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More falls in cerebellar ataxia when standing on a slow up-moving tilt of the support surface

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Abstract

We investigated how subjects with cerebellar ataxia (CA) adapt their postural stability and alignment to a slow and small tilt of the support surface allowing for online postural corrections. Eight subjects with CA and eight age- and gender-matched healthy control subjects participated in the study. Subjects stood eyes closed for 1 minute after which the support surface was tilted 5° toes-up at a ramp velocity of 1°/s. The toes-up position was held for 2.5 minutes after which the surface rotated back down to level with identical tilt characteristics. As reflected by the large number of falls, subjects with CA had marked difficulty adapting their posture to the up-moving incline in contrast to control subjects. Subjects with CA who lost their balance had faster trunk velocity and excessive backward trunk reorientation beginning within the first second after onset of the tilting surface. In contrast, the down-moving tilt to level did not result in instability in CA subjects. These results suggest that instability and falls associated with CA derives from an inability to maintain trunk orientation to vertical while standing on a slow-moving or unstable surface. This study underscores the importance of the cerebellum in the online sensory control of the upper body orientation during small amplitude and slow velocity movements of the support surface.

Keywords

Postural Balance; Accidental Fall; Torso; Movement Disorders; Motor Activities

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CONFLICT OF INTEREST (COI) STATEMENT

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INTRODUCTION

Falls and postural instability are common in individuals with cerebellar ataxia [1, 2]. Cerebellar damage has shown to cause postural instability when standing on fast moving surfaces with large perturbations [3–7]. Postural responses in patients with cerebellar disorders are hypermetric but with normal latencies and inability to scale response amplitudes to predicted perturbation amplitudes [4, 7, 8]. Such fast perturbations limit the possibility of corrections during movement execution so postural response scaling is based on sensory predictions, a key role of the cerebellum in motor control (internal model) [9, 10]. For example, in upper limb reaching, it has been shown that corrections occurring during movement cause error accumulation in subjects with cerebellar ataxia, which results in increased end-point errors [11].

The role of the cerebellum in postural stability when adapting to slow and small perturbations of the supporting surface remains poorly understood. When standing on a slow upward tilting surface of small amplitude, multiple postural adjustments must be made. These adjustments are especially important in ankle dorsiflexion and needs to be proportional to the surface motion to maintain upright balance. We have previously shown that healthy adults respond to this minor perturbation by maintaining trunk orientation to vertical while allowing ankle rotation during the surface motion, even with eyes closed [12]. Thus, it is not clear whether subjects with cerebellar ataxia, who are known to have difficulty walking or standing on an inclined surface and who accumulate errors with motor tasks, are able to correct their movement during slow movements to maintain postural stability.

In the present study, we investigated the role of the cerebellum in adapting to a slowly inclining surface during standing in subjects with cerebellar ataxia (CA) and healthy adults. We hypothesized that the cerebellum significantly contributes to this slow adaptation process involving a gradual recalibration of sensory information to optimize motor performance. Thus, it is expected that cumulative errors, due to multiple postural adjustments, would lead to decreased stability in subjects with CA standing on a slow inclining surface. Therefore, we expect that measures of segmental orientation, to maintain verticality, rather than postural stability as measured by sway would be more affected by a slow and small incline of the supporting surface.

PATIENTS AND METHODS

Subjects

Eight subjects with cerebellar ataxia (CA) (age: 58 years [SD 7], height: 169 cm [SD 11] and weight 77 kg [SD 14]) and eight age- and gender-matched healthy control subjects (age: 57 years [SD 6], height: 171 cm [SD 11] and weight: 75 kg [SD 13]) participated in the study. Table 1 summarizes the diagnosis, onset, disease severity with the scale for the assessment and rating of ataxia (SARA) [13] and balance function in the subjects with CA. All subjects were screened with a health history evaluation to ensure that they were free of musculoskeletal and other neurological impairments that could affect postural control. All participants were ambulatory and did not require any assisting device. Prior to their participation in the experiment, all subjects gave their informed consent in accordance to the

Institutional Review Board of the Oregon Health & Science University regulations and the Declaration of Helsinki.

