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Physiological arousal accompanying postural responses to external perturbations after stroke

Pollock CL¹, Carpenter MG², Hunt MA¹, Gallina A^{1,3}, Vieira TM^{3,4}, Ivanova TD⁵, Garland SJ⁵.

¹ Department of Physical Therapy, University of British Columbia, Vancouver, Canada

² School of Kinesiology, University of British Columbia, Vancouver, Canada

³ Laboratorio di Ingegneria del Sistema Neuromuscolare (LISiN), Dipartimento di Elettronica e Telecomunicazioni, Politecnico di Torino, Italy

⁴ Escola de Educação Física e Desportos, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

⁵ Faculty of Health Sciences, Western University, London, Canada

Abbreviations: EDA, electrodermal activation; ANS, autonomic nervous system; kg, kilogram; COM, center of mass; APCOP, anterior-posterior center of pressure; BM, body mass; EMG, electromyography; BOS, base of support; MG, medial gastrocnemius; LG, lateral gastrocnemius; SOL, soleus; CMSA, Chedoke McMaster Stroke Assessment Scale; CB&M, Community Balance and Mobility Scale; ABC, Activities-specific Balance Confidence Scale HDsEMG, high-density surface electromyography; RMS, root mean square

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Corresponding Author:

S. Jayne Garland, PhD PT

Professor and Dean, Faculty of Health Sciences

Western University

Arthur & Sonia Labatt Health Sciences Bldg, Rm 200

London, ON, N6A 5B9

Canada

Phone: 519-661-4239

Email: jgarland@uwo.ca

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Highlights:

1. The physiological arousal responses to perturbations in standing post-stroke were established.
2. People post-stroke show higher physiological arousal when anticipating perturbations than controls.
3. Habituation to self-triggered perturbations was present in controls, but not in people post-stroke.

Abstract

Objective: The purpose of this study was to examine simultaneously the level of physiological arousal and the postural response to external perturbations in people post-stroke compared to age-matched controls to build a more comprehensive understanding of the effect of stroke on postural control and balance self-efficacy.

Methods: Participants stood with each foot on separate force platforms. Ten applications of loads of 2% body weight at the hips perturbed the participant anteriorly under two conditions: investigator-triggered or self-triggered (total 20). Electrodermal activity (EDA; measurement of physiological arousal), electromyography (EMG) of the ankle plantarflexor muscles and anterior-posterior center of pressure measurements were taken pre-perturbation (anticipatory) and post-perturbation (response) and compared between the initial (first two) and final (last two) perturbations.

Results: Participants post-stroke demonstrated significantly higher levels of anticipatory EDA and anticipatory paretic plantarflexor EMG during both self- and investigator-triggered conditions compared to controls. Anticipatory EDA levels were higher in the final perturbations in participants post-stroke in both conditions, but not in controls. Habituation of the EDA responses post-perturbation was exhibited in the self-triggered perturbations in controls, but not in participants post-stroke.

Conclusions: Physiological arousal and postural control strategies of controls revealed habituation in response to self-triggered perturbations, whereas this was not seen in participants post-stroke.

Significance: Understanding the physiological arousal response to challenges to standing balance post-stroke furthers our understanding of postural control mechanisms post-stroke.

Introduction

Neuromuscular control of standing balance is known to be impaired after stroke (Garland et al. 2009). Response to surface translations have characterized the postural reactions of people post-stroke as being asymmetrical favoring the non-paretic leg (Marigold et al. 2004; van Asseldonk et al. 2006), accompanied by muscle activation which is delayed, and of decreased amplitude, in the paretic limb with poor intra-limb muscle coordination (Badke and Duncan 1983; Marigold and Eng 2006). In particular, the plantarflexor muscles in people post-stroke demonstrate impaired responses to external perturbations (Pollock et al. 2014). The impairment in standing balance following stroke has also been shown to result in increased attention to postural control, proposed to be related to decreased balance confidence (or balance self-efficacy) (Brown et al. 2002; Orrell et al. 2009).

Mounting evidence suggests that physiological arousal modulated by the autonomic nervous system (ANS) may influence postural control (Horslen and Carpenter 2011; Sibley et al. 2014). Physiological arousal can be measured indirectly by electrodermal activation (EDA), a measurement of skin conductance. Measurements of EDA have been used to examine changes in physiological arousal associated with changes in level of attention, cognitive effort, and emotion during tasks (Critchley et al. 2000). Changes in the level of attention and/or emotion surrounding maintenance of standing balance following stroke may result in increased levels of physiological arousal during tasks that threaten balance. This is important to consider as increased levels of arousal in general have been shown to alter postural control in healthy subjects regardless of the nature of the associated emotion (Horslen and Carpenter 2011).

