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Local Dynamic Stability of Trunk During Gait is Responsive to Rehabilitation in Subjects with Primary Degenerative Cerebellar Ataxia

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Abstract

This study aimed to assess the responsiveness to the rehabilitation of three trunk acceleration-derived gait indexes, namely the harmonic ratio (HR), the short-term longest Lyapunov's exponent (sLLE), and the step-to-step coefficient of variation (CV), in a sample of subjects with primary degenerative cerebellar ataxia (swCA), and investigate the correlations between their improvements (Δ), clinical characteristics, and spatio-temporal and kinematic gait features. The trunk acceleration patterns in the antero-posterior (AP), medio-lateral (ML), and vertical (V) directions during gait of 21 swCA were recorded using a magneto-inertial measurement unit placed at the lower back before (T0) and after (T1) a period of inpatient rehabilitation. For comparison, a sample of 21 age- and gait speed-matched healthy subjects ($HS_{matched}$) was also included. At T1, sLLE in the AP ($sLLE_{AP}$) and ML ($sLLE_{ML}$) directions significantly improved with moderate to large effect sizes, as well as SARA scores, stride length, and pelvic rotation. $sLLE_{ML}$ and pelvic rotation also approached the $HS_{matched}$ values at T1, suggesting a normalization of the parameter. HRs and CV did not significantly modify after rehabilitation. $\Delta sLLE_{ML}$ correlated with Δ of the gait subscore of the SARA scale ($SARA_{GAIT}$) and Δstride length and $\Delta sLLE_{AP}$ correlated with Δpelvic rotation and $\Delta SARA_{GAIT}$. The minimal clinically important differences for $sLLE_{ML}$ and $sLLE_{AP}$ were $\geq 36.16\%$ and $\geq 28.19\%$, respectively, as the minimal score reflects a clinical improvement in SARA scores. When using inertial measurement units, $sLLE_{AP}$ and $sLLE_{ML}$ can be considered responsive outcome measures for assessing the effectiveness of rehabilitation on trunk stability during walking in swCA.

Keywords Gait Analysis · Rehabilitation · Postural Balance · Cerebellar Ataxia · Gait Stability · Inertial Measurement Units

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Introduction

Due to the cerebellum's inability to process multisensory features and provide adequate computation and corrections to perturbations [1–5], subjects with degenerative cerebellar ataxia (swCA) exhibit poor joint coordination, abnormal intra-limb joint, and upper and lower body segment coupling during walking [5–9]. Ataxic gait is additionally characterized by incoordination between the upper and lower bodies, which results in increased upper body oscillations with a lack of local trunk stability, transforming the trunk into a generator of perturbations during walking. This causes an unstable, staggering, and wide-based gait, which correlates with disease progression and leads to impaired balance and an increased risk of falling [10–15].

SwCA attempts to cope for center of mass deviations by increasing the base of support and coactivating muscles at single and multi-joint levels, in order to stiffen the lower limb joints [16–18]. Nonetheless, approximately 85% of swCA experience injurious falls. Intensive and repetitive rehabilitation focusing on balance, gait, and activities of daily living has proved to be effective in improving motor performance of swCA [19–27]. Particularly, truncal ataxia and trunk-limb coordination were shown to be effective targets for rehabilitation [19, 20, 22, 28]. Therefore, identifying responsive measures to quantify the improvements in trunk instability during gait may provide clinicians with useful information for designing rehabilitative interventions and assessing their effectiveness.

In this regard, instrumented gait analysis is a useful tool for capturing gait abnormalities and improvements after interventions in swCA, providing specific measures that outperform traditional clinical assessment tools in terms of accuracy and sensitivity to changes and allowing separate investigation of several aspects of gait ataxia [29–32].

Recently, a series of trunk acceleration-derived gait measures have been proposed to assess gait imbalance [29, 33–43]. Particularly, three indexes, namely the harmonic ratios (HRs), short-time longest Lyapunov's exponent (sLLE), and step-to-step coefficient of variation (CV), showed the best ability to characterize the trunk behavior during gait of swCA [36–38].

Therefore, the primary aim of this study was to assess the internal responsiveness to rehabilitation of HRs, sLLE, and CV in terms of the magnitude of changes after rehabilitation. Furthermore, we aimed to assess (i) the external responsiveness of the gait stability indexes, as well as the minimal clinically important differences reflecting clinical improvements after rehabilitation, and (ii) the spatio-temporal and kinematic gait parameters that correlate with the improvements in the gait stability indexes and clinical improvements following rehabilitation in swCA.

We hypothesized that, in addition to characterizing swCA gait behavior, HRs, sLLE, and CV could be responsive outcomes for rehabilitative interventions, and that their improvements could correlate with clinical improvements after rehabilitation.

Materials and Methods

Subjects

We collected data samples from 21 swCA (8 females, 13 males) aged 51.33 ± 12.17 years and diagnosed with primary degenerative cerebellar ataxia since 10.71 ± 7.14 years, who underwent an inpatient rehabilitation program at the Traumatic Orthopedic Surgical Institute (ICOT) in Latina, Italy.

Table 1 shows the diagnoses and clinical characteristics of all subjects. The Scale for the Assessment and Rating of Ataxia (SARA) [44, 45] and its gait subscore ($SARA_{GAIT}$) were administered to assess disease severity. SwCA with gait impairment due to extracerebellar symptoms (spasticity, polyneuropathy, cognitive impairment (MMSE score > 24), oculomotor abnormalities, and visual deficits according to the Snellen visual acuity test) was excluded, as well as subjects with concomitant other neurologic or orthopedic conditions. We only included subjects who could walk without assistance and had gait problems that were exclusively cerebellar in nature at the time of their initial evaluation within a larger group of swCA from a rare disease center [13, 18, 36, 46].

SwCA were matched with a dataset of 89 walking trials from healthy subjects (HS) for group comparison using a 1:1 optimal data matching procedure with the propensity score difference method [47]. Each HS repeated the gait task twice, walking at both self-selected and slower speeds to reduce the effect of gait speed on other gait parameters and to gather the largest sample size possible for speed-matched comparisons [18, 34, 36, 48]. The propensity scores were calculated using logistic regression analysis and age and speed as covariates [49–53]. As a control group, 21 age- and speed-matched healthy subjects ($HS_{matched}$) (11 females, 10 males), aged 56.61 ± 10.92 years, were included after the matching procedure. An independent sample t-test confirmed the effectiveness of the matching procedure (Table 1).

Before the experimental procedure, both swCA and HS provided informed consent in accordance with the Helsinki Declaration. The local ethics committee (CE Lazio 2, protocol number 0139696/2021) approved the study.

Procedures

Gait data were collected by fixing a magneto-inertial measurement unit (BTS GWALK, BTS, Milan, Italy) at the fifth lumbar vertebrae level via an ergonomic belt and connecting it to a laptop via Bluetooth. The "Walk +" protocol of the G-STUDIO software (G-STUDIO, BTS, Milan, Italy) was used to detect trunk linear acceleration patterns in the antero-posterior (AP), medio-lateral (ML), and vertical (V) directions at a sampling rate of 100 Hz, as well as to detect right and left heel strikes, toe-off, spatio-temporal parameters, and pelvic kinematics. swCA were asked to walk at their own pace along a corridor 30 m long and 3 m wide with no external sensory cues before (T0) and at the end of their 4-week rehabilitation period (T1). Walking trials with at least 20 consecutive correctly recorded strides [54–56] were included in the analyses. HRs, CV, and sLLE in the three spatial directions were also calculated as the trunk acceleration-derived gait indexes. Details on the calculation of the indexes are provided in the supplementary material.

