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ARTICLE

Reactive stepping after a forward fall in people living with incomplete spinal cord injury or disease

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Abstract

Study design Cross sectional.

Objectives To compare the reactive stepping ability of individuals living with incomplete spinal cord injury or disease (SCI/D) to that of sex- and age-matched able-bodied adults.

Setting A tertiary SCI/D rehabilitation center in Canada.

Methods Thirty-three individuals (20 with incomplete SCI/D) participated. Participants assumed a forward lean position in standing whilst 8–12% of their body weight was supported by a horizontal cable at waist height affixed to a rigid structure. The cable was released unexpectedly, simulating a forward fall and eliciting one or more reactive steps. Behavioral responses (i.e., single step versus non-single step) were compared using a Chi-square test. The following temporal parameters of reactive stepping were compared using *t*-tests: the onset of muscle activation in 12 lower extremity muscles (six per limb) and step-off, step contact and swing time of the stepping leg.

Results Behavioral responses were significantly different between groups ($\chi^2 = 13.9$ and $p < 0.01$) with participants with incomplete SCI/D showing more non-single step responses (i.e., multi-steps and falls). The onsets of muscle activation were more variable in participants with incomplete SCI/D, but only the stepping tibialis anterior showed a significantly slower onset in this group compared with able-bodied adults ($t = -2.11$ and $p = 0.049$). Movement timing of the stepping leg (i.e., step-off, step contact, and swing time) was not significantly different between groups.

Conclusions Reactive stepping ability of individuals with incomplete SCI/D is impaired; however, this impairment is not explained by temporal parameters. The findings suggest that reactive stepping should be targeted in the rehabilitation of ambulatory individuals with SCI/D.

Introduction

Spinal cord injury or disease (SCI/D) affects ~10.5 out of every 100,000 people worldwide [1]. SCI/D results from damage to the spinal cord either due to a traumatic (e.g., motor vehicle accident or fall) or a nontraumatic (e.g., tumor or infection) event. The resulting sensorimotor deficits make everyday movements, such as standing and walking, difficult. In particular, it can be challenging for individuals with SCI/D to maintain their balance, defined here as maintaining the vertical projection of one's center of mass (i.e., the weighted average position of all parts of the body according to mass) within the base of support (i.e., the area of support beneath a person or object, including points of contact) [2, 3], during standing and walking tasks [4–6]. Indeed, up to 75% of individuals with incomplete SCI/D fall at least once annually and most of these falls occur while walking [7–9].

Balance control during standing and walking is essential for stability and preventing falls. When a disturbance to one's balance is predictable, proactive balance strategies are used [10]. For example, when one

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knowingly begins walking on a slippery surface, one may walk slower, with smaller steps and a flatter foot-floor angle [11]. However, when a perturbation (i.e., slippery surface) is unexpected and one slips, reactive balance responses are required to prevent a fall [10]. A common response to a loss of balance when standing or walking is taking one or more rapid, reactive steps [12]. The purpose of reactive stepping is to increase the size of the base of support, maintaining the center of mass within it, for a balance recovery reaction [13].

Poor reactive stepping is related to an increased likelihood of falls in individuals who have experienced a stroke [14] and older adults [15]; however, it is unknown if and how reactive stepping ability is impaired in individuals with incomplete SCI/D. Reactive stepping ability can be quantified with the lean-and-release test [16]. This test simulates a forward fall from standing and has been used to evaluate reactive stepping ability in older adults [17] and individuals who have experienced a stroke [14]. It requires individuals to adopt a forward lean position with ~10% of their body weight supported through a horizontal cable attached at waist height. The unexpected release of the cable provokes one or more reactive steps. The lean-and-release test is a safe and standardized measure used to evaluate reactive stepping parameters, such as behavioral response, the time from the release to the initiation of the reactive step (i.e., foot-off) and the swing duration of the stepping leg [18]. These behavioral and temporal parameters have been used to characterize reactive stepping deficits in older adults [17] and individuals who have experienced a stroke [14, 19].