Perturbation tasks that manipulate the perception of threat and the knowledge of timing of a perturbation have demonstrated modulation of physiological arousal levels both in

anticipation of a perturbation, and in response to perturbations (Sibley et al. 2008; Sibley et al. 2010; Sibley et al. 2014). Larger increases in physiological arousal in response to postural threat have been found in older adults than in young adults, which may be related to a change with aging in the perception of ability to recover from postural threat (Carpenter et al. 2006). Physiological arousal responses to perturbations have been shown to habituate in healthy subjects with repeated exposure to the same low-threat perturbation stimuli, whereas levels of arousal in anticipation of a perturbation remain stable (Sibley et al. 2010). Because the autonomic nervous system can be affected by stroke (Korpelainen et al. 1999), it is possible that attentional demands and emotional state may interact with balance-related neuromuscular impairments after stroke. Examining self-triggered versus investigator-triggered perturbations will uncover the effects of knowledge of and control over the timing of perturbation on both the physiological arousal and postural reaction to external perturbations following stroke.

The relationship between the perception of threat to standing balance and the postural strategy (e.g. increased postural muscle activity resulting in limited movement of the centre of mass (COM) and the anterior-posterior centre of pressure (APCOP)), adopted during a standing balance task has been established in healthy individuals (Adkin et al. 2002; Brown and Frank 1997; Carpenter et al. 2001; Carpenter et al. 2006; Sibley et al. 2008). During external perturbations, healthy individuals demonstrate a lower COM and reduced APCOP displacement and velocity when expected perturbations are introduced under conditions of perceived risk to standing balance (Brown and Frank 1997; Carpenter et al. 2001). These changes have been suggested to be secondary to a change in the postural control strategy in anticipation of a challenge to standing balance. Anticipatory postural strategies are associated with a tighter control of the COM and APCOP, which is suggested to ensure a more effective postural reaction

to a perturbation, such that there is less displacement of the COM within the base of support (BOS) and therefore less risk of a fall (Brown and Frank 1997; Horak et al. 1989; Horslen et al. 2013; Santos et al. 2010a and 2010b). Over a course of repeated perturbations, healthy subjects have been shown to demonstrate a habituated response to perturbation by the second trial whereas subjects with central nervous system impairment (Parkinson's Disease) showed a delayed habituation which has contributed to a decreased efficiency of motor learning (Nanhoe-Mahabier et al. 2012). During conditions of increasing level of challenge to standing balance, anticipatory postural strategies that limited body movement in response to external perturbations have been found in people post-stroke at lower levels of challenge than healthy controls (Pollock et al. 2014). How this postural strategy changes under conditions of perceived threat (external perturbations) and with repeated exposure is not known.

The purpose of this study was to examine simultaneously the level of physiological arousal and the postural response to external perturbations in people post-stroke compared to age-matched controls to build a more comprehensive understanding of the effect of stroke on postural control and balance self-efficacy. We hypothesized that: (1) people post-stroke would demonstrate higher levels of physiological arousal, as measured by electrodermal activation, and heightened ankle plantarflexor muscle activity than age-matched controls in anticipation of external perturbations; (2) physiological arousal and plantarflexor muscle activation would be less when both people post-stroke and healthy participants control the timing of the perturbation (self-triggered) vs. investigator-triggered perturbations of uncertain timing; (3) the anticipatory postural strategies used in participants post-stroke would result in less COM and APCOP displacement and velocity in response to perturbations compared to controls and; (4) repeated exposure to perturbations would result in habituation of levels of physiological arousal, COM

and APCOP displacement and velocity, and plantarflexor muscle activity during self-triggered external perturbations in people post-stroke, whereas healthy controls would demonstrate habituation of postural reactions during both conditions.