Table 1 Sample characteristics and gait assessments at T0 and T1

	swCA	T0 (mean (SD))	T1 (mean (SD))	p-value (T0 vs T1)	Cohen's d	HS
Disease duration (years)	10.71 (7.14)					
CA subtype (n)	SAOA 10					
	SCA1 5					
	SCA2 2					
	SCA3 2					
	SCA6 1					
	SCA8 1					
SARA (total)		14.74 (7.84)	9.69 (3.95)	0.01	0.66	
SARA$_{GAIT}$		3.09 (0.99)	2.43 (1.03)	0.00 ●	0.73	
Age (years)		51.33 (12.17)			56.61 (10.92)	51.33 (12.17)
Gait speed (m/s)		1.04 (0.25)	1.02 (0.25)	0.17 ●	0.31	1.01 (0.15)
HR$_{AP}$		1.86 * (0.37)	1.85 * (0.44)	0.89	0.03	2.51 (0.53)
HR$_{ML}$		1.85 * (0.39)	1.81 * (0.42)	0.58	0.12	2.44 (0.44)
HR$_V$		1.90 * (0.43)	1.89 * (0.50)	0.96	0.01	2.81 (0.57)
sLLE$_{AP}$		0.95 * (0.29)	0.75 * (0.21)	0.03	0.75	0.55 (0.26) †
sLLE$_{ML}$		0.61 * (0.18)	0.41 (0.13)	0.00	0.86	0.34 (0.16) †
sLLEv		0.62 * (0.31)	0.49 * (0.19)	0.06	0.43	0.33 (0.20) †
Step-to-step CV (%)		39.73 * (20.42)	42.58 * (19.00)	0.38	0.22	18.55 (11.45) †
Stride length (m)		1.14 * (0.23)	1.19 * (0.25)	0.04	0.46	1.27 (0.19)
Stance phase duration (% gait cycle)		65.42 * (3.45)	63.98 * (3.53)	0.11	0.36	62.11 (4.38) †
Swing phase duration (% gait cycle)		34.70 * (3.26)	36.02 * (3.53)	0.12	0.35	37.89 (4.38) †
Double support phase duration (% gait cycle)		30.16 * (7.21)	28.38 * (6.99)	0.22	0.27	23.49 (6.75)
Single support phase (% gait cycle)		35.26 * (3.92)	35.61 * (4.16)	0.67	0.09	38.62 (3.47)
Cadence (steps/min)		107.63 (12.12)	105.72 (9.22)	0.44	0.17	101.82 (12.52) †
Pelvic tilt (°)		2.11 (0.82)	2.19 (0.93)	0.63	0.10	2.90 (1.02)
Pelvic obliquity (°)		1.97 * (1.11)	2.47 * (1.47)	0.07 ●	0.48	5.19 (2.65)
Pelvic rotation (°)		5.84 * (2.65)	7.84 (4.63)	0.03	0.49	8.12 (3.11) †

swCA, subjects with degenerative cerebellar ataxia; *HS*, age- and gait speed-matched healthy subjects; *SAOA*, sporadic adult-onset ataxia; *SCA*, spino-cerebellar ataxia; SARA, scale for the assessment and rating of ataxia; *SARA$_{GAIT}$*, gait subscore of the SARA scale; *HR*, harmonic ratio; *sLLE*, short-term largest Lyapunov's exponent; *AP*, antero-posterior direction; *ML*, medio-lateral direction; *V*, vertical direction; *CV*, coefficient of variation; ●, p-values calculated using Wilcoxon test following significant Shapiro–Wilk test (SARA$_{GAIT}$, $p = 0.01$; gait speed, $p = 0.01$; pelvic obliquity, $p = 0.03$); †, p-values calculated using Mann–Whitney test following significant Shapiro–Wilk test in HS subgroup (sLLE$_{AP}$, $p = 0.00$; sLLE$_{ML}$, $p = 0.00$; sLLE$_V$, $p = 0.04$; step-to-step CV, $p = 0.01$; stance phase duration, $p = 0.02$; swing phase duration, $p = 0.02$; cadence, $p = 0.00$; pelvic rotation, $p = 0.01$); *significant differences between swCA and HS values

The rehabilitation program consisted of a 4-week inpatient intensive training. All subjects received 3 h of day rehabilitation per day, with at least 1 h of exercise-based rehabilitation 6 days a week, for a total of 18 h and 6 h of exercise therapy per week. Based on the talk test, the exercises were performed at a moderate intensity. Exercises focused on static balance and trunk stabilization, dynamic balance, trunk-limb coordination, and stretching exercises to treat or prevent contractures [19, 20, 22, 26]. Static balance exercises were performed using both "hands-off" (e.g., standing on one leg or maintaining specific posture such as side bridging) and "hands-on" interventions (e.g., rhythmic stabilization of the trunk in quadruped, supine, lateral position, and half-kneeling positions); dynamic balance exercises were performed through the repetitive execution of postural transfers from lying to standing positions; trunk-limb coordination was trained by asking participants to move their upper or lower limbs alternately while stabilizing the trunk in supine (e.g., raising feet alternately while maintaining supine bridge position), lateral (e.g., raising one leg or one arm while maintaining a stable side-lying position), prone (e.g., raising arms or legs alternately while maintaining quadruped position), or vertical (e.g., moving feet forward alternately while maintaining kneeling position) positions. Participants also performed exercises aiming at reducing their postural sway by using an instrumented

balance board with visual feedback (Tecnobody, Prokin Balance System, Tecnobody, Italy).

Statistical Analysis

Based on previously reported gait improvements after rehabilitation [20], we calculated a sample size of at least 15 swCA to reliably detect a high effect size ($d = 0.8$), assuming a two-sided detection criterion that allows for a maximum type I error rate of 0.05 and type II error rate of 0.80 in a paired sample t-test procedure.

The Shapiro–Wilk test was used to check for the normality of the distributions. To identify significant changes in clinical and gait parameters at T1, a paired t-test or Wilcoxon test was used. Cohen's d with Hedge's correction was used to calculate internal responsiveness [57, 58].

To identify significant differences between swCA and HS at T0 and the gait parameters that approached normative values at T1, the unpaired t-test or Mann–Whitney test was used.

Gait variable and SARA and SARA$_{PG}$ score changes at T1 were expressed as delta (Δ) values using the following formula:

$$\Delta = 100 \times \frac{\text{value}_{T1} - \text{value}_{T0}}{\text{value}_{T0}}$$

To identify the correlations between the Δs of the modified gait stability indexes and the Δs of the clinical, spatio-temporal, and kinematic gait parameters, Spearman's correlation coefficients were calculated. To account for tied scores, we applied the tie correction factor to the correlation coefficients according to the formula:

$$r_s = 1 - \frac{6 \sum d_i^2}{n(n^2 - 1) - \sum (t_i^3 - t_i)},$$

where d_i represents the difference between the ranks of corresponding values for the two variables, n is the number of observations, and t_i is the number of tied ranks for each group of ties. The term $\sum (t_i^3 - t_i)$ represents the sum of the cubes of the number of ties minus the number of ties for each distinct number of tied values, summed across all sets of ties.

The external responsiveness of the modified trunk acceleration-derived indexes was assessed using an anchor-based method [57] using the smallest detectable change of the SARA scale (3.5 points) in subjects who improved their SARA$_{GAIT}$ scores as the criterion for clinical improvement [59]. Receiver operating characteristic curves were plotted and the area under the curves (AUCs) were calculated. AUC values > 0.70 were considered for satisfying external responsiveness. The value that maximized the sum of sensitivity and specificity was used to determine the

minimally clinically important differences (MCID). At the MCID value, positive and negative likelihood ratios (LRs) were calculated and transformed into post-test probabilities using Fagan's nomograms. Δs of the externally responsive trunk acceleration-derived gait indexes was classified as the binary variable based on their MCIDs, and $\Delta SARA_{GAIT}$ was categorized as lacking improvement ($\Delta SARA_{GAIT} < 1$), improving by 1 point ($\Delta SARA_{GAIT} \geq 1$), or improving by 2 points or higher ($\Delta SARA_{GAIT} \geq 2$). To observe differences in baseline variables and improvements after rehabilitation using the MCID-based category as a between-groups factor, a Mann–Whitney test for continuous independent variables was used.

All the statistical analyses were set at 95% significance level and 80% power and performed using the IBM SPSS vers.27, JASP vers.0.17.2.1, NCSS 2023 software, and the "Pingouin" Python package, vers.0.5.3 [60].

Results

Internal Responsiveness Findings

The results of the clinical and gait parameter assessments at T0 and T1 are reported in Table 1.

At T0, significant differences between swCA and HS were found in all the gait parameters except for gait speed and pelvic tilt. Following rehabilitation, swCA significantly improved their SARA and SARA$_{GAIT}$ scores, stride length, pelvic rotation, and sLLE$_{AP}$ with medium-to-large effect sizes and sLLE$_{ML}$ with large effect size (Table 1, Fig. 1). At T1, sLLE$_{ML}$ and pelvic rotation were no longer different from HS$_{matched}$ (Fig. 2).

