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Exploring gait adaptations to perturbed and conventional treadmill training in Parkinson's disease: Time-course, sustainability, and transfer

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A B S T R A C T

Background: Gait impairment is a major motor symptom in Parkinson's disease (PD), and treadmill training is an effective non-pharmacological treatment option.

Research question: In this study, the time course, sustainability and transferability of gait adaptations to treadmill training with and without additional postural perturbations were investigated.

Methods: 38 PD patients (Hoehn & Yahr 1–3.5) were randomly allocated to eight weeks of treadmill training, performed twice-weekly for 40 min either with (perturbation treadmill training [PTT], n = 18) or without (conventional treadmill training [CTT], n = 20) additional perturbations to the treadmill surface. Spatiotemporal gait parameters were assessed during treadmill walking on a weekly basis (T0–T8), and after three months follow-up (T9). Additional overground gait analyses were performed at T0 and T8 to investigate transfer effects.

Results: Treadmill gait variability reduced linearly over the course of 8 weeks in both groups ($p < .001$; Cohen's d (range): −0.53 to −0.84). Only the PTT group significantly improved in other gait parameters (stride length/time, stance-/swing time), with stride time showing a significant between-group interaction effect (Cohen's d = 0.33; p = .05). Additional between-group interactions indicated more sustained improvements in stance (Cohen's d = 0.85; p = .02) and swing time variability in the PTT group (Cohen's d = 0.82; p = .03) at T9. Overground gait improvements at T8 existed only in stance (d = -0.73; p = .04) and swing time (d = 0.73; p = .04).

Discussion: Treadmill stride-to-stride variability reduced substantially and linearly, but transfer to overground walking was limited. Adding postural perturbations tended to increase efficacy and sustainability of several gait parameters. However, since between-group effects were small, more work is necessary to support these findings.

1. Introduction

Gait impairments present as one of the major clinical features of Parkinson's Disease (PD), with the cardinal motor symptoms tremor, rigidity, bradykinesia and postural instability strongly contributing to the progressive decline throughout the disease course (Jankovic, 2008). Altered gait characteristics have been demonstrated in PD patients, including reduced stride length, increased stride time and stance phase proportion, as well as high stride-to-stride variability (Galna, Lord, Burn, & Rochester, 2015; Hass et al.,

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2012; Morris et al., 2017). As a consequence of these gait deficits, patients suffer from reduced mobility and quality of life (Soh, Morris, & McGinley, 2011), and demonstrate an alarmingly high risk of falling (Fasano, Canning, Hausdorff, Lord, & Rochester, 2017).

Treatment response to dopaminergic therapy diminishes with time, and several features of gait are refractory to pharmacological treatment (Galna et al., 2015). This highlights the importance of complementary non-pharmacological treatments, particularly exercise and physical therapy (Abbruzzese, Marchese, Avanzino, & Pelosin, 2016). Recent meta-analyses provide evidence for the efficacy of various exercise modalities in improving gait impairment in PD (Tomlinson et al., 2014), with treadmill training being particularly promising (Mehrholz et al., 2015). Improved stride length and stride-to-stride variability have been demonstrated following several weeks of treadmill practice for both, overground (Nadeau, Pourcher, & Corbeil, 2014; Tseng, Yuan, & Jeng, 2015) and treadmill (Ganesan, Sathyaprabha, Pal, & Gupta, 2015; Studer et al., 2017) walking, respectively.

One major limitation of treadmill training is that it does not entirely reflect the typical demands of ambulation in natural environments (Bello & Fernandez-Del-Olmo, 2012; Frenkel-Toledo et al., 2005). Recently, we demonstrated that eight weeks of treadmill therapy with additional postural perturbations produced favorable effects on overground gait speed, and was particularly effective in improving dynamic balance control in PD patients (Steib et al., 2017). Further, a single session of perturbed treadmill walking improved gait variability (Klamroth et al., 2016) and motor output complexity (Pasluosta et al., 2017) to a larger extent compared to standard treadmill training.

Although emerging evidence supports the efficacy of treadmill interventions, the time course of treadmill gait adaptations has not yet been described. Further, few studies have investigated the sustainability of initial adaptations and the extent of transfer to overground walking (Mehrholz et al., 2015). Lastly, this is the first study investigating whether adding postural perturbations to treadmill practice leads to more pronounced and sustainable gait adaptations. Consequently, this study aimed at 1) analyzing spatiotemporal gait adaptations to eight weeks of treadmill training with or without additional postural perturbations on a weekly basis; 2) evaluating the sustainability of changes over three months; and 3) assessing transfer effects to overground gait in both training regimes.

2. Methods

2.1. Design and participants

This study is a secondary analysis of data from a randomized controlled trial (trial registration ID: NCT01856244) (Steib et al., 2017). Forty-three PD patients were randomly assigned to either perturbation treadmill training (PTT) or conventional treadmill training (CTT), two times a week for eight weeks. Participants were recruited based on predefined inclusion and exclusion criteria (Steib et al., 2017). A computer-generated block-randomization stratified by Hoehn & Yahr stage (H&Y 1–2/2.5–3.5) was used, and group assignment concealed. Patients gave written informed consent prior to participation, and the study was approved by the local ethics committee.

