HOKKAIDO UNIVERSITY

Title	Quantitative evaluation of gait ataxia by accelerometers
Author(s)	Shirai, Shinichi; Yabe, Ichiro; Matsushima, Masaaki et al.
Citation	Journal of the Neurological Sciences, 358(1-2), 253-258 https://doi.org/10.1016/j.jns.2015.09.004
Issue Date	2015-11-15
Doc URL	https://hdl.handle.net/2115/63578
Rights	© 2015. This manuscript version is made available under the CC-BY-NC-ND 4.0 license http://creativecommons.org/licenses/by-nc-nd/4.0/
Rights(URL)	https://creativecommons.org/licenses/by-nc-nd/4.0/
Type	journal article
File Information	manuscript.pdf

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Clinical Research Paper

Quantitative evaluation of gait ataxia by accelerometers

Shinichi Shirai [a,b], Ichiro Yabe [a], Masaaki Matsushima [a], Yoichi M. Ito [c], Mitsuru Yoneyama [d], Hidenao Sasaki [a]

[a] Department of Neurology, Hokkaido University Graduate School of Medicine, Sapporo, Japan

[b] Department of Neurology, Kushiro Rosai Hospital, Kushiro, Japan

[c] Department of Biostatistics, Hokkaido University Graduate School of Medicine, Sapporo, Japan.

[d] MCHC R&D Synergy Center, Inc. Yokohama, Japan

Correspondence to Hidenao Sasaki, h-isasak@med.hokudai.ac.jp

Word counts of Text; 2,041 words (excluding of abstract, acknowledgement, captions and references)

Word counts of Abstract; 197 words

Number of Tables; 2

Number of Figures; 3

Number of References; 14

Conflict of interest: We used triaxial accelerometers that were owned by LSI Medience Corporation.

Key words; cerebellar ataxia, quantitative evaluation, accelerometer, biomarker, the Scale for the Assessment and Rating of Ataxia (SARA), gait analysis

Abstract

An appropriate biomarker for spinocerebellar degeneration (SCD) has not been identified. Here, we performed gait analysis on patients with pure cerebellar type SCD and assessed whether the obtained data could be used as a neurophysiological biomarker for cerebellar ataxia. We analyzed 25 SCD patients, 25 patients with Parkinson's Disease as a disease control, and 25 healthy control individuals. Acceleration signals during 6 minutes of walking and 1 minute of standing were measured by two sets of triaxial accelerometers that were secured with a fixation vest to the middle of the lower and upper back of each subject. We extracted two gait parameters, the average and the coefficient of variation of motion trajectory amplitude, from each acceleration component. Then, each component was analyzed by correlation with the Scale for the Assessment and Rating of Ataxia (SARA) and the Berg Balance Scale (BBS). Compared with the gait control of healthy subjects and concerning correlation with severity and disease specificity, our results suggest that the average amplitude of medial-lateral (upper back) of straight gait is a physiological biomarker for cerebellar ataxia. Our results suggest that gait analysis is a quantitative and concise evaluation scale for the severity of cerebellar ataxia.

1. Background

A useful biomarker is an index that assists in the diagnosis of disease or the determination of disease severity. Diagnostic markers are important at preclinical or initial stages, while surrogate markers are important after the diagnosis. Biomarkers play an important role when novel treatments are discovered and clinical trials are performed.

Although there are various types of biomarkers such as molecular markers and imaging markers, an appropriate maker for neurodegenerative disease has not been identified. Thus, we use clinical evaluation scales. However, it is important to identify an appropriate biomarker in order to evaluate the efficiency of a given clinical trial.

Here, we performed gait analyses in patients with pure cerebellar type spinocerebellar degeneration (SCD) and assessed whether the obtained data could be used as a neurophysiological biomarker for cerebellar ataxia.

Here we performed gait analysis in patients with pure cerebellar type spinocerebellar degeneration (SCD) and assessed whether the obtained data could be used as a neurophysiological biomarker for cerebellar ataxia.

2. Subjects and Methods

2.1. Subjects

From June 1, 2013 to August 31, 2014, we analyzed 25 SCD patients that included 16 patients with spinocerebellar ataxia (SCA 6), 2 patients with SCA31, 3 patients with dominant-inherited cerebellar cortical atrophy (DCCA), and 4 patients with cortical cerebellar atrophy (CCA). These SCD patients included 11 males and 14 females with an average age of 62.4±12.0 years (range, 24～83 years). We also analyzed 25 patients with Parkinson's disease (PD) as a disease control (13 male and 12 female; average age, 63.3±9.0 years; range 38-80 years) and 25 healthy control subjects (12 male and 13 female; average age, 57.6±17.1 years; range 32-84 years). The mean age and male-female ratio of the PD group and healthy control group were not significantly different from those of the SCD group .

We evaluated the clinical severity of each patient in the SCD group using the Scale for the Assessment and Rating of Ataxia (SARA) [1, 2] and the Berg Balance Scale (BBS) [3, 4]. The mean SARA of the SCD group was 13.26±4.43, while the mean Unified Parkinson's Disease Rating Scale (UPDRS) part III was 18.48±8.4760.

This study was approved by the ethics panels of Hokkaido University Hospital and Kushiro Rosai Hospital.

2.2. Methods (Fig. 1)

Acceleration signals were measured during 6 min walking and 1 min standing tasks by two sets of triaxial accelerometers (Mimamori-gait system, LSI Medience; size, 7.5 cm × 5 cm × 2 cm; weight, 95 g) that were secured with a fixation vest to the middle of the subject's lower and upper back. When in the standing position, the subjects were evaluated with their eyes open for 1 min and then their eyes closed for another 1 min. An assistant remained beside the subjects in order to prevent falls, however, no falls occurred. The subjects were evaluated while they shuttle-walked a 30 m straight line for 6 min (6-min walk test (6MWT) [5]). Similar tasks were performed in the JASMITT study[6] and in other studies. When standing in the anatomical position, the orientation of the three acceleration axes, X, Y, and Z, were medial/lateral (ML), vertical (VT), and anterior/posterior (AP), respectively. Data were collected at a sampling frequency of 100 Hz and stored on a secure digital memory card inserted into the device for later analysis.