Correlation Findings

Both $\Delta sLLE_{ML}$ and $\Delta sLLE_{AP}$ correlated with $\Delta SARA_{GAIT}$. $\Delta sLLE_{ML}$ correlated with Δstride length, whereas $\Delta sLLE_{AP}$ correlated with Δpelvic rotation (Table 2).

External Responsiveness Findings

Nine swCA (40.91%) outperformed the smallest detectable SARA change score among the 11 (52.38%) swCA who improved their SARA$_{GAIT}$ score by 1 point or more. Both sLLE$_{ML}$ and sLLE$_{AP}$ revealed good external responsiveness to SARA improvements (AUCs ≥ 0.70). According to MCID, $\Delta sLLE_{ML} \geq 36.16\%$ and $\Delta sLLE_{AP} \geq 28.19\%$ were deemed as necessary to improve SARA scores with 70% and 67% probabilities, respectively (Table 3).

Twelve (57.14%) and 11 (52.38%) swCA were classified as improved according to the MCIDs of sLLE$_{ML}$ and sLLE$_{AP}$, respectively. We found significant differences
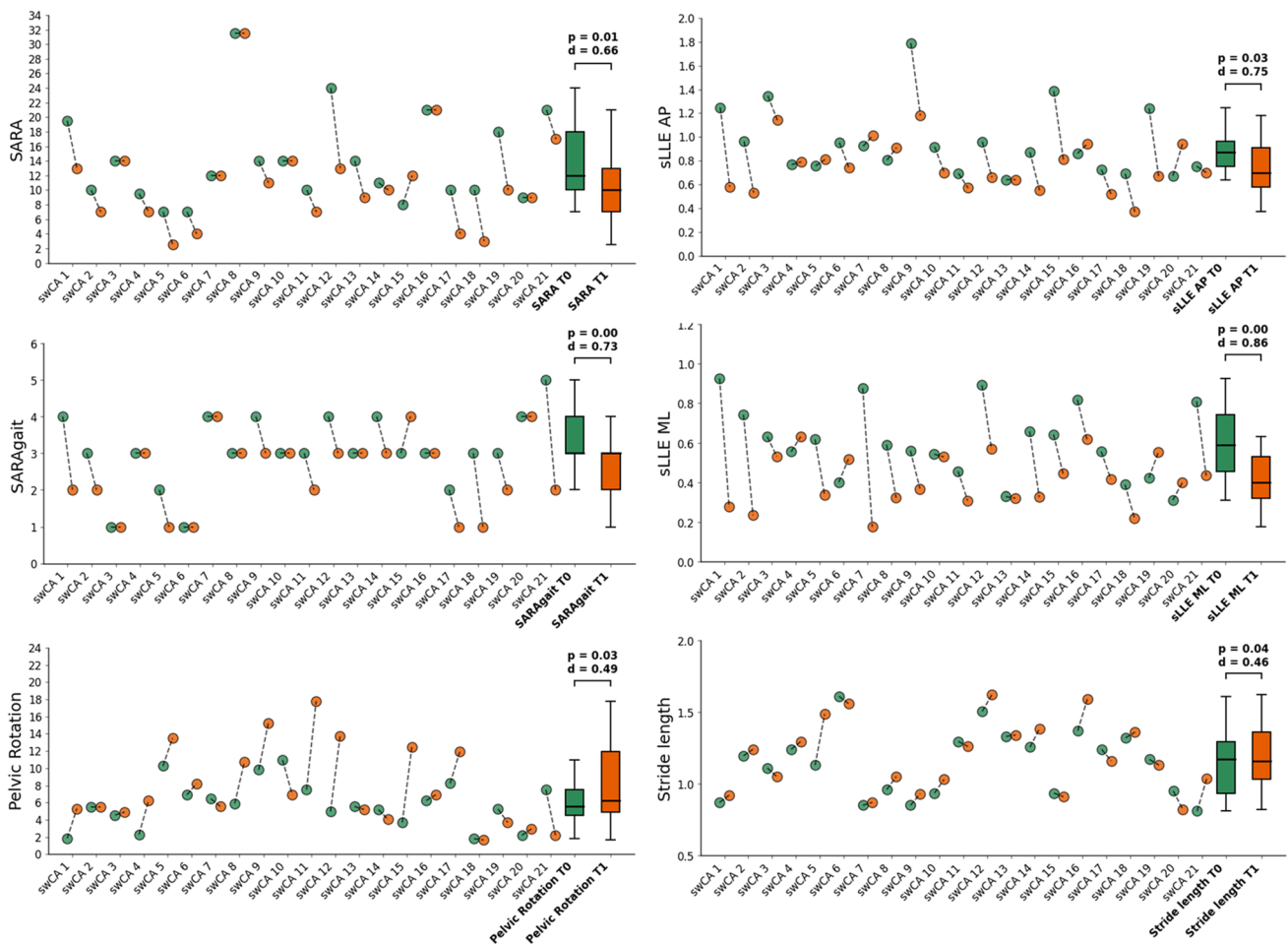
Fig. 1 Significant differences between T0 (green) and T1 (orange). The jitter elements represent the values for each subject at T0 and T1. Paired sample *t*-test was performed on SARA, $sLLE_{AP}$, $sLLE_{ML}$, and pelvic rotation after verifying the normality of distributions (Shap-iro–Wilk test, $p > 0.05$). Wilcoxon test was performed on $SARA_{GAIT}$ (Shapiro–Wilk test, $p = 0.01$). Above the boxplots, Cohen's *d* as the effect size and *p*-values

in $sLLE_{ML}$ baseline values, and Δstride length, based on $sLLE_{ML}$ improvements, and in $sLLE_{AP}$ baseline values and Δpelvic rotation, based on $sLLE_{AP}$ improvements (Table 4). Three subjects (14.29%) improved both their $SARA_{GAIT}$ values and sLLE values. After removing these subjects from the analysis, no differences in $\Delta SARA_{GAIT}$ were found based on $sLLE_{ML}$ and $sLLE_{AP}$ improvements (Table 4). Significant differences between T0 and T1 were maintained in $sLLE_{ML}$ and $sLLE_{AP}$ even after repeating a paired sample *t*-test by removing swCA with $\Delta SARA_{GAIT} > 1$ ($sLLE_{ML}$, $p = 0.00$, Cohen's $d = 0.76$; $sLLE_{AP}$, $p = 0.02$, Cohen's $d = 0.60$).

Discussion

The main objective of this study was to assess the responsiveness of seven trunk acceleration-derived gait indexes to intensive rehabilitation training in a sample of swCA by determining the magnitude of their modification and quantifying the minimal improvements required to identify subjects who clinically improved following rehabilitation. We also aimed at identifying significant correlations between the improvements in trunk acceleration-derived gait indexes and the improvements in clinical and kinematic measures.

We found that sLLE in the AP and ML directions significantly modified following rehabilitation with medium-to-high internal ($0.75 < d > 0.86$, Table 1, Fig. 1) and good external (AUCs ≥ 0.70, Table 3) responsiveness. Following rehabilitation, $sLLE_{ML}$ also approached normative values (Fig. 2). Furthermore, $\Delta sLLE_{ML}$ and $\Delta sLLE_{AP}$ moderately correlated with $\Delta SARA_{GAIT}$ (Table 2), with MCIDs $\geq 36.16\%$ and $\geq 28.19\%$, respectively, required to detect clinically significant variations in SARA scale values after rehabilitation (Table 3).

