An observational study of balance and proprioception function in patients with spinocerebellar ataxias type 3

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Research

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Abstract

Background

Postural instability is one of the most disabling features of spinocerebellar ataxias type 3 (SCA3) and often leads to falls that reduce mobility and functional capacity. This study aimed to quantitatively analyse static and dynamic balance and proprioception function on postural control in patients with SCA3 using the Pro-kin system and optimise rehabilitation programmes for them.

Methods

Eight-one clinically diagnosed SCA3 patients (38 women, 43 men; aged 39.00 ± 9.66) and 62 healthy controls were studied and evaluated using the Pro-kin system (PK254P, Tecnobody S.r.l, Dalmine, Italy). The measurements included (1) a static balance test in two visual feedback conditions: eyes open (EO) and eyes closed (EC); (2) a dynamic balance test measuring limits of stability (LOS); and (3) a proprioception function test to obtain proprioceptive measurements on a multiaxial balance evaluator for both right and left lower limbs.

Results

Compared to controls, SCA3 patients showed significantly higher values of all static balance outcome variables with eyes open and eyes closed, implying postural instability. SCA3 patients showed significantly higher values in the standard deviation of body sway along the medio-lateral (ML) axis and in the velocity of body sway along the anterior-posterior (AP) axis. The overall scores and the scores for all eight LOS components were significantly lower in the SCA3 patients than in the controls. The mean values of AP index (API), ML index (MLI), Stability index (SI) and average trace error (ATE) were significantly greater in SCA3 patients compared to HC subjects, while API showed a trend toward higher values.

Conclusions

SCA3 patients have a significant postural control disorder, and are likely to fall on the AP plane and prefer performing postural adjustments in the ML direction; a decreased proprioception function in the knee and ankle is also evident. Visual cues and proprioception should be emphasized in balance rehabilitation training. Attention should also be paid to improve muscle strength and range of motion.

Trial registration

The Chinese clinical test registration center. ChiCTR1800020133. Registered 15 december 2018 - Retrospectively registered, http://www.chictr.org.cn/showprojen.aspx?proj=33950

Background

Spinocerebellar ataxias (SCAs) are a large, complex group of autosomal dominant neurodegenerative diseases characterised by progressive cerebellar ataxia with oculomotor dysfunction, dysarthria, pyramidal and extrapyramidal signs, peripheral neuropathy and cognitive impairments[1−2]. To date, more than 40 types of SCAs are described[3]. Spinocerebellar ataxia type 3 (SCA3), which is also known as Machado-Joseph disease (MJD), is currently the most common subtype of SCAs, accounting for nearly 50% of all SCA patients in the Chinese population[4]. SCA3 is caused by a cytosine-adenineguanine (CAG) trinucleotide repeat expansion on chromosome 14q32.1, resulting in an expanded polyglutamine repeat in the encoded ataxin-3 protein[5−6].

Balance impairments in SCA3 are characterised by increased postural sway and poor balance control during both static and dynamic tasks[7]. These impairments are the most frequent initial clinical manifestation in SCA3, which can be quickly recognised by patients as a sign of onset[8]. As the disease progresses, SCA3 patients usually show an uncoordinated, unstable, wide-based gait[9]. Postural stability is one of the main factors of SCA3 directly affecting gait[7−8]. Various underlying complications, such as muscle atrophy, change of muscle tone and joint motion limitation, give rise to postural instability[10]. Such deficits in SCA3 patients are progressive in nature and are strongly associated with an increased risk of falling[11−12], which in turn affects their posture and balance control. These problems are considered the main cause of worsening the quality of life and independence of these individuals[13]. Studies have shown that rehabilitation training may improve the balance function of SCA patients[14−16], but there is no consistent recommendation for rehabilitation training. It is therefore necessary to evaluate postural stability to optimise rehabilitation programmes for SCA3 patients to improve their function, reduce the risk of falling and improve their quality of life.

In a study that assessed balance in patients with SCA, Aizawa *et al.*[17] used the Tinetti balance test, the Scale for the Assessment and Rating of Ataxia (SARA) and the International Cooperative Ataxia Rating Scale (ICARS) to evaluate disease severity. A study used the Berg Balance Scale (BBS) to observe the balance in patients with SCA[18]. In the EuroSCA fall study[11], patients were asked to complete a fall questionnaire and the SARA. However, these common semi-quantitative clinical scales and questionnaires for balance assessment used in these studies are, to some extent, subjectively influenced[19] and cannot detect minor balance deficits in mildly disabled patients[20]. Further, these scales are often used in the later stages of the disorder, meaning early identification of patients who have a potential for postural instability is not possible[21]. The development of an objective method for identifying postural stability in patients with SCA3 in the early stages is therefore essential.