2.2. Intervention

The intervention protocol and the prototypic treadmill device used in this study has been previously described (Klamroth et al., 2016; Steib et al., 2017). In brief, it consists of a standard medical treadmill (Mercury, h/p/cosmos medical GmbH) mounted on a platform construction (zebris Medical GmbH) which contains three pneumatic actuators (30 mm lifting capacity) placed in a triangle below the platform surface. The actuators are controlled separately and, via a micro-controller, are set to constantly varying positions. This induces small tilting movements of the treadmill surface, resulting in continuously varying surface inclinations. This simulation of an uneven ground induces additional postural challenge to the patient during walking. PD patients in the control group walked on the identical treadmill but without perturbations. All participants performed 16 sessions, two times per week over a period of maximally nine weeks. One treadmill session was structured into 30 min training in the allocated condition, and additional five minutes warm-up and cool-down, respectively. Based on patients' self-perceived exertion and difficulty of the task, treadmill walking speed was individually progressed during the intervention period (starting with 70% of individual overground walking speed). Both groups increased their treadmill walking speed from T0 to T8, with no significant difference between groups (change PTT: +0.19 ± 0.11 m/s; CTT: +0.17 ± 0.10 m/s). Patients were encouraged to walk without handrail support but were allowed to do so if necessary. Seven patients (PTT = 3, CTT = 4) made use of handrail support during parts of the training phase (max. 8 sessions), and another five patients (PTT = 3, CTT = 2) exercised with handrails for more than 50% of all sessions. The exercise sessions were supervised by trained physiotherapists providing standardized and rigorously restricted instructions (Steib et al., 2017).

2.3. Data collection and analysis

Treadmill-based gait parameters were recorded at baseline (T0), at the beginning of every training week prior to the training sessions (T1-T7), within one week post-intervention (T8), and after a three months follow-up (T9). Data were collected using a treadmill-integrated pressure sensor matrix (108.4 × 47.4 cm, 7169 pressure/force sensors; FDM-T zebris Medical GmbH, Isny, Germany), and gait parameters were extracted using the corresponding software package (zebris FDM, zebris Medical GmbH, Isny, Germany). This procedure was pilot tested in our group (Klamroth et al., 2016), and was also successfully applied by others to investigate treadmill gait in elderly and neurologic populations (Faude, Donath, Roth, Fricker, & Zahner, 2012; Kalron, Dvir, Frid, &

Achiron, 2013). Data were recorded during one minute of treadmill walking with a constant and individually defined gait speed (70% of overground walking speed at T0). All treadmill-based gait analyses were performed after 4 min warm-up on the treadmill and without handrail use when possible (handrails use (n): T1 = 8, T8 = 3, T9 = 2). Assessors at T0, T8 and T9 were blinded to group allocation. Gait analyses during the intervention period (T1-T7) were performed by therapists supervising the training.

Additional overground gait analyses were performed at T0 and T8 in order to estimate potential transfer effects. Data were collected with inertial sensors (SHIMMER 2 sensors, Shimmer Sensing, Dublin, Ireland) consisting of gyroscopes and accelerometers, attached to the lateral side of each shoe. The system has been previously validated in PD patients (Schlachetzki et al., 2017). For data collection, patients walked with their self-selected comfortable walking speed 4x10 meter. Based on a validated machine learning algorithm, turning strides were excluded and only straight strides used for calculation of stride parameters (Barth et al., 2015). Details on the computation of the overground stride parameters can be found in (Rampp et al., 2015).

All gait analyses were performed in patients stable on medication. Spatiotemporal gait parameters were calculated from individual strides for all gait parameters (exception: treadmill gait asymmetry) in order to obtain comparable data from both gait analysis systems (treadmill vs. overground). Variability measures (coefficient of variation: $CV = \left(\frac{standard\ deviation}{mean} * 100\%\right)$) and symmetry measures (symmetry index (Sadeghi, Allard, Prince, & Labelle, 2000): $SI = \frac{(X_R - X_L)}{0.5 \times (X_R + X_L)} \times 100\%$) were calculated.

2.4. Statistical analysis

All statistical analyses were performed with IBM SPSS statistics software (version 25.0 for Windows). As this was a secondary analysis, no a-priori sample size estimation was performed. All data were initially explored and tested for normality using the Shapiro-Wilk test. Homogeneity of groups in demographic and baseline variables were analyzed using independent samples *t*-test for interval variables, Chi-square test for categorical data, and Mann-Whitney *U* test for ordinal variables.

