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Responsiveness to rehabilitation of balance and gait impairment in elderly with peripheral neuropathy

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ABSTRACT

Elderly people with peripheral neuropathy of the lower limbs (PNLL) demonstrate a typical balance and gait impairment because of sensory ataxia. There is evidence that rehabilitation produces important gains on balance and gait. However, responsiveness to rehabilitation of balance and gait measures is unknown in PNLL. Aim of the current work is to evaluate the responsiveness to rehabilitation of balance, gait and sensory ataxia measures in elderly with PNLL.

Twenty-five elderly with PNLL attending physiotherapy and occupational therapy during inpatient rehabilitation were recruited. Balance and gait measures (including static posturography, TUG test and the 10 m walking test) were administered on admission and discharge. An accelerometer secured to the trunk was used for TUG recording and static balance assessment. Static balance was tested with open and closed eyes, so as to assess sensory ataxia.

Following rehabilitation, patients improved gait [admission vs discharge, mean(SD): 0.86(0.33) vs 0.98 (0.32) m/s], TUG [18.7(7.8) vs 15.1(5.2) s] and turning [46.2(15.3) vs 53.3(15.3) °/s]. However, none of 12 static balance parameters derived from trunk acceleration significantly changed. Principal component analysis showed that before training, eyes closed and eyes open balance correlated with orthogonal components (one and two vs. three and four). After training, eyes open and eyes closed balance were more similar to each other being both correlated with component one.

Responsiveness to rehabilitation is larger for gait than static balance measured by trunk acceleration. However, exercise can also have a beneficial effect on sensory ataxia by making eyes closed balance more similar to eyes open balance.

1. Introduction

Poor balance and gait impairment are major problems for people with peripheral neuropathy of the lower limbs (PNLL (Caronni et al., 2016a,b; Hurvitz et al., 2001)).

Balance (i.e. the ability not to fall (Winter, 1995)) is traditionally divided into static and dynamic, the former indicating the ability to stand still in upright position and the latter indicating the ability to move while standing. Both static and dynamic balance are impaired in people with PNLL and these patients suffer from a typical balance and gait impairment because of sensory ataxia (Nardone and Schieppati, 2010). Sensory ataxia is a motor syndrome caused by impaired sensory feedback from peripheral nerves and characterised by loss of coordination and precision when a movement is performed without vision. Affecting both upper and lower limbs, sensory ataxia also affects upright stance and gait. It is well known that sensory ataxia causes important deficit to people with PNLL and thus recovery from sensory ataxia can be a significant benefit for them (Riva et al., 2014).

A range of different balance and gait measures are used in clinical practice and clinical trials to assess treatments' effectiveness. Posturography is often used for measuring static balance. Force platforms are classically used for posturography (Furman, 1993) and in recent times, accelerometers secured to the trunk are also used for body sway recording (Moe-Nilssen and Helbostad, 2002). In a typical static balance assessment, the patient is asked to maintain quiet stance in different conditions, such as first with eyes open and then eyes closed. By comparing these tasks, sensory ataxia during quiet stance is easily quantified. Several scales are available for balance assessment and the majority of them evaluate

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both static and dynamic balance (Franchignoni et al., 2010). Moreover, many measures of dynamic balance have been proposed as well. Interestingly, a link between gait and dynamic balance has been repeatedly shown and different authors have proposed some gait parameters as dynamic balance indicators (Caronni et al., 2018; Hwa-ann and Krebs, 1999).

To our knowledge, a comparison of the responsiveness to rehabilitation of the different gait and balance measures in PNLL has never been reported. Responsiveness is the ability of a measure to detect a clinically significant change in the patient (Kirshner and Guyatt, 1985). With this regard, even if there is poor consensus on which outcome measure should be preferred, there is sound evidence that rehabilitation is an effective treatment for elderly with balance and gait impairment, which produces clinically important gains (Province et al., 1995). Comparing responsiveness is important. Different gait and balance measures actually explore different aspects of gait and balance, which could respond in different ways to rehabilitation. In this regard, it is a common clinical experience that not all the aspects of gait and balance are equally responsive to rehabilitation. As an example, patients often increase their gait speed with a much smaller improvement of gait kinematics (Mulroy et al., 2010).

On this basis, in the current work we report the modifications after rehabilitation of gait and balance measures in elderly patients with PNLL. In particular, we want to compare the responsiveness of static balance measures derived from trunk acceleration recordings with that of other balance and gait measures.

Implications of this analysis are twofold. From the pathophysiology perspective the current work shows *how* PNLL elderly improve after rehabilitation, from the responsiveness perspective the current work enables the planning of clinical trials (e.g. sample size calculation). Two scenarios are possible in the pathophysiology perspective. Patients evenly improve their static and dynamic balance and gait or, on the contrary, they show an improvement of only some of these variables. In the latter scenario, the current work would be a useful guide for the clinicians involved in PNLL rehabilitation. Highlighting the motor components that do not improve with conventional rehabilitation offers an opportunity for developing better tailored exercise programs.