Our objective was to compare the reactive stepping ability (i.e., behavioral and temporal parameters) of individuals with incomplete SCI/D to that of sex- and age-matched able-bodied (AB) adults using the lean-and-release test. We hypothesized that compared with the AB participants, individuals with incomplete SCI/D would take more steps to recover their balance and have a slower response to the release as demonstrated by the studied temporal parameters. The findings will have important implications for clinical practice, such as suggesting whether or not reactive stepping ability should be addressed in the rehabilitation of individuals with incomplete SCI/D.

Methods

In this cross-sectional study, participants with incomplete SCI/D and AB matches attended one testing session at the Lyndhurst Centre, KITE, Toronto Rehabilitation Institute-University Health Network (TRI-UHN).

Participants

Individuals with incomplete SCI/D were recruited through flyers posted at the Lyndhurst Centre, KITE, TRI-UHN, and the Centre's central recruiting database. This database contains the names of previous inpatients of the Lyndhurst Centre who consented to receive notifications of research studies. Interested individuals with SCI/D who met the following criteria were included in the study: (1) ≥18 years old; (2) traumatic or nonprogressive, nontraumatic cause of SCI/D; (3) > one year since injury or onset of neurological symptoms; (4) American Spinal Injury Association Impairment Scale (AIS) C or D; (5) moderate level of trunk control (i.e., score of ≥2 on the Berg Balance Scale Reaching Forward Task [20] or the ability to reach forward >5 cm with an outstretched arm in standing); (6) ability to stand independently for > 30 s (s) without assistance; and (7) no condition, other than the SCI/D, that affected balance or walking ability (e.g., stroke and vestibular disorder). Individuals with SCI/D were excluded if they had: (1) severe contractures or spasticity in the lower extremities that prevented one's ability to maintain an upright posture; (2) a pressure injury of grade >2 on the pelvis or trunk, where the safety harness was donned; and (3) a history of a lower extremity fragility fracture, suggesting low bone density.

AB participants, who were recruited through emails sent to listservs of the Lyndhurst Centre, were included based on the following criteria: (1) the absence of a condition or injury that affects balance or walking; (2) no history of a lower extremity fragility fracture; (3) the ability to ambulate independently without a gait aid or ankle-foot orthosis. The AB participants were sex- and age-matched (±3 years) to the participants with incomplete SCI/D.

Sample size calculation

Data from AB adults [18] and individuals who had experienced a stroke [14] were used for the sample size calculation as reactive stepping ability had not previously been investigated for individuals with SCI/D. Foot-off timing, an alpha of 0.05, and a power of 0.8 resulted in 13 participants per group [21].

Experimental procedure

Participants donned a safety harness and stood on a dual force plate with each foot on a separate force plate component, each measuring 251 × 502 mm (AccuSway Dual, Advanced Mechanical Technology Inc., Watertown, USA) (Fig. 1). An additional dual force plate was placed anteriorly to the force plate on which the participants stood. A horizontal cable at waist height attached the harness to the release mechanism

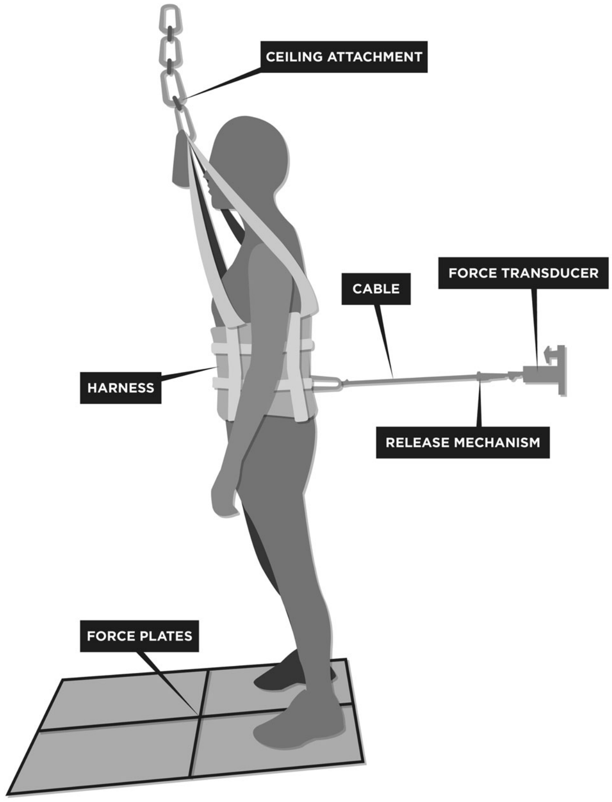

Fig. 1 Set-up of the lean-and-release test. An image of a participant in the forward lean position