We extracted two gait parameters, the average and the coefficient of variation (CV) of the motion trajectory amplitude, from each acceleration component by the following methods:

1. The acceleration signal was integrated twice in the time domain and processed with high-pass filtering based on a moving-window average to generate motion trajectory, namely, relative displacement [7].

2. The upper and lower envelopes of the trajectory signal (denoted as Y_1 and Y_2) were obtained by spline interpolation of its positive and negative peaks, respectively.

3. The amplitude time series was defined as $(Y_1 - Y_2)/2$, and divided into two parts: signals corresponding to straight walking and to turning around the cone.

4. The average and CV of the amplitude time series were calculated separately for each part, which yielded the desired gait parameters.

To quantify body motion during standing, we examined parameters as follows:

1. The three acceleration components $a_x(t)$, $a_y(t)$, and $a_z(t)$ were smoothed by a moving-window average with a window size of 5.6 s to generate three

baseline signals: $B_x(t)$, $B_y(t)$, and $B_z(t)$.

2. Three parameters for quantifying baseline drifts due to slow body movements were calculated as $\max[|B_x(t) - B_x(0)|]$ (maximum drift along ML), $\max[|B_z(t) - B_z(0)|]$ (maximum drift along AP), and $\max[\{[B_x(t) - B_x(0)]^2 + [B_y(t) - B_y(0)]^2 + [B_z(t) - B_z(0)]^2\}^{0.5}]$ (maximum total drift).

3. Two parameters for quantifying fluctuations due to rapid body movements were provided by the standard deviation of $a_x(t) - B_x(t)$ (fluctuation along ML) and $a_z(t) - B_z(t)$ (fluctuation along AP).

2.3. Statistical analysis

We used Student's t-test for inter-group comparison and Pearson's correlation coefficients for disease severity and each parameter analysis. The JMP® Pro 11.2.0 software program (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses. We considered the results significant if $p<0.05$. The test of significance was adjusted for multiple testing using a Bonferroni step-down (Holm) correction.

3. Results

We compared each parameter of SCD patients to that of PD and healthy control subjects in Table 1. A number of parameters of SCD

measured on the upper and lower back showed significantly larger values, while the VT amplitude of straight gait and turning showed significantly smaller values ($p<0.001$).

We compared each parameter of the healthy control group by upper and lower back. The average amplitudes of ML and VT in SCD patients were larger than in healthy control subjects and those of AP in SCD were similar to that in healthy control subjects. The CV of ML and VT were lower in the upper back, while the CV of AP was lower in the lower back. These results show significant differences by Student's t-test. Thus, we chose the upper back of ML and VT, and the lower back of AP as an evaluation positions (Supplemental Figure).

Correlation of each parameter with the clinical severity and their p-value is shown in Table 2. A number of parameters showed a high correlation with BBS and SARA. The average amplitude and CV of straight gait showed a higher correlation than these parameters in standing and turning. In particular, the average amplitude of ML (upper back) and CV of VT (upper back) correlated most significantly with severity (Fig. 2). In addition, these parameters correlated significantly with the SARA gait item (Supplemental

Table 1).

We compared the average amplitude of ML (upper back) and CV of VT (upper back) of SCD patients with those of PD patients as the disease control. The average amplitude of ML (upper back) of SCD patients was significantly larger than that of PD patients (Fig. 3). Compared with the gait control of healthy control subjects, correlation with severity, and disease specificity, our results suggest that a physiological biomarker for cerebellar ataxia may be the average amplitude of ML (upper back) during straight gait.

We compared the correlation of each gait parameter with severity between that observed in the first 3 minutes and to that of the last 3 minutes (Supplemental Table 2). Each coefficient of correlation of the first and last 3 minutes was applied to a Brand-Altman plot, which demonstrated an intraclass correlation coefficient of 0.976, indicating that the results were not significantly different.

4. Discussion

Few studies have conducted quantitative analysis of gait disability in ataxic patients. Previously, we reported that SARA did not correlate with the total length traveled or the root mean square area of body sway as measured

by body stabilometry[8]. Some reports of gait analysis in PD patients have evaluated acceleration, but not amplitude or CV[9].

Menz et al. reported that the magnitude of pelvis accelerations increased, while head accelerations were not affected by the walking surface when walking on an irregular surface[10]. In the present study, when we compared each parameter of the healthy control group by upper and lower back, the CV of ML and VT were lower in the upper back, while the CV of AP was lower in the lower back. Therefore, we chose the upper back of ML and VT, and the lower back of AP as evaluation positions.

We measured both mean amplitude and CV. The severity of cerebellar ataxia correlated strongest with the average amplitude of ML of straight gait in our study. The CV may indicate the control of gait. Thus, we selected the site with more control in healthy control subjects according to the CV data.

Our results suggest that the parameter of gait analysis may be a biomarker for cerebellar ataxia. We used clinical evaluation scales of cerebellar ataxia to determine the effect of the intervention trial. However, we need a greater number of objective patients in order to detect the effect of intervention using a category characteristics scale rather than a metric

variable scale[11].

A previous study showed that 250 patients per group were required to detect a 50% reduction of disease progression within 1 year using SARA[11]. We used the Unified Multiple System Atrophy Rating Scale (UMSARS), a clinical evaluation scale of cerebellar ataxia and multiple system atrophy (MSA). Sample size estimation showed that an interventional trial with 258 patients would be able to detect a 30% effect size in 1-year UMSARS motor examination decline rates at 80% power[12].

A previous study indicated that fewer patients were required for the 9-hole peg test (9HPG)[11]. 9HPG is a metric variable of the amount of time required to perform the task. This suggests that a novel biomarker as a metric variable is needed to achieve an interventional study with fewer patients.