Computerised posturography tests have the advantage of being more sensitive and specific than clinical tests. Bunn L M *et al.*[22] used an infrared motion-capture system to investigate stance instability in SCA6 and determine how it is affected by varying stance width. Nanetti L *et al.*[23] used the Tetrax® posturography system to show a progressive impairment of stance performance in the SCA1 preclinical phase. In a study, the analysis of trunk motion and muscle responses in SCA patients was shown using the SwayStar system[24]. Nonetheless, subjects of prior studies almost always examine other SCA subtypes, and most posturography studies have focused mainly on measuring body sway using the stability index. Very few studies have attempted to determine the characteristics of postural stability from both static and dynamic aspects, which provide a foundation for characterizing patients' postural and balance instability[25]. In addition, the proprioception function has been shown to yield additional information on postural stability[26], yet to the best of our knowledge, there is no study on this aspect in SCA3 patients. The Pro-kin system is a new type of visual feedback instrument equipped with a balance force platform and computer[27]. This system can be used to test static and dynamic balance and the proprioception function and overcomes the deficiencies of balance detection in prior studies.

We previously used the Pro-kin system to assess the static and dynamic stability of SCA3 clinically, and the results proved to be effective[28]. To the best of our knowledge, our previous study is the only study about static and dynamic balance in SCA3 patients. However, no intensive study exists that examines the overall postural stability in SCA3 patients. Our study therefore to analyze the differences between SCA3 patients and healthy control people in both balance ability and proprioception function using the Pro-kin system; our purpose is to find the targets requiring key intervention, so as to guide the selection and design of clinical rehabilitation training methods and improve the effect of rehabilitation training intervention.

Methods

Participants

A cohort of 81 patients (43M/38F, aged 39.00 ± 9.66) with a diagnosis of molecular-confirmed SCA3[29] was assessed at the Department of Rehabilitation Medicine, the First Affiliated Hospital, Fujian Medical University between October 2018 and December 2019. The inclusion criteria were (1) definite genetic diagnosis of SCA3, (2) aged over 14 years, (3) Mini-Mental State Examination score (MMSE)≥27, (4) ability to stand independently in the upright position for 30 s, and (5) a willingness to participate. Exclusion criteria were (1) unstable vital signs and uncontrolled hypertension; (2) presence of cognitive impairment, visual or hearing pathologies; (3) unable to stand independently for 30 s with eyes closed; (4) lack of sensitivity in the lower limbs; (5) musculoskeletal, cardiovascular or respiratory system impairments or other accompanying ailments; (6) engagement in another rehabilitative study protocol; or (7) recent oral medication that would affect balance.

A cohort of 62 age- and gender-matched healthy control (HC) subjects (31M/31F, aged 40.18 ± 10.99) were enrolled as a reference population. The controls showed no evidence of balance deficits; comorbidities, such as diabetes, hypertension, rheumatic, or oncological diseases; vision problems; or musculoskeletal, cardiovascular, or respiratory system problems. The age, height and weight of the subjects were collected.

The protocol was approved by the Ethics Committee of the First Affiliated Hospital, Fujian Medical University. The study's design and procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained prior to participation.

Experimental Design

We conducted an observational study between SCA3 patients and HC subjects at the same time of the day. The Pro-kin system (Prokin 254 (Pro-Kin Software Stability), TecnoBody S. r. l., Dalmine, 24044 Bergamo, Italy) was used to assess postural stability, which is based on assessing the movement of the centre of pressure (COP) and measuring proprioceptive on a multiaxial balance evaluator for lower limbs. A rehabilitation therapist blinded to the groups conducted the assessments. All participants received the following postural stability assessments in a naturally and brightly lit and quiet room: (1) a static balance test in two visual feedback conditions: eyes open (EO) and eyes closed (EC); (2) a dynamic balance test measuring limits of stability (LOS); (3) a proprioception function test measuring proprioceptive on a multiaxial balance evaluator for both right and left lower limbs. Each test was repeated three times and the mean scores were recorded. The assessment lasted approximately 45 minutes. The participants were oriented to the test in the evaluation mode before performing the actual test. Postural stability was evaluated in terms of three types of balance outcomes (static and dynamic balance indices, proprioception function indices) in both groups for comparison. Participants are evaluated as shown in Fig. 1.