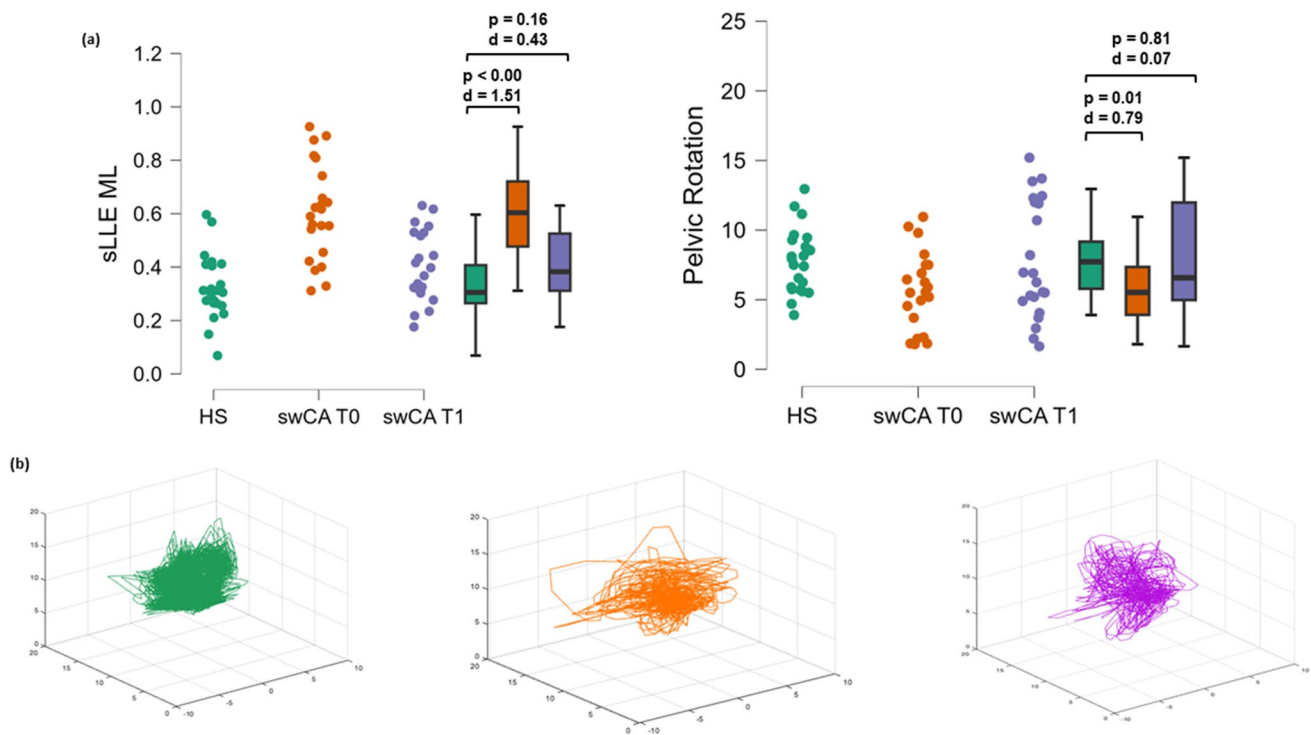sLLE quantifies the local dynamic stability of a system [61–63], accurately reflecting the gait instability of swCA

Fig. 2 a Differences in short-term longest Lyapunov's exponent (sLLE) in the medio-lateral (ML) direction, and pelvic rotation between HS (green) and swCA at T0 (orange) and swCA at T1 (purple). Cohen's *d* as the effect size and *p*-values in a *t*-test or Wilcoxon test procedure are reported. **b** 3D-reconstructed state space of the acceleration and its time-delayed copies (time delay of ten data samples) in the medio-lateral direction of a representative age- and speed-matched healthy subject (green), and a swCA at baseline (orange) and after the rehabilitation period (purple)

Table 2 Correlation analysis findings

		$\Delta SARA_{GAIT}$[*]	ΔPelvic rotation	ΔStride length
$\Delta sLLE_{ML}$	ρ	0.41	0.18	0.51
	p-value	0.03	0.22	0.01
$\Delta sLLE_{AP}$	ρ	0.43	0.41	−0.07
	p-value	0.03	0.03	0.62

Δ, %difference between the last and the first assessment; *sLLE*, short-term largest Lyapunov's exponent; *AP*, antero-posterior direction; *ML*, medio-lateral direction; *SARA_GAIT*, subscore of the SARA scale, ρ, Spearman's correlation coefficient; *, Spearman's rho coefficients accounting for tied scores

caused by the inability to recover from small perturbations [33, 36, 38]. However, to the best of our knowledge, this is the first time that its responsiveness to interventions has been investigated in swCA. Because the acceleration patterns in this study were recorded at the lower back level, and trunk ataxia has been described as being susceptible to improvement in swCA [19, 64], we could argue that sLLE may capture improvements in the ability of the trunk to cope with the center of mass displacements during gait. In that regard, it represents a potentially useful tool to assess the efficacy of intensive rehabilitation treatments. We additionally found that subjects with higher baseline sLLE values improved the most in dynamic trunk stability after rehabilitation (Table 4). Although our findings did not reach statistical significance,

Table 3 External responsiveness findings

	AUC	MCID	Se	Sp	LR+	LR−	PTP+	PTP−
$\Delta sLLE_{ML}$	0.75 (0.41–0.91)	≥36.16%	0.78	0.77	3.37	0.28	70%	16%
$\Delta sLLE_{AP}$	0.70 (0.36–0.88)	≥28.19%	0.66	0.77	2.89	0.43	67%	23%

AUC, area under the ROC curve; *MCID*, minimal clinically important difference; *Se*, sensitivity; *Sp*, specificity; *LR+*, positive likelihood ratio; *LR−*, negative likelihood ratio; *PTP+*, positive post-test probability; *PTP−*, negative post-test probability; *ΔsLLE*, percentage improvement of short-term longest Lyapunov's exponent following rehabilitation; *ML*, medio-lateral direction of the acceleration signals; *AP*, antero-posterior direction of the acceleration signals

Table 4 Significant differences according to MCIDs

		ΔsLLE$_{ML}\geq36.16\%$	ΔsLLE$_{ML}<36.16\%$	p-value	ΔsLLE$_{AP}\geq28.19\%$	ΔsLLE$_{AP}<28.19\%$	p-value
SARA$_{GAIT}$ T0 (n, %)	1	2 (9.52)	0		0	2 (9.52)	
	2	1 (4.76)	1 (4.76)		1 (4.76)	1 (4.76)	
	3	7 (33.33)	3 (14.29)		5 (23.81)	5 (23.81)	
	4	2 (9.52)	5 (23.81)		5 (23.81)	2 (9.52)	
SARA T0 (mean (SD))		16.22 (8.18)	12.37 (4.22)	0.30	14.50 (5.34)	13.50 (7.57)	0.37
ΔSARA (%, mean (SD))		33.92 (26.59)	17.56 (29.45)	0.20	28.82 (33.59)	19.92 (23.26)	0.24
SARA$_{GAIT}$ T0 (mean (SD))		3.44 (0.73)	2.75 (0.96)	0.08	3.36 (0.67)	2.70 (1.06)	0.24
ΔSARA$_{GAIT}$ (n, %)	<1	2 (9.52)	8 (38.10)		2 (9.52)	8 (38.10)	
	≥1	4 (19.05)	4 (19.05)		6 (28.57)	2 (9.52)	
	≥2	3 (14.29)	0		3 (14.29)	0	
ΔSARA$_{GAIT}$ (%, mean (SD))		34.44 (24.31)	9.03 (22.32)	**0.03**	30.45 (28.37)	8.33 (18.00)	**0.04**
ΔSARA$_{GAIT}$* (%, mean (SD))		22.22 (19.48)	9.03 (22.32)	0.27	19.79 (25.56)	8.33 (18.00)	0.56
sLLE$_{AP}$ T0 (mean (SD))		0.88 (0.17)	0.99 (0.36)	**0.02**	1.11 (0.35)	0.84 (0.20)	**0.03**
sLLE$_{ML}$ T0 (mean (SD))		0.72 (0.17)	0.52 (0.14)	**0.01**	0.65 (0.18)	0.56 (0.19)	0.28
Gait speed T0 (m/s, mean (SD))		1.08 (0.21)	1.02 (0.28)	0.57	1.07 (0.27)	1.03 (0.24)	0.75
Stride length (m, mean (SD))		1.09 (0.24)	1.17 (0.22)	0.52	1.18 (0.23)	1.01 (0.23)	0.34
ΔStride length (%, mean (SD))		11.27 (10.78)	0.28 (8.33)	**0.02**	5.94 (9.26)	3.95 (12.63)	0.47
Stance phase (%gait cycle, mean (SD))		65.53 (4.74)	65.35 (2.29)	0.97	64.65 (2.94)	66.12 (3.86)	0.47
Swing phase (%gait cycle, mean (SD))		34.77 (4.39)	34.65 (2.29)	0.97	34.12 (3.56)	35.34 (2.94)	0.47
Double support phase (%gait cycle, mean (SD))		30.81 (10.03)	29.67 (4.56)	0.73	28.29 (6.01)	31.86 (8.05)	0.39
Single support phase (%gait cycle, mean (SD))		34.72 (5.32)	35.67 (2.64)	0.59	34.26 (4.30)	36.36 (3.34)	0.35
Cadence (steps/min, mean (SD))		113.41 (10.40)	103.30 (11.85)	0.06	108.19 (13.28)	107.02 (11.38)	0.86
Pelvic obliquity (°, mean (SD))		2.05 (1.12)	1.92 (1.16)	0.78	1.92 (0.89)	2.04 (1.37)	0.86
Pelvic rotation (°, mean (SD))		5.49 (2.62)	6.10 (2.75)	0.57	5.89 (2.98)	5.78 (2.39)	0.78
ΔPelvic rotation (%, mean (SD))		30.77 (75.45)	0.81 (59.64)	0.32	39.49 (48.61)	− 11.38 (58.23)	**0.02**