Treadmill gait characteristics were analyzed for within- and between-group differences, using separate two-level linear mixed models specified for each gait parameter. The experimental factors 'group' (PTT, CTT) and 'time' (continuous, T0-T8) as well as two-way interactions ('group' × 'time') were integrated as fixed factors. A random intercept and random slope model was estimated, with 'individuals' (patients) and 'time' included as random effects. The assumed covariance matrix was diagonal at level 1 (within subjects) and unstructured at level 2 (between subjects). Effect sizes were calculated using Cohen's *d*.

Sustainability of training effects were examined by analyzing treadmill gait change from posttest (T8) to follow-up (T9). In addition, overground gait changes from baseline (T0) to posttest (T8) were analyzed in order to evaluate transfer effects. Due to non-normal distribution of most variables, change was assessed within groups using the Wilcoxon signed-rank test, and between groups using the Mann-Whitney *U* test.

3. Results

Demographic characteristics of the 38 included PD patients are reported in Table 1. At baseline, there were no significant differences between the PTT and CTT group for demographics or gait parameters.

Table 1
Participants‘ characteristics.

	PTT n = 18		CTT n = 20		p-value
	Mean	SD	Mean	SD	
Age (years)	67.6	8.2	62.5	7.9	0.055
Gender (male/female)	11/7		16/4		0.200†
Height (cm)	174.6	8.8	175.8	8.6	0.663
BMI (kg/m$^{2)}$	24.6	1.9	25.6	2.3	0.156
Disease duration (years)	7.9	4.0	7.3	4.4	0.644
LEDD (mg/d)	630.4	331.1	645.7	280.8	0.879
Hoehn&Yahr	2.6	0.5	2.5	0.5	0.492#
H&Y 1–2 (n)	3.0		6.0		
H&Y 2.5–3.5 (n)	15.0		14.0		
UPDRS-III (score)	17.7	6.1	20.4	8.2	0.257
UPDRS item gait	0.8	0.6	0.9	0.4	0.698#
UPDRS item postural stability	1.0	0.5	0.9	0.5	0.513#
MoCA (score)	25.8	3.7	25.6	3.9	0.850
Gait speed baseline (m/s)	1.4	0.2	1.4	0.2	0.740

†Chi Square test; #Mann-Whitney *U* test; PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; LEDD: Levodopa equivalent daily dose; H&Y: Hoehn and Yahr disease stage; UPDRS-III: Motor score of the Unified Parkinson's disease rating scale; MoCA: Montreal Cognitive Assessment.

Table 2
Estimates of average growth rate per week for treadmill gait parameters (T0 – T8).

Outcome	Time Effects											Interaction Effects				
	PTT (n = 18)					CTT (n = 20)					All (n = 38)	Group by Time				
	Estimate[a]	SE	Effect Size		p	Estimate[a]	SE	Effect Size		p	p	Estimate[b]	SE	Effect Size		p
Stride length (cm)	0.39	0.17	0.39	Small	**0.02**	0.02	0.16	0.02	Marginal	0.88	0.10	0.37	0.23	0.26	Small	0.11
Stride time (ms)	4.40	1.74	0.41	Small	**0.02**	−0.37	1.63	−0.04	Marginal	0.82	0.15	4.77	2.38	0.33	**Small**	**0.05**
Stance time (% gait cycle)	−0.06	0.03	−0.34	Small	**0.04**	0.01	0.03	0.04	Marginal	0.82	0.25	0.06	0.04	0.27	Small	0.10
Swing time (% gait cycle)	0.06	0.03	0.34	Small	**0.04**	−0.01	0.03	−0.04	Marginal	0.82	0.25	0.06	0.04	0.27	Small	0.10
Stride length CV (%)	−0.16	0.03	−0.75	Large	**0.00**	−0.17	0.03	−0.84	**Large**	**0.00**	**0.00**	0.01	0.05	0.03	Marginal	0.86
Stride time CV (%)	−0.15	0.03	−0.81	Large	**0.00**	−0.12	0.03	−0.71	**Moderate**	**0.00**	**0.00**	0.02	0.04	0.10	Marginal	0.56
Stance time CV (%)	−0.04	0.01	−0.53	Moderate	**0.00**	−0.05	0.01	−0.70	**Moderate**	**0.00**	**0.00**	0.01	0.02	0.10	Marginal	0.54
Swing time CV (%)	−0.10	0.03	−0.56	Moderate	**0.00**	−0.11	0.03	−0.69	**Moderate**	**0.00**	**0.00**	0.02	0.04	0.07	Marginal	0.68
Step length asymmetry (%)	−0.04	0.17	−0.04	Marginal	0.80	0.06	0.16	0.06	Marginal	0.71	0.95	0.10	0.23	0.07	Marginal	0.66
Step time asymmetry (%)	0.04	0.07	0.10	Marginal	0.54	0.07	0.06	0.18	Small	0.27	0.21	0.03	0.09	0.05	Marginal	0.76
Stance time asymmetry (%)	−0.03	0.10	−0.05	Marginal	0.76	0.09	0.09	0.16	Small	0.34	0.62	0.12	0.13	0.14	Marginal	0.38
Swing time asymmetry (%)	−0.03	0.10	−0.05	Marginal	0.76	0.09	0.09	0.16	Small	0.34	0.62	0.12	0.13	0.14	Marginal	0.38

a,b Estimates of fixed effects were derived from the linear mixed models and provide the average growth rate per week within groups (a) and between groups (b) over 8 weeks treadmill training; PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; SE: standard Error of the estimate; CV: coefficient of variation; bold values indicate a statistically significant effect ($p \leq 0.05$).