Another problem in the use of an evaluation scale of cerebellar ataxia is the lack of consideration of differences in pathogenesis or gene mutations. The cerebellum plays a role as a comparator, which gains feed-forward control by reserving short-term memory in the cerebellar cortex and long-term memory in the cerebellar nucleus by afferent feed-back from

effector organs. However, we evaluate cerebellar cortex disordered disease, cerebellar nucleus disordered disease, and feed-back pathway disordered disease using the same evaluation scale. SARA is a scale constructed to assess various types of SCD[1]. Study of the natural course of SCD using SARA indicates that the type of SCD or the different repeat number results in a different deterioration rate[13]. Therefore, a clinical evaluation scale that considers the pathological findings or clinical symptoms of each disease is needed in interventional studies. In Friedreich's ataxia, there has been a successful interventional study of alpha-tocopherol using the specific scale that reflects its clinical symptoms, the Friedreich's Ataxia Rating Scale[14]. However, it is difficult to produce each evaluation scale and carry out an interventional study for each disease because of the number of patients required. Since ataxic gait is a common early symptom of SCD, quantitative analysis of gait abnormality is most essential for the early intervention.

In the present study, gait distance also correlated significantly with SARA (data not shown). However, not every medical institution has sufficient space to perform the 6MWT, which is advantageous for CV and mean amplitude. Moreover, according to the comparison between the first

and last 3 minutes of gait, which were not significantly different, we may be able to shorten the gait minutes. Further study is needed to assess whether gait analysis over a short distance can be used as a biomarker for SCD.

While we have not established a quantitative evaluation for SCD, our gait analysis is more quantitative and concise than previous evaluation scales, SARA and BBS, which are bound to symptoms. It is unclear whether SARA is the best scale for ataxia, but, since there is no alternative, we assessed the coefficient correlation to SARA. Follow up study is needed to assess SARA and gait analysis to determine the deterioration rate and to calculate the sample size.

The establishment of a quantitative evaluation by gait analysis is important to determine the deterioration rate and to estimate the effect size in order to construct a plan of interventional trial with less patients and more significant results.

5. Conclusion

Our results suggest that gait analysis is a quantitative and concise evaluation scale for the severity of cerebellar ataxia.

Acknowledgements

We thank all of the patients and control subjects for their cooperation. This work was supported in part by a Grant-in-Aid for the Research Committee for Ataxic Diseases of the Research on Measures for Intractable Diseases from the Ministry of Health, Welfare and Labor, Japan, and by a Grant-in-Aid from the Takeda Science Foundation.

We thank Kazufumi Tsuzaka MD, PhD, chief of the department of Neurology Kushiro Rosai Hospital and Tetsuya Ueda of LSI Medience Corporation for their assistance in this study.

We thank LSI Medience Corporation for use of the triaxial accelerometers.

Figure Captions.

Figure 1. Diagrams of the gait analysis.

Acceleration signals were measured by two sets of triaxial accelerometers secured with a fixation vest to the subject's lower and upper back. We extracted two gait parameters, the average and the coefficient of variation (CV) of the motion trajectory amplitude.

Figure 2. The correlation of each parameter with Scale for the Assessment and Rating of Ataxia (SARA).

The average amplitude of ML and CV of VT of the upper back correlated most significantly with severity.

Figure 3. The comparison of the candidate parameter of spinocerebellar degeneration (SCD) patients with Parkinson's Disease (PD) patients.

The average amplitude of ML of SCD patients is significantly higher than that of PD patients.

Supplemental Figure. A comparison of each parameter of healthy control subjects by upper / lower back.

In the upper back, the CV of medial/lateral (ML) and vertical (VT) are significantly low, while the CV of anterior/posterior (AP) is significantly high.

References

[1] Schmitz-Hubsch T, du Montcel ST, Baliko L, Berciano J, Boesch S, Depondt C, et al. Scale for the assessment and rating of ataxia: development of a new clinical scale. Neurology. 2006; 66: 1717-1720.

[2] Sato K, Yabe I, Soma H, Yasui K, Ito M, Shimohata T, et al. [Reliability of the Japanese version of the Scale for the Assessment and Rating of Ataxia (SARA)]. Brain Nerve. 2009; 61: 591-595.

[3] Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. Can J Public Health. 1992; 83 Suppl 2: S7-11.

[4] Matsushima M, Yabe I, Uwatoko H, Shirai S, Hirotani M, Sasaki H. Reliability of the Japanese version of the Berg balance scale. Intern Med. 2014; 53: 1621-1624.

[5] ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002; 166: 111-117.

[6] Katsuno M, Banno H, Suzuki K, Takeuchi Y, Kawashima M, Yabe I, et al. Efficacy and safety of leuprorelin in patients with spinal and bulbar muscular atrophy (JASMITT study): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010; 9: 875-884.

[7] Yoneyama M. Visualising gait symmetry/asymmetry from acceleration data. Comput Methods Biomech Biomed Engin. 2015; 18: 923-930.

[8] Yabe I, Matsushima M, Soma H, Basri R, Sasaki H. Usefulness of the Scale for Assessment and Rating of Ataxia (SARA). J Neurol Sci. 2008; 266: 164-166.

[9] Terashi H, Utsumi H, Ishimura Y, Takazawa T, Okuma Y, Yoneyama M, et al. Deficits in scaling of gait force and cycle in parkinsonian gait identified by long-term monitoring of acceleration with the portable gait rhythmogram. ISRN Neurol. 2012; 2012: 306816.

[10] Menz HB, Lord SR, Fitzpatrick RC. Acceleration patterns of the head and pelvis when walking on level and irregular surfaces. Gait Posture. 2003; 18: 35-46.

[11] Schmitz-Hubsch T, Fimmers R, Rakowicz M, Rola R, Zdzienicka E, Fancellu R, et al. Responsiveness of different rating instruments in spinocerebellar ataxia patients. Neurology. 2010; 74: 678-684.

[12] Wenning GK, Geser F, Krismer F, Seppi K, Duerr S, Boesch S, et al. The natural history of multiple system atrophy: a prospective European cohort study. Lancet Neurol. 2013; 12: 264-274.

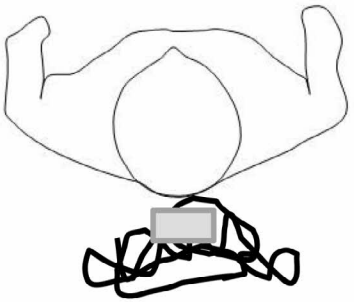
[13] Jacobi H, Bauer P, Giunti P, Labrum R, Sweeney MG, Charles P, et al. The natural history of spinocerebellar ataxia type 1, 2, 3, and 6: a 2-year follow-up study. Neurology. 2011; 77: 1035-1041.

