Title: Between-limb synchronization for control of standing balance in individuals with stroke

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ABSTRACT

Background: During standing, forces and moments exerted at the feet serve to maintain stability in the face of constant centre-of-mass movement. These actions are temporally synchronized in healthy individuals. Stroke is typically a unilateral injury resulting in increased sensori-motor impairment in the contra-lesional compared with the ipsi-lesional lower-limb, which could lead to reduced between-limb synchronization for control of standing balance. The purpose of this study is to investigate between-limb synchronization of standing balance control in individuals with stroke; a potentially important index of control of upright stability.

Methods: Twenty healthy controls and 33 individuals with unilateral stroke were assessed. Stability was assessed during a 30-second quiet standing trial by measuring data from two force plates (one per foot). Limb-specific centre of pressure was calculated. Between-limb synchronization was defined as the coefficient of the correlation between the left and right foot for both the antero-posterior and medio-lateral centre of pressure time series. Synchronization, weight-bearing symmetry, and root mean square of the total centre of pressure excursion were compared between controls and stroke participants.

Findings: Stroke participants swayed more, were more asymmetric, and had less between-limb synchronization than healthy controls. Among individuals with stroke, reduced between-limb synchronization was related to increased postural sway in the medio-lateral direction and increased weight-bearing asymmetry.

Interpretation: Individuals with stroke have reduced temporal synchronization of centre of pressure fluctuations under the feet when controlling quiet standing. The clinical significance of reduced synchronization remains to be determined, although it appears linked to increased medio-lateral sway and weight-bearing asymmetry.

INTRODUCTION

Individuals with stroke have a high incidence of falls (Forster and Young, 1995), which may be linked to impaired standing balance control compared to aged-matched controls (Geurts et al., 2005). Further understanding of the underlying challenges to balance control after stroke is required. One approach to quantitatively assess balance control is the measurement of postural sway in standing using force plates. In many populations, a composite measure of centre of pressure (COP) sway reveals balance control challenges and increased falls risk (Maki et al., 1992). Current postural sway measures typically examine excursion of the total COP under both feet combined. However, the application of this approach is complex after stroke due to the possible contribution of limb-specific control problems and/or central balance control challenges. For individuals post-stroke, the interest is not only in the overall COP excursion, but the interpretation of this compromised control, specifically related to paretic-limb control and strategy to stand (e.g. weight-bearing asymmetry). It is likely that a single composite measure of COP will be inadequate to reveal underlying determinants of balance control. As a result, we view it important to specifically understand the paretic limb control (limb specific coupling to the non-paretic limb) and the strategy (stance symmetry) to complement more conventional measures of overall COP.

A previous study used two force plates to analyse COP profiles under each foot separately in individuals with stroke (Genthon et al., 2008b). This study, which was limited to examination of typical amplitude and frequency COP measures under each foot, found that the non-paretic lower-limb contributes more to the control of standing balance than the paretic limb. Measurement of COP profiles under each foot during standing can also be used to examine correlation of COP profiles in time. The strength of the correlation can indicate between-limb synchronization of stability control (Winter et al., 1993). Between-limb correlations of antero-posterior (AP) and medio-lateral (ML) COP profiles reveal moderate to high correlation coefficients in healthy individuals (Winter et al., 1993, Mochizuki et al., 2005).

We argue that use of two force plates to assess standing balance in individuals with stroke can provide information on three potentially independent measures of control of standing posture: 1) weight-bearing symmetry, 2) contribution of each limb to maintenance of stable posture, and 3) synchronization between the limbs. The purpose of this study is to examine differences in between-limb synchronization in individuals with stroke compared to healthy controls, and to determine if asynchrony is related to the control of postural sway and stance loading asymmetry.