and a force transducer (Fig. 1). Participants were instructed to lean forward from the ankles, not the hips; distribute weight evenly between both legs; and do what was necessary to recover his/her balance, if and when the release occurred. Participants were instructed to lean forward until a researcher confirmed that 8–12% of their body weight was supported through the cable, which was measured using the force transducer. This target value was chosen to control for the consistency of the size of the perturbation relative to body weight, which aligned with previous work on individuals who had experienced a stroke [14]. A researcher stood behind and to the side of the participant and manually triggered the release. Upon the release, participants fell forward eliciting reactive stepping. In the event of a loss of balance, participants were supported by the harness and ceiling attachment in addition to receiving physical assistance from one of the researchers. Participants were not instructed to take the minimum amount of steps possible; their natural responses were observed. Participants performed up to ten lean-and-release trials that consisted of participants leaning for up to 30 s, as tolerated. Three false trials (i.e., mechanism was not released) were interspersed amongst the lean-and-release trials in an attempt to reduce the engagement of proactive balance strategies.

Data acquisition

Birth month and year, sex, weight, and fall history in the previous three months were collected from each participant. A fall was defined as coming to rest on the ground or another lower surface unintentionally [22]. Participants with incomplete SCI/D were asked to provide the following additional information: AIS score, neurological level of injury, time post-injury, cause of injury, and gait aid and/or braces used for daily ambulation. Participants with incomplete SCI/D were also asked if they had a fear of falling, defined as a lasting concern about falling resulting in avoidance or curtailing of activities despite being capable of doing them [23].

Behavioral responses to the lean-and-release test were observed and documented by a researcher near to the participant for each trial. Behavioral responses were classified as a single step (i.e., a single foot-off with a single foot contact, with a second step of the opposite foot permitted only for realignment), a multi-step (i.e., a single foot-off with a single foot contact followed by at least one more step of the same or opposite foot necessary to recover balance), or a fall (i.e., inability to recover balance without external assistance).

Surface electromyography (EMG) (Bagnoli, Delsys Inc., Natick, MA, USA) was used to record the onset of muscle activation of lower extremity muscles relative to timing of the release (i.e., <1 N of body weight through the cable); this temporal parameter is henceforth referred to as reaction timing. EMG recordings were obtained from six lower extremity muscles bilaterally: tibialis anterior (TA), soleus (SOL), medial gastrocnemius (MG), rectus femoris (RF), vastus lateralis (VL), and biceps femoris (BF).

The two dual force plates were used to record the movement timing of the stepping response relative to the timing of the release. Foot-off of the stepping leg occurred when <1% of the participant's body weight registered on the respective posterior force plate. Foot contact of the stepping leg occurred when >1% of the participant's body weight registered on a force plate (posterior or anterior force plate depending on the distance of the reactive step). Swing time was defined as the time between foot-off and foot contact of the stepping leg.

Prior to the lean-and-release test, gait speed was measured in order to provide descriptive information about the mobility status of participants. An electric gait mat (Zeno Walkway, Zenometrics LLC, Havertown, PA, USA) was used to measure gait speed. Participants walked two lengths across the mat (14 ft) at their preferred walking speed with starting and end points and turns occurring off the mat. Gait speed was provided as an output from the ProtoKinetics Movement Analysis Software v. 508c2.

Data analysis

Demographic and injury-related data were reported as frequency counts or mean and standard deviation, as appropriate. To summarize the behavioral responses of each group, the total number of trials in which single step, multi-step, and fall responses was observed were reported for each group. A Chi-Square test was used to identify group differences of the behavioral data, comparing the proportion of single step and non-single step (i.e., multi-step or fall) responses. This binary measure of behavioral responses was used in previous clinical research literature [24].