[14] Lynch DR, Willi SM, Wilson RB, Cotticelli MG, Brigatti KW, Deutsch EC, et al. A0001 in Friedreich ataxia: biochemical characterization and effects in a clinical trial. Mov Disord. 2012; 27: 1026-1033.

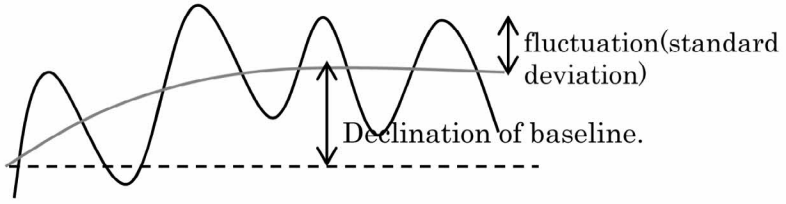
Figure 1. Diagrams of the gait analysis

Two sets of triaxial accelerometers secured with a fixation vest to the subject's lower and upper back

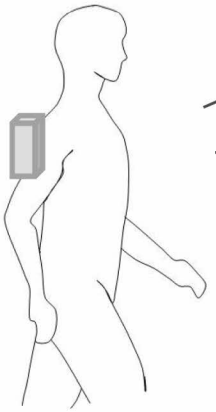
In standing position

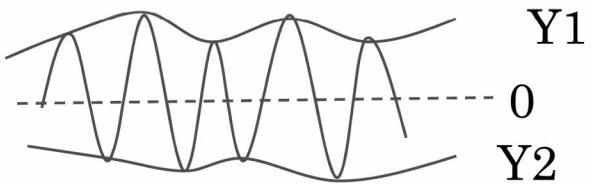


Fluctuation of acceleration



In gait position





Integration twice

Acceleration → relative displacement

amplitude = (Y1-Y2)/2

- mean amplitude
  low in medial/lateral, high in vertical.
- coefficient of variation (CV=standard deviation/ mean value)
  low if the gait is controlled well.

Figure 2. The correlation of each parameter with Scale for the Assessment and Rating of Ataxia (SARA).

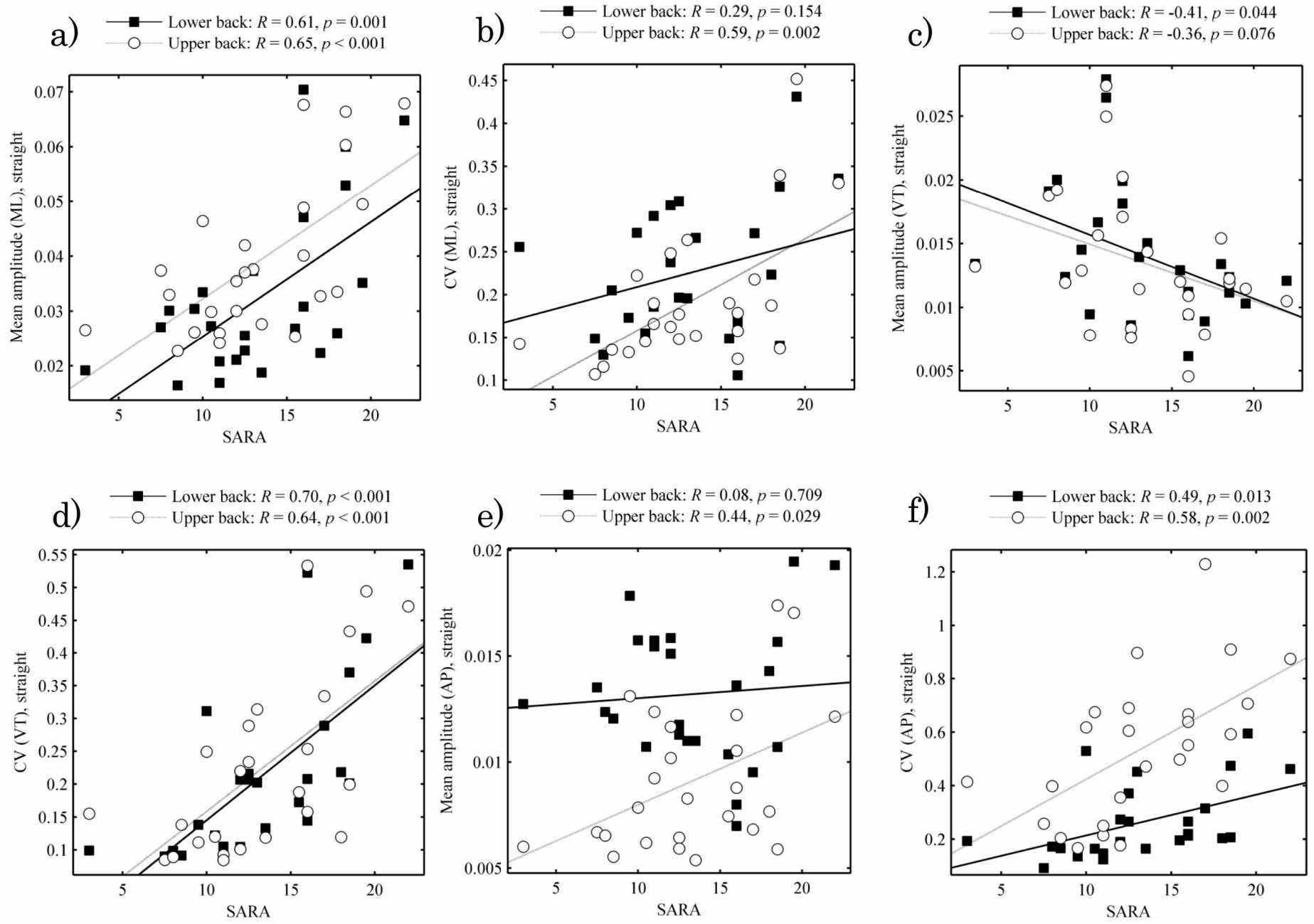
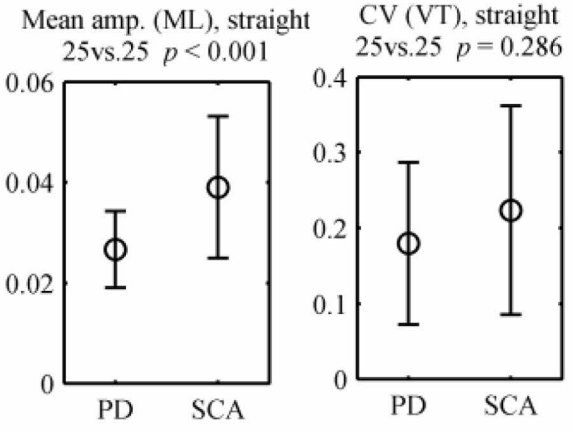