METHODS

Data for this study were gathered as part of the Heart and Stroke Foundation Centre for Stroke Recovery Longitudinal Database. Individuals with stroke receiving treatment at one of the four participating hospitals (one acute care and three rehabilitation hospitals) were recruited for this database. The purpose of the database is to monitor sensori-motor and cognitive recovery post-stroke. Data from the initial assessment of 33 consecutive participants who met the inclusion/exclusion criteria and had completed a standing balance test (as described below) were included in this study. The inclusion criteria for individuals selected for this specific study were: 1) able to stand independently (no aid or physical support) for at least 10s, and 2) able to understand and follow instructions. Individuals with bilateral strokes or measurable sensori-motor impairment in both lower limbs, as assessed with the Chedoke-McMaster Stroke Assessment (Gowland et al., 1993), were excluded. For comparison, 20 healthy controls with no known neurological or musculoskeletal illness or injury that could affect balance control were also recruited and completed the same balance test. Participant characteristics are described in Table 1. This study was approved by the Research Ethics Board at each participating institution and subjects provided written informed consent prior to participation.

Table 1: Participant characteristics. Values presented are means (standard deviation; range), or counts.

	Stroke participants	Healthy controls
Age (years)	61 (14; 28-90)	27 (5; 20-37)
Sex (number)		
Women	10	9
Men	23	11
Time since stroke (days)	133 (194; 10-861)	-
Time since stroke (number)		
< 1 month	9	-
1-3 months	9	-
3-6 months	9	-
6 months – 1 year	3	-
> 1 year	3	-
Affected or non-dominant side (number)		
Left	17	19
Right	16	1
National Institutes of Health Stroke Scale (Goldstein et al., 1989)	4.6 (4.1; 0-15)	-
Chedoke-McMaster Stroke Assessment (Gowland et al., 1993)		
Leg	4.6 (1.3; 3-7)	-
Foot	4.2 (1.6; 1-7)	-
Berg Balance Scale (Berg et al., 1989)	37.9 (15.6; 4-56)	-

Two force plates were positioned side-by-side so that they were as close together as possible without touching (<1mm apart). Subjects stood with one foot on each force plate in a standardized position (feet oriented at 14° with 0.17m between the heels (McIlroy and Maki, 1997)) with each foot equidistant from the midline between both plates. Subjects were instructed to stand as still as possible for 30s. Ground-reaction forces and moments were sampled at 200Hz, and were low-pass filtered using a 4th order dual-pass Butterworth filter at 10Hz prior to processing. AP and ML COP were calculated separately for both force plates and the total COP under both feet combined was also calculated.

The AP and ML COP and force time series' for each force plate were divided into five-second-long epochs and outcome variables were calculated for each epoch. Note that it was necessary to crop 5 seconds of data for one trial of one healthy control (due to a technical error) and 10 seconds of data from one trial from one stroke participant (due to reduced standing tolerance). As a result, there were 119 healthy control epochs (20 subjects x 6 epochs – 1 epoch) and 196 stroke participant epochs (33 subjects x 6 epochs – 2 epochs) available for analysis.

Stance load symmetry was defined as the mean force recorded by the force plate under the affected (or non-dominant) limb and was expressed as a percentage of body weight. Absolute stance load symmetry was defined as the mean force recorded by the force plate under the less-loaded limb. The root mean square (RMS) of the AP and ML COP time series was calculated for each force plate and for total COP under both feet; the RMS provides a measure of the amplitude of postural sway (de Haart et al., 2004). Synchronization of COP motion between both feet was calculated by cross-correlating COP under the left and right foot. The mean AP and ML COP was subtracted from the time series and the right and left COP were cross-correlated on a point-by-point basis (Mochizuki et al., 2005). The correlation coefficient at time zero was determined (ρ_0) as COP motion should be synchronized at the same point in time (Winter et al., 1993). To account for potential time lag in COP fluctuations in both limbs, the peak of the cross-correlation function within ± 1 s of time zero ($\rho_{\max}$), and the timing of the peak lag were also determined (Figure 1).

Figure 1: Sample COP time series and cross-correlation functions. Panels A1-3 show two epochs of simulated data, panels B1-3 show data from one epoch for a healthy control, and panels C1-3 show data from one epoch for a stroke participant. Note the expanded scale on the cross-correlation function graph in panel A3 and the lower correlation coefficients calculated for these epochs. Absolute stance loading asymmetry was similar for both epochs (49% body weight for the healthy control, and 45% body weight for the stroke participant). COP correlation coefficients, shown in panel B3, were high for the healthy control (AP: 0.97; ML: -0.97) and $\rho_{\max}$ occurred at time zero. Both ρ_0 and $\rho_{\max}$ were low for the stroke participant (AP ρ_0 : 0.07; ML ρ_0 : -0.18; AP $\rho_{\max}$: 0.25; ML $\rho_{\max}$: -0.23). The peaks of the cross correlation functions occurred at a time lag for the stroke participant.