Methods

Ten people with chronic stroke (>1 year post-stroke) and ten age-matched controls provided written informed consent to participate in this study. Participants post-stroke were recruited from local community stroke groups and controls were recruited from the university community, including a healthy aging fitness program (non-structured, self-directed activity levels). Individuals with hemiparesis post-stroke were included if they were ambulatory, with or without a walking aid, and could stand independently for a minimum of five minutes. Individuals were excluded if in addition to stroke, they had any health conditions that negatively impacted balance. Controls were included if they were free from neurological or musculoskeletal impairment which resulted in decreased balance. The study conformed to the standards set by the latest revision of the *Declaration of Helsinki* and was approved by the University of British Columbia Clinical Research Ethics Board.

The severity of motor impairment following stroke was measured at the foot and ankle using the Chedoke-McMaster Stroke Assessment (CMSA, (Gowland et al., 1993). The CMSA describes seven stages of motor recovery; 0/7 refers to flaccid paralysis and 7/7 refers to movement equated to a "normal" sensory-perceptual-motor system (Gowland et al., 1995). Both participants post-stroke and controls were assessed for ambulatory balance with the Community Balance and Mobility Scale (CB&M, /96; Howe et al. 2006; Knorr et al. 2010), and for balance

related self-efficacy using the Activities-specific Balance Confidence Scale (ABC, /100; Botner et al. 2005; Myers et al. 1996).

Experimental protocol

Participants stood with their arms at their sides, barefoot with their feet shoulder-width apart, with each foot on a separate floor-mounted force platform (AMTI OR6-6, Advanced Mechanical Technology, Watertown, MA). Baseline quiet standing data were collected for 30 seconds and served as a comparator for changes in anticipation of a perturbation.

A belt was secured around the pelvis of each participant and was attached to a horizontal cable in front of the participant. External loads were applied via a cable-pulley system attached to the front of the belt (Fig.1). The EDA and postural responses were examined by repetition of the same stimulus (load drop) with only the knowledge of stimulus timing being altered. Postural control research paradigms can manipulate attentional demands by providing knowledge of the timing of impending postural disturbances (Badke et al. 1987; Sibley et al. 2008). All participants were exposed to 5 unexpected load drops prior to data collection for familiarization. During data collection, participants remained standing in comfortable stance and external loads were applied through the belt by dropping loads of 2% body mass (BM) into a basket from a height of 40 cm. The load was maintained in the basket for 10 seconds and then removed. This was repeated ten times, with 15-30 s (random timing) of quiet standing between perturbations. Load drops were either self-triggered by participants or investigator-triggered using a button which initiated the release of the load suspended by an electromagnet. A screen in front of the participants prevented them from seeing when the loads were dropped which was of importance particularly during the investigator-triggered condition in which the exact timing of the load drop was not known. Half of the participants experienced the self-triggered prior to investigator-

triggered perturbations and the other half had the opposite order. In the self-triggered condition, participants were instructed to regain comfortable stance once the load was removed and to press the button when they felt ready for the next perturbation. The exact timing of the load application was detected by a force transducer in-line with the cable (Fig. 1). During the investigator-triggered perturbations, loads were dropped once the APCOP position (monitored by the researcher in real-time) returned to that during quiet stance. In some instances, participants did not return to this position; therefore the load drop was triggered once their COP position appeared stable on visual inspection on the computer monitor (no longer than 20 seconds). Rest was provided for participants as required.

Electrodermal activation

EDA was measured using electrodes affixed to the palmer surface of the right hand in controls and the non-paretic hand of participants post-stroke (Sibley et al. 2014) because the EDA response has been shown to be suppressed on the paretic side (Muslumanoglu et al. 2002). Electrodes were placed on the hypothenar and thenar eminences. A 50 mV current was applied between the two electrodes and the skin conductance was measured as an estimate of physiological arousal of the participant. EDA signal was collected at a sampling frequency of 2048 Hz. The EDA was measured for 30 s in standing, prior to participants donning the hip belt described above, and this represented a baseline level of physiological arousal during standing. During the perturbation trials, the mean EDA was measured 1 second prior to the perturbation. The change in EDA amplitude from the baseline quiet stance trial was calculated. The peak EDA directly following the perturbation was measured and the change from the pre-perturbation level was calculated.

Kinetic and kinematic data

Kinetic data were collected using two floor-mounted force platforms (detailed above), sampled at 2048 Hz. Mean APCOP displacement and velocity were calculated one second prior to the perturbation and peak values were measured one second immediately following load drop. Percentage weight-bearing through the paretic leg for participants post-stroke and the right leg for controls was calculated from the vertical component of the ground reaction force of the each limb divided by the total vertical ground reaction force from both platforms, multiplied by 100.