Figure 3. The comparison of the candidate parameter of SCD patients with PD patients.



Suppl. Figure. The comparison of each parameter of healthy control subjects by upper / lower back.

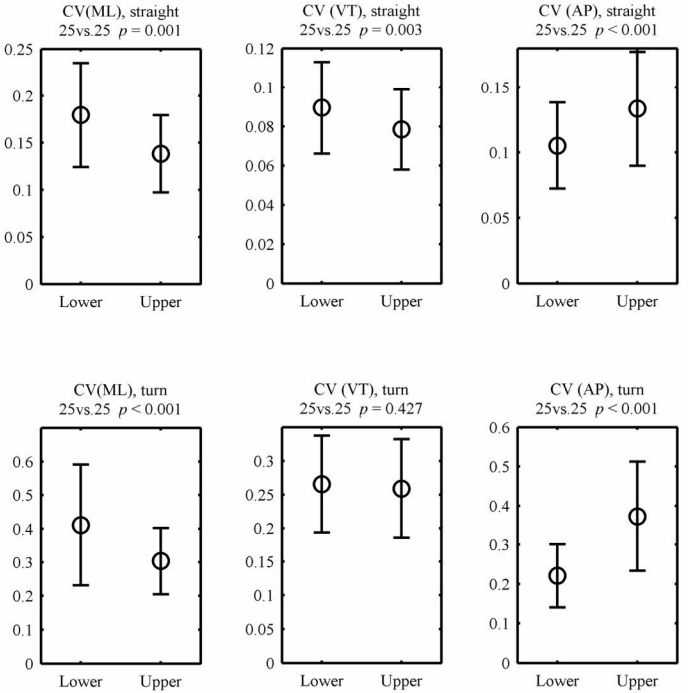


Table 1 .Comparison of SCD patients with disease control patients and healthy control subjects.

			Patient		Disease Control			Healthy Control		
			Mean	SD	Mean	SD	P	Mean	SD	p
lower back	straight	Mean amp.(ML)	0.0322	0.0152	0.0233	0.0066	0.011	0.0179	0.0056	<0.001*
		CV(ML)	0.2258	0.0789	0.1236	0.0360	<0.001*	0.1795	0.0555	0.020
		Mean amp. (VT)	0.0140	0.0054	0.0139	0.0064	0.948	0.0206	0.0060	<0.001*
		CV (VT)	0.2121	0.1298	0.1652	0.0784	0.129	0.0895	0.0234	<0.001*
		Mean amp. (AP)	0.0132	0.0032	0.0119	0.0050	0.273	0.0152	0.0026	0.020
		CV (AP)	0.2634	0.1379	0.1798	0.0829	0.012	0.1053	0.0329	<0.001*
	turn	Mean amp. (ML)	0.0369	0.0127	0.0270	0.0073	0.001	0.0260	0.0062	<0.001*
		CV(ML)	0.3129	0.1278	0.2275	0.0991	0.011	0.4107	0.1800	0.032
		Mean amp. (VT)	0.0103	0.0044	0.0103	0.0053	0.994	0.0165	0.0054	<0.001*
		CV (VT)	0.3987	0.1664	0.3266	0.0860	0.060	0.2654	0.0719	<0.001*
		Mean amp. (AP)	0.0121	0.0031	0.0113	0.0063	0.560	0.0146	0.0027	0.005
		CV (AP)	0.4361	0.2165	0.3135	0.0969	0.013	0.2205	0.0806	<0.001*
	open eye	Baseline (ML)	0.2214	0.1596	0.2094	0.1608	0.791	0.1179	0.0672	0.004
		Baseline (AP)	0.4048	0.3425	0.4286	0.3169	0.800	0.4010	0.3379	0.969
		Baseline (total)	0.4654	0.3581	0.4916	0.3305	0.790	0.4317	0.3297	0.730
		Fluctuation (ML)	0.0992	0.0422	0.0715	0.0407	0.023	0.0561	0.0148	<0.001*
		Fluctuation (AP)	0.1344	0.0486	0.0930	0.0398	0.002	0.0918	0.0219	<0.001*
	closed eye	Baseline (ML)	0.1913	0.1466	0.1459	0.0882	0.191	0.1221	0.0745	0.041
		Baseline (AP)	0.4381	0.3153	0.3427	0.1977	0.206	0.3230	0.1667	0.113
		Baseline (total)	0.4854	0.3341	0.3877	0.2163	0.226	0.3492	0.1611	0.073
		Fluctuation (ML)	0.1337	0.0693	0.0782	0.0314	0.001	0.0621	0.0222	<0.001*
		Fluctuation (AP)	0.1888	0.1022	0.0976	0.0344	<0.001*	0.0986	0.0241	<0.001*
upper back	straight	Mean amp. (ML)	0.0390	0.0140	0.0271	0.0074	<0.001*	0.0233	0.0053	<0.001*
		CV(ML)	0.1929	0.0808	0.1237	0.0357	<0.001*	0.1382	0.0410	0.004
		Mean amp. (VT)	0.0135	0.0054	0.0138	0.0064	0.847	0.0197	0.0050	<0.001*
		CV (VT)	0.2234	0.1375	0.1744	0.1018	0.158	0.0784	0.0205	<0.001*
		Mean amp. (AP)	0.0091	0.0034	0.0101	0.0066	0.520	0.0106	0.0019	0.066
		CV (AP)	0.5382	0.2666	0.2615	0.1346	<0.001*	0.1335	0.0437	<0.001*
	turn	Mean amp. (ML)	0.0424	0.0125	0.0344	0.0088	0.011	0.0326	0.0073	0.001
		CV(ML)	0.2688	0.1047	0.2082	0.0925	0.035	0.3032	0.0990	0.239
		Mean amp. (VT)	0.0102	0.0041	0.0102	0.0049	0.981	0.0160	0.0048	<0.001*
		CV (VT)	0.4321	0.2177	0.3479	0.1053	0.088	0.2589	0.0731	<0.001*
		Mean amp. (AP)	0.0100	0.0033	0.0104	0.0077	0.824	0.0101	0.0021	0.912
		CV (AP)	0.6986	0.2400	0.4851	0.1456	<0.001*	0.3728	0.1398	<0.001*
	open eye	Baseline (ML)	0.2469	0.2317	0.2005	0.1440	0.399	0.1378	0.0736	0.030
		Baseline (AP)	0.2997	0.1512	0.5240	0.3582	0.006	0.2661	0.1945	0.499
		Baseline (total)	0.4291	0.3839	0.6158	0.3933	0.096	0.2980	0.1951	0.134
		Fluctuation (ML)	0.1097	0.0515	0.0786	0.0466	0.030	0.0683	0.0158	<0.001*
		Fluctuation (AP)	0.1224	0.0498	0.0973	0.0387	0.053	0.0762	0.0181	<0.001*
	closed eye	Baseline (ML)	0.2421	0.1551	0.2018	0.1291	0.323	0.1155	0.0831	<0.001*
		Baseline (AP)	0.4685	0.3563	0.5592	0.3704	0.382	0.3356	0.1969	0.109
		Baseline (total)	0.5360	0.3610	0.6366	0.4203	0.368	0.3624	0.2017	0.041
		Fluctuation (ML)	0.1483	0.0801	0.0851	0.0339	<0.001*	0.0712	0.0194	<0.001*
		Fluctuation (AP)	0.1862	0.0950	0.0962	0.0368	<0.001*	0.0843	0.0184	<0.001*