In order to estimate the strength of the correlations that might be obtained due to random chance, the cross-correlation function was calculated in cases where two signals are uncorrelated. Twenty 30-second long simulated signals were generated. These signals consisted of a sine wave (amplitude: 2 units, range: -1 to +1, period: 3.14s) paired with a series of randomly-generated numbers that ranged between -1 and +1. The sine wave served as the COP under one foot, and the random numbers served as the COP under the other foot. The signals were analysed, as described above, to determine ρ_0 , $\rho_{\max}$ and the $\rho_{\max}$ lag (Figure 1).

Repeated measures analysis of variance (ANOVA) on rank-transformed data was used to compare RMS of total AP and ML COP, and RMS of AP and ML COP under each foot, stance loading asymmetry, and between-limb AP and ML COP correlations between the two subject groups (healthy controls and stroke participants). A t-test was used to determine if the time lag in $\rho_{\max}$ was different from zero. Synchronization, weight-bearing asymmetry and postural sway variables were averaged for each subject and Spearman correlations were used to explore relationships between these variables in stroke participants. For all statistical analyses alpha was set at 0.05.

RESULTS

Stroke participants showed increased postural sway compared with controls (Table 2); RMS of total AP and ML COP, and RMS of AP and ML COP under both limbs were higher in individuals with stroke than controls ($P_s < 0.0006$). In general, AP COP under each foot was positively correlated, and ML COP was negatively correlated (Figure 1). The absolute COP cross-correlations were, on average, lower for stroke participants compared to controls indicating poorer temporal synchrony, although this relationship was only statistically significant for the ML correlation ($P = 0.0013$). Healthy controls were more likely than stroke participants to show the highest synchronization at time zero; ρ_0 and $\rho_{\max}$ were equivalent in 58% and 42% of epochs for controls (AP and ML, respectively), but only 40% and 15% of epochs for stroke participants. The time lags for $\rho_{\max}$ were not statistically different from zero for either group (healthy controls AP $\rho_{\max}$ lag $P = 0.29$; ML $\rho_{\max}$ lag $P = 0.081$; stroke participants AP $\rho_{\max}$ lag $P = 0.94$; ML $\rho_{\max}$ lag $P = 0.29$). There was also no evidence for a consistent direction of time lag for $\rho_{\max}$ within individual participants; therefore, absolute time lag at $\rho_{\max}$ was compared between the groups. For both AP and ML correlation, stroke participants showed a greater lag at $\rho_{\max}$ than healthy controls ($P_s < 0.041$).

Table 2: Standing balance measures. Between-group differences in measures of postural sway, weight-bearing asymmetry, and between-limb synchronization. Values presented are means with standard deviations in parentheses. The p-value is for the repeated-measures ANOVA on rank-transformed data comparing the two groups.

	Stroke participants	Healthy controls	p-value
RMS of AP COP (mm)			
Total			
Affected/non-dominant side	4.9 (2.7)	2.5 (1.2)	<0.0001
Unaffected/dominant side	4.3 (2.8)	2.3 (1.1)	<0.0001
	5.9 (3.8)	2.9 (1.7)	<0.0001
RMS of ML COP (mm)			
Total			
Affected/non-dominant side	2.8 (2.6)	1.1 (0.9)	<0.0001
Unaffected/dominant side	1.3 (0.9)	0.6 (0.4)	<0.0001
	1.3 (1.3)	0.8 (0.7)	0.0005
Stance load symmetry (% body weight)	42.9 (12.0)	48.8 (2.4)	0.039
Absolute stance load symmetry (% body weight)	39.8 (9.5)	47.9 (1.7)	<0.0001
Synchronization			
AP ρ_0 (correlation coefficient)	0.74 (0.30)	0.83 (0.20)	0.081
AP $\rho_{\max}$ (correlation coefficient)	0.77 (0.23)	0.85 (0.15)	0.086
AP $\rho_{\max}$ lag (ms)	23 (24)	13 (13)	0.59
Absolute AP $\rho_{\max}$ lag (ms)	89 (22)	43 (12)	0.040
ML ρ_0 (correlation coefficient)	-0.37 (0.45)	-0.65 (0.39)	0.0013
ML $\rho_{\max}$ (correlation coefficient)	-0.54 (0.28)	-0.73 (0.26)	0.0004
ML $\rho_{\max}$ lag (ms)	-1 (47)	-7 (34)	0.49
Absolute ML $\rho_{\max}$ lag (ms)	304 (352)	163 (308)	0.0061