2. Methods

2.1. Participants

In the current retrospective study we recruited 25 elderly patients affected by axonal PNLL attending the rehabilitation clinic of Casa di Cura del Policlinico in Milano (May 2016 – September 2018).

Patients were included if (i) older than 65 years, (ii) admitted to inpatient rehabilitation because of PNLL-related disability, (iii) able to complete the Timed Up and Go (TUG) test without touching assistance in less than 40 s and (iv) able to keep upright stance with arms by their side, feet together and eyes closed for at least 15 s. Patients were excluded because of (i) an acute medical condition, (ii) a condition causing by itself a locomotor impairment (e.g. concomitant Parkinson disease), (iii) the need for touching assistance or gait aids to keep stance with feet together and eyes closed.

All patients were diagnosed with axonal PNLL after a nerve conduction study of the lower limbs. Well accepted criteria were used for the axonal PNLL diagnosis (Caronni et al., 2016a,b). Briefly, patients were diagnosed with PNLL in case of reduced amplitude (or absence) of both sural nerves' sensory nerve action potentials associated with roughly symmetrical reduction of peroneal nerves' compound muscle action potentials amplitude. Normal or slightly reduced nerve conduction velocities were also necessary for the axonal PNLL diagnosis.

Patients completed inpatient physiotherapy and occupational therapy one-on-one sessions (see Supplementary Materials 1). All participants gave their written informed consent to participate in this retrospective cohort study, which received internal ethical approval (PRO.05.M.03).

2.2. Gait, transfers and balance assessment

At the beginning (T0) and at the end (T1) of the rehabilitation program, a battery of gait and balance tests was administered to each participant. All measurements were part of the patients' routine assessment.

The 10 m walking test (Studenski et al., 2011) was used for calculating gait speed along a linear trajectory. Patients were asked to walk straight while a clinician used a stopwatch to measure the time spent to travel the central 6 m of the 10 m linear trajectory.

Participants completed the TUG test with an inertial measurement unit (IMU) (mHT-mHealth Technologies, Bologna, Italy) secured to their lower trunk to approximate body center of mass during data collection (instrumental TUG test, ITUG). The same ITUG protocol detailed in our previous work (Caronni et al., 2018) was also used here. The conventional three-meters TUG test was performed. To avoid falls, patients were also asked to walk and to complete the TUG test at their comfortable speed.

In each session, the 10 m walking test and the TUG test were repeated five times each. Exactly as in our previous analysis, trials were analysed individually and the median of the five trials was calculated for each measure.

The Mini-BESTest (MB (Franchignoni et al., 2010)) scale was chosen as an accepted clinical measure of static and dynamic balance.

Whenever possible, patients were evaluated without gait aids.

2.3. Static balance assessment

The static balance assessment consisted in the following tasks: standing still with (i) feet apart (FA) and eyes open (EO), (ii) feet apart and eyes closed (EC), (iii) feet together (FT) and eyes open and (iv) feet together and eyes closed. Each task lasted 30 s. In the FA condition, feet were 29.7 cm apart (i.e. the width of a A4 page), which is approximately the same as shoulder width apart.

Standing still with FT-EC (i.e. the Romberg task (Lanska and Goetz, 2000)) can be quite challenging for people with PNLL. To increase the sample size, we expanded the inclusion criteria so as to recruit people able to stand with FT-EC for at least 15 s (see above). To make comparable the different recordings, only the first 15 s of each task were analysed. Finally, for each task, the first 2 s were discarded and data analysis was eventually restricted to a 13 s vector. At session beginning, all patients completed a 30 s FA-EO trial, which was not included in the analyses.

The same IMU used for ITUG recording was also used for recording trunk acceleration during the static balance assessment. Also in this case, the IMU was secured to the lower back, in the lumbar region. Techical details on the IMU used here are given in Supplementary Materials 1.

2.4. Signal processing

Gyroscopes signals from the IMU were used to split the TUG test into five subsequent phases: sit to stand (STS), walk 1 (W1), turn 1 (T1), walk 2 (W2) and turn and sit (TAS). The duration of each phase was measured as well as the total TUG duration (TTD). In addition, mean vertical angular velocity during turn 1 (T1 gyro) and during the turn phase of TAS (T2 gyro) were calculated. The TUG splitting procedure is described in detail in our previous work (Caronni et al., 2019, 2018). Note that with this splitting procedure, the TUG test returns measures of transfers (e.g. STS duration),