SD, standard deviation; CV, coefficient of variation; ML, medial/lateral; VT, vertical; AP, anterior-posterior

*: significantly different adjusted with a Bonferroni step-down (Holm) correction.

Table 2. Correlation of each parameter with clinical severity and p-value.

			SARA	(p)	BBS	(p)
lower back	straight	Mean amplitude (ML)	0.61	0.001	-0.62	0.001
		CV (ML)	0.29	0.154	-0.43	0.034
		Mean amplitude (VT)	-0.41	0.044	0.51	0.010
		CV (VT)	0.70	**<0.001***	-0.79	**<0.001***
		Mean amplitude (AP)	0.08	0.709	-0.05	0.825
		CV (AP)	0.49	0.013	-0.69	**<0.001***
	turn	Mean amplitude (ML)	0.36	0.082	-0.36	0.074
		CV (ML)	0.02	0.919	-0.24	0.239
		Mean amplitude (VT)	-0.38	0.060	0.49	0.012
		CV (VT)	0.49	0.012	-0.67	**<0.001***
		Mean amplitude (AP)	0.05	0.822	-0.01	0.951
		CV (AP)	0.40	0.050	-0.65	**<0.001***
upper back	straight	Mean amplitude (ML)	0.65	**<0.001***	-0.70	**<0.001***
		CV (ML)	0.59	0.002	-0.66	<**0.001***
		Mean amplitude (VT)	-0.36	0.076	0.49	0.013
		CV (VT)	0.64	**<0.001***	-0.81	**<0.001***
		Mean amplitude (AP)	0.44	0.029	-0.50	0.011
		CV (AP)	0.58	0.002	-0.78	**<0.001***
	turn	Mean amplitude (ML)	0.24	0.245	-0.22	0.296
		CV (ML)	0.34	0.092	-0.57	0.003
		Mean amplitude (VT)	-0.26	0.207	0.37	0.069
		CV (VT)	0.35	0.084	-0.61	0.001
		Mean amplitude (AP)	0.52	0.008	-0.63	<0.001
		CV (AP)	0.34	0.097	-0.60	0.002

			SARA	(p)	BBS	(p)
lower back	open eye	Baseline (ML)	0.46	0.021	-0.40	0.045
		Baseline (AP)	-0.18	0.388	0.31	0.132
		Baseline (total)	-0.03	0.898	0.16	0.432
		Fluctuation (ML)	0.34	0.099	-0.38	0.064
		Fluctuation (AP)	0.31	0.126	-0.36	0.074
	closed eye	Baseline (ML)	0.32	0.121	-0.47	0.018
		Baseline (AP)	0.30	0.149	-0.34	0.092
		Baseline (total)	0.30	0.144	-0.35	0.083
		Fluctuation (ML)	0.42	0.039	-0.58	0.003
		Fluctuation (AP)	0.37	0.067	-0.47	0.018
upper back	open eye	Baseline (ML)	0.07	0.738	-0.27	0.195
		Baseline (AP)	0.15	0.471	-0.19	0.376
		Baseline (total)	-0.04	0.851	-0.11	0.605
		Fluctuation (ML)	0.29	0.163	-0.36	0.079
		Fluctuation (AP)	0.53	0.007	-0.57	0.003
	closed eye	Baseline (ML)	0.29	0.165	-0.47	0.018
		Baseline (AP)	0.39	0.051	-0.48	0.015
		Baseline (total)	0.40	0.045	-0.52	0.008
		Fluctuation (ML)	0.43	0.032	-0.60	0.002
		Fluctuation (AP)	0.55	0.004	-0.65	**<0.001***

SARA, Scale for the Assessment and Rating of Ataxia; BBS, Berg Balance Scale; CV, coefficient of variation; ML, medial/lateral; VT, vertical; AP, anterior/posterior

*: significantly different adjusted with a Bonferroni step-down (Holm) correction.

Suppl. Table 1.