AP=antero-posterior; COP=centre of pressure; ML=medio-lateral; RMS=root mean square

We observed a high level of within-trial variability in ρ_0 for some individuals; that is, for some individuals, ρ_0 varied from epoch-to-epoch (see example in Figure 2). Therefore, those individuals who, on average, had low ρ_0 were not necessarily asynchronous but may have displayed transient periods of low synchronization among periods of moderate-to-high synchronization.

Figure 2: Within-trial variability in between-limb synchronization. Panel A shows AP COP and Panel B shows ML COP under both feet across the entire 30s trial for two different individuals with stroke. Cross-correlation coefficients at time zero (ρ_0) for each 5 second epoch are noted at the top of each figure. Periods of transient asynchrony are evident for the individual in Panel A from 10-20s, and for the individual in Panel B from 5-10s and from 20-25s. Note also the increased contribution of the unaffected limb for balance control for the individual in Panel A, evident by increased magnitude of AP COP fluctuations on the unaffected side compared to the affected side. Moderate-to-high ρ_0 is observed in most epochs despite the large between-limb differences in magnitude of COP fluctuations.

Because there was no consistent time lag for $\rho_{\max}$ for either controls or individuals with stroke, ρ_0 was analysed further for relationships with sway and stance loading asymmetry. Reduced AP ρ_0 was significantly related to increased RMS of total ML COP (correlation coefficient=-0.43, $P=0.012$; Table 3), and there was a trend toward a significant relationship between ML ρ_0 and RMS of total ML COP (correlation coefficient=0.32, $P=0.072$). There were no significant relationships between synchronization indices and RMS of total AP COP (absolute correlation coefficients<0.18, $P_s>0.34$). There were no statistically significant relationships between synchronization and RMS of AP or ML COP for each limb separately (absolute correlation coefficients<0.32, $P_s>0.074$). Increased absolute stance loading asymmetry was related to reduced synchronization between limbs (absolute correlation coefficients>0.44; $P_s<0.01$). Scatter plots for the significant relationships are presented in Figure 3.

Figure 3: Scatter plots showing relationship between synchronization and ML RMS and stance loading asymmetry. Relationships between AP COP ρ_0 and ML RMS (panel A) and absolute load asymmetry (panel C), and between ML COP ρ_0 and ML RMS (panel B) and absolute load asymmetry (panel D) are plotted. Absolute load asymmetry is the percentage of body weight recorded on the less-loaded foot. Statistically significant correlations were found for the relationships presented. Data for healthy controls are also presented, but correlation analyses were not performed for controls due to the low range of RMS and load asymmetry observed in this group.

As expected, the simulated data were uncorrelated and yielded low ρ_0 and $\rho_{\max}$ (Figure 1). The average ρ_0 over the 30 simulated trials was 0.0008 (standard deviation: 0.033) and ρ_0 ranged from -0.085 to 0.078. Absolute values of $\rho_{\max}$ were <0.98 and ρ_0 and $\rho_{\max}$ were never equivalent in the simulated data. The mean lag for $\rho_{\max}$ was close to zero (14ms) but there was a high degree of variability over

trials (standard deviation: 714ms) and over epochs within each trial (standard deviation range: 393-983ms). Nine individuals with stroke and two healthy controls showed ML COP cross-correlation characteristics similar to the uncorrelated data; that is, ρ_0 and $\rho_{\max} < 0.1$; $\rho_0 \neq \rho_{\max}$; and $\rho_{\max}$ lag standard deviation > 400 ms. Only one of these individuals (a stroke participant) showed these same characteristics for AP COP cross-correlation.