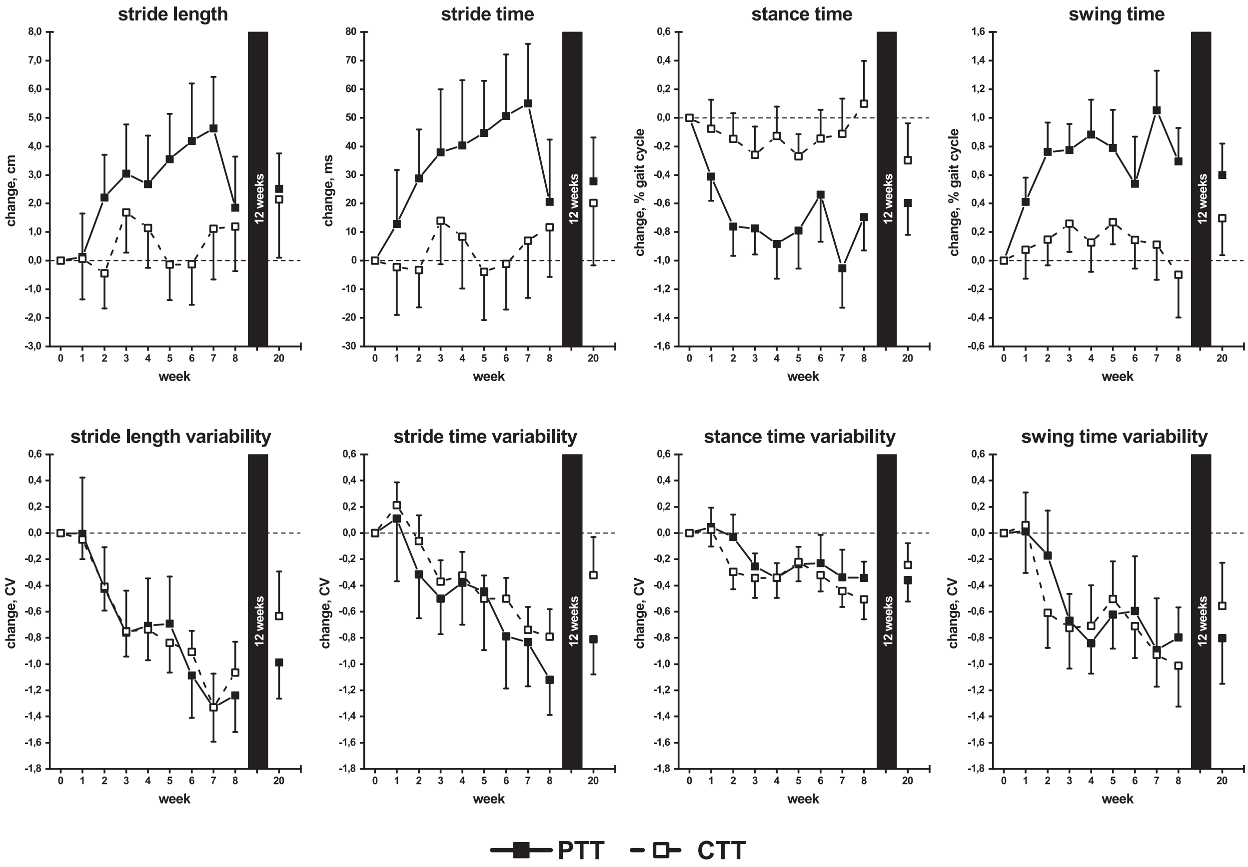

Fig. 1. Change from baseline in treadmill gait characteristics showing significant improvement over time; PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; Error bars: standard error (SE).

3.1. *Treadmill gait adaptations*

Estimates of fixed effects for change in treadmill gait parameters are presented in Table 2. Significant changes in several gait parameters were observed over the course of eight weeks training (Fig. 1).

Gait variability significantly decreased in both groups, with moderate to large effect sizes ($p < .001$; d(range): −0.53 to −0.84). Post-hoc tests revealed the strongest within-group effects for stride time CV in the PTT group ($p \leq .001$; $d = -0.81$), and stride length CV in the CTT group ($p < .001$; $d = -0.84$). No significant between-group differences existed for change over time ($p > .05$).