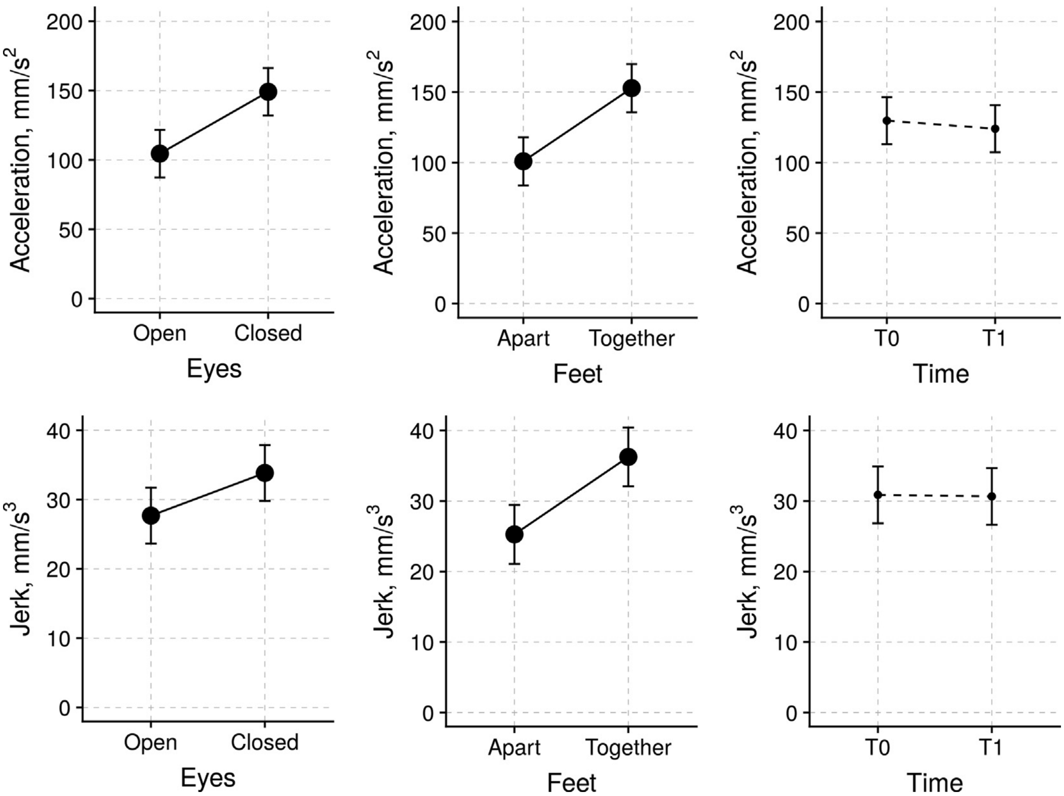

Fig. 1. Static posturography: trunk acceleration and jerk RMS. Trunk acceleration and jerk were significantly larger with feet together than with feet apart and with eyes closed than with eyes open (three-way ANOVAs; large dots, continuous line). No significant effect of time was found (small dots, dashed line). T0: before rehabilitation; T1: after rehabilitation. Least-squares means and their 95% confidence intervals are plotted.

walking (e.g. W1 duration) and walking along curved trajectories (e.g. T1 duration and T1 gyro).

IMU's accelerometers were used to measure trunk acceleration in the transverse plane during the static balance tasks (i.e. FA-EO, FT-EO, FA-EC and FT-EC). A trigonometric procedure was applied to correct the accelerometer tilt along the left–right and anterior-posterior axes (Moe-Nilssen and Helbostad, 2002). Vertical acceleration was not considered for the current analysis. Trunk jerk was calculated by differencing the tilt-corrected trunk acceleration. Resultant trunk acceleration and jerk vectors magnitude, in the transverse plane, were calculated for each temporal instant according to Pythagorean theorem. Root mean square (RMS), which quantifies the dispersion of trunk acceleration ($Trunk_{acc}$) and trunk jerk ($Trunk_{jerk}$), were eventually calculated for the 13 s vectors.

Romberg ratios (RR) were calculated according to the classical formula: balance measure with the eyes closed/balance measure with the eyes open, where the balance measures are: FA-$Trunk_{acc}$, FT-$Trunk_{acc}$, FA-$Trunk_{jerk}$, FT-$Trunk_{jerk}$. Four RRs were obtained (i.e. FA-RR-$Trunk_{acc}$, FT-RR-$Trunk_{acc}$, FA-RR-$Trunk_{jerk}$, FT-RR-$Trunk_{jerk}$).

Static balance traces 13 s long are shorter than generally used in posturography (Carpenter et al., 2001). Therefore, a control analysis was also run in the sub-sample of 21 patients who completed the full 30 s static balance tasks on both admission and discharge. For this new analysis, the RMS of $Trunk_{acc}$ and $Trunk_{jerk}$ (and the corresponding RRs) were calculated from 28 s long acceleration traces (i.e. the full trials after discarding the first two seconds).

2.5. Statistics

Repeated measures three-way ANOVAs were used to evaluate the effect of feet position (FA vs FT), eyes (EO vs EC) and treatment (T0 vs T1) on $Trunk_{acc}$ and $Trunk_{jerk}$. Repeated measures two-way ANOVAs were calculated on RR-$Trunk_{acc}$ and RR-$Trunk_{jerk}$. Linear mixed-effects model was used for ANOVA calculation. Normality of residuals was checked and data transformed as needed (logarithmic or inverse transformation).