Analog data were collected at a sampling frequency of 2000 Hz (Cortex ver. 4, Motion Analysis Corp., CA, USA). The force plate and force transducer data were filtered using a 4th order low-pass Butterworth filter with the cut-off frequency of 4 Hz. EMG data were full-wave rectified. An integrated protocol algorithm, adapted from previous work [25, 26], was used to detect the onset of EMG activation of each muscle in the stepping and supporting legs. The average of the entire 30-s rectified EMG signal was calculated, including the period of inactivity prior to the release and the period of EMG activation during the reactive stepping phase. The algorithm integrated the difference between the rectified signal and the average value. The integrated signal decreased in amplitude until the onset of EMG activity, where the amplitude started to increase. The lowest point of the integrated difference signal was detected as the onset of EMG activity. One author (KC) manually checked the EMG activation plots to confirm or revise the automatically detected onset points. The plots without an identifiable onset were rejected and not included in the analysis (see Fig. 2b). Of the total 348 EMG mean onsets across all participants, 18 (5.2%) were rejected. One participant with incomplete SCI/D was excluded from the EMG onset analysis because there were no identifiable onset points out of the trials performed.

A Shapiro–Wilk test determined the normalcy of the reaction timing (i.e., EMG onset) and movement timing (i.e., foot-off, foot contact, and swing duration) data of the stepping leg. As all data sets met the assumption of normality, parametric statistical tests were used. We first compared reaction and movement timing between single step responses and the first step of multi-step responses to determine whether the temporal parameters of the stepping leg differed between these two types of responses. As there were no differences in reaction and movement timing between responses for both incomplete SCI/D and AB matched groups ($p = 0.08$–0.89), single step and multi-step responses were analyzed collectively for each group. Independent samples t-tests were used to compare the reaction and movement timing between the two groups of participants. For all statistical tests, alpha was set to 0.05 and SPSS 25 (IBM, Armonk, NY, USA) was used.

Results

Participants

Twenty individuals with incomplete SCI/D participated; however, four of these participants were unable to sufficiently recover their balance (i.e., fell on every trial) during the lean-and-release test; thus, their data were excluded from further analyses (Table 1). Therefore, the following results included 16 individuals with incomplete SCI/D (13 females, 3 males; mean age 54.3 (13.2) years). The mean (SD) time post-injury for the group was 6.2 (9.3) years, and nine (56.3%) participants had a nontraumatic cause of SCI/D. The neurological level of injury ranged from C1-L5. Seven participants (43.8%) with SCI/D reported experiencing at least one fall in the past 3 months and 10 (62.5%) reported having a fear of falling. See Table 1 for participant characteristics.

Thirteen AB matches (nine females, four males; mean age 58.1 (11.1) years) participated. None of the AB participants experienced a fall in the three months prior to participation and none reported having a fear of falling.

Behavioral response

All participants with incomplete SCI/D were able to complete 9–10 trials of the lean-and-release test with the exception of two participants who were only able to complete seven and four trials. Participants with SCI/D were able to reach the 8–12% body weight support threshold for 94.1% of trials. All AB participants completed ten lean-and-release trials and reached the body weight support threshold for all trials performed. On average, participants with incomplete SCI/D showed more multi-steps and falls than the AB matches (Table 2). A significant difference in the distribution of single step versus non-single step responses was found between groups ($\chi^2 = 13.9$ and $p < 0.01$).

Reaction timing

With respect to reaction timing, the AB participants showed a consistent pattern of muscle activation during the stepping response (Fig. 2a for single participant data; Fig. 3a for group data). Following the release, the stepping SOL and MG were activated to initiate the step. Activation of the stepping TA, BF, and in some cases the RF, followed to swing the stepping leg forward and clear the ground. Simultaneously, muscles of the supporting limb were