Balance Measurement

We placed and fixed the four locks of the system under the force platform to conduct the static balance test[27]. All participants stood barefoot on the platform in a standard standing position with arms hanging comfortably at their sides and feet placed symmetrically at the corresponding position on the platform. In the EO trials, participants were instructed to look straight ahead and gaze at a specific target 80 cm away. In the EC trials, the participants were denied visual feedback, but they were instructed to face forward as if looking straight ahead. Each trial lasted 30 seconds. Five key parameters are measured[30]: (1) sway range standard deviation (SD) along the anterior-posterior (AP) and medio-lateral (ML) directions (OE + CE); (2) velocity of body sway along the AP and ML directions (OE + CE) [mm/s]; (3) ellipse area (EA) (OE + CE) [mm^2]; (4) total sway path length (SP) (OE + CE) [mm]; and (5) the Romberg of the EA (R_{EA}) and SP (R_{SP}) [%] [31]. COP is the point of application of forces exchanged between feet and ground. SD is defined as the mean error of the COP displacement, EA is the ellipse that contains the COP trajectory, and SP is the length that contains the COP trajectory. Specifically, the highest SD value identifies the preferred direction of the postural adjustments performed by the subject. The highest velocity value indicates that the sway is significant in this direction. The Romberg of the EA (R_{EA}) and SP (R_{SP}) were evaluated as the ratio between EC and EO. Higher R_{EA} and R_{SP} values reflect greater instability with closed eyes. In total, we measured 14 outcome variables based on five parameters (Fig. 2).

The circular force platform can tilt 20° in all directions from the horizontal, and the degree of surface instability of the platform can be adjusted from level 10 (most stable) to level 1 (least stable) using the microprocessor-based actuator control incorporated in the system. The most stable level (level 10) was used to examine the dynamic balance test, and the medium stable level (level 5) was used in the proprioception function test in all participants.

In the dynamic balance test, all participants were asked to stand on the platform to perform the LOS test. They were asked to shift their centre of mass, without changing their foot position, towards the targets that appeared randomly in eight different directions only once. The direction of the target was indicated on the screen by a blinking target. Participants were required to achieve the target from the centre position using the shortest vertical or horizontal path. The path used was given a score by the instrument; the total LOS score and the LOS results in all directions, including forward (FW), backward (BW), right (RT), left (LT), forward-right (FW-RT), forward-left (FW-LT), backward-right (BW-RT) and backward-left (BW-LT) were recorded [%] [32]. In a particular direction, the maximum achievable perfect score was 100. A lower score indicated greater sway (Fig. 3).

For the proprioception function test, participants placed the right foot on the balance board and the left foot on a fixed support platform equal to the balance board[33]. Participants had to focus on the monitor and draw lines on the screen by moving their right foot (on the balance board) within 120 seconds. Their motor task is to try to superimpose the lines drawn by the movements of their foot on those drawn by the system. Then, the left lower limb was tested for two key parameters: (a) balance control indices: AP index (API), ML index (MLI) and stability index (SI) [°] and (b) the Average Trace Error (ATE) [%] [33], the preassessment of lower limb proprioception. The smaller the value, the better the lower limb proprioception function and balance control (Fig. 4).

To reduce the risk of falls and minimise interference from external support, a trainer stayed close alongside or behind the participants.

Statistical Analyses

All statistical analyses were performed using GraphPad version 8.0.1. The normality of the distribution of all postural parameters variables was assessed using Kolmogorov-Smirnov tests. Following the results of these tests, variables with normal distribution and variables in non-normal distribution were expressed as mean ± SD and median (range), respectively. Two-independent sample *t*-tests and Mann-Whitney *U* tests were used to analyse normally and non-normally distributed measures, respectively, and to confirm the statistical difference of the two groups and the two lower limbs according to the normality assumption. Chi-squared tests were used to assess the gender difference between SCA3 patients and HC subjects. Statistical test outcomes were considered significant at $p < 0.05$.

Results

Static Balance Test Analysis

Table 1 shows the values of all static balance outcome variables for the two groups. We compared the values between SCA3 patients and HC subjects for the EO and EC conditions separately. The statistical analysis revealed that all indices were significantly worse for SCA3 patients compared to HC subjects (all $ps < 0.0001$), suggesting worse balance in SCA3 patients. Particularly, in both EO and EC conditions, the SD of body sway values along the ML axis were all greater than the AP axis in SCA3 patients and velocity of body sway values along the AP axis showed a trend toward higher values than the ML axis.

Table 1

Values of the postural indices in SCA3 patients and HC subjects in eyes open (EO) and eyes closed (EC) conditions during Static Balance Test

Visual conditions	**Postural indices**	**SCA3**	**HC**	***P* value**
EO	EA	2206.00 ± 2240.00 (1560.00)	342.70 ± 180.70 (296.80)	<0.0001[1]
	SP	798.20 ± 392.90 (713.70)	307.00 ± 89.50 (296.00)	<0.0001[1]
	SDap	9.89 ± 4.79 (9.33)	4.61 ± 1.46 (4.33)	<0.0001[1]
	SDml	10.63 ± 4.75	4.27 ± 1.18 (4.00)	<0.0001[1]
	Vap	21.93 ± 11.90 (19.67)	8.26 ± 2.00 (7.84)	<0.0001[1]
	Vml	20.62 ± 9.69 (18.67)	8.40 ± 2.27 (8.00)	<0.0001[1]
EC	EA	8105.00 ± 7133.00 (8244.00)	843.00 ± 528.00 (689.50)	<0.0001[1]
	SP	1932.00 ± 1156.00 (1770.00)	538.60 ± 166.40	<0.0001[1]
	SDap	18.79 ± 8.14	6.80 ± 2.14 (6.67)	<0.0001[1]
	SDml	19.90 ± 9.22	6.44 ± 2.19 (6.00)	<0.0001[1]
	Vap	56.93 ± 36.42 (53.33)	14.13 ± 4.48 (12.84)	<0.0001[1]