For mean spatiotemporal gait parameters, a significant between-group interaction ($p = .05$; $d = 0.33$) indicated that stride time only improved in the PTT group. In addition, post-hoc tests revealed significant improvements in stride length ($p = .02$; $d = 0.39$), stride time ($p = .02$; $d = 0.41$), stance time ($p = .04$; $d = -0.34$), and swing time ($p = .04$; $d = 0.34$) in the PTT group, exclusively.

3.2. *Sustainability of treadmill gait adaptations*

Changes from post-intervention (T8) to three months follow-up (T9) are presented in Fig. 2 and Table 3. Significant between-group interactions existed for stance time CV ($p = .02$; $d = 0.85$) and swing time CV ($p = .03$; $d = 0.82$), indicating that gait variability increased only in the CTT group (stance time CV: $p \leq .01$; $d = 1.63$; swing time CV: $p = .01$; $d = 1.43$), while no significant changes existed in the PTT group. In addition, post-hoc tests revealed decreased step length asymmetry ($p = .02$; $d = -1.47$) in the CTT group.

3.3. *Transfer to overground gait*

Transfer effects are presented in Table 4. When considering the entire sample, significant changes in overground gait parameters at T8 were observed only for stance- and swing time, with a significantly decreased stance time ($d = -0.73$; $p = .04$) and a corresponding increase in swing time ($d = 0.73$; $p = .04$).

When considering group allocation, post-hoc tests for the observed changes in stance- and swing time revealed that these effects

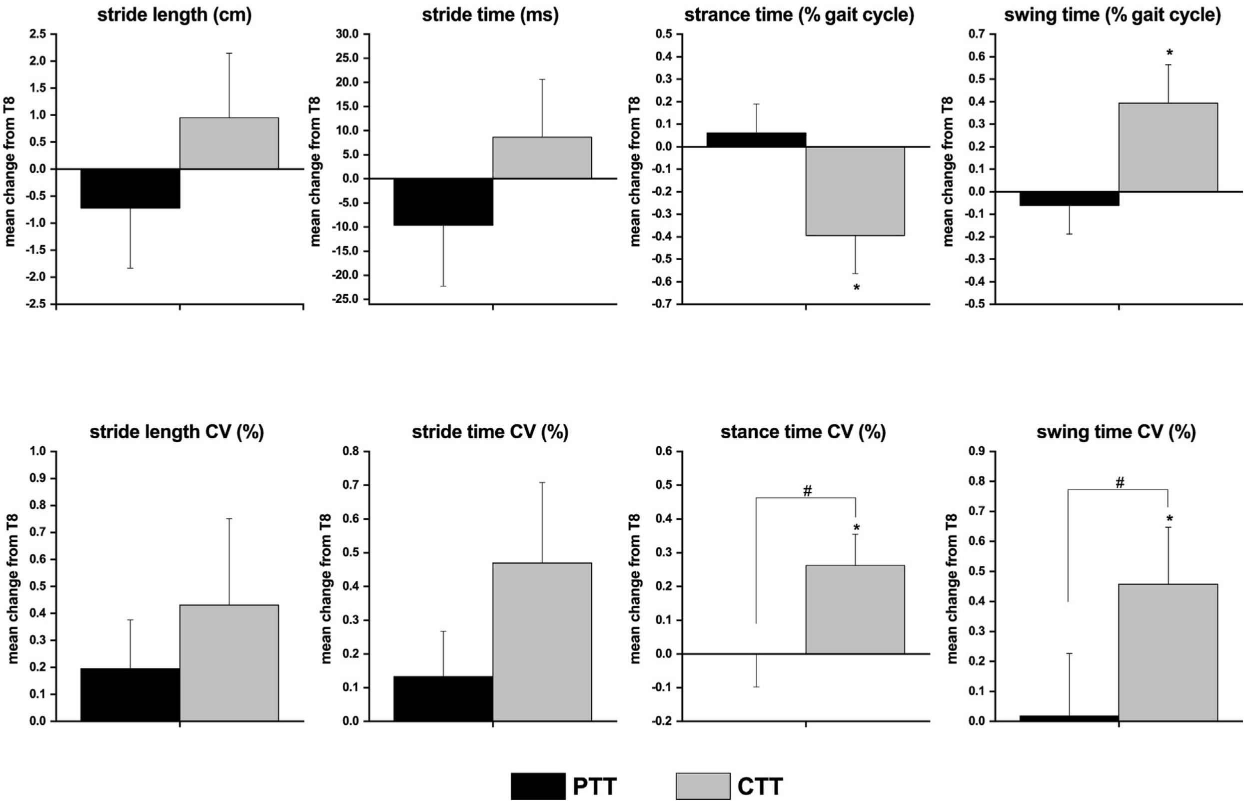

Fig. 2. Mean change from post-intervention (T8) to follow-up (T9) for gait characteristics showing significant improvement with intervention; PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; Error bars: standard deviation (SD); * indicates significant within-group change from T8 (p ≤ .05); # indicates significant between-group difference in change scores (p ≤ .05).