The Wilcoxon signed rank test was used to compare gait, transfers and static balance measures on T0 vs T1. Because of multiple paired comparisons, the customary 0.05 type I error probability was corrected according to Holm-Bonferroni. Cohen's d (Cohen, 1992) for paired data was used to quantify the difference between T1 and T0 measures and, being *scale free*, Cohen's d of different measures can be compared.

We used Bland-Altman plots (Bland and Altman, 1999) and the principal component analysis (PCA) to evaluate in greater detail the agreement between static balance with EO and EC, on admission and discharge. Full details on the Bland-Altman plots and on the PCA are given as Supplementary Materials 1.

R 3.3.0 (R Core Team, 2017) was used for figures and statistics.

3. Results

Twenty five older adult subjects (13 male and 12 female) aged between 60 and 85 (mean age, SD: 76.5, 6.7) completed all study conditions (see Table I-S2 in Supplementary Materials 2 for participants' clinical features).

Fig. 1 shows the sample $Trunk_{acc}$ and $Trunk_{jerk}$ in different stance conditions (i.e. EO vs EC; FA vs FT), before and after rehabilitation. As expected, $Trunk_{acc}$ and $Trunk_{jerk}$ were significantly larger with EC than with EO (see Supplementary Materials 2). In addition, $Trunk_{acc}$ and $Trunk_{jerk}$ were significantly larger with FT than with FA. Three-way ANOVAs showed a significant effect of eyes ($F_{1,\ 24} = 52.78$, $p < 0.001$) and feet position ($F_{1,\ 24} = 60.35$, $p < 0.001$) on $Trunk_{acc}$ and a significant effect of eyes ($F_{1,\ 24} = 41.23$, $p < 0.001$) and feet position ($F_{1,\ 24} = 67.81$, $p < 0.001$) on $Trunk_{jerk}$. No significant effect of time was found for $Trunk_{acc}$ ($F_{1,\ 24} = 0.87$, $p = 0.360$) and $Trunk_{jerk}$

Table 1
Gait, balance and transfers measures, before and after rehabilitation. Left, TTD: total TUG duration; STS, W1, T1, W2, TAS, T1 gyro and T2 gyro were obtained from the TUG test. STS: sit to stand; W1: first walking phase; T1: first turning phase; W2: second walking phase; TAS: turn and sit; T1 gyro: vertical angular velocity during T1; T2 gyro: vertical angular velocity during the second turning phase; MB: Mini-BESTest balance scale. Right, acc: trunk acceleration RMS; jerk: trunk jerk RMS. FA: feet apart; FT: feet together; EO: eyes open; EC: eyes closed. Grey cells: T1 measures significantly different from T0 (Wilcoxon signed rank test, type I error probability corrected according to Holm-Bonferroni). p, raw type I error probability; p_{HB}, type I error probability corrected according to Holm-Bonferroni. Median and IQR (in brackets) are given for the MB ordinal score. Mean and SD (in brackets) are used for the remaining measures. The Shapiro-Wilk test was used to test the normality of the different measures (see Supplementary Materials 2).

	T0	T1	p p_{HB}		T0	T1	p p_{HB}
Gait speed (m/s)	0.86 (0.33)	0.98 (0.32)	0.001 0.018	**FA-EO acc**	81.7 (36.0)	76.7 (30.7)	0.491 1.000
TTD (s)	18.7 (7.8)	15.1 (5.2)	< 0.001 < 0.001	**FA-EC acc**	128.1 (69.7)	117.3 (52.8)	0.287 1.000
STS (s)	1.87 (0.93)	1.42 (0.44)	0.003 0.045	**FT-EO acc**	136.9 (43.0)	123.0 (40.7)	0.442 1.000
W1 (s)	4.71 (2.23)	3.73 (1.43)	< 0.001 < 0.001	**FT-EC acc**	172.2 (69.2)	179.1 (86.4)	0.442 1.000
T1 (s)	4.13 (1.40)	3.52 (1.01)	0.001 0.018	**FA-EO jerk**	23.6 (5.7)	22.8 (4.1)	0.353 1.000
W2 (s)	3.53 (2.00)	2.60 (1.26)	< 0.001 < 0.001	**FA-EC jerk**	28.0 (10.1)	26.6 (7.3)	0.411 1.000
TAS (s)	4.42 (2.03)	3.83 (1.81)	0.010 0.140	**FT-EO jerk**	32.8 (11.9)	31.5 (11.8)	0.731 1.000
T1 gyro (°/s)	46.2 (15.3)	53.3 (15.3)	< 0.001 < 0.001	**FT-EC jerk**	39.0 (18.8)	41.7 (20.7)	0.396 1.000
T2 gyro (°/s)	53.4 (19.3)	62.1 (19.2)	0.001 0.018	**FA acc RR**	1.63 (0.88)	1.56 (0.50)	0.895 1.000
MB	14 (5)	16 (7)	0.032 0.416	**FT acc RR**	1.27 (0.45)	1.49 (0.52)	0.191 1.000
				FA jerk RR	1.18 (0.25)	1.17 (0.18)	0.731 1.000
				FT jerk RR	1.18 (0.40)	1.31 (0.34)	0.210 1.000

($F_{1,\ 24}$ = 0.00, p = 0.954). No significant effect of time and feet was found for RR-Trunk$_{acc}$ and RR-Trunk$_{jerk}$ and no significant interaction was found for any of the four ANOVAs (not shown). The full ANOVA tables for each of the four dependent variables (i.e. Trunk$_{acc}$, Trunk$_{jerk}$, RR-Trunk$_{acc}$ and RR-Trunk$_{jerk}$) are given as Supplementary Materials 2 (Table II-S2 to Table V-S2).