	Age	Onset age	Disease duration	SARA	SARA (gait)	SARA (standing)	BBS	Gait Distance
Mean amplitude (ML), straight, lower back	-0.17	-0.30	0.21	0.61	0.63	0.56	-0.62	-0.68
	0.411	0.143	0.320	0.001	<0.001	0.004	0.001	<0.001
CV (ML), straight, lower back	0.32	0.38	-0.09	0.29	0.33	0.30	-0.43	-0.20
	0.116	0.061	0.688	0.154	0.105	0.144	0.034	0.327
Mean amplitude (VT), straight, lower back	-0.25	-0.25	-0.02	-0.41	-0.49	-0.51	0.51	0.89
	0.223	0.238	0.924	0.044	0.013	0.009	0.010	<0.001
CV (VT), straight, lower back	0.01	-0.06	0.10	0.70	0.75	0.72	-0.79	-0.78
	0.983	0.788	0.632	<0.001	<0.001	<0.001	<0.001	<0.001
Mean amplitude (AP), straight, lower back	0.18	0.20	-0.03	0.08	0.01	0.03	-0.05	0.14
	0.386	0.336	0.898	0.709	0.953	0.883	0.825	0.506
CV (AP), straight, lower back	0.36	0.37	-0.01	0.49	0.59	0.54	-0.69	-0.67
	0.080	0.071	0.974	0.013	0.002	0.005	<0.001	<0.001
Mean amplitude (ML), turn, lower back	-0.35	-0.36	0.01	0.36	0.37	0.27	-0.36	-0.41
	0.091	0.078	0.949	0.082	0.067	0.201	0.074	0.040
CV (ML), turn, lower back	0.49	0.42	0.13	0.02	0.05	0.04	-0.24	-0.06
	0.013	0.037	0.538	0.919	0.811	0.850	0.239	0.769
Mean amplitude (VT), turn, lower back	-0.34	-0.28	-0.11	-0.38	-0.47	-0.41	0.49	0.81
	0.100	0.176	0.618	0.060	0.019	0.040	0.012	<0.001
CV (VT), turn, lower back	0.32	0.13	0.33	0.49	0.56	0.51	-0.67	-0.61
	0.120	0.550	0.110	0.012	0.004	0.009	<0.001	0.001
Mean amplitude (AP), turn, lower back	0.23	0.21	0.05	0.05	-0.01	0.05	-0.01	0.09
	0.260	0.313	0.828	0.822	0.974	0.819	0.951	0.684
CV (AP), turn, lower back	0.47	0.41	0.11	0.40	0.53	0.47	-0.65	-0.57
	0.019	0.043	0.600	0.050	0.006	0.018	<0.001	0.003
Mean amplitude (ML), straight, upper back	-0.02	-0.17	0.26	0.65	0.71	0.59	-0.70	-0.78
	0.940	0.404	0.210	<0.001	<0.001	0.002	<0.001	<0.001
CV (ML), straight, upper back	0.26	0.24	0.04	0.59	0.61	0.57	-0.66	-0.38
	0.210	0.244	0.861	0.002	0.001	0.003	<0.001	0.058
Mean amplitude (VT), straight, upper back	-0.21	-0.22	0.00	-0.36	-0.46	-0.49	0.49	0.87
	0.311	0.301	0.999	0.076	0.020	0.014	0.013	<0.001
CV (VT), straight, upper back	0.01	0.04	-0.04	0.64	0.74	0.70	-0.81	-0.80
	0.949	0.854	0.844	<0.001	<0.001	<0.001	<0.001	<0.001
Mean amplitude (AP), straight, upper back	-0.09	-0.05	-0.07	0.44	0.38	0.44	-0.50	-0.25
	0.674	0.831	0.725	0.029	0.061	0.026	0.011	0.226
CV (AP), straight, upper back	0.41	0.30	0.19	0.58	0.69	0.64	-0.78	-0.72
	0.042	0.144	0.359	0.002	<0.001	<0.001	<0.001	<0.001
Mean amplitude (ML), turn, upper back	-0.35	-0.38	0.05	0.24	0.24	0.12	-0.22	-0.31
	0.090	0.061	0.830	0.245	0.255	0.584	0.296	0.136
CV (ML), turn, upper back	0.59	0.39	0.33	0.34	0.39	0.38	-0.57	-0.34
	0.002	0.051	0.106	0.092	0.057	0.064	0.003	0.097
Mean amplitude (VT), turn, upper back	-0.23	-0.20	-0.06	-0.26	-0.35	-0.32	0.37	0.79
	0.266	0.346	0.761	0.207	0.085	0.122	0.069	<0.001
CV (VT), turn, upper back	0.44	0.18	0.43	0.35	0.44	0.48	-0.61	-0.54
	0.030	0.390	0.031	0.084	0.030	0.016	0.001	0.005
Mean amplitude (AP), turn, upper back	0.18	0.15	0.05	0.52	0.54	0.50	-0.63	-0.37
	0.391	0.464	0.819	0.008	0.006	0.010	<0.001	0.069
CV (AP), turn, upper back	0.45	0.32	0.24	0.34	0.45	0.42	-0.60	-0.55
	0.024	0.124	0.258	0.097	0.023	0.037	0.002	0.004