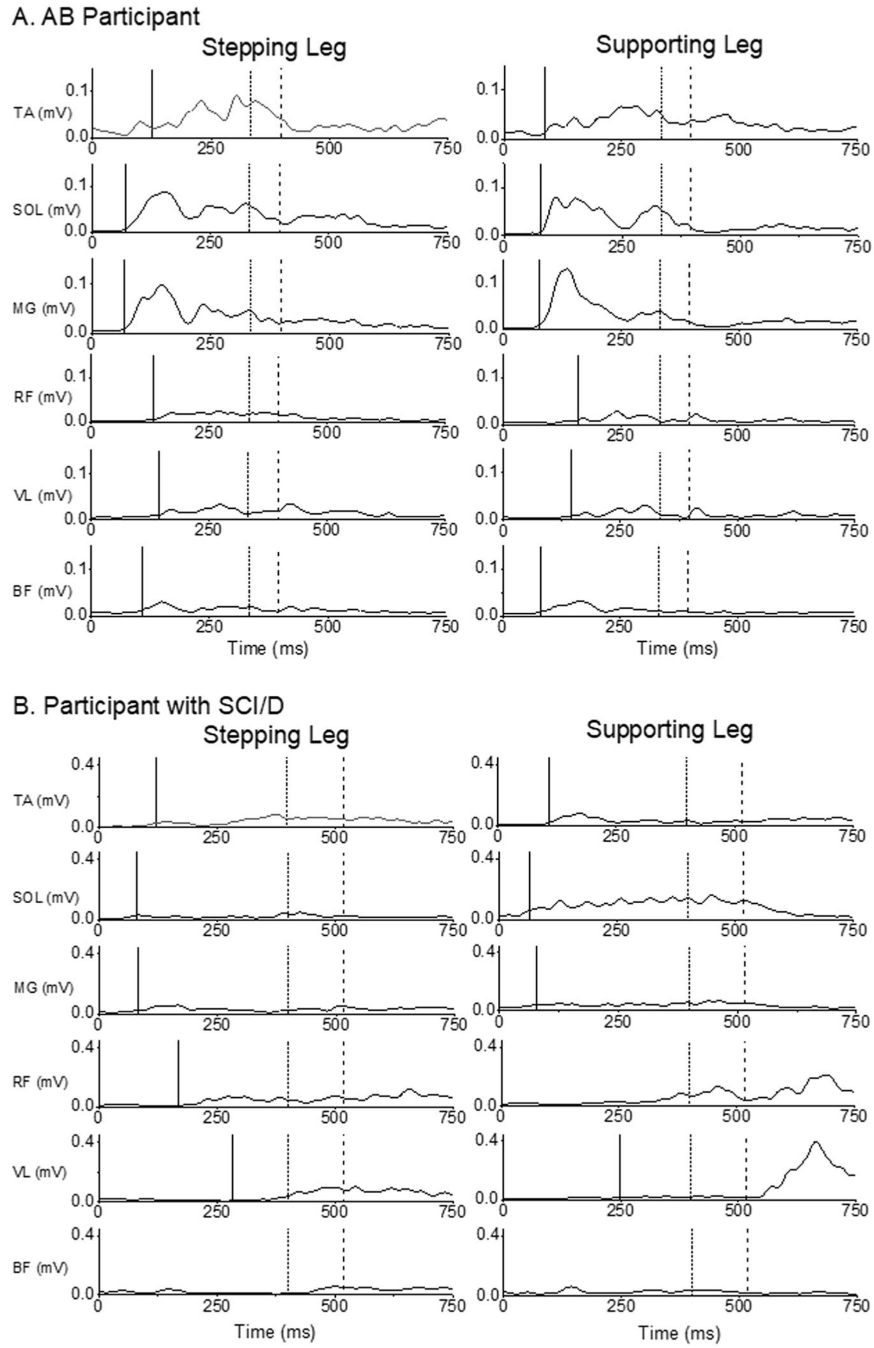

Fig. 2 Activation pattern of six lower extremity muscles, bilaterally, for a single participant. Average activation pattern of the stepping (left plots) and supporting (right plots) legs are shown for: **a** an able-bodied (AB) participant (female, 56 years old) and **b** a participant with incomplete spinal cord injury/disease (SCI/D) (male, 70 years old). Time 0 s signifies the point of release. First vertical line (solid) identifies the average onset of EMG activation. Second vertical line (dashed) identifies the average foot-off timing. Third vertical line (dotted) identifies the average foot contact timing over ten trials

activated (RF, SOL, and BF, followed by MG, TA, and VL) as the limb accepted weight.