Variables were represented as the mean ± standard deviation and for variables with skewed distribution, the median was presented in parentheses

Abbreviations: EA,ellipse area; SP,sway path; SDap and SDml, standard deviation of COP displacement in the anterior-posterior and medio-lateral direction;Vap and Vml,velocity of body sway along anterior-posterior and medio-lateral direction.

[1]Mann-Whitney *U* test

Visual conditions	Postural indices	SCA3	HC	*P* value
	Vml	45.51 ± 26.94 (42.67)	14.53 ± 4.89 (13.67)	<0.0001[1]
Variables were represented as the mean ± standard deviation and for variables with skewed distribution, the median was presented in parentheses				
Abbreviations: EA,ellipse area; SP,sway path; SDap and SDml, standard deviation of COP displacement in the anterior-posterior and medio-lateral direction;Vap and Vml,velocity of body sway along anterior-posterior and medio-lateral direction.				
[1]Mann-Whitney *U* test				

We then quantified the impact of loss of visual feedback on balance performance by comparing the Romberg indices (R_{EA} and R_{SP}) **(**Fig. 5**).**Our results show that, R_{EA} was higher in SCA3 patients compared to HC subjects (SCA3 patients 408.6 ± 210.4; HC subjects 275.5 ± 130.9, $p < 0.0001$); R_{SP} was also significantly affected (SCA3 patients 238.3 ± 74.8; HC subjects 176.0 ± 43.3, $p < 0.0001$).

Dynamic Balance Test Analysis

Table 2 shows the LOS scores of the SCA3 patients and HC subjects. The SCA3 patients had significantly lower total LOS score and overall scores for all eight components of the LOS scores compared to the HC subjects, the difference between groups was significant (all *ps* < 0.05). In SCA3 patients, the LOS score for all directions was asymmetrically affected. In particular, the forward LOS scores was lower than other components of the LOS scores.

Table 2
Dynamic Balance Test analysis between patients of SCA3 and health control subjects

Limits of stability (LOS)	SCA3	HC	*P* value
Total LOS score	59.15 ± 17.94(62.17)	75.73 ± 16.94(78.47)	<0.0001[2]
Right	48.00 ± 19.94	67.14 ± 17.05	<0.0001[1]
Forward right	50.16 ± 25.77	67.27 ± 26.98(73.52)	<0.0001[2]
Forward	43.40 ± 22.16(45.83)	55.17 ± 24.87	0.0038[2]
Forward left	50.06 ± 29.45	65.77 ± 24.58(68.94)	0.0005[2]
Left	51.36 ± 20.29	67.27 ± 19.05	<0.0001[1]
Backward left	75.87 ± 24.67(82.00)	88.16 ± 16.13(96.73)	0.0002[2]
Backward	79.20 ± 25.00(88.33)	96.35 ± 11.03(100.00)	<0.0001[2]
Backward right	78.44 ± 22.18(84.00)	88.88 ± 17.60(99.07)	<0.0001[2]
Variables were represented as the mean ± standard deviation and for variables with skewed distribution, the median was presented in parentheses			
Abbreviations: LOS means the limits of stability; RT means right; FW-RT means forward-right; FW means forward; FW-LT means forward-left; LT means left; BW-LT means backward-left; BW means backward; BW-RT means backward-right.			
[1]Two-independent samples *t* test			
[2]Mann-Whitney *U* test			

Proprioception Function Test

Table 3 shows the analysis of the proprioception function. We first compared all outcome variables between SCA3 patients and HC subjects for the right and left lower limbs. The mean API, MLI ,SI and ATE values were significantly greater in SCA3 patients compared to HC subjects (all *ps* < 0.0001).While API showed a trend toward higher values ($p < 0.05$). Second, we compared the values of all outcome variables between the right and left lower limbs for SCA3 patients and HC subjects separately. No significant worsening occurred between the right and left lower limbs for all indices in these two groups.