Table 3
Sustainability of treadmill gait adaptations from post-intervention (T8) to follow-up (T9).

Outcome	Time Effects											Interaction Effects		
	PTT (n = 15)					CTT (n = 19)					All (n = 34)	Group by Time		
	Median[a]	Range	Effect Size[b]		*p*	Median[a]	Range	Effect Size[b]		*p*	*p*	Effect Size[b]		*p*
Stride length (cm)	−0.29	15.37	−0.24	Small	0.65	0.16	19.23	0.24	Small	0.60	0.94	0.28	Small	0.42
Stride time (ms)	7.38	160.09	0.30	Small	0.57	0.02	195.72	0.24	Small	0.60	0.98	0.30	Small	0.40
Stance time (% gait cycle)	0.16	1.91	0.94	Large	0.10	−0.41	2.98	**−1.03**	**Large**	**0.05**	0.38	0.61	Moderate	0.09
Swing time (% gait cycle)	−0.16	1.91	−0.94	Large	0.10	0.41	2.98	**1.03**	**Large**	**0.05**	0.38	0.61	Moderate	0.09
Stride length CV (%)	0.19	2.35	0.45	Moderate	0.39	0.08	6.34	0.46	Moderate	0.33	0.19	0.06	Marginal	0.85
Stride time CV (%)	0.06	2.11	0.45	Moderate	0.39	0.27	4.63	0.94	Large	0.06	0.37	0.28	Small	0.42
Stance time CV (%)	0.01	1.54	0.12	Marginal	0.82	0.22	1.68	**1.63**	**Large**	**0.01**	0.06	**0.85**	**Large**	**0.02**
Swing time CV (%)	0.05	3.41	0.09	Marginal	0.87	0.39	3.59	**1.43**	**Large**	**0.01**	0.06	**0.82**	**Large**	**0.03**
Step length asymmetry (%)	0.78	21.83	0.12	Marginal	0.82	−1.33	15.78	**−1.47**	**Large**	**0.02**	0.17	0.43	Moderate	0.22
Step time asymmetry (%)	−0.97	9.61	−1.00	Large	0.08	0.68	8.42	0.17	Small	0.75	0.42	0.56	Moderate	0.12
Stance time asymmetry (%)	−0.32	14.60	−0.30	Small	0.57	−1.62	12.11	−0.89	Large	0.12	0.12	0.33	Small	0.35
Swing time asymmetry (%)	−0.32	14.60	−0.30	Small	0.57	−1.62	12.11	−0.89	Large	0.12	0.12	0.33	Small	0.35

a Change from post-intervention (T8) to follow-up (T9); b Effect size calculation is based on ranks derived from non-parametric tests (corresponding effect size r transformed into Cohens‘ d); PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; CV: Coefficient of variance; bold values indicate statistically significant effect ($p \leq 0.05$).

Table 4
Overground gait adaptations from baseline (T0) to post-intervention (T8).

Outcome	Time Effects											Interaction Effects		
	PTT (n = 18)					CTT (n = 20)[c]					All (n = 38)	Group by Time		
	Median[a]	Range	Effect Size[b]		p	Median[a]	Range	Effect Size[b]		P	p	Effect Size[b]		p
Stride length (cm)	4.00	28.50	0.67	Moderate	0.18	1.00	42.00	−0.04	Marginal	0.93	0.41	0.49	Moderate	0.14
Stride time (ms)	−6.64	424.71	−0.61	Moderate	0.22	−3.76	418.57	0.48	Moderate	0.30	0.09	0.08	Marginal	0.82
Stance time (% gait cycle)	−0.43	4.70	**−1.32**	**Large**	**0.02**	−0.05	3.95	−0.18	Small	0.70	**0.04**	0.54	Small	0.11
Swing time (% gait cycle)	0.43	4.70	**1.32**	**Large**	**0.02**	0.05	3.95	0.18	Small	0.70	**0.04**	0.54	Small	0.11
Stride length CV (%)	0.23	22.65	−0.21	Small	0.66	0.65	13.20	0.90	Large	0.07	0.12	0.30	Small	0.37
Stride time CV (%)	−0.30	3.35	−0.40	Small	0.41	0.08	4.25	−0.25	Small	0.56	0.82	0.34	Small	0.30
Stance time CV (%)	0.08	4.70	0.25	Small	0.60	0.20	5.30	−0.19	Small	0.67	0.53	0.01	Marginal	0.97
Swing time CV (%)	−0.30	8.10	−0.92	Large	0.08	0.33	10.10	0.60	Moderate	0.20	0.92	**0.82**	**Large**	**0.02**
Stride length asymmetry (%)	1.47	10.89	0.64	Moderate	0.20	0.01	23.07	0.13	Marginal	0.78	0.26	0.18	Small	0.60
Stride time asymmetry (%)	−0.04	1.92	0.23	Small	0.54	0.04	1.69	0.76	Large	0.12	0.51	0.51	Moderate	0.14
Stance time asymmetry (%)	0.40	10.95	0.46	Moderate	0.34	0.31	7.08	0.36	Small	0.44	0.22	0.02	Marginal	0.95
Swing time asymmetry (%)	0.40	10.95	0.46	Moderate	0.34	0.31	7.08	0.36	Small	0.44	0.22	0.02	Marginal	0.95
Gait velocity (m/s)	0.05	0.69	0.67	Moderate	0.18	0.02	0.80	0.14	Marginal	0.75	0.20	0.38	Small	0.25