In contrast there was greater variability in the average EMG onset of the participants with SCI/D (compare size of error bars in Fig. 3a, b). However, there were a few exceptions; the SOL and MG bilaterally, and the supporting RF, were consistently activated early after the release to shift weight from the stepping limb onto the supporting limb.

The onset of the stepping TA in individuals with SCI/D occurred significantly later (mean difference = 38.8 ms (ms), 95% CI 0.16–78 ms, $p = 0.049$, $t = -2.11$) later than that of the AB participants. The onsets of the remaining eleven muscles were not significantly different between groups.

Movement timing

The mean and standard deviation of the timing of foot-off, foot contact, and swing duration for both groups are reported in Table 3. There were no significant differences found between groups.

Table 1 Demographics of the participants with incomplete SCI/D

	Sex	Age (years)	Time post-injury (years)	Level of injury[a]	Cause of injury	LE strength (/120)[b]	Gait speed without aid (m/s)	Usual walking aid	mini-BESTest Score (/28)	Fall history[c]	Fear of falling
PBT01	F	61	1	C3	Surgery	83.5	0.71	4WW	10	1	Y
PBT04	F	54	1	T10	Surgery	75	0.4	4WW	4	0	N
PBT05	F	32	3.5	C4	Stenosis	92	1.26	None	25	1	N
PBT06	M	70	1.8	T1	Osteomyelitis	104.5	1.24	Cane	19	0	N
PBT08	M	60	3.2	C5	Bike fall	115	1.28	None	25	0	N
PBT10	F	43	3.9	T6	Surgery, meningioma	102.5	1.05	None	24	1	Y
PBT12	F	87	2.6	T4	Meningioma	94	0.89	Cane	22	0	N
PBT13	F	57	2.9	C2	Transverse myelitis	88	0.72	Cane	17	0	Y
PBT14	F	59	1.1	C1	Fall	81.5	0.43	4WW	4	0	Y
PBT16	F	55	9.1	C5	Fall	94	1.17	Cane	20	1	Y
PBT17	F	38	1.3	T4	AVM	74.5	0.94	4WW	5	1	N
PBT18	F	54	13	C4	Car accident	78.5	0.81	Cane	14	0	Y
PBT20	F	56	1.2	L5	Surgery	72.5	0.87	None	20	0	Y
PBT23	F	38	6.8	T11	Gym accident (fall)	91	1.03	None	26	1	Y
PBT24	M	51	7.9	C3	Gym accident (trampoline)	97	1.29	Poles or 4WW	15	0	Y
PBT25	F	53	39	C4	Fall	76	0.95	Poles	18	1	Y
Mean (SD) or count	13F 3M	54 (13)	6.2 (9.3)			89 (12)	0.94 (0.28)		17 (7.5)	7	10
PBT02[d]	M	64	6.8	T6	Staph infection	80	0.18	4WW	6	0	N
PBT15[d]	M	49	21	T5	Tumor	76	0.41	Canes	1	12	N
PBT19[d]	M	56	16.3	L1	Virus	66.5	0.21	2WW	0	0	Y
PBT21[d]	F	69	4.8	C5	Virus	72	0.42	4WW	3	0	N

LE lower extremity, *mini-BESTest*, mini-Balance Evaluation Systems Test, *C* cervical, *T* thoracic, *L* lumbar, *AVM* arteriovenous malformation, *4WW* 4-wheeled walker, *2WW* 2-wheeled walker

[a]Denotes neurological level of injury

[b]LE strength measured with manual muscle testing of 12 muscles per LE. Maximum score per muscle is 5, resulting in a total score of 120 for 2 LE

[c]Denotes retrospective falls in the previous 3 months

[d]Denotes participants excluded from data analyses, unable to walk without gait aid

Table 2 Behavioral responses by group

	Behavioral response		
Group	Single step	Multi-step	Fall
AB matches	55 (45)%	45 (45)%	0%
SCI/D	29 (39)%	66 (41)%	5 (12)%

Percentage (±1 standard deviation) of trials that showed single step, multi-step, and fall responses by group