Table 3
Proprioception Function Test indices between patients of SCA3 and health control subjects

indices	lower Limb	SCA3	HC	*P* value
API	R	3.65 ± 2.42(3.12)	1.84 ± 1.29(1.37)	<0.0001*
	L	3.56 ± 2.33(2.95)	1.63 ± 1.21(1.28)	<0.0001*
	P value	0.9076*	0.2593*	
MLI	R	3.44 ± 1.96(3.07)	2.03 ± 1.21(1.61)	<0.0001*
	L	3.22 ± 1.74(2.71)	1.79 ± 1.02(1.50)	<0.0001*
	P value	0.5604*	0.1981*	
SI	R	1.83 ± 0.86(1.54)	1.05 ± 0.04(1.00)	<0.0001*
	L	1.94 ± 0.91(1.71)	1.17 ± 0.33(1.11)	<0.0001*
	P value	0.2819*	0.041*	
ATE	R	38.13 ± 23.56(31.67)	30.95 ± 22.77(26.67)	0.0741*
	L	44.64 ± 28.86(39.33)	35.52 ± 22.77(29.67)	0.0519*
	P value	0.1788*	0.2033*	

Variables were represented as the mean ± standard deviation and for variables with skewed distribution, the median was presented in parentheses

Abbreviations: API, anterior-posterior index; MLI, medio-lateral index; SI, stability index; ATE, average trace error.

* Mann-Whitney *U* test

Discussion

Although previous studies have examined postural control problems in spinocerebellar ataxias patients, the nature of postural instability and the pathophysiological and biomechanical mechanism of balance in SCA3 patients remain unknown.Also, no targeted rehabilitation program has been proposed in these studies. The Pro-kin system is an ideal tool for the evaluation of balance function at present. It can not only judge the cause and degree of balance function damage, but also evaluate the effect of treatment and rehabilitation. In this study, the Pro-kin system was used to assess the static balance, dynamic balance and proprioception function of SCA3 patients. Our main findings show that the function of visual afference affects postural control in SCA3 patients; these patients have predominant instability in the AP plane and prefer performing ML direction postural adjustments; the distribution of centre of gravity in SCA3 patients is asymmetrical, and they have a worse ability to shift the weight forward; notably, SCA3 patients have a decreased proprioception function, mainly in the knee and ankle joints.

The SCA3 patients consistently exhibited increased postural instability in all experimental conditions compared with HC subjects. We observed the existence of a predominant alteration of body sway velocity in the AP axis in SCA3 patients in both EO and EC conditions. This demonstrated that our patients have more AP falls. Mohan *et al.*[34] quantitatively assessed the balance in spinocerebellar ataxia type 1 and found that SCA1 patients had global impairment of balance and a significantly greater body sway in the AP direction than in the ML direction. A previous study of trunk movements revealed that autosomal dominant spinocerebellar ataxia patients have worse trunk sway and predominant instability in the AP direction[24]. Our study is in line with these related studies. Therefore, maintaining good control of body sway in the AP direction should be of high priority in preventing falls and in balance training programs in patients with SCA3.

Besides these similar phenomena, our study also found that SCA3 patients showed a significant trend toward higher values in the standard deviation of body sway along the ML axis. The findings suggest that SCA3 patients prefer performing ML direction postural adjustments. Thus, the ML standard deviation is one of the most reliable markers of postural instability in SCA3[35–36] and can be used to analyse postural instability in SCA3 in future studies. Moreover, this finding can explain why SCA3 patients adopt an abnormally typically broad-based gait and have marked difficulties performing tandem gait[9]. The increased values in the ML standard deviation may reflect an attempt to maintain stabilising movements during a quiet stance, which may be a compensatory strategy to reduce their intrinsic instability in the AP direction. Impairments in the activation function of the synaptic transmission between the climbing fibres and Purkinje cells inhibits cortical motor activation via a complex neural pathway involving the dentate nucleus, which could be related to abnormal postural sways in SCA3 patients[37–38]. Previous studies have demonstrated that cerebellar transcranial magnetic stimulation (TMS) is capable of facilitating motor cortical activation via modulation of Purkinje cell excitability[39–40]. Therefore, TMS is recommended to activate the function of the cerebellar to improve balance.

The main functions of the cerebellum are to maintain postural stability, regulate muscle tone and coordinate the voluntary movement of muscles. Control of postural stability is a multifaceted process and involves the integration of sensory information from proprioception, vision and vestibular systems[41]. As one of the main results, the presented findings highlight that SCA3 patients had statistically significant higher Romberg indices values in both R_{EA} and R_{SP} compared to HC subjects, which reflected that an absence of visual control or insufficient input of visual information inenhances an increase in postural sway in SCA3 patients[24]. During the dynamic balance process, asymmetrically affected component LOS scores in all eight directions indicated that SCA3 patients have less adaptive capacity to effect correct postural control in all directions according to the task requirement, even with visual cues[34]. Our results contradict the common physiological model in which vision helps control postural stability[42]. Owing to the neuronal loss occurrings in the basal ganglia, SCA3 patients have a deficit in reweighting various sensor-motor loops. When adapting to novel situations, this deficit affects the integration of sensory information for postural stability[43]. This may reflect the predominant involvement of the spinocerebellum (anterior lobe) in SCA3, as the anterior lobe is associated with visual input[44]. Therefore, visual cues may be required in balance rehabilitation so as to compensate for the decreased balance function caused by cerebellar factors in SCA3.

