, in term of changes of the FTF degree, support the rehabilitation effectiveness in patients with lower (early) and higher (advanced) forward trunk flexion severity.

The lack of specific knowledge on the pathophysiology of FTF in PD hampers clinicians to address specific rehabilitation strategies. Ideally, treatments might act on both peripheral and central mechanisms and may, therefore, be difficult. Of great future potential is the development of specific rehabilitative approaches to treat this highly disabling disorder. Despite this, the literature on this topic is scant. Only two RCTs have investigated treatment effects on isolated FTF or combined with lateral deviation reporting positive effects [4,5]. With the limit of methodological differences among studies, the present RCT study agrees that greater improvements from specific rehabilitation approaches are expected in the management of FTF. According to the composite pathophysiology of the disorder, two main rehabilitation approaches can be roughly distinguished to hinder the progression of the misalignment. On the one hand, biomechanical approaches (i.e. lumbar supports, high-level walking devices, manipulative physiotherapy) originated from the hypothesis that postural abnormalities result from poor spine stability caused by trunk muscular imbalance and passive elements deterioration [1,3].

On the other hand, neurophysiological approaches are based on the hypothesis that CNS dysfunctions related to neuromotor control of the trunk along with impaired proprioception, poor CNS control of body posture and body schema disorders are crucial [1,3,6]. In our view, a clear-cut distinction between the two main rehabilitation approaches should be overcome, and the strict interplay between CNS control and body biomechanics constraints should be addressed [6,7]. Some of the elements of the four-week trunk-specific exercise program should be considered highly innovative. The key features were the trunk passive and active correction exercises, the use of visual and proprioceptive feedback to improve the neuromotor control of the trunk consciously and the use "dual-task" exercises during functional tasks [7]. The trunk passive and active correction exercises may have reduced the biomechanical constraints and in turn, the trunk neural control. The elongation of shortened muscles, in fact, has two synergistic effects. From one hand, the improvement in the viscoelastic muscle properties facilitates muscle contraction in a more physiologic pattern. From the other hand, the synergistic effects of the muscle-tendon unit lengthening may decrease the spinal reflex excitability of alpha motor neurons throughout the modulation of I-alpha spinal inhibitory interneurons [22]. Despite the lack of electromyographic assessment of the training effects, the specific training might be interpreted with large training effects on all the muscle patterns involved in trunk stabilization and

orientation [3].

The improvements in balance are intriguing. Patients with more severe FTF exhibited poorer postural control in both static and dynamic conditions confirming the strict interplay between postural orientation and postural equilibrium. Secondly, balance improvements observed from T0 to T2 may be the results of improvements in postural control and stability. The use of visual and proprioceptive feedbacks may have played as sensory cues to select the most appropriate postural reaction to maintain trunk alignment improving sensorimotor strategies and reweighting. Feed-forward postural adjustments are one of the primary mechanisms used by the CNS to meet trunk functional challenge [6,7]. Anticipatory control, indeed, is required to warrant spine stability and to prepare the trunk for the reactive moments from limb movements.

In contrast, feedback postural adjustments are activated when unpredictable disturbances threaten trunk stability. Based on these theoretical principles, the experimental treatment followed at least, in general, these neurophysiological principles based on two main aspects: active unconsciousness of self-correction and trunk stabilization [6,7]. Interestingly, patients learned progressively to acquire the best trunk alignment without any sensory feedback during the execution of active three-dimensional self-corrections during static and functional tasks. This important achievement might have to be ascribed to the use of "dual-task" exercises. Literature supports the importance of integrating dual-task training in improving gait velocity without increasing fall risk [23]. It could not be excluded that the training effects observed at follow-up resulted from the continuation of self-practice home sessions. Our novel findings confirm preliminary evidence on the straight influence of postural orientation on postural control and for the first time suggest the adoption of dual-task training in the management of postural orientation deficits in PD [24]. The study limitations are the lack of patient stratification by FTF severity, neuroimaging/neurophysiological assessments and mood disturbances assessment. The exclusion of patients with on-off fluctuations may be a selection bias. Since the EG training was conceived as a single training, it is not possible to draw any conclusion on the individual contribution of the three groups of exercises on the primary endpoint. However, the training effects may rely on synergies between the three groups of exercises rather than their single effects. It could be argued that the longer the camptocormia duration the lower the chance to gain improvements given the wellknown structural changes induced by prolonged postural abnormalities. The strengths of the present study are the comprehensive rehabilitation approach to forward trunk flexion, the low dropout rate, which suggests the feasibility of the rehabilitation training.