Table 1 reports gait, balance and transfers measures, before and after rehabilitation. After rehabilitation, PNLL patients significantly improved their gait speed, TTD and the duration of the different phases of the TUG test (i.e. W1, T1 and W2). Patients also significantly increased their vertical angular velocity during T1 and T2 and significantly increased the MB total score.

Fig. 2 shows the effect size (Cohen's d) of the different gait, balance and transfers measures. According to the Cohen's classification, four gait measures (i.e. gait speed, T1 gyro and T2 gyro) and the TTD showed a large improvement (i.e. Cohen's d > 0.8) after rehabilitation. The improvement was medium for the walking phases of the TUG test (i.e. W1, T1 and W2) and TUG transfers (i.e. STS and TAS) and small for the MB score.

The effect size of the static balance measures ranged from negligible (five variables) to small (three variables). Note the negative effect size of four measures, indicating a change opposite to what is expected in the case of a patient's improvement. Table 1 also reports the Wilcoxon signed rank test for the static balance measures. Also this *non-conservative* analysis shows no treatment effect for any of the static balance measures.

ANOVAs on the static balance measures from the sub-sample of 21 patients who completed the full 30 s static balance tasks are given as Supplementary Materials 3. To note, the analysis of the complete accelerometer traces and that of the short ones returned the very same findings.

3.1. Modification of static balance after exercise

It is actually surprising that, after rehabilitation, patients with PNLL consistently improved straight walking, walking along curved trajectories and transfers, with no apparent modification

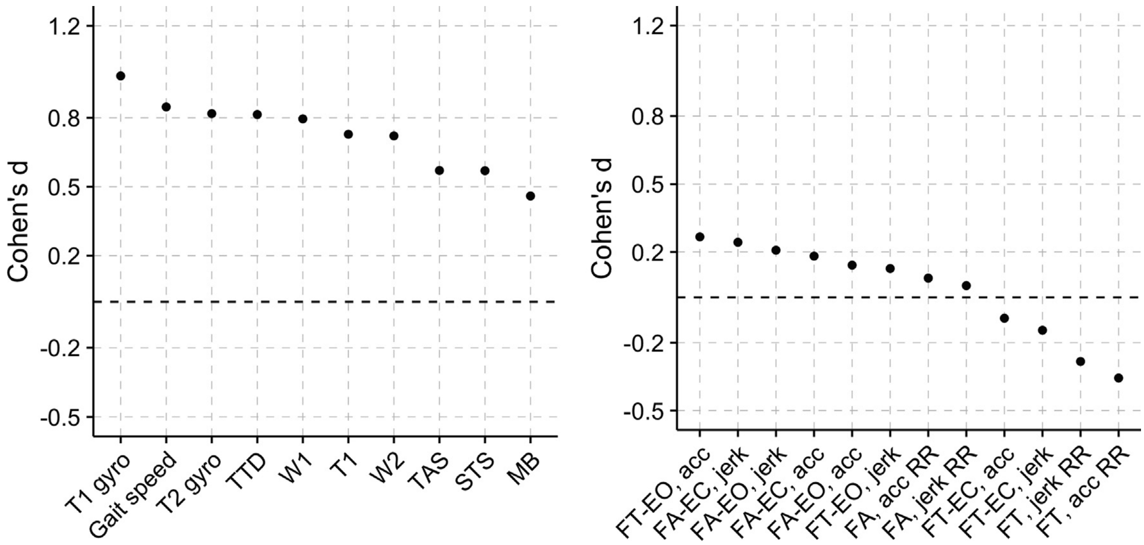

Fig. 2. Cohen's d of gait, transfers and static balance measures. Cohen's d was considerably larger for gait and transfers measures (left panel) than for static balance measures (right panel). Positive Cohen's d values indicates the patients improvement after rehabilitation.