The results of this study showed that the total LOS score and overall scores for all eight components of the LOS scores of patients with SCA3 were smaller, which was significantly different from that of healthy controls. Also, LOS score of forward was the lowest and LOS score of back was highest in all eight components of the LOS scores in SA3 patients, which was consistent with the results measured in the health control group under the same conditions. In normal activities, the range of body stability limit is smaller than the theory, and the range of stability limit is tilted at different angles in multiple directions. There are more activities in forward and back direction in human activities, so the limit of stability range in forward and back direction has greater influence on daily life[45]. Melzer *et al.* [46] thought that the forward LOS was related to the muscle strength of flexor metatarsus and extensor dorsum of the ankle joint, and believed that the muscle strength of metatarsophalangeal flexor played a more obvious role in the prevention of falls. It is suggested to increase the imitative movement exercises such as retrieving in the balance training, and increase the forward and backward movement range through the muscle strength training of metatarsal flexus, so as to contribute to the body balance.Therefore, in the balance training of patients withSCA3, attention should be paid to the training of muscle strength of trunk and lower limbs, so as to expand the range of stability limits of forward and backward, especially forward.

Proprioception is a nerve impulse that is sent to the central nervous system by mechanical receptors located in joints, joint capsules, ligaments, muscles, tendons and skin. It can be divided into strength sense, motion sense and position sense. Instead of weakening somatosensory feedback by standing on foam to analyse the interactions between postural stability and proprioceptive function[47], in this work, we performed the lower limb proprioceptive function test. To the best of our knowledge, this study is the first to analyse the proprioception of the left and right feet separately in SCA3 patients. We found that our patients obtained larger values for API, MLI ,SI and ATE compared to HC subjects, and there was a trend toward higher values in API, suggesting that postural instability in SCA3 patients correlates with a deficient proprioception function and a quantitative reduction in muscle strength, mainly in the knee and ankle joints[26]. The pathological involvement of spinocerebellar proprioceptive input and the loss of the integrity of the medial somatosensory descending system may explain abnormal postural control[48]. Patients presented a locking of knees and ankles and muscular rigidity, causing abnormal joint movements related to postural instability. When human body is about to fall after receiving small and slow interference, the body mainly relies on ankle joint regulation to restore postural stability (ankle joint strategy). The decline of ankle joint position sense affects the implementation of ankle strategy, which may be the cause of poor balance in SCA3 patients. We suggest that SCA3 patients receive a proprioceptive-motor training rehabilitation program and stretching and strength exercises. Unexpectedly, no significantly better proprioception function was observed for the right lower limb compared to the left lower limb in our SCA3 patients. Since all the patients are right dominant, it remains to be seen why patients’ right lower limbs lost the advantage of a better proprioception function to control balance.

As our study was an observational study, we have not provided information on changes in postural stability over time in our patients. As posturography cannot identify the specific constraints underlying postural instability, the predictive validity of these measurements in monitoring disease progression remains un-explored.

Conclusions

In this study, the Pro-kin system was used to analyse static and dynamic balance and proprioception function on postural control in patients with SCA3 using the Pro-kin system. Our patients have a significant postural control disorder; they are likely to fall in the AP plane and prefer performing ML direction postural adjustments. Decreased proprioception function in the knee and ankle was also observed. Impaired postural stability in our SCA3 patients relates to abnormal integration of the somatosensory descending system and/or inappropriate cerebellar motor commands. Neurorehabilitation in SCA3 patients should engage movement and the integration of various sensorial inputs, such as perception and vision. The description of the characteristics of postural stability in SCA3 patients presented herein can be used as criteria to distinguish the disease severity in SCA3 patients in future studies.

Abbreviations

SCA3:spinocerebellar ataxias type 3; EO:eyes open; EC:eyes closed; LOS:limitsof stability; ML:medio-lateral; AP:anterior-posterior; API:anterior-posterior index;MLI: medio-lateral index; SI:Stability index; ATE:average trace error; MJD:Machado-Joseph disease; CAG:cytosine-adenineguanine; SARA:Scale for the Assessment and Rating of Ataxia; ICARS:the International Cooperative Ataxia RatingScale; BBS: the Berg Balance Scale; HC:healthy control; COP:the centre of pressure; SD:sway range standard deviation; EA:ellipse area; SP: sway path; REA:the Romberg of the ellipse area ; RSP: the Romberg of the sway path; FW:forward; BW:backward; RT:right; LT:left; FW-RT:forward-right; FW-LT:forward-left;BW-RT:backward-right; BW-LT:backward-left; TMS:transcranial magnetic stimulation

Declarations

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Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study complied with the principles of the Declaration of Helsinki and the protocol was approved by the ethics committee of the First Affiliated Hospital of Fujian Medical University (Approval No: MRCTA, ECFAH of FMU[2018]201.). The subjects were given the written informed consent form, and they signed the consent form before joining this study.