Δ, differences between the assessment before and after rehabilitation; *SARA*, scale for the assessment and rating of ataxia; *SARA*$_{GAIT}$, gait subscore of the SARA scale; *sLLE*, short-term largest Lyapunov's exponent; *AP*, antero-posterior direction; *ML*, medio-lateral direction; *p*-values were calculated using Mann–Whitney test; *, statistical analysis performed by excluding swCA with ΔSARA$_{GAIT}>1$; bolded values represent significant differences

it is worth noting that a substantial number of subjects with cerebellar ataxia (swCA) who improved the most in sLLE$_{ML}$, 33.33%, specifically (Table 4), had poorer gait quality at baseline, according to their SARA$_{GAIT}$ scores. This observation is consistent with existing literature [20, 65] reporting the effectiveness of rehabilitation training in swCA in more severely disabled swCA, regardless of disease duration, implying that individuals with swCA may be able to improve their dynamic trunk stability despite ongoing degeneration.

Notably, unlike other studies investigating the effects of rehabilitation on gait parameters [19, 20, 24], gait speed did not improve in our sample, suggesting that sLLE may capture the effects of rehabilitation regardless of gait speed. The differences in gait speed improvements observed in our study compared to existing literature can be attributed to differences in rehabilitation environments, methods of gait speed assessment, and the nature of exercise programs implemented. Miyai et al. [19] and Keller et al.

[24] documented increases in gait speed following 4 and 6 weeks of rehabilitation programs, respectively, focusing specifically on gait training. Ilg et al. [20] also observed gait improvements following a 16-week rehabilitation period, observing improvements in gait speed after an 8-week follow-up, and involved participants engaging in home-based exercises following intensive rehabilitation. In contrast, our study involved inpatient swCA and did not emphasize specialized gait training, such as on uneven terrain, outdoor settings, or treadmill training with variable gait speeds. This could partly explain the lack of significant gait improvement findings. However, a direct comparison with Miyai et al. is challenging, as they did not specify the tools used for gait speed assessment or the distance for gait measurement. Keller et al. [24] employed an optoelectronic system to measure gait over a 6-m path, significantly shorter than the 30-m distance that we used in our study, leading to the recording of a considerably fewer number of consecutive

gait strides. Ilg et al. [20], on the other hand, measured gait parameters over 12–15 strides using an optoelectronic system. Their study found that increased walking speeds were achieved after an 8-week period of home exercises following 4 weeks of supervised intensive rehabilitation, resulting in a considerably longer observation period compared with our study. Thus, the disparities in our study's findings could be attributed to the different lengths and types of rehabilitation programs.

As in previous studies on swCA rehabilitation [20], we also found significant modifications in stride length (Table 1, Fig. 1) that positively correlated with the improvements in $sLLE_{ML}$ (Table 2). Moreover, stride length improvements were significantly higher in swCA who improved their $sLLE_{ML}$ by the 36.16% MCID (Table 4). Because of the use of a single magneto-inertial measurement unit in this study, we were unable to assess the effects of rehabilitation on step width, a well-known increased gait parameter in swCA attempting to compensate for balance impairment during gait [1, 7, 13, 15, 66, 67]. However, given the inverse correlation between step width and stride length, the correlation between Δstride length and $\Delta sLLE_{ML}$ in this study may reflect a decrease in the need for compensating by widening the base of support due to improvements in trunk stability [20].

Moreover, pelvic rotation approached normative values after rehabilitation (Table 1, Fig. 2) and correlated with improvements in $sLLE_{AP}$. Moreover, pelvic rotation improvements were significantly higher in swCA who improved their $sLLE_{ML}$ by the $\geq 28.19\%$ MCID (Table 4). Considering that impaired trunk-lower limb coordination [10], increased coactivation of lower limb muscles [18], and chaotic upper trunk behavior [68] may cause compensatory reductions in pelvic mobility during gait [36], it is possible to hypothesize that the proposed rehabilitation training, which included a large proportion of trunk stability-focused exercises, induced swCA to increase their pelvic movement due to improvements in trunk stability during gait.

However, useful biomarkers of gait instability and falls risk in swCA [36, 37], and HR and CV did not show responsiveness to rehabilitation in this study. HR represents a measure of the symmetry of acceleration signals reflecting gait symmetry or trunk smoothness during gait [56, 69], which has been reported as responsive to rehabilitation in subjects with Parkinson's disease [35]. The results of this study lead us to hypothesize that, in swCA, the proposed intensive rehabilitation training may be more effective on trunk stability rather than trunk smoothness or symmetry as measured. However, because we measured the symmetry of trunk behavior during gait through HR only, we cannot exclude that other measures in the gait symmetry domain would have improved following rehabilitation. As regards the CV, a lack of reduction of variability in spatial gait

parameters is expected in swCA. However, in this study, we only assessed the step-to-step variability. Conversely, Ilg et al. reported a reduction of the temporal variability in limb coordination during gait after rehabilitation [20–22]. Since we could not assess interlimb variability due to the use of a single lumbar-mounted magneto-inertial measurement unit, the responsiveness to the rehabilitation of other gait variability measures should be further investigated.

This study presents several limitations to be accounted for a better interpretation of the results. First, we only included swCA who could walk independently, excluding subjects with more severe disability, to which our findings cannot be directly extended. Additionally, because of the small sample size, we could not investigate differences between the subtypes of degenerative CA. Notably, we discovered that the three subjects who improved the most in $SARA_{GAIT}$ also improved the most in sLLE. Despite the internal responsiveness of sLLE did not change substantially after removing these three subjects, we cannot rule out an overrepresentation of subjects with the greatest improvements in $SARA_{GAIT}$ scores on sLLE improvements due to the small number of subjects who improved their $SARA_{GAIT}$ scores by more than 1 point. As a result, our study deserves to be replicated with larger samples in order to better understand the factors that predict sLLE responsiveness after rehabilitation.

Furthermore, we only evaluated subjects with inherited degenerative CA; thus, our findings deserve to be confirmed on subjects with other cerebellar or afferent gait disorders. Although recommended in cerebellar disorders [45], another limitation of this study is represented by the use of SARA improvements as the criterion for external responsiveness calculations. Since a clear definition of responsiveness and minimal clinically important change scores for SARA are lacking [32, 70–72], in this study, we used the SDC scores as the external criterion. However, we cannot exclude that our results may vary by using other clinical scales as the criterion for clinical improvement definitions.

Conclusions

In this study, we aimed at assessing the responsiveness of trunk acceleration-derived HR, sLLE, and CV, to a 4-week intensive rehabilitation program. sLLE in the ML and AP directions revealed good internal and external responsiveness, and moderately correlated with the improvements in $SARA_{GAIT}$ subscore, stride length, and pelvic rotation. The findings of this study suggest that trunk stability can be effectively quantified using sLLE and improve after rehabilitation. Because of the usability and affordability of magneto-inertial measurement units, sLLE can be considered a useful additional outcome measure for assessing the effectiveness of intensive rehabilitation treatments, particularly when

focusing on improvements in trunk stability during gait. Further studies including larger populations are needed to confirm these results and investigate long-term responsiveness.

Declarations

Ethics Approval The study was approved by the local ethics committee (CE Lazio 2, protocol number 0139696/2021).

Competing Interests The authors declare no competing interests.