Experimental Setup & Protocol

As illustrated in Fig. 1A, each trial consisted of a 1-minute baseline period of quiet stance with eyes closed to avoid anticipation of the upcoming surface motion and to obtain a stable upright standing baseline. The force platform was then tilted 5° toes-up (Tilt-Up) at a ramp velocity of 1°/s. Surface tilts were driven by a computer-controlled hydraulic system, with the axis of surface rotation located at approximately ankle height. The surface tilted at a constant velocity with a cosine function at the start and end of the ramp to limit acceleration and create gradual, rather than abrupt, onset and offset of surface tilts, without activating short-latency, somatosensory-triggered destabilizing bursts of the gastrocnemius muscle [14–16]. The support surface was held in the up position (5°) for 2.5 minutes to allow subject to adapt to their posture to the incline surface. A Tilt-Down motion to bring back the foot position to a flat surface (0°) followed with the same displacement characteristics as the toes-up tilt (1°/s). All subjects maintained quiet stance on the stationary flat surface for a minimum of 3 minutes for them to stabilize their posture following the toes-up adaptation and slow Tilt-Down motion. Two trials were performed in all participants except for two of the CA subjects who only performed one trial due to excessive fatigue.

During each trial, the subjects stood upright on the force platform with their head facing forward, arms crossed and wearing a blindfold ensuring that vision was occluded for the duration of the trial. Subjects stood with their bare feet spaced at comfortable width, at approximately hip width. The position of the feet was marked on the floor to ensure subjects were tested in the same position on all trials. Subjects wore a safety harness attached to an overhead beam to ensure safety during trials without providing directional/spatial cues for postural alignment. The subjects were instructed to “stand in a relaxed way and try to maintain your balance”. To further assure subject safety, a research assistant stood beside all subjects during each trial.

Measurements

Body kinematics were recorded at 60 Hz using an 8-camera motion analysis system (Motion Analysis, Santa Rosa, CA) and 22 retro-reflective markers placed bilaterally on the trunk, hips, legs, feet and tilting surface. Marker positions were then used to calculate the orientation of body segment angles (shank, thigh and trunk) on the right side of the body. The shank segment was defined from the lateral malleolus to the axis of rotation of the knee, the thigh segment from the axis of rotation of the knee to the greater trochanter and the trunk segment from the greater trochanter to the seventh cervical vertebra. Segment angular velocity was obtained from the first derivative of the angular position.

Subjects stood on a custom-made dual-plate force platform with four vertical force sensors beneath each foot. Forces were sampled at 120 Hz and the center of pressure (COP) was calculated from the combined vertical forces of each force plate [17]. COP data were low-pass filtered at 0.1 Hz using a dual-pass 2nd order Butterworth filter. For two CA subjects,

collection of the force platform data failed. As illustrated in Fig. 1B, the center of mass (COM) closely followed the COP position hence COM data was used for these subjects.

Analyses

Each trial was coded as a loss of balance (LOB) or a non-loss of balance trial (No LOB). Trials were identified as LOB if the subject needed to be caught or touched by the research assistant and/or the safety harness to prevent falling, if the subject took one or more steps, or if the subject touched or held onto the research assistant. The time of onset of the LOB was detected by a sudden reduction in vertical forces as registered by the force plates and also visually, by analyzing video recordings of the sessions as well as with motion analysis data used for kinematic analysis. LOB occurred only in the CA group in 11/14 of the trials. Ten of these trials with LOB could be analyzed for kinematic strategy, CoP displacement and variability for up to the moment of LOB. The LOB in these 10 trials occurred after a minimum of 1.3 seconds (mean onset of LOB was 1.9 seconds), hence sufficient data was available to analyze prior to LOB. After LOB, subjects were supported to recover balance and instructed to reposition the displaced foot so the trial could be continued. In order to analyze data for these trials post LOB, the COP displacement was calculated in relation to the heels of the subjects for all trials. Thus, during trials with LOB involving a displacement of the feet, we could continue to quantify changes in COP displacement while excluding the LOB intervals.

Kinematic strategies were quantified from body segment displacements in response to the upward surface tilts by measuring the angular displacement and velocity of the shank, thigh and trunk segment in the sagittal plane with respect to the gravity-vertical reference. In addition, we measured peak backward angular displacement and velocity. This additional metric allowed for the comparison of trunk kinematics of all subject prior to any intervention from the assistant or reaction from the subjects (stepping or grasping).