AB able-bodied, *SCI/D* spinal cord injury/disorder

Discussion

In this study, we found that reactive stepping ability was impaired in participants with incomplete SCI/D compared with age- and sex-matched AB individuals when considering the behavioral outcome of this test, but in contrast to work done in other populations, the temporal parameters did not differ with the exception of the onset of the stepping TA. Those with incomplete SCI/D demonstrated a higher occurrence of multi-step responses and falls, and the onset of their stepping TA was delayed, during the lean-and-release test. The delay in onset of the stepping TA may be explained by the fact that there is greater motor cortex activity during dorsiflexion compared with plantarflexion, which is thought to be more peripherally controlled [27–29]. These findings were not surprising given that the spinal cord plays an important role in balance reactions [30]. Hence, our hypotheses were only partially supported;

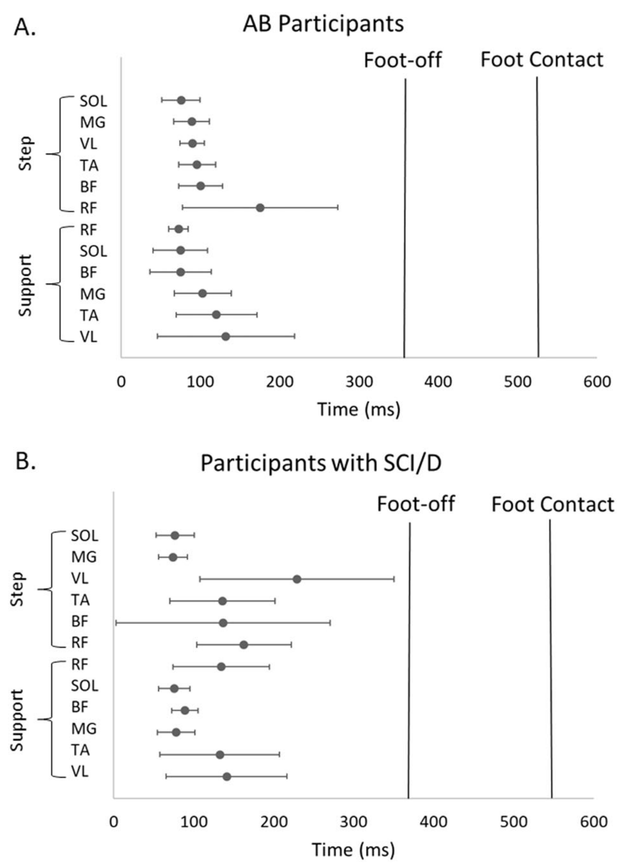

Fig. 3 Average timing of the onset of muscle activation by group: **a** able-bodied (AB matches); **b** participants with incomplete spinal cord injury/disease (SCI/D). Muscles are plotted in order of activation; the first six muscles are of the stepping leg and the latter six are of the supporting leg. Error bars reflect the standard deviation of each mean value. step, stepping leg; support, supporting leg

Table 3 Mean (SD) of timing of foot-off, foot contact, and swing duration by group

	AB Matches	SCI/D	*p*-value
Foot-off (ms)	366 (89)	376 (70)	0.74
Foot contact (ms)	528 (127)	558 (94)	0.46
Swing (ms)	160 (50)	183 (51)	0.24

AB able-bodied, *SCI/D* spinal cord injury/disorder

individuals with incomplete SCI/D required more steps to regain their balance, but the majority of temporal parameters did not differ between groups.

Similar to our findings in individuals with incomplete SCI/D, ineffective stepping responses have been documented in some individuals who have experienced a stroke. Specifically, individuals living with stroke have shown inadequate foot clearance or a complete absence of a step attempt during the lean-and release test, resulting in a fall [13, 18, 31]. Likewise, healthy older adults have a greater tendency to take multiple steps [32–34] or fail to recover their balance altogether [35] compared with their younger counterparts. Further, older adults had a reduced step length compared with younger AB adults during reactive stepping [36–39]. Short step lengths may also explain why our participants with incomplete SCI/D showed a greater proportion of multi-steps and falls compared with AB individuals. This behavioral difference was not explained by deficits in movement timing. Rather, the participants with incomplete SCI/D may have taken shorter steps, requiring multi-step responses to reposition the center of mass within the base of support following the release. The inability to execute a sufficiently sized compensatory step was recently reported in another study, where participants with incomplete SCI/D were found to have an impaired ability to widen their lateral margin of stability (i.e., the distance between their extrapolated center of mass and the lateral border of their base of support) when attempting a reactive step in response to a slip perturbation while walking [40]. It is possible that the participants in our study also took small compensatory steps (i.e., short step length); however, 3D motion analysis would be required to confirm this suggestion.