Baseline (ML), open eye, lower back	-0.07	-0.16	0.13	0.46	0.41	0.35	-0.40	-0.17
	0.728	0.459	0.528	0.021	0.045	0.088	0.045	0.408
Baseline (AP), open eye, lower back	-0.33	-0.21	-0.21	-0.18	-0.19	-0.24	0.31	0.41
	0.105	0.307	0.325	0.388	0.363	0.254	0.132	0.040
Baseline (total), open eye, lower back	-0.29	-0.20	-0.15	-0.03	-0.05	-0.11	0.16	0.29
	0.158	0.328	0.470	0.898	0.800	0.619	0.432	0.156
Fluctuation (ML), open eye, lower back	0.04	0.06	-0.03	0.34	0.38	0.32	-0.38	-0.21
	0.851	0.772	0.872	0.099	0.062	0.118	0.064	0.306
Fluctuation (AP), open eye, lower back	-0.14	-0.06	-0.14	0.31	0.32	0.26	-0.36	-0.09
	0.498	0.770	0.515	0.126	0.116	0.214	0.074	0.663
Baseline (ML), closed eye, lower back	-0.41	-0.38	-0.07	0.32	0.33	0.41	-0.47	-0.15
	0.042	0.065	0.740	0.121	0.109	0.042	0.018	0.479
Baseline (AP), closed eye, lower back	-0.16	-0.15	-0.01	0.30	0.30	0.23	-0.34	0.03
	0.460	0.470	0.963	0.149	0.139	0.268	0.092	0.900
Baseline (total), closed eye, lower back	-0.22	-0.20	-0.05	0.30	0.31	0.25	-0.35	0.02
	0.286	0.341	0.832	0.144	0.135	0.233	0.083	0.919
Fluctuation (ML), closed eye, lower back	0.07	0.14	-0.12	0.42	0.48	0.46	-0.58	-0.23
	0.757	0.509	0.572	0.039	0.016	0.020	0.003	0.273
Fluctuation (AP), closed eye, lower back	-0.07	-0.01	-0.11	0.37	0.40	0.37	-0.47	-0.08
	0.736	0.969	0.617	0.067	0.046	0.068	0.018	0.709
Baseline (ML), open eye, upper back	0.11	-0.03	0.23	0.07	0.09	0.28	-0.27	-0.12
	0.589	0.903	0.266	0.738	0.682	0.184	0.195	0.567
Baseline (AP), open eye, upper back	-0.06	-0.05	-0.01	0.15	0.20	0.20	-0.19	0.18
	0.792	0.803	0.976	0.471	0.329	0.348	0.376	0.401
Baseline (total), open eye, upper back	0.04	-0.06	0.15	-0.04	-0.01	0.15	-0.11	0.08
	0.870	0.785	0.468	0.851	0.978	0.479	0.605	0.700
Fluctuation (ML), open eye, upper back	0.13	0.17	-0.05	0.29	0.33	0.28	-0.36	-0.18
	0.526	0.426	0.808	0.163	0.106	0.180	0.079	0.384
Fluctuation (AP), open eye, upper back	0.08	0.07	0.03	0.53	0.54	0.51	-0.57	-0.32
	0.689	0.741	0.899	0.007	0.006	0.009	0.003	0.115
Baseline (ML), closed eye, upper back	0.04	0.02	0.04	0.29	0.25	0.44	-0.47	-0.12
	0.836	0.914	0.867	0.165	0.221	0.028	0.018	0.559
Baseline (AP), closed eye, upper back	-0.17	-0.21	0.06	0.39	0.45	0.40	-0.48	-0.13
	0.409	0.309	0.778	0.051	0.025	0.050	0.015	0.536
Baseline (total), closed eye, upper back	-0.18	-0.21	0.05	0.40	0.45	0.44	-0.52	-0.16
	0.393	0.310	0.817	0.045	0.025	0.027	0.008	0.448
Fluctuation (ML), closed eye, upper back	0.06	0.13	-0.11	0.43	0.47	0.49	-0.60	-0.25
	0.784	0.541	0.587	0.032	0.017	0.012	0.002	0.227
Fluctuation (AP), closed eye, upper back	0.09	0.11	-0.04	0.55	0.58	0.57	-0.65	-0.24
	0.670	0.591	0.866	0.004	0.003	0.003	<0.001	0.246

SARA: Scale for the Assessment and Rating of Ataxia, BBS: Berg Balance Scale,

ML: medial/lateral, VT: vertical, AP: anterior/posterior

Upper; coefficient of correlation, Lower; p-value

Supplement Table 2. Correlation between earlier and latter SARA.

			through	(p)	first	(p)	latter	(p)
lower back	straight	Mean amp. (ML)	0.61	0.001***	0.61	0.001***	0.60	0.001***
		CV(ML)	0.29	0.154	0.23	0.268	0.29	0.163
		Mean amp. (VT)	-0.41	0.044	-0.39	0.052	-0.42	0.039*
		CV (VT)	0.7	<0.001****	0.65	<0.001****	0.72	<0.001****
		Mean amp. (AP)	0.08	0.709	0.09	0.673	0.07	0.749
		CV (AP)	0.49	0.013*	0.42	0.038*	0.49	0.012*
	turn	Mean amp. (ML)	0.36	0.082	0.39	0.054	0.31	0.135
		CV(ML)	0.02	0.919	-0.02	0.930	0.07	0.727
		Mean amp. (VT)	-0.38	0.06	-0.37	0.065	-0.38	0.059
		CV (VT)	0.49	0.012*	0.45	0.024*	0.52	0.008**
		Mean amp. (AP)	0.05	0.822	0.01	0.962	0.06	0.759
		CV (AP)	0.4	0.05	0.37	0.072	0.36	0.077
upper back	straight	Mean amp. (ML)	0.65	<0.001****	0.68	<0.001****	0.61	0.001***
		CV(ML)	0.59	0.002***	0.50	0.012*	0.60	0.002***
		Mean amp. (VT)	-0.36	0.076	-0.35	0.091	-0.37	0.065
		CV (VT)	0.64	<0.001****	0.61	0.001***	0.63	0.001***
		Mean amp. (AP)	0.44	0.029*	0.44	0.027*	0.41	0.043*
		CV (AP)	0.58	0.002***	0.51	0.010*	0.59	0.002***
	turn	Mean amp. (ML)	0.24	0.245	0.29	0.157	0.19	0.363
		CV(ML)	0.34	0.092	0.21	0.318	0.42	0.037*
		Mean amp. (VT)	-0.26	0.207	-0.27	0.198	-0.25	0.226
		CV (VT)	0.35	0.084	0.38	0.063	0.36	0.074
		Mean amp. (AP)	0.52	0.008**	0.39	0.054	0.50	0.011*
		CV (AP)	0.34	0.097	0.32	0.115	0.36	0.073

SARA, Scale for the Assessment and Rating of Ataxia; BBS, Berg Balance Scale; CV, coefficient of variation; ML, medial/lateral; VT, vertical; AP, anterior/posterior

***: p<0.05, **: p<0.01, ***: p<0.005, ****: p<0.001 statistically significant.**