References

1. Cabaraux P, Agrawal SK, Cai H, Calabro RS, Carlo C, Loic D, et al. Consensus paper: ataxic gait. Cerebellum [Internet]. Cerebellum; 2022 [cited 2022 Sep 20]. Available from: https://pubmed.ncbi.nlm.nih.gov/35414041/.
2. Cabaraux P, Gandini J, Kakei S, Manto M, Mitoma H, Tanaka H. Dysmetria and errors in predictions: the role of internal forward model. Int J Mol Sci [Internet]. Multidisciplinary Digital Publishing Institute (MDPI). 2020 [cited 2021 Jul 21];21:1–21. Available from: /pmc/articles/PMC7555030/.
3. Manto M. Motor control: CRF regulates coordination and gait. Curr Biol [Internet]. Curr Biol; 2017 [cited 2023 Nov 15];27:R847–50. Available from: https://pubmed.ncbi.nlm.nih.gov/28898648/.
4. Manto M. The underpinnings of cerebellar ataxias. Clin Neurophysiol Pract [Internet]. Clin Neurophysiol Pract; 2022 [cited 2023 Nov 15];7:372–87. Available from: https://pubmed.ncbi.nlm.nih.gov/36504687/.
5. Manto M, Serrao M, Filippo Castiglia S, Timmann D, Tzvi-Minker E, Pan MK, et al. Neurophysiology of cerebellar ataxias and gait disorders. Clin Neurophysiol Pract [Internet]. Clin Neurophysiol Pract; 2023 [cited 2023 Sep 12];8:143–60. Available from: https://pubmed.ncbi.nlm.nih.gov/37593693/.
6. Bodranghien F, Bastian A, Casali C, Hallett M, Louis ED, Manto M, et al. Consensus paper: revisiting the symptoms and signs of cerebellar syndrome. Cerebellum. Springer New York LLC. 2016;15:369–91.
7. Serrao M, Pierelli F, Ranavolo A, Draicchio F, Conte C, Don R, et al. Gait pattern in inherited cerebellar ataxias. Cerebellum [Internet]. Cerebellum; 2012 [cited 2021 Mar 23];11:194–211. Available from: https://pubmed.ncbi.nlm.nih.gov/21717229/.
8. Ilg W, Golla H, Thier P, Giese MA. Specific influences of cerebellar dysfunctions on gait. Brain [Internet]. Brain; 2007 [cited 2023 Nov 15];130:786–98. Available from: https://pubmed.ncbi.nlm.nih.gov/17287287/.
9. Israeli-Korn SD, Barliya A, Paquette C, Franzén E, Inzelberg R, Horak FB, et al. Control of Movement: intersegmental coordination patterns are differently affected in Parkinson's disease and cerebellar ataxia. J Neurophysiol [Internet]. American Physiological Society; 2019 [cited 2021 Jul 21];121:672. Available from: /pmc/articles/PMC6397403/.
10. Caliandro P, Iacovelli C, Conte C, Simbolotti C, Rossini PM, Padua L, et al. Trunk-lower limb coordination pattern during gait in patients with ataxia. Gait Posture. 2017;57:252–7 (**Elsevier B.V.**).
11. Martino G, Ivanenko YP, Serrao M, Ranavolo A, d'Avella A, Draicchio F, et al. Locomotor patterns in cerebellar ataxia. J Neurophysiol [Internet]. J Neurophysiol; 2014 [cited 2022 Sep 20];112:2810–21. Available from: https://pubmed.ncbi.nlm.nih.gov/25185815/.
12. Conte C, Pierelli F, Casali C, Ranavolo A, Draicchio F, Martino G, et al. Upper body kinematics in patients with cerebellar ataxia. Cerebellum. Springer New York LLC; 2014;13:689–97.
13. Serrao M, Chini G, Casali C, Conte C, Rinaldi M, Ranavolo A, et al. Progression of gait ataxia in patients with degenerative cerebellar disorders: a 4-year follow-up study. Cerebellum [Internet]. Springer New York LLC; 2017 [cited 2021 Apr 21];16:629–37. Available from: https://pubmed.ncbi.nlm.nih.gov/27924492/.
14. Morton SM, Bastian AJ. Relative contributions of balance and voluntary leg-coordination deficits to cerebellar gait ataxia. https://doi.org/101152/jn007872002 [Internet]. American Physiological SocietyBethesda, MD ; 2003 [cited 2021 Jul 21];89:1844–56. Available from: https://journals.physiology.org/doi/abs/10.1152/jn.00787.2002.
15. Conte C, Serrao M, Cuius L, Ranavolo A, Conforto S, Pierelli F, et al. Effect of restraining the base of support on the other biomechanical features in patients with cerebellar ataxia. Cerebellum [Internet]. Cerebellum; 2018 [cited 2023 Nov 16];17:264–75. Available from: https://pubmed.ncbi.nlm.nih.gov/29143300/.
16. Mari S, Serrao M, Casali C, Conte C, Martino G, Ranavolo A, et al. Lower limb antagonist muscle co-activation and its relationship with gait parameters in cerebellar ataxia. Cerebellum [Internet]. Springer New York LLC; 2014 [cited 2021 Apr 21];13:226–36. Available from: https://pubmed.ncbi.nlm.nih.gov/24170572/.
17. Martino G, Ivanenko YP, d'Avella A, Serrao M, Ranavolo A, Draicchio F, et al. Neuromuscular adjustments of gait associated with unstable conditions. J Neurophysiol [Internet]. American Physiological Society; 2015 [cited 2021 Jun 8];114:2867–82. Available from: https://pubmed.ncbi.nlm.nih.gov/26378199/.
18. Fiori L, Ranavolo A, Varrecchia T, Tatarelli A, Conte C, Draicchio F, et al. Impairment of global lower limb muscle coactivation

during walking in cerebellar ataxias. Cerebellum. 2020;19:583–96 (**Springer**).

19. Miyai I, Ito M, Hattori N, Mihara M, Hatakenaka M, Yagura H, et al. Cerebellar ataxia rehabilitation trial in degenerative cerebellar diseases. Neurorehabil Neural Repair [Internet]. Neurorehabil Neural Repair; 2012 [cited 2023 Nov 16];26:515–22. Available from: https://pubmed.ncbi.nlm.nih.gov/22140200/.

20. Ilg W, Synofzik M, Brötz D, Burkard S, Giese MA, Schöls L. Intensive coordinative training improves motor performance in degenerative cerebellar disease. Neurology [Internet]. Neurology; 2009 [cited 2022 Sep 20];73:1823–30. Available from: https://pubmed.ncbi.nlm.nih.gov/19864636/.

21. Ilg W, Brötz D, Burkard S, Giese M, Schöls L, Synofzik M. Long-term effects of coordinative training in degenerative cerebellar disease. Mov Disord [Internet]. Mov Disord; 2010 [cited 2021 Jul 19];25:2239–46. Available from: https://pubmed.ncbi.nlm.nih.gov/20737551/.

22. Synofzik M, Ilg W. Motor training in degenerative spinocerebellar disease: ataxia-specific improvements by intensive physiotherapy and exergames. Biomed Res Int [Internet]. Biomed Res Int; 2014 [cited 2023 Nov 16];2014. Available from: https://pubmed.ncbi.nlm.nih.gov/24877117/.

23. Morrison S, Russell DM, Kelleran K, Walker ML. Bracing of the trunk and neck has a differential effect on head control during gait. J Neurophysiol [Internet]. American Physiological Society; 2015 [cited 2021 Jun 23];114:1773–83. Available from: https://pubmed.ncbi.nlm.nih.gov/26180113/.

24. Keller JL, Bastian AJ. A home balance exercise program improves walking in people with cerebellar ataxia. Neurorehabil Neural Repair [Internet]. Neurorehabil Neural Repair; 2014 [cited 2023 Nov 16];28:770–8. Available from: https://pubmed.ncbi.nlm.nih.gov/24526707/.

25. Fleszar Z, Mellone S, Giese M, Tacconi C, Becker C, Schöls L, et al. Real-time use of audio-biofeedback can improve postural sway in patients with degenerative ataxia. Ann Clin Transl Neurol [Internet]. Ann Clin Transl Neurol; 2018 [cited 2023 Nov 16];6:285–94. Available from: https://pubmed.ncbi.nlm.nih.gov/30847361/.