Postural stability before, during and after tilting was also quantified to determine if subjects adapted to each surface positions. The mean position and variability (i.e., standard deviation) of the COP in the direction of the perturbation (i.e., the anterior-posterior direction). As illustrated in Fig. 1A, COP measures were obtained during five 45-second intervals: 1) before incline (baseline), 2) early and 3) later during the incline and 4) early and 5) later after the returning to neutral position. These different intervals were selected to assess postural stability immediately after surface motions and after adaptation (or re-adaptation) to the new surface position.

Levene's test for homogeneity of variances and Mauchle's Sphericity test were non-significant ($p < 0.120$) for the mean of COP during the intervals standing on a flat or inclined surface, therefore a repeated measures analysis of variance [intervals x groups] and main effects were explored with Tukey HSD test. Due to the small sample size, non-parametric statistics (Mann-Whitney U test) were used to investigate differences between control vs. CA subjects that maintained or lost their balance. Spearman Rank Order Correlation (r_s) was used to investigate the relationship between the disease severity and loss of balance in the CA group. The significance level was set at $p < 0.05$.

RESULTS

Postural alignment deficits with cerebellar ataxia

Subjects with CA showed marked difficulty in adapting their posture to a low-amplitude (5°) very slow (1°/s) up-moving incline, in contrast to control subjects who showed no difficulty performing the task, as seen in Table 2 and in Fig. 2. During Tilt-Up, in 11 (7 different individuals) out of 14 trials, subjects with CA needed to be caught or took a step in at least one of the trials attempted. Loss of balance occurred in every attempt in 4 subjects, on the first attempt only in one participant and on the second trial only in one other subject (2 subjects only performed 1 trial: one with and one without LOB). In contrast, standing on a Tilt-Down moving surface was not as challenging for subjects with CA in that subjects were caught or took a step in only 2 trials (2 different individuals, 1 on the first and 1 on the second attempt). Control subjects easily adapted to the slowly moving surface as they remained stable in all trials. There was no relationship between loss of balance during the surface tilts and disease severity (total SARA score $r_s = -0.15$, $p > 0.05$).

Control subjects maintained balance on the up- and down-rotating surface with minimal change in their postural alignment except for ankle rotation that followed the surface motion (5°), e.g. an ankle strategy, in which ankle rotation was larger than the trunk motion described below. Subjects with CA who were able to maintain balance on the up-moving surface generated a hip strategy, as seen in Fig. 2B (No LOB). This hip strategy was expressed by a forward trunk tilt from initial position, combined with a backward tilt of the thigh segment. When subjects with CA lost their balance (No LOB) during the Tilt-Up incline, they reoriented their trunk backward instead of forward to maintain balance.

There was no difference in initial trunk, thigh or shank segment orientation between groups ($p > 0.05$) and differences were only observed in trunk segment orientation (as reflected in Fig. 2B). In fact, during toes-up surface tilting, the peak trunk extension was larger in CA subjects who lost their balance (9°) in contrast to control subjects who only moved slightly (3°, $U=5$, $Z=3.9353$, $p < 0.001$). In addition, trunk peak extension velocity during the toes-up tilt was larger in CA subjects with loss of balance in contrast to control subjects (17.6 mm/s vs. 7.2 mm/s, $U=16$, $Z=3.3942$, $p < 0.001$).

Postural stability on a tilted surface in subjects with cerebellar ataxia

In all conditions, subjects with CA had larger COP sway, as measured by the standard deviation of their COP displacement, compared to control subjects (Fig. 1C). Sway was more than 2-fold that of control subjects (118% larger with a main effect of group: $F(1,12)=73.980$ $p < 0.001$). Both subjects with CA and control subjects adjusted their COP position backward when standing on the incline (Fig. 1C [$F(4,48)=7.957$ $p < 0.05$, incline (I and II) vs. baseline and the post-incline periods]).

DISCUSSION

This study showed that adapting to a very slow, low amplitude, toes up-tilting incline is compromised in subjects with cerebellar ataxia, as reflected by their hypermetric trunk extension responses, frequent loss of equilibrium. Postural control during these very slow

surface rotations are not reflexive but involve on-line sensory feedback and integration from the somatosensory and vestibular systems.