a Change from post-intervention to follow-up; b Effect size calculation is based on ranks derived from non-parametric tests (corresponding effect size r transformed into Cohens‘ d); c Asymmetry parameters derived from n = 19; PTT: Perturbation Treadmill Training; CTT: Conventional Treadmill Training; CV: Coefficient of variance; bold values indicate a statistically significant effect ($p \leq 0.05$).

were only statistically significant in the PTT group (stance time: p = .02; d = −1.32; swing time: p = .02; d = 1.32). However, the between-group interaction effects were non-significant (p = .11; d = 0.54). Additionally, a significant between-group interaction effect was found for swing time CV (p = .02; d = 0.82), with a trend for reduced variability in the PTT group (p = .08; d = −0.92), and a moderately increased variability in the CTT group at T8 (p = .20; d = 0.60).

4. Discussion

Results from the present study demonstrate that eight weeks of treadmill training improved Parkinsonian gait characteristics, with the largest effects existing for reduced stride-to-stride variability. Augmenting the training with postural perturbations led to larger improvements in stride time and resulted in more sustained effects for stance and swing time variability, suggesting a more steady and stable ambulation on the treadmill. Importantly, the observed gait adaptations were mainly restricted to treadmill walking, supporting increasing evidence for task-specific adaptations and limited transfer effects. The only effects on overground gait were found for stance- and swing time. Interestingly, these changes were restricted to the perturbation training group, which needs further attention and confirmation in larger scaled studies.

4.1. Treadmill gait adaptations

Various treadmill gait adaptations emerged throughout the intervention period, with the most substantial effects seen for variability of gait. Stride-to-stride variability markedly decreased over the course of the intervention in both training groups, with the time course indicating an almost linear reduction (Fig. 1). High stride-to-stride variability has been associated with disease progression (Hass et al., 2012), and is indicative of increased fall risk in PD (Hausdorff, 2009). Since variability of gait is refractory to dopaminergic therapy (Galna et al., 2015), our findings emphasize the high relevance of treadmill training for gait rehabilitation and fall prevention. These results are in line with previous studies demonstrating reductions in overground (Nadeau et al., 2014; Tseng et al., 2015) and treadmill (Ganesan et al., 2015; Studer et al., 2017) gait variability following regular treadmill exercise.

Adding postural perturbations to the training led to additional increases in stride time. Prolonged stride time is associated with disease progression (Hass et al., 2012) and an indicator of reduced rhythm of gait in PD (Morris et al., 2017). As patients' gait speed was constant for all time points, these data are indicative of qualitative gait improvements rather than an increased walking speed. The additional postural challenge and constant perturbation of gait regularity may have led to these adaptations, expressing in a more rhythmic gait under less challenging situations (unperturbed treadmill walking). From a motor learning perspective, the random nature of perturbations results in high practice variability, contextual interference, and increased task challenge, all of which have been associated with improved motor learning outcome (Abbruzzese et al., 2016; Kitago & Krakauer, 2013). As between-group effects were small and statistically significant results limited to stride time, more work is needed to clarify the added value of perturbations.

An unexpected and rather unsystematic drop in stride length and stride time performance was observed from T7 to T8 in the PTT group (Fig. 1). There appeared to be no obvious outliers that could entirely explain this phenomenon. An alternative reason might be the fact that gait analyses at T0, T8 and T9 were incorporated into a larger assessment session including other gait and balance assessments, while at T1–T7 solely treadmill gait analyses were performed prior to practice. Further, assessments at T0, T8 and T9 were performed by a blinded assessor (SS), while assessments at T1–T7 were performed by the therapists. Consequently, there could be a certain bias induced by the observer, the special test situation at T0 and T8, or both.

4.2. Sustainability of effects

Treadmill gait assessment at three months post-intervention revealed that patients partially retained their improvements. Importantly, sustainability was significantly higher for stance and swing time variability in patients training with additional perturbations, and this effect was strong.