Consent for publication

The authors consent this article for the publication of Journal of NeuroEngineering and Rehabilitation.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Dr. X-H Liu carried out study concept and designed the experiment study. Dr. A Sikandar and Dr. W-H Lin recruited SCA3 patients for this study, Dr. Y Li and Dr. H-L Xu performed the experiments and collected the data. Dr. N Wang, Dr. J Ni, and Dr. W-J Chen involved in study concept and design and acquisition of data. Dr. Z-Y Wang and Dr. S-R Gan analyzed the data, drafted, edited and revised the manuscript. All authors read and approved the final manuscript.

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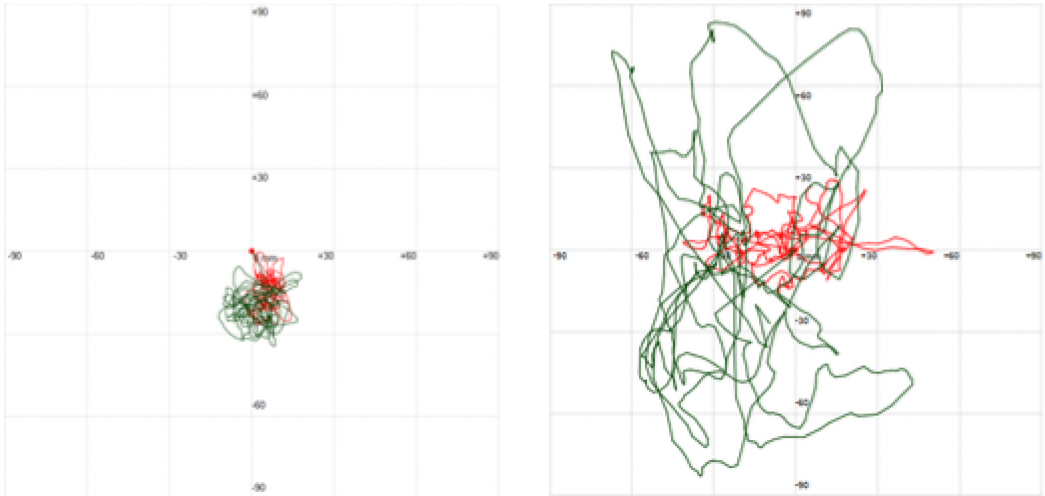
Figures

(a) (b)

Figure 1

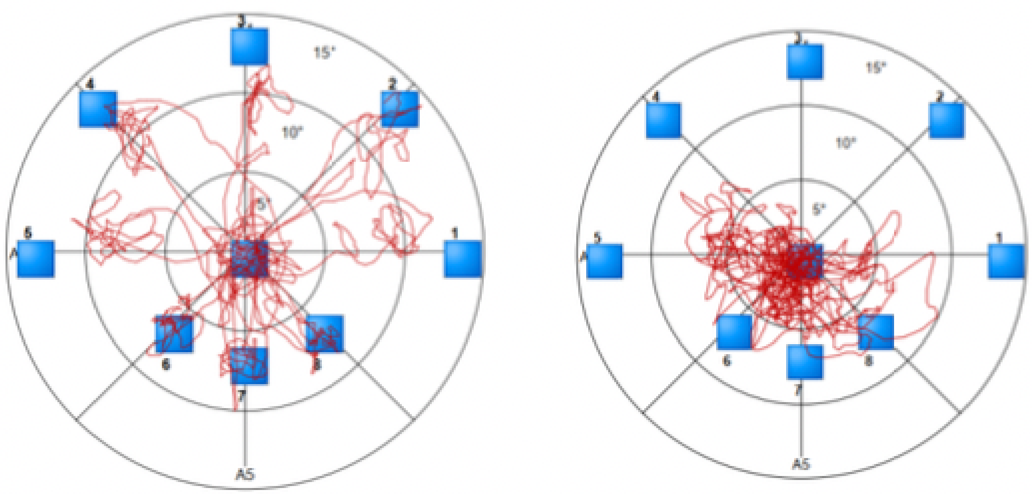
The figure shows the Pro-kin system.(a) patient was tested balance function (b)patient was tested in the proprioception function



(a) (b)

Figure 2

The figure shows the actual recording of the path of postural sway during Static Balance Test in (a) a control subject and (b) a SCA3 patient. The red trajectory means in eyes open,the green trajectory means in eyes closed.



(a) (b)

Figure 3

The figure shows the actual recording of the path of postural sway during Limits of stability (LOS) task in (a) a control subject and (b) a SCA3 patient.