Table 3: Relationships between synchronization and standing balance measures. The values shown are Spearman correlation coefficients with associated p-values in parentheses.

	AP ρ_0	ML ρ_0
RMS of AP COP (mm)		
Total	-0.039 (0.83)	-0.17 (0.35)
Affected/non-dominant side	0.25 (0.15)	-0.31 (0.075)
Unaffected/dominant side	-0.11 (0.56)	-0.0030 (0.99)
RMS of ML COP (mm)		
Total	-0.43 (0.012)	0.32 (0.072)
Affected/non-dominant side	-0.09 (0.60)	-0.11 (0.55)
Unaffected/dominant side	-0.084 (0.64)	-0.16 (0.38)
Stance load symmetry (% body weight)	0.32 (0.068)	-0.29 (0.096)
Absolute stance load symmetry (% body weight)	0.44 (0.0099)	-0.48 (0.005)

AP=antero-posterior; COP=centre of pressure; ML=medio-lateral; RMS=root mean square

DISCUSSION

During quiet standing in healthy individuals, both feet work together in a synchronized way, exerting forces on the ground to regulate motion of the centre of mass and maintain stability (Winter et al., 1998). This is evident in moderate-to-high correlations in COP fluctuations between the two feet (Winter et al., 1993), with little or no time lag in the peak of the cross-correlation function (Mochizuki et al., 2005, Mochizuki et al., 2006). In the AP direction, these fluctuations are in-phase (positively correlated), whereas in the ML direction they are anti-phase (negatively correlated) (Winter et al., 1993).

Individuals with stroke show reduced between-limb synchronization in AP and ML COP fluctuations compared with healthy controls. Stroke commonly results in unilateral dyscontrol, which has been shown to manifest in reduced weight-bearing on the more affected side (Laufer et al., 2003) and reduced contribution of the more affected side to the control of standing balance (Genthon et al., 2008b). The current study found that stroke can also lead to reduced temporal synchronization of COP fluctuations under the feet to maintain stability during quiet standing; this has not been previously reported in the literature and may reflect a potentially important index of the state of central nervous system control of balance after stroke. However, a determination of the potential clinical significance requires further investigation.

We observed a high degree of between-subject variability in ρ_0 (see Figure 3 and standard deviations in Table 2), and a high degree of within-subject variability in ρ_0 in some subjects. This means that a low ρ_0 may reflect continuous dyscontrol, or may be largely driven by one or two transient periods of low synchronization. An epoch with low synchronization within a trial that predominantly shows moderate-to-high synchronization may be reflective of transient periods of dyscoordination and/or instability, rather than a continuous or ongoing control problem. Such an observation highlights the need to examine time-varying characteristics of postural sway in addition to summary measures of overall performance (Loughlin et al., 2003). In light of this finding, other methods for investigating synchronization between COP fluctuations under the two feet, such as cross-approximate entropy (Hong et al., 2007) or wavelet cross-spectrum (Lee, 2002) may be more appropriate than the cross-

correlation. Comparison of different methods for measuring between-limb synchronization is beyond the scope of the current study but should be investigated in future work.

When random data were cross-correlated with a sine wave we observed the following characteristics of the cross-correlation function: 1) low ρ_0 and $\rho_{\max}$ (<0.1); 2) $\rho_0 \neq \rho_{\max}$; and 3) standard deviation of $\rho_{\max}$ lag >400 ms. Approximately 10% of individuals in our sample showed these characteristics of the ML COP cross-correlation function. This could be partly explained by a smaller range of ML than AP COP fluctuations, making the ML COP cross-correlation more susceptible to noise. However, the higher single-limb RMS of ML COP in the individuals with stroke compared with the healthy controls (Table 2) suggests that a small range of ML COP can not entirely explain the poor correlations in these individuals and that reduced control may be a contributing factor.