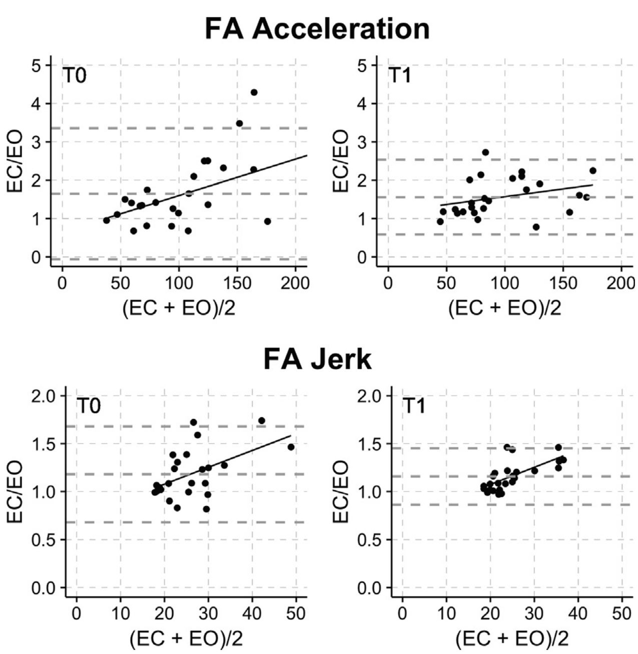

Fig. 3. Bland-Altman plots, feet apart. Dashed upper and lower grey lines: limits of agreement. Dashed middle grey line: ratio mean value. A linear pattern is evident in all four plots, with balance ratios increasing when static balance is poor. Note that after training, the amplitude of the limits of agreement is reduced. Linear regression analysis. Acceleration, T0: $y = 0.23 * x + 52.5$, adjusted $R^2 = 0.16$, $p = 0.028$. Acceleration, T1: $y = 0.40 * x + 29.3$, adjusted $R^2 = 0.46$, $p < 0.001$. Jerk, T0: $y = 0.43 * x + 11.6$, adjusted $R^2 = 0.57$, $p < 0.001$. Jerk, T1: $y = 0.52 * x + 9.0$, adjusted $R^2 = 0.83$, $p < 0.001$.

of static balance. This discrepancy was investigated further with Bland-Altman plots and the PCA.

Fig. 3 shows the Bland-Altman plots of the $Trunk_{acc}$ and $Trunk_{jerk}$ in the FA conditions. A linear pattern is evident in all four plots, with RRs increasing considerably when static balance is poor. After training, limits of agreement are reduced in amplitude, a trend suggesting that training makes balance with EC more similar to balance with EO. The same pattern was also observed in the FT condition (not shown; width of the limits of agreement, T0 vs T1: FA $Trunk_{acc}$ 3.42 vs 1.95; FA $Trunk_{jerk}$ 1.00 vs 0.59; FT $Trunk_{acc}$ 2.19 vs 2.03; FT $Trunk_{jerk}$ 1.86 vs 1.31).

The PCA further evaluated this finding. Fig. 4 shows the scree plot for the static balance measures on admission and discharge. Five and four principal components (PCs) had an eigenvalue larger than one on admission and discharge, respectively. From visual inspection, it is also apparent that the point of inflexion of the scree curve is at PC3 for admission data and at PC2 for discharge data. Similarly, the parallel analysis suggests to retain the first two PCs on admission data and the first PC only on discharge. It is noteworthy that all three methods agree that fewer components are enough to explain data on discharge than on admission.

On admission data, both five components (minimum communality: 1.1; fit based upon off diagonal values: 1; percentage of residuals with absolute value larger than 0.05: 11%) and four components (minimum communality: 1.0; fit based upon off diagonal values: 0.96; percentage of residuals with absolute value larger than 0.05: 44%) solutions were satisfactory. On discharge, a four components solution was satisfactory (minimum communality: 1.1; fit based upon off diagonal values: 0.98; percentage of residuals with absolute value larger than 0.05: 47%), but a three components solution was not (minimum communality: 1.0; fit based upon off diagonal values: 0.95; percentage of residuals with absolute value larger than 0.05: 68%). To make easier the comparison of admission and discharge PCA, we eventually retained four components at both T0 and T1.

On admission, measures of balance with the eyes closed were the only static balance measures with high loadings on PC1 and PC2 (Fig. 5), while only measures of balance with the eyes open had high loadings on PC3 and PC4 (Table VII-S in Supplementary Materials 2). On discharge, both eyes open and eyes closed balance showed high loadings on PC1, while PC2 still exclusively correlated with eyes closed balance.

If we go on to consider further only components with more than three measures with loading >0.6 (see Methods), two PCs exclusively related to EC balance explained a large part of data variability before training. After training, EO and EC measures explain together the largest part of data variability.

4. Discussion

We report here the responsiveness to rehabilitation of different balance, transfers and gait measures in elderly with PNLL.