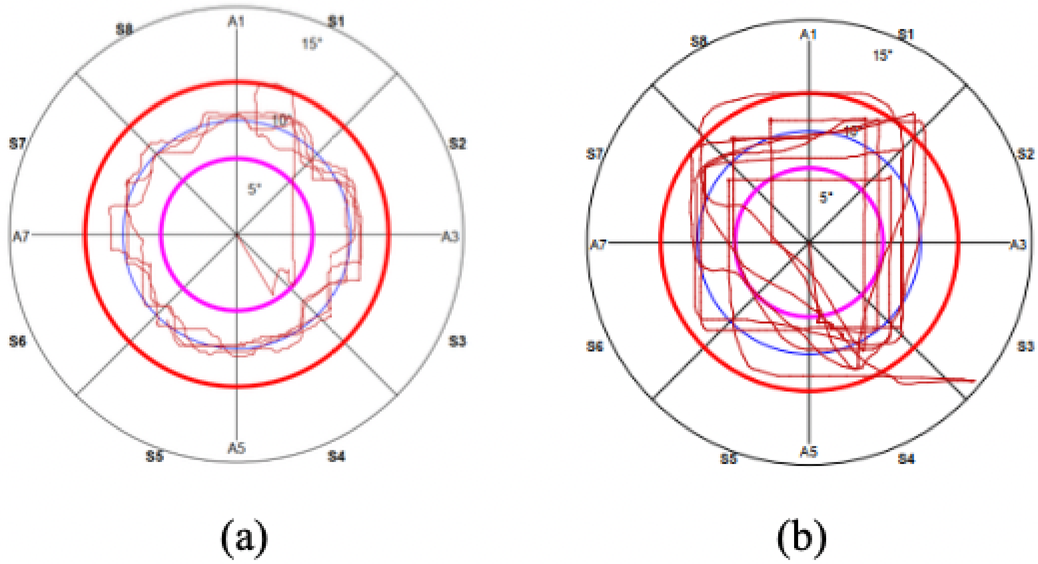


Figure 4

The figure shows the actual recording of the path of postural sway during Proprioceptive multiaxial assessment in right lower limb in (a) a control subject and (b) a SCA3 patient.

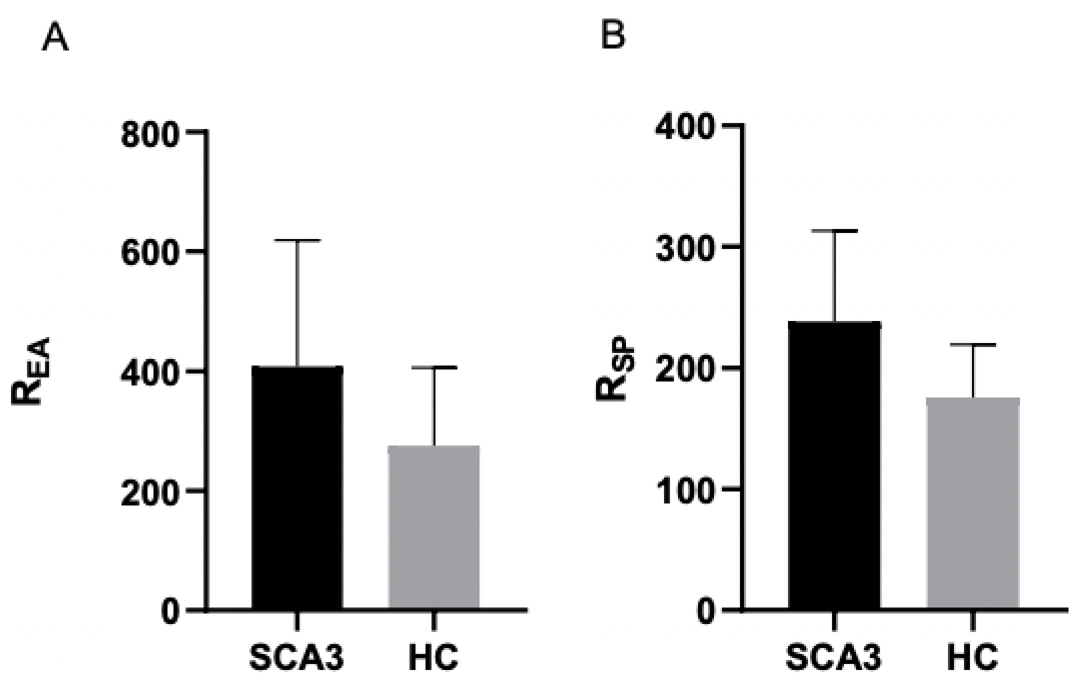


Figure 5

The comparison of REA and RSP between SCA3 patients and health controls: (A) REA values was significantly higher in SCA3 patients compared to health control; (B) RSP values was significantly higher in SCA3 patients compared to health controls.