Subjects with CA had more difficulty maintaining balance on an Up- than Down-moving surface rotation. These findings are consistent with previous studies showing that the backward moving direction (ie, tilt-Up) is most challenging for upright standing subjects with CA [4, 5]. The reason for more difficulty balancing during toes up than toes down surface tilts is not known but may be related to the relative biomechanical difficulty in using tibialis anterior muscles and hip extensors to prevent backward displacement of the COM behind the heels compared to using gastrocnemius and soleus muscles and hip flexors to prevent forward displacement of the COM over the toes [18, 19]. Ankle range of motion in dorsiflexion is also smaller compared to plantarflexion [20] and the COP in normal upright stance is located more posteriorly than anteriorly in relation to the foot limits of stability [21]. In addition, the downward tilt in this experiment was a movement going from dorsiflexion to a neutral position and not an actual plantarflexion (i.e., not challenging the COP anteriorly) which could also explain the additional difficulty in maintaining balance in the Up-moving surface rotation.

Interestingly, CA subjects more easily adapted to a fast-moving surface ($60^\circ/\text{s}$) [4] in contrast to our slower tilt velocity protocol ($1^\circ/\text{s}$), suggesting that subjects with CA have more difficulty regulating continuous sensory feedback control of postural orientation than in triggering a fast, automatic postural response [7]. Recent sensory feedback models explain the scaling of muscle activity due to perturbations at different accelerations and velocities [22]. The loss of equilibrium we observed in subjects with CA could be due to deficiencies in somatosensory and vestibular feedback processing and to inappropriate scaling of online postural corrections, especially in the trunk (ie, accumulation of errors as observed in studies of upper-limb reaching [11]). Alternatively, use of vestibular input as a sensory reference for vertical orientation may have been compromised by impaired vestibulo-cerebellar function, which was not tested.

Falls in subjects with CA standing on a slow up-moving incline seemed to be caused by a change in postural alignment characterized by an early backward reorientation of the trunk segment. As illustrated in Fig. 2B, right panel, after 1° of upward surface tilt, cerebellar subjects who lost their balance, showed large backward movements of the trunk and thigh, in contrast to control subjects and CA subjects who tilted their trunks forward to maintain balance. Early hypermetric shifts in the trunk segmental orientation in individuals with CA has previously been observed in trunk flexion during fast surface tilts [4, 7]. In the present study, an extension of the trunk was observed in subjects with CA that lost their balance while subjects who were able to maintain balance reoriented their trunk forward (Fig. 2B right panel). This early extension of the trunk in subjects with CA might indicate an inability to coordinate multiple joints simultaneously resulting in lack of global control of the trunk in space [23, 24] and/or the result of error accumulation in postural alignment adjustments [11]. It is not clear whether the extension observed in the trunk is an active reorientation of the segment to follow the support surface or whether the lack of flexion adjustment in the trunk was responsible for the backward reorientation of the trunk segment leading to a loss of balance.

There was no difference in mean COP position between groups as both controls and subjects with CA adjusted their position to the incline similarly. Subjects with CA have been found to have increased sway in comparison to controls and our findings are consistent with previous studies [3, 25, 26]. Postural sway in subjects with CA did not further increase when standing on the inclined surface. Together with the hypermetric trunk responses observed, increased sway variability may still further amplify a less favorable position to maintain postural equilibrium when orientation of the standing surface changes, especially if subjects with CA sway closer to their limits of stability.

The relatively small number of subjects and various etiologies of the subjects with CA limits the generalization of these results. Although we could not find a learning or familiarization pattern in our dataset, we cannot exclude that participants did not learn the task because of the limited number of trials and the same test order (flat, up-wards tilt and tilt back down to flat). Future studies should investigate whether subjects with CA can learn to maintain balance with repeated trials and whether falls and postural instability in subjects with CA depend on the speed or amplitude of the surface perturbation. In addition, a better understanding of the role of the visual system in adapting to a slow moving support surface with CA would help provide important information that could help guide compensatory strategies in rehabilitation. Finally, it would also be relevant to determine whether the location of the cerebellar lesion affects the ability to maintain balance on a slow moving support surface.

This study demonstrates that individuals with CA experience more falls arising more from an inability to maintain trunk orientation vertical when standing on a rotating surface rather than changes in postural sway. These hypermetric extension responses seem to be caused by a deficit in sensory feedback control during the online adaptation to slow and long perturbations likely resulting in error accumulation.

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ABBREVIATIONS

ABC	Activities specific Balance Confidence scale
BESTest	Balance Evaluation Systems Test
CA	cerebellar ataxia
COM	center of mass
COP	center of pressure
DTR	deep tendon reflex
LOB	loss of balance
MSA-C	Multiple System Atrophy cerebellar dysfunction subtype

SAOA	Sporadic adult-onset ataxia
SARA	scale for the assessment and rating of ataxia
SCA	Spinocerebellar ataxia

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Figure 1.