The lean-and-release has been used in clinical practice with the stroke population [19] and our findings suggest that it may prove useful in SCI/D rehabilitation practice. This test has the potential to discriminate between individuals with SCI/D and AB individuals; however, based on our study results we suggest a noninstrumented version of the lean-and-release test would suffice for clinical practice. Differences between the AB participants and participants with SCI/D were primarily seen in the behavioral response, suggesting that this parameter may be the most valid; however, this will need to be confirmed with psychometric testing. In other populations, this variable has shown to be predictive of falls [13, 17]. As the behavioral component of the lean-and-release test does not require equipment or training and takes little time to complete, the clinical utility of a noninstrumented version is likely high [41]. Despite the importance of reactive stepping for fall prevention and balance recovery, it is not commonly assessed in clinical practice [42–44].

Our findings suggest that the lean-and-release test is appropriate for a subset of the incomplete SCI/D population, specifically individuals who are able to take more than one step independently. The four individuals with incomplete SCI/D who were unable to complete the lean-and-release test required a gait aid for ambulation. Further, their preferred gait speeds were slower than those participants who were able to complete the lean-and-release test (0.18–0.42 m/s versus 0.40–1.29 m/s).

Our sample of participants does not represent the Canadian SCI/D population in that a higher proportion of females and nontraumatic causes of SCI/D were included. Despite the higher proportion of males that experience SCI/D [45], a greater number of females were enrolled in this study. One possible explanation is that females have a greater concern about falling. Studies involving older adults and individuals who have experienced a stroke found that females were more likely to have a fear of falling compared with their male counterparts [46–49]. Our sample also had a greater proportion of individuals with nontraumatic than traumatic SCI/D. In previous literature, the prevalence of traumatic SCI/D was reported as greater than nontraumatic [45], but this trend is shifting [50, 51].

The incidence proportion of falls reported for our participants (i.e., 43.8% reported falling at least once in the past 3 months) is smaller than the incidence proportion reported in the majority of other studies involving individuals with incomplete SCI/D [52]. The difference is likely due to the duration of fall monitoring; while we queried the past 3 months of participants' lives, many previous retrospective studies have queried the past 6 or 12 months [52]. Hence, our findings likely underestimate the incidence proportion of falls among our participants.

One limitation of this work is that participants were aware that the release would occur, making it difficult to truly evaluate reactive balance control. We attempted to reduce the initiation of proactive balance strategies by including false trials that were interspersed within the release trials, and by randomizing the timing of the release from trial to trial.

In conclusion, individuals with incomplete SCI/D have a deficit in reactive stepping ability compared with age- and sex-matched AB adults, as exhibited by the greater occurrence of non-single step responses. However, this deficit is not due to differences in temporal parameters of the stepping response.

Data archiving

De-identified data may be available upon request and approval from the institutional Research Ethics Board.

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Author contributions KC was responsible for designing the collection protocol, recruiting able-bodied adults, collecting and analysing data, interpreting results, and writing the paper. JWL was responsible for the analysis of the data. He contributed to the designing of the collection protocol, collecting of data, and providing feedback on the paper. JU was responsible for screening potential participants with SCI/D. She contributed to collecting data and providing feedback on the paper. JY contributed to collecting data and providing feedback on the paper. KM was responsible for designing the collection protocol. He provided feedback on the analytical methods and provided feedback on the paper. KEM was responsible for creating the research questions and study design, designing the collection protocol, recruiting and screening participants with SCI/D, interpreting results, and writing the paper.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of ethics Ethical approval for the study was obtained from the Research Ethics Boards of the University Health Network and the University of Toronto. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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