5. Conclusion

FFT might be reversibly in patients with PD. The trunk-specific training can significantly improve not only postural orientation but also postural control by improving particular sensorimotor strategies. These preliminary findings need for validation in a more extensive study.

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Author contributions statement

All Authors have approved the final article.

MG: study coordination, analysis and interpretation of data, drafting the article.

MT: conception and study design, study supervision, interpretation of data and revising the manuscript critically.

FM: clinical assessment, revising the article.

GB: acquisition of clinical data.

ED and NP: patients' treatment.

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CG: the conception and design of the study, acquisition of instrumental data, revising the article.Acknowledgements

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Conflict of interest statement

None.

References

- [1] K.M. Doherty, B. Pp van de Warrenburg, M.C. Peralta, L. Silveira-Moriyama, J.P. Azulay, O.S. Gershanik, B.R. Bloem, Postural deformities in Parkinson's disease, Lancet Neurol. 10 (2011) 538–549.
- [2] A. Fasano, C. Geroin, A. Berardelli, B.R. Bloem, A.J. Espay, M. Hallett, A.E. Lang, M. Tinazzi, Diagnostic criteria for camptocormia in Parkinson's disease: a consensus-based proposal, Park. Relat. Disord. (2018), https://doi.org/10.1016/j. parkreldis.2018.04.033.
- [3] P. Srivanitchapoom, M. Hallett, Camptocormia in Parkinson's disease: definition, epidemiology, pathogenesis and treatment modalities, J. Neurol. Neurosurg. Psychiatry 87 (2016) 75–85.
- [4] M. Bartolo, M. Serrao, C. Tassorelli, R. Don, A. Ranavolo, F. Draicchio, C. Pacchetti, S. Buscone, A. Perrotta, A. Furnari, P. Bramanti, L. Padua, F. Pierelli, G. Sandrini, Four-week trunk-specific rehabilitation treatment improves lateral trunk flexion in Parkinson's disease, Mov. Disord. 25 (2010) 325–331.
- [5] M. Capecci, C. Serpicelli, L. Fiorentini, G. Censi, M. Ferretti, C. Orni, R. Renzi, L. Provinciali, M.G. Ceravolo, Postural rehabilitation and Kinesio taping for axial

postural disorders in Parkinson's disease, Arch. Phys. Med. Rehabil. 95 (2014) 1067-1075.