26. Ilg W, Bastian AJ, Boesch S, Burciu RG, Celnik P, Claaßen J, et al. Consensus paper: management of degenerative cerebellar disorders. Cerebellum [Internet]. Cerebellum; 2014 [cited 2023 Nov 16];13:248–68. Available from: https://pubmed.ncbi.nlm.nih.gov/24222635/.

27. He M, Zhang H nan, Tang Z chu, Gao S guang. Balance and coordination training for patients with genetic degenerative ataxia: a systematic review. J Neurol [Internet]. J Neurol; 2021 [cited 2023 Nov 16];268:3690–705. Available from: https://pubmed.ncbi.nlm.nih.gov/32583055/.

28. Freund JE, Stetts DM. Use of trunk stabilization and locomotor training in an adult with cerebellar ataxia: a single system design. Physiother Theory Pract [Internet]. Physiother Theory Pract; 2010 [cited 2023 Nov 16];26:447–58. Available from: https://pubmed.ncbi.nlm.nih.gov/20649489/.

29. Ilg W, Seemann J, Giese M, Traschütz A, Schöls L, Timmann D, et al. Real-life gait assessment in degenerative cerebellar ataxia: toward ecologically valid biomarkers. Neurology [Internet]. NLM (Medline); 2020 [cited 2021 Apr 21];95:e1199–210. Available from: https://pubmed.ncbi.nlm.nih.gov/32611635/.

30. Thierfelder A, Seemann J, John N, Harmuth F, Giese M, Schüle R, et al. Real-life turning movements capture subtle longitudinal and preataxic changes in cerebellar ataxia. Mov Disord [Internet]. Mov Disord; 2022 [cited 2023 Nov 16];37:1047–58. Available from: https://pubmed.ncbi.nlm.nih.gov/35067979/.

31. Rochester L, Galna B, Lord S, Mhiripiri D, Eglon G, Chinnery PF. Gait impairment precedes clinical symptoms in spinocerebellar ataxia type 6. Mov Disord [Internet]. Mov Disord; 2014 [cited 2023 Nov 16];29:252–5. Available from: https://pubmed.ncbi.nlm.nih.gov/24301795/.

32. Shirai S, Yabe I, Takahashi-Iwata I, Matsushima M, Ito YM, Takakusaki K, et al. The responsiveness of triaxial accelerometer measurement of gait ataxia is higher than that of the scale for the assessment and rating of ataxia in the early stages of spinocerebellar degeneration. Cerebellum [Internet]. Cerebellum; 2019 [cited 2023 Nov 16];18:721–30. Available from: https://pubmed.ncbi.nlm.nih.gov/30993540/.

33. Hoogkamer W, Bruijn SM, Sunaert S, Swinnen SP, Van Calenbergh F, Duysens J. Toward new sensitive measures to evaluate gait stability in focal cerebellar lesion patients. Gait Posture. 2015;41:592–6 (**Elsevier**).

34. Castiglia SF, Tatarelli A, Trabassi D, De Icco R, Grillo V, Ranavolo A, et al. Ability of a set of trunk inertial indexes of gait to identify gait instability and recurrent fallers in Parkinson's disease. Sensors [Internet]. MDPI AG; 2021 [cited 2021 Jun 23];21. Available from: https://pubmed.ncbi.nlm.nih.gov/34063468/.

35. Castiglia SF, Trabassi D, De Icco R, Tatarelli A, Avenali M, Corrado M, et al. Harmonic ratio is the most responsive trunk-acceleration derived gait index to rehabilitation in people with Parkinson's disease at moderate disease stages. Gait Posture [Internet]. Gait Posture; 2022 [cited 2022 Sep 15];97:152–8. Available from: https://pubmed.ncbi.nlm.nih.gov/35961132/.

36. Castiglia SF, Trabassi D, Tatarelli A, Ranavolo A, Varrecchia T, Fiori L, et al. Identification of gait unbalance and fallers among subjects with cerebellar ataxia by a set of trunk acceleration-derived indices of gait. Cerebellum [Internet]. Cerebellum; 2022 [cited 2022 Sep 15]; Available from: https://pubmed.ncbi.nlm.nih.gov/35079958/.

37. Caliandro P, Conte C, Iacovelli C, Tatarelli A, Castiglia SF, Reale G, et al. Exploring risk of falls and dynamic unbalance in cerebellar ataxia by inertial sensor assessment. Sensors (Basel) [Internet]. Sensors (Basel); 2019 [cited 2024 Jan 25];19. Available from: https://pubmed.ncbi.nlm.nih.gov/31861099/.

38. Chini G, Ranavolo A, Draicchio F, Casali C, Conte C, Martino G, et al. Local stability of the trunk in patients with degenerative cerebellar ataxia during walking. Cerebellum 2016 161 [Internet]. Springer; 2016 [cited 2021 Jul 21];16:26–33. Available from: https://link.springer.com/article/10.1007/s12311-016-0760-6.

39. Zanin M, Olivares F, Pulido-Valdeolivas I, Rausell E, Gomez-Andres D. Gait analysis under the lens of statistical physics. Comput Struct Biotechnol J [Internet]. Comput Struct Biotechnol J; 2022 [cited 2023 Nov 16];20:3257–67. Available from: https://pubmed.ncbi.nlm.nih.gov/35782747/.

40. Shah V V., Rodriguez-Labrada R, Horak FB, McNames J, Casey H, Hansson Floyd K, et al. Gait variability in spinocerebellar ataxia assessed using wearable inertial sensors. Mov Disord [Internet]. Mov Disord; 2021 [cited 2023 Nov 16];36:2922–31. Available from: https://pubmed.ncbi.nlm.nih.gov/34424581/.

41. Shirai S, Yabe I, Matsushima M, Ito YM, Yoneyama M, Sasaki H. Quantitative evaluation of gait ataxia by accelerometers. J Neurol Sci [Internet]. Elsevier; 2015 [cited 2021 Apr 21];358:253–8. Available from: https://pubmed.ncbi.nlm.nih.gov/26362336/.

42. Matsushima A, Yoshida K, Genno H, Ikeda S ichi. Principal component analysis for ataxic gait using a triaxial accelerometer. J Neuroeng Rehabil [Internet]. J Neuroeng Rehabil; 2017 [cited 2023 Nov 16];14. Available from: https://pubmed.ncbi.nlm.nih.gov/28464831/.

43. Hickey A, Gunn E, Alcock L, Del Din S, Godfrey A, Rochester L, et al. Validity of a wearable accelerometer to quantify gait in spinocerebellar ataxia type 6. Physiol Meas [Internet]. Physiol Meas; 2016 [cited 2023 Nov 16];37:N105–17. Available from: https://pubmed.ncbi.nlm.nih.gov/27779133/.

44. Schmitz-Hübsch T, Montcel ST du, Baliko L, Berciano J, Boesch S, Depondt C, et al. Scale for the assessment and rating of ataxia. Neurology [Internet]. Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology; 2006 [cited 2021 Jul 22];66:1717–20. Available from: https://n.neurology.org/content/66/11/1717.

45. Perez-Lloret S, van de Warrenburg B, Rossi M, Rodríguez-Blázquez C, Zesiewicz T, Saute JAM, et al. Assessment of ataxia rating scales and cerebellar functional tests: critique and recommendations. Mov Disord [Internet]. Mov Disord; 2021 [cited 2023 Nov 16];36:283–97. Available from: https://pubmed.ncbi.nlm.nih.gov/33022077/.

46. Serrao M, Casali C, Ranavolo A, Mari S, Conte C, Chini G, et al. Use of dynamic movement orthoses to improve gait stability and trunk control in ataxic patients. Eur J Phys Rehabil Med. 2017;53:735–43.

47. Yao XI, Wang X, Speicher PJ, Hwang ES, Cheng P, Harpole DH, et al. Reporting and guidelines in propensity score analysis: a systematic review of cancer and cancer surgical studies. J Natl Cancer Inst [Internet]. J Natl Cancer Inst; 2017 [cited 2021 Dec 1];109. Available from: https://pubmed.ncbi.nlm.nih.gov/28376195/.

48. Castiglia SF, Trabassi D, Conte C, Ranavolo A, Coppola G, Sebastianelli G, et al. Multiscale entropy algorithms to analyze complexity and variability of trunk accelerations time series in subjects with Parkinson's disease. Sensors (Basel) [Internet]. Sensors (Basel); 2023 [cited 2023 Sep 12];23. Available from: https://pubmed.ncbi.nlm.nih.gov/37430896/.