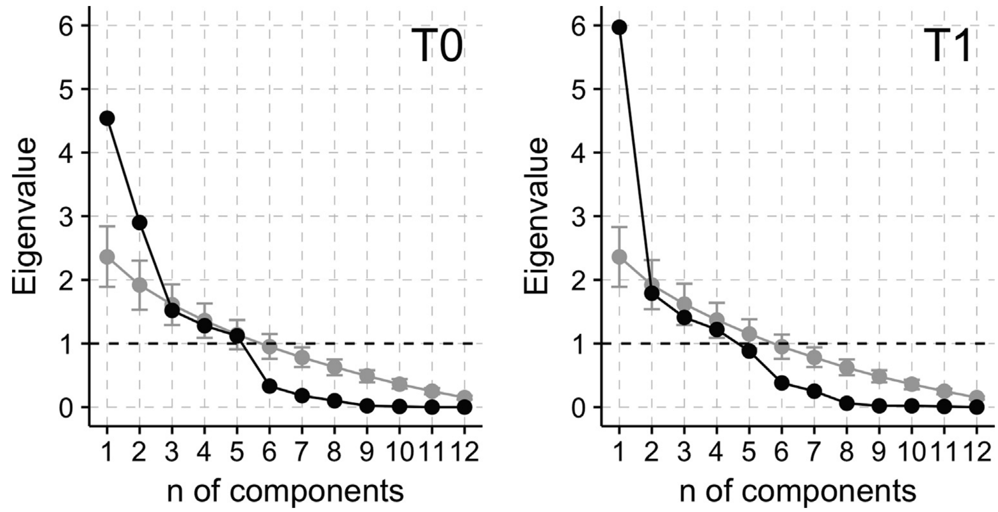

Fig. 4. Scree plots of the principal component analysis. Left panel: admission data (T0); right panel: discharge data (T1). Black plots: scree plots obtained from the principal component analysis of the 12 static posturographic measures. Grey plots: parallel analysis scree plots with 95% confidence interval of the mean eigenvalues.

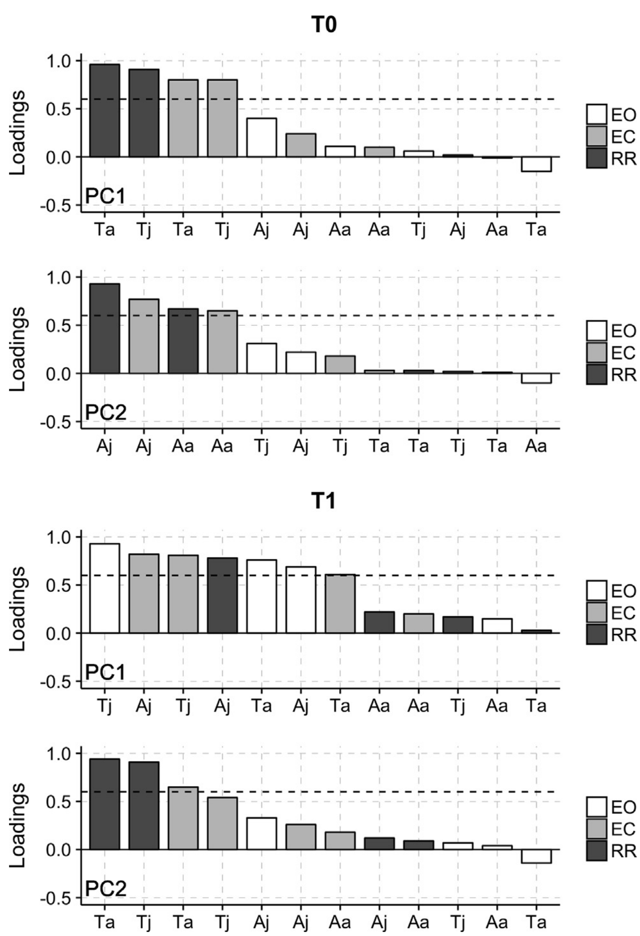

Fig. 5. Loadings of the principal component analysis. The first (PC1) and the second (PC2) components are shown for both admission (T0) and discharge (T1) posturography data. EO: standing with the eyes open; EC: standing with the eyes closed; RR: Romberg ratio; A: feet apart; T: feet totgether; a: acceleration; j: jerk. Black dashed line: loading 0.6.

The current work suggests that elderly PNLL patients benefit from rehabilitation with important improvements on gait speed, both on easy trajectories (e.g. straight walking) and difficult ones (e.g. walking along curved trajectories). Rehabilitation also produces a moderate improvement of transfers (e.g. sit to stand) and a small (but significant) improvement of the overall balance.

Surprisingly enough, no significant improvement of any of the 12 static balance measures was found. From a clinical point of view, we feel that this is an unexpected result. In fact, it is a common clinical finding that patients with poor balance actually get better balance with training, an observation also supported by different studies (Gordt et al., 2018; Missaoui and Thoumie, 2009). With this regard it is important to stress that previous works showed that trunk acceleration can be used as a valid measure of static balance (Whitney et al., 2011) and our results are in line with these reports. In fact, we show here that trunk acceleration and jerk correctly show the worsening of balance that occurs when standing with feet together and when standing with the eyes closed.

The Bland-Altman plot and the PCA showed that the similarity between static balance with EC and static balance with EO balance increases after training. The PCA showed that, on admission, EO and EC balance measures correlate with different (i.e. unrelated) PCs. More precisely, the first and the second PCs (i.e. the two PCs explaining the largest part of data variability) positively correlated with EC balance while EO balance showed high loads on the third and fourth components. On discharge, the first PC correlates high with static balance with both EO and EC.