- [6] N. Smania, A. Picelli, S. Negrini, M. Romano, Neurophysiological basis of rehabilitation of adolescent idiopathic scoliosis, Disabil. Rehabil. 30 (10) (2008) 763–771.
- [7] M. Romano, A. Negrini, S. Parzini, M. Tavernaro, F. Zaina, S. Donzelli, S. Negrini, SEAS (Scientific Exercises Approach to Scoliosis): a modern and effective evidence based approach to physiotherapic specific scoliosis exercises, Scoliosis 10 (2015) 3, https://doi.org/10.1186/s13013-014-0027-2.
- [8] R.B. Postuma, D. Berg, M. Stern, W. Poewe, C.W. Olanow, W. Oertel, J. Obeso, K. Marek, I. Litvan, A.E. Lang, G. Halliday, C.G. Goetz, T. Gasser, B. Dubois, P. Chan, B.R. Bloem, C.H. Adler, G. Deuschl, MDS clinical diagnostic criteria for Parkinson's disease, Mov. Disord. 30 (2015) 1591–1601.
- [9] M.F. Folstein, S.E. Folstein, P.R. McHugh, 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician, J. Psychiatr. Res. 12 (3) (1975) 189–198.
- [10] S. Pandey, H. Kumar, Assessment of striatal & postural deformities in patients with Parkinson's disease, Indian J. Med. Res. 144 (5) (2016) 682–688, https://doi.org/ 10.4103/ijmr.IJMR_502_15.
- [11] C.G. Goetz, W. Poewe, O. Rascol, C. Sampaio, G.T. Stebbins, C. Counsell, N. Giladi, R.G. Holloway, C.G. Moore, G.K. Wenning, M.D. Yahr, L. Seidl, Movement disorder society task force report on the Hoehn and Yahr staging scale: status and recommendations. The movement disorder society task force on rating scales for Parkinson's disease, Mov. Disord. 19 (9) (2004) 1020–1028.
- [12] J. Bettany-Saltikov, E. Parent, M. Romano, M. Villagrasa, S. Negrini, Physiotherapeutic scoliosis-specific exercises for adolescents with idiopathic scoliosis, Eur. J. Phys. Rehabil. Med. 50 (1) (2014) 111–121.
- [13] Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease, The unified Parkinson's disease rating scale (UPDRS): status and recommendations, Mov. Disord. 18 (2003) 738–750.
- [14] Z.S. Nasreddine, N.A. Phillips, V. Bédirian, S. Charbonneau, V. Whitehead, I. Collin, J.L. Cummings, H. Chertkow, The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment, J. Am. Geriatr. Soc. 53 (2005) 695–699.
- [15] C.L. Tomlinson, R. Stowe, S. Patel, C. Rick, R. Gray, C.E. Clarke, Systematic review of levodopa dose equivalency reporting in Parkinson's disease, Mov. Disord. 25 (2010) 2649–2653.
- [16] N.G. Margraf, R. Wolke, O. Granert, A. Berardelli, B.R. Bloem, R. Djaldetti, A.J. Espay, A. Fasano, Y. Furusawa, N. Giladi, M. Hallet, J. Jankovic, M. Murata, M. Tinazzi, J. Volkmann, D. Berg, G. Deuschl, Consensus for the measurement of the camptocormia angle in the standing patient, Park. Relat. Disord. (52 2018 Jul) 1–5, https://doi.org/10.1016/j.parkreldis.2018.06.013.
- [17] Kellogg International Work Group on the prevention of Falls by the Elderly, Report of the kellogg international work group on the prevention of falls by the elderly. The prevention of falls in later life, Dan. Med. Bull. 34 (1987) 1–24.
- [18] N. Luo, L.C. Tan, Y. Zhao, P.N. Lau, W.L. Au, S.C. Li, Determination of the longitudinal validity and minimally important difference of the 8-item Parkinson's Disease Questionnaire (PDQ-8), Mov. Disord. 24 (2) (2009 Jan 30) 183–187, https://doi.org/10.1002/mds.22240 PubMed PMID: 18972545.
- [19] L. Chiari, A. Bertani, A. Cappello, Classification of visual strategies in human postural control by stochastic parameters, Hum. Mov. Sci. 19 (2000) 817–842.
- [20] A.L. Leddy, B.E. Crowner, G.M. Earhart, Utility of the Mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with Parkinson disease, J. Neurol. Phys. Ther. 35 (2011) 90–97.
- [21] L.A. King, K.C. Priest, A. Salarian, D. Pierce, F.B. Horak, Comparing the mini-BESTest with the Berg balance scale to evaluate balance disorders in Parkinson's disease, Parkinsons Dis. (2012) 375419, https://doi.org/10.1155/2012/375419.
- [22] A. Valero-Cabré, M. Oliveri, M. Gangitano, A. Pascual-Leone, Modulation of spinal cord excitability by subthreshold repetitive transcranial magnetic stimulation of the primary motor cortex in humans, Neuroreport 12 (2001) 3845–3848.
- [23] C. Strouwen, E.A.L.M. Molenaar, L. Münks, S.H.J. Keus, J.C.M. Zijlmans, W. Vandenberghe, B.R. Bloem, A. Nieuwboer, Training dual tasks together or apart in Parkinson's disease: results from the DUALITY trial, Mov. Disord. 32 (2017) 1201–1210.
- [24] C. Geroin, N. Smania, F. Schena, E. Dimitrova, E. Verzini, F. Bombieri, F. Nardello, M. Tinazzi, M. Gandolfi, Does the Pisa syndrome affect postural control, balance, and gait in patients with Parkinson's disease? An observational cross-sectional study, Park. Relat. Disord. 21 (2015) 736–741.