The present study revealed that the degree of synchronization was linked to postural sway and stance symmetry. As noted, reduced synchronization was related to increased total postural sway (i.e. under both feet combined) in the ML direction but not in the AP direction. Total ML COP fluctuations rely on hip abductor/adductor activity, whereas AP COP fluctuations largely rely on ankle dorsiflexion/plantarflexion. In contrast, while AP COP fluctuations under each foot rely on dorsiflexion and plantarflexion, ML COP fluctuations under each foot rely on ankle inversion/eversion (Winter et al., 1993). Therefore, reduced synchronization of ankle activity may be related to increased amplitude of proximal, but not distal, corrective actions. It should also be noted, however, that the ML and AP COP measures are not completely independent and are influenced in part by foot orientation (Rougier, 2008). To limit between-subject variability, we adopted a standard foot position in the current study but it is possible that some of the ML COP measures are influenced by asymmetry in control of ankle plantarflexor and dorsiflexors. Further work is required to identify the potential source of underlying problems in temporal asynchrony of ML and/or AP COP control.

Reduced synchronization was also related to increased absolute weight-bearing asymmetry. Previous studies found similar relationships between weight-bearing asymmetry and the contribution of each limb to control of quiet stance (Genthon et al., 2008b, Genthon and Rougier, 2005, Rougier and Genthon, 2009). It is possible that, for highly-asymmetric individuals, the unloaded limb makes such a small contribution to postural control that temporal synchronization of COP under both feet is irrelevant. It is also possible that weight-bearing asymmetry is a symptom of profound limb dyscontrol, and that it is this dyscontrol rather than asymmetry itself that is related to reduced synchronization. Because individuals with stroke had greater stance load asymmetry than controls it is possible that between-group differences in weight-bearing symmetry are responsible for between-group differences in synchronization. Due to the limited range of stance load symmetry values in the control group we examined the relationship between stance load asymmetry and synchronization in the stroke group only. Future studies could investigate this relationship further by manipulating stance load asymmetry (e.g. by asking controls to bear more weight on one side).

The results of this study have implications for the clinical assessment of standing balance control post-stroke. Because stroke is often a unilateral injury there is clinical interest in understanding how both lower limbs work independently and together to control balance. To this end, the evaluation of weight-bearing asymmetry (Laufer et al., 2003), the contribution of each limb to the control of balance (Genthon et al., 2008b), and between-limb synchronization can be clinically meaningful. While weight-bearing asymmetry can be estimated using the mean ML COP location when standing on a single force plate (Genthon et al., 2008a) this estimate may be highly dependent on slight variations in foot position. The contribution of each limb to standing balance control and the synchronization COP fluctuations under the feet can only be evaluated with recordings from two separate force plates.

This study included a heterogeneous stroke population, evident by a wide range of clinical impairment and function scores (see Table 1). We purposely chose not to limit inclusion/exclusion criteria such that we could potentially generalize our findings to individuals with hemiparesis post-stroke who have some independent standing function. One participant could not stand for the entire

30s duration of the trial. Clinical balance assessment of this individual, using the Berg balance scale (Berg et al., 1989), would indicate he has no standing function (i.e. he scored zero on item 2: standing unsupported). Despite the low clinical balance score this subject could stand independently for at least 20s and it was still possible to obtain meaningful information regarding his standing balance control in this limited trial duration. Note that this individual was assessed at admission to in-patient rehabilitation 19 days post-stroke and would be expected to regain independent standing with rehabilitation and recovery from stroke. Therefore, we believe it is appropriate and worthwhile to quantitatively assess standing balance control, even during a short duration of quiet standing, to inform clinical care.

The purpose of this study was to characterize between-limb synchronization of COP fluctuations for the control of standing balance in individuals with stroke compared to healthy controls, and to relate reduced synchronization to more typical measures of postural control (i.e. sway variability and stance asymmetry). Future larger studies will investigate clinical characteristics that are related to reduced synchronization (e.g. lower-limb motor impairment) and if synchronization improves with recovery and rehabilitation from stroke.

CONCLUSIONS

This study demonstrates reduced between-limb synchronization in COP fluctuations to maintain a stable quiet standing posture in individuals with stroke compared with healthy controls. Reduced synchronization was related to increased medio-lateral postural sway and increased weight-bearing asymmetry, although the clinical significance of these relationships requires further investigation. These findings support the clinical utility of two force plates to examine activity under each foot separately rather than relying on analysis of the total COP under both feet combined, particularly when assessing individuals with stroke.

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