Static balance (and thus trunk acceleration and jerk) is finely controlled by the nervous system. From a latent variable point of view, PCA components could represent the noise degrading the motor command for upright stance (larger the noise, larger the acceleration and jerk dispersion). Neural signals are corrupted by noise (Harris and Wolpert, 1998). In this framework, the PCA results indicates that, before rehabilitation, noise with EC is uncorrelated to noise with EO. More specifically, on admission, the noise in the motor command when this is driven by proprioception (i.e. EC) is uncorrelated to the noise in the motor command driven by the eyesight. On the contrary, the first PCA component observed on discharge suggests that after rehabilitation noise in proprioception is similar to the noise of the visual system. Given that PNLL patients recruited here had no significant visual impairment (see inclusion criteria), noise in proprioception after rehabilitation would be more similar to the physiologic noise of the sensorymotor system. This modification towards physiologic noise would have obvious benefits on gait, thus giving a possible explanation of the gait improvement observed after rehabilitation in this patients' sample. With this regard it is noteworthy that motor learning induces modifications of gait PCs (Hinkel-Lipsker and Hahn, 2018) and that the effects of motor noise can be minimised by learning (Cohen and Sternad, 2009).

We feel that these results are of interest for different reasons.

Responsiveness studies, in which outcome measures are evaluated, are fundamental for choosing the appropriate sample size when planning a clinical trial. Consider a RCT in which a new intervention for elderly people with PNLL is tested against the control treatment. With this regard, the rehabilitation program administered to the patients recruited here can be easily considered the control group receiving *usual care*. The researcher chooses T1 gyro as the main outcome and makes the hypothesis that the new intervention is at least twice as effective the control treatment. The t test is chosen for assessing the between groups difference at treatment end (type 1 error probability 0.05; power 0.8). From the current study, the researcher knows that standard rehabilitation produces a 7.1°/s average increases of T1 gyro, from 46.2°/s (SD: 15.3°/s) to 53.3°/s (SD: 15.3°/s). On these premises, 74 people per group should conclude the RCT. Because of its much lower responsiveness, if FT-EO trunk acceleration would be chosen as the main outcome, 134 people per group should complete the trial (Faul et al., 2007).

Moreover, these results are also important for the clinician. Our results point out that what is done everyday in real world rehabilitation gyms may not be enough for ameliorating the static balance deficit in PNLL patients and their sensory ataxia. New rehabilitative modalities in which balance is trained with the help of augmented movement feedback and in low light conditions (such as with exergaming or augmented reality training (Shih et al., 2016)) could be of help in this regard.

We are aware of some limitations of our work. We show here that exercise is ineffective on static balance in PNLL patients. Because of the risk of a type 2 error, one has to be cautious when concluding that treatment is not effective. Even if several reports have shown the validity of trunk acceleration for assessing static balance, at our knowledge validation of the accelerometer used here against a criterion reference is missing. Moreover, even if we feel it to be unlikely, we cannot rule out that an accelerometer with different technical specifications could return different results. We cannot rule out as well that other instrumental measures of static balance have proper responsiveness to rehabilitation and this aspect surely deserves further development. Responsiveness to rehabilitation of trunk acceleration and jerk could be compared with that of classical measures obtained from force platforms (Nardone and Schieppati, 2010), to trunk displacement or angular velocity (de Warrenburg et al., 2005) or to computationally-advanced balance measures, such as stability indices (Ladislao and Fioretti, 2007). Posturographic traces 13 s long are shorter than usually recommended (Carpenter et al., 2001) and the reliability of static balance assessments of that duration remains to be understood. With this regard, the fact that the analysis on the 13 s traces and that on the subgroup of patients able to complete the full 30 s static balance tasks return the same results is encouraging. The study's sample size is relatively small, even if similar to that of other studies on the responsiveness of instrumental movement measures (Bolink et al., 2015; Hoff et al., 2001). Moreover, effect sizes were calculated here on paired data and no comparison group was recruited. It could be assumed that training with no or altered visual control of balance and gait is more effective than conventional exercise in PNLL patients. It would therefore be of interest to compare this type of intervention (for example focused on standing with the eyes closed on stable or unstable surfaces) with the exercise program completed here and the effect sizes obtained from this comparison would furthermore simplify the planning of future clinical trials (see above).

We show here that elderly patients with PNLL can enjoy important gait improvements after conventional inpatient rehabilitation consisting in physiotherapy and occupational therapy. On the contrary, no change of static balance (as measured by trunk acceleration) was observed. Responsiveness to conventional rehabilitation seems thus larger for gait than for static balance measures obtained from trunk acceleration. However, we show here that exercise actually has an effect also on static balance, making standing with the eyes closed more similar to standing with the eyes open. The increased agreement between these two standing conditions is consistent with the view that exercise makes noise when standing with the eyes closed closer to the physiologic noise of the sensory-motor system.

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Declaration of Competing Interest

Nothing to disclose.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbiomech.2019.07.007.

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