49. Lindemann U. Spatiotemporal gait analysis of older persons in clinical practice and research. Zeitschrift für Gerontol und Geriatr 2019 532 [Internet]. Springer; 2019 [cited 2021 Jul 22];53:171–8. Available from: https://link.springer.com/article/10.1007/s00391-019-01520-8.

50. Huijben B, van Schooten KS, van Dieën JH, Pijnappels M. The effect of walking speed on quality of gait in older adults. Gait Posture [Internet]. Elsevier B.V.; 2018 [cited 2021 Mar 23];65:112–6. Available from: https://pubmed.ncbi.nlm.nih.gov/30558916/.

51. Schniepp R, Wuehr M, Neuhaeusser M, Kamenova M, Dimitriadis K, Klopstock T, et al. Locomotion speed determines gait variability in cerebellar ataxia and vestibular failure. Mov Disord [Internet]. John Wiley & Sons, Ltd; 2012 [cited 2021 Jul 22];27:125–31. Available from: https://movementdisorders.onlinelibrary.wiley.com/doi/full/10.1002/mds.23978.

52. Fukuchi CA, Fukuchi RK, Duarte M. Effects of walking speed on gait biomechanics in healthy participants: a systematic review and meta-analysis. Syst Rev [Internet]. Syst Rev; 2019 [cited 2021 Dec 1];8. Available from: https://pubmed.ncbi.nlm.nih.gov/31248456/.

53. Craig JJ, Bruetsch AP, Huisinga JM. Coordination of trunk and foot acceleration during gait is affected by walking velocity and fall history in elderly adults. Aging Clin Exp Res 2018 317 [Internet]. Springer; 2018 [cited 2021 Jul 22];31:943–50. Available from: https://link.springer.com/article/10.1007/s40520-018-1036-4.

54. Kroneberg D, Elshehabi M, Meyer AC, Otte K, Doss S, Paul F, et al. Less is more - estimation of the number of strides required to assess gait variability in spatially confined settings. Front Aging Neurosci [Internet]. Frontiers Media S.A.; 2019 [cited 2021 Mar 23];11. Available from: https://pubmed.ncbi.nlm.nih.gov/30719002/.

55. Riva F, Bisi MC, Stagni R. Gait variability and stability measures: minimum number of strides and within-session reliability. Comput Biol Med [Internet]. Comput Biol Med; 2014 [cited 2021 Dec 1];50:9–13. Available from: https://pubmed.ncbi.nlm.nih.gov/24792493/.

56. Pasciuto I, Bergamini E, Iosa M, Vannozzi G, Cappozzo A. Overcoming the limitations of the harmonic ratio for the reliable assessment of gait symmetry. J Biomech [Internet]. Elsevier Ltd; 2017 [cited 2021 Mar 23];53:84–9. Available from: https://pubmed.ncbi.nlm.nih.gov/28104246/.

57. Husted JA, Cook RJ, Farewell VT, Gladman DD. Methods for assessing responsiveness: a critical review and recommendations. J Clin Epidemiol [Internet]. J Clin Epidemiol; 2000 [cited 2021 Dec 1];53:459–68. Available from: https://pubmed.ncbi.nlm.nih.gov/10812317/.

58. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. Front Psychol [Internet]. Front Psychol; 2013 [cited 2021 Dec 1];4. Available from: https://pubmed.ncbi.nlm.nih.gov/24324449/.

59. Schmitz-Hübsch T, Fimmers R, Rakowicz M, Rola R, Zdzienicka E, Fancellu R, et al. Responsiveness of different rating instruments in spinocerebellar ataxia patients. Neurology [Internet]. Neurology; 2010 [cited 2023 Nov 16];74:678–84. Available from: https://pubmed.ncbi.nlm.nih.gov/20177122/.

60. Vallat R. Pingouin: statistics in Python. J Open Source Softw. 2018;3:1026 (**The Open Journal**).

61. Raffalt PC, Kent JA, Wurdeman SR, Stergiou N. Selection procedures for the largest Lyapunov exponent in gait biomechanics. Ann Biomed Eng [Internet]. Ann Biomed Eng; 2019 [cited 2023 Nov 16];47:913–23. Available from: https://pubmed.ncbi.nlm.nih.gov/30701396/.

62. Mehdizadeh S. The largest Lyapunov exponent of gait in young and elderly individuals: a systematic review. Gait Posture [Internet]. Gait Posture; 2018 [cited 2023 Nov 16];60:241–50. Available from: https://pubmed.ncbi.nlm.nih.gov/29304432/.

63. Toebes MJP, Hoozemans MJM, Furrer R, Dekker J, Van Dieën JH. Local dynamic stability and variability of gait are associated with fall history in elderly subjects. Gait Posture [Internet]. Gait Posture; 2012 [cited 2021 May 5];36:527–31. Available from: https://pubmed.ncbi.nlm.nih.gov/22748312/.

64. Ilg W, Timmann D. Gait ataxia—specific cerebellar influences and their rehabilitation. Mov Disord [Internet]. John Wiley & Sons, Ltd; 2013 [cited 2021 Jul 22];28:1566–75. Available from: https://movementdisorders.onlinelibrary.wiley.com/doi/full/10.1002/mds.25558.

65. Matsushima A, Maruyama Y, Mizukami N, Tetsuya M, Hashimoto M, Yoshida K. Gait training with a wearable curara® robot for cerebellar ataxia: a single-arm study. Biomed Eng Online [Internet]. Biomed Eng Online; 2021 [cited 2024 Jan 17];20. Available from: https://pubmed.ncbi.nlm.nih.gov/34496863/.

66. Mitoma H, Hayashi R, Yanagisawa N, Tsukagoshi H. Characteristics of parkinsonian and ataxic gaits: a study using surface electromyograms, angular displacements and floor reaction forces. J Neurol Sci [Internet]. Elsevier; 2000 [cited 2021 Jul 22];174:22–39. Available from: http://www.jns-journal.com/article/S0022510X99003299/fulltext.

67. Serrao M, Chini G, Bergantino M, Sarnari D, Casali C, Conte C, et al. Identification of specific gait patterns in patients with cerebellar ataxia, spastic paraplegia, and Parkinson's disease: a non-hierarchical cluster analysis. Hum Mov Sci [Internet]. Hum Mov Sci; 2018 [cited 2022 Sep 20];57:267–79. Available from: https://pubmed.ncbi.nlm.nih.gov/28967438/.

68. Serrao M, Ranavolo A, Casali C. Neurophysiology of gait. Handb Clin Neurol [Internet]. Elsevier B.V.; 2018 [cited 2021 Apr 21]. p. 299–303. Available from: https://pubmed.ncbi.nlm.nih.gov/29903447/.

69. Brach JS, McGurl D, Wert D, VanSwearingen JM, Perera S, Cham R, et al. Validation of a measure of smoothness of walking. Journals Gerontol Ser A [Internet]. Oxford Academic; 2011 [cited

2021 Jul 22];66A:136–41. Available from: https://academic.oup.com/biomedgerontology/article/66A/1/136/532030.

70. Monte TL, Reckziegel ER, Augustin MC, Silva ASP, Locks-Coelho LD, Barsottini O, et al. NESSCA validation and responsiveness of several rating scales in spinocerebellar ataxia type 2. Cerebellum [Internet]. Cerebellum; 2017 [cited 2023 Nov 16];16:852–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28456900/.

71. Traschütz A, Adarmes-Gómez AD, Anheim M, Baets J, Brais B, Gagnon C, et al. Responsiveness of the scale for the assessment and rating of ataxia and natural history in 884 recessive and early onset ataxia patients. Ann Neurol [Internet]. Ann Neurol; 2023 [cited 2023 Nov 16];94:470–85. Available from: https://pubmed.ncbi.nlm.nih.gov/37243847/.

72. Maas RPPWM, van de Warrenburg BPC. Exploring the clinical meaningfulness of the Scale for the Assessment and Rating of Ataxia: a comparison of patient and physician perspectives at the item level. Park Relat Disord [Internet]. Elsevier Ltd; 2021 [cited 2023 Nov 17];91:37–41. Available from: http://www.prd-journal.com/article/S1353802021003084/fulltext.