A. Illustration of the surface position during one trial. The trials started with a 1-minute baseline period of quiet stance followed by a 5° toes-up tilt. The support surface was held in the up position for 2.5 minutes and followed by a 5° toes-down tilt. Thereafter, the surface was held horizontal for a minimum of 3 minutes. Shaded areas represent the five, 45 seconds intervals before, during and after the inclines used for analysis. B. Representative example of the center of mass (COM) and center of pressure (COP) displacement during tilting in a representative subject with cerebellar ataxia (grey) and in a control subject (black). C. Top row shows example stabilograms from a control and a cerebellar subject for the duration of each interval presented. Below are mean position and sway (i.e., 95% Confidence interval [C.I.]) of the COP during the five intervals. Data shown is from all subjects and all trials with intervals with loss of balance removed. * denotes significant differences of main effects.

A. Examples of segment reorientation during up-moving tilt

No loss of balance (no LOB) **Loss of balance (LOB)**

B. Mean segment reorientation during up-moving tilt

Figure 2.

A. Examples of segment orientation (right-side markers illustrated only) in one control subject and one subject with cerebellar ataxia. Each data point represent the raw data at each second during the surface tilt corresponding to each degree of surface tilt-up rotation. The cerebellar subject lost balance and took a step (with the left foot). B. Mean group segment orientation of the shank, thigh and trunk segments are shown on the left at initial position (0° , light grey) and at 5° upward tilt of the surface in controls and subjects with cerebellar ataxia that maintained balance (No LOB, 3 trials in 3 different subjects). Subjects with cerebellar ataxia who lost their balance (LOB, 11 trials in 7 different subjects) are at 2° of upward tilt of the surface corresponding to pre-balance loss. On the right, mean shank (bottom), thigh (middle) and trunk (top) segment orientation at each degree (0 to 5°) during up-moving tilt of the surface in subjects with cerebellar ataxia who lost their balance (LOB, grey), who did not lose their balance (No LOB, dashed grey) and controls (black with grey shaded area corresponding to $\pm$ SD of the control subject data).

Table 1

Cerebellar ataxia subject characteristics.

Patient	Diagnosis	Duration ¹ (years)	Sex	Age (years)	SARA					BESTest ² (%)	ABC ² (%)
					Total (/40)	Gait (/8)	Stance (/6)	Sitting (/4)			
1	SCA-6 ⁵	3	F	48	8.5	2	2	0	70	78	
2	SAOA	3	F	58	11	2	2	0	82	71	
3	SCA-6 ⁵	9	F	58	12	2	3	0	58	38	
4	SCA-15 ³	> 20	F	65	14.5	3	2	0	51	26	
5	MSA-C ⁴	2	F	68	14.5	3	3	1	64	33	
6	SCA-6	9	M	64	15	3	3	1	57	70	
7	SAOA	5	F	49	17.5	2	3	1	68	8	
8	SAOA ⁶	4	M	56	18	5	3	1	48	md	

¹ Symptom onset

² 0% = worst performance and 100% = best performance

³ SCA-15 suspected, not confirmed genetically (available on a research basis only) but consistent symptoms, duration and family history

⁴ Sleep apnea (autonomic feature)

⁵ Slightly brisk DTR

⁶ Brisk DTR with up going toes

ABC= Activities specific Balance Confidence Scale, BESTest= Balance Evaluation Systems Test, DTR= Deep Tendon Reflexes, MSA-C=Multiple System Atrophy cerebellar dysfunction subtype, SCAO = Sporadic adult-onset ataxia, SARA= Scale for the assessment and rating of ataxia (score of 0=normal), SCA = Spinocerebellar ataxia, md = missing data.

Table 2

Loss of balance (LOB) during the UP and DOWN tilt in subjects with cerebellar ataxia and in healthy controls when standing on an inclined surface.

	Tilt-UP		Tilt-DOWN	
	LOB at least once	LOB on all attempts	LOB at least once	LOB on all attempts
Cerebellar	7/8 (88%)	5/8 (63%)	2/8 (25%)	0/8 (0%)
Controls	0/8 (0%)	0/8 (0%)	0/8 (0%)	0/8 (0%)