These findings have several implications. First, irrespective of group allocation, all patients were able to partially preserve their gait improvements. This is in accordance with previous studies showing that treadmill therapy may have lasting carry over effects on patients' mobility and fall risk (Herman, Giladi, & Hausdorff, 2009). More importantly, the retained effects on gait performance are indicative of motor learning (i.e. neuroplasticity) (Bello & Fernandez-Del-Olmo, 2012). Treadmill training is a goal-based, highly repetitive and intense motor practice stimulus, which has been proposed to be an essential feature for inducing motor learning in neurorehabilitation (Abbruzzese et al., 2016; Petzinger et al., 2013). In addition, treadmill walking not only leads to intense task practice; it also presents an aerobic training stimulus, which has been suggested to enhance neural plasticity (Petzinger et al., 2013; Taubert, Villringer, & Lehmann, 2015), thereby particularly facilitating motor memory consolidation in PD (Steib et al., 2018). Thus, treadmill practice seems to provide a specifically favorable training stimulus. These findings are of great importance since PD patients demonstrate reduced motor learning abilities (Nieuwboer, Rochester, Müncks, & Swinnen, 2009) that are not improved by pharmacotherapy (Marinelli, Quartarone, Hallett, Frazzitta, & Ghilardi, 2017).

The sustainability for stance- and swing time variability was higher in perturbed compared to conventional treadmill training. This may indicate that this training regime presents a particularly effective modality for inducing neuroplasticity, potentially due to its unpredictable and challenging nature (Abbruzzese et al., 2016; Kitago & Krakauer, 2013). However, effects were limited to a few gait parameters and need further validation.

4.3. Transfer to overground gait

To the best of our knowledge, this was the first study analyzing spatiotemporal gait adaptations to treadmill training both on and off the treadmill in PD. Treadmill walking presents an artificial condition, and treadmill gait has been shown to differ from overground walking in PD (Frenkel-Toledo et al., 2005; Warlop, Detrembleur, Stoquart, Lejeune, & Jeanjean, 2018). Thus, it has been suggested that gait changes on the treadmill might reflect successful task adaptation, rather than an actual improvement in gait performance (Bello & Fernandez-Del-Olmo, 2012). Consequently, a critical question is whether treadmill training can positively impact overground walking performance and if gait adaptations on and off the treadmill are interlinked.

Our findings suggest that transfer to overground walking is limited, and effects only partially correspond to gait adaptations on the treadmill. One reason for this finding may be the short training duration. Nadeau et al. (2014) found improved overground gait variability after 24 weeks of treadmill training in PD patients, while Tseng et al. (2015) failed to see this effect after 12 weeks of intervention. Further, gait changes on the treadmill might be indicative of successful task adaptation, but not an actual improvement in gait performance (Bello & Fernandez-Del-Olmo, 2012). It is suggested that treadmills act as an external pacemaker (Frenkel-Toledo et al., 2005), leading to a less variable and more regular gait pattern in PD patients (Frenkel-Toledo et al., 2005; Warlop et al., 2018). However, the fact that we familiarized patients to treadmill walking prior to study entry, and that a gradual and sustained reduction of variability existed, rather than a spontaneous change, at least challenge this point. Lastly, the limited transfer might be partially explained by differences in the assessment regimes. Gait parameters on the treadmill were measured at a fixed gait speed for each patient, while speed is not constant during overground gait analysis.

Interestingly, the significant overground improvements in stance- and swing time were only seen in the PTT group. In addition, a significant between-group interaction effect suggested reduced swing time variability in the PTT group, but an increased variability in the CTT group. This finding may support our assumption that practice conditions during perturbed treadmill walking better reflect the demands of ambulation in everyday life environments, and thus, would explain the better transfer. Additionally, as discussed above, the nature of perturbations, inducing high practice variability, contextual interference and task challenge, may provide a particularly beneficial motor learning stimulus, leading to the superiority compared to conventional treadmill practice. However, since transfer was generally low and between-group effects were only found for selective parameters, larger scaled studies are needed to further clarify these findings.

4.4. Limitations

Some limitations need to be mentioned. First, the sample size of this trial was small, and thus statistical power is limited. Secondly, gait characteristics (e.g. stride length) may have had limited room for improvement, given that individuals' treadmill walking speed was held constant at all assessment time points. Some patients were unable to walk on the treadmill without additional handrail support for parts of the intervention. Since handrail use may affect gait patterns (Bello, Marquez, Camblor, & Fernandez-Del-

Olmo, 2010) and minimize the need for dynamic postural control, this might have reduced treatment response in these patients. However, the proportion of handrail users did not systematically differ between both intervention groups.

4.5. Conclusions

In summary, PD patients demonstrated marked gait adaptations to the eight-week treadmill intervention, which were partially retained after three months follow-up. These findings support previous research on preserved neuroplasticity in PD patients. The largest improvements were seen in stride-to-stride variability on the treadmill, which decreased almost linearly over time in both groups. Perturbed treadmill training demonstrated interesting trends for larger improvements and sustainability of effects in selected gait variables, which need further attention and confirmation in future studies. Another important finding was that transfer to overground walking was limited in most variables. More work is warranted to elucidate which gait adaptations transfer to enhanced performance in real life scenarios, and which aspects are purely an adaptation to treadmill walking.

Ethical approval

Ethics committee of the Friedrich-Alexander University Erlangen-Nürnberg (Re.-No. 181_12 B)

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2019.01.007.

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