Twenty two passive reflective markers were affixed to participants according to a modified Helen Hayes marker set (Kadaba et al. 1989). Eight high-speed digital cameras (Raptor-E, Motion Analysis Corp, Santa Rosa, CA, USA) sampled the movement of the reflective markers at 120 Hz. Kinematic data were analyzed with a custom-written program in MATLAB (The Mathworks Inc., Natick, MA, USA) that was used in a previous study to quantify kinematics during movement (Pollock et al. 2012). COM was calculated from marker coordinate data and using published anthropometric values (Dempster and Gaughran 1967). COM velocity was calculated as the derivative of COM displacement. Mean anterior-posterior COM displacement and COM velocity were calculated one second prior to the perturbation and peak values were measured one second following load drop.

Surface EMG recordings

Skin over the plantarflexor muscles was shaved and cleaned with a mild abrasive prior to placement of electrode grids. High-density surface electromyography (HDsEMG) data from the soleus (SOL) (24 electrode grid, 2 cm interelectrode distance), medial (MG) and lateral gastrocnemius (LG) (20 electrode grids each, 1.5 cm interelectrode distance) were collected bilaterally (OT Bioelettronica, Turin, Italy) at 2048 Hz. HDsEMG signals were analyzed in bipolar configurations resulting in 18 EMG signals from the SOL muscle and 16 from each of

the MG and LG muscles. The EMG signal amplitude was normalized to baseline quiet stance (QS). All three plantarflexor muscles have been shown to be active during quiet standing (Loram et al. 2005; Vieira et al. 2012). In the current study, the amplifier used to collect EMG had a noise level of $0.8\mu\text{V}$ while the average signal of the plantarflexor muscles during baseline QS were $5.0\text{-}20.0\mu\text{V}$, consistent with reports in the literature (Vieira et al. 2016). The normalization of EMG signal amplitude to QS when there was absolutely no threat of a perturbation was intended to reveal any anticipatory strategy that participants might use prior to experiencing the external perturbations. Root mean square (RMS) amplitude of each bipolar EMG configuration was measured for one second prior to the perturbation and one second immediately following the load drop. The median RMS amplitude was calculated across the bipolar signals for each plantarflexor muscle before and after the perturbation.

Statistical analysis

The performance of right and left legs of controls were first compared using paired t-tests. As there were no significant differences between the right and left legs of controls for all outcomes, data from the right leg were considered for the control group. Next, the three ankle plantarflexor muscle amplitudes were compared within each leg using three-way ANOVAs, including factors of experience with repeated perturbations (average of last two perturbations (final) compared to average of first two perturbations (initial)), condition (investigator- compared to self-triggered perturbations), and muscle (MG, LG, SOL). As there was no difference between MG and LG in any group, we chose to report only MG findings. Pre-perturbation RMS EMG amplitudes from MG and SOL were compared to that during the baseline quiet stance trial (when there was no possibility of a perturbation) using paired t-tests. Parameters derived from APCOP and RMS EMG amplitude of MG and SOL muscles were compared using mixed model

three-way ANOVAs with Bonferroni post-hoc analysis, including two within-subject factors of experience and condition, and one between-group factor of control (C), paretic (P) and non-paretic (NP) leg comparisons. EDA and COM parameters were compared using similar mixed model ANOVAs with Bonferroni correction for the within-subject factors of experience and condition, and a between-group factor (stroke and control). Data were analyzed separately in two time periods: pre-perturbation and post-perturbation to capture anticipatory preparation for, and response to, perturbation. When between-factor interactions were evident, post-hoc pairwise comparisons revealed the nature of the interaction. Significance was set at an alpha of 0.05.

Results

Participants

Table 1 shows the characteristics of participants post-stroke and controls. Age was not significantly different between groups ($p = 0.65$). The participants post-stroke had achieved independent ambulation (with or without walking aid) post-stroke. All participants with stroke were engaged in, at minimum, a walking exercise program. Motor recovery following stroke as measured with the CMSA, showed scores of the foot and ankle of participants post-stroke ~~showed~~ with an IQR of 3-6 out of 7. A CMSA score of 3/7 reflects a motor control impairment which can be described as: marked spasticity present, some voluntary movement, synergistic patterns with inability to move quickly between plantarflexion and dorsiflexion. A motor control impairment scored as CMSA 5/7 can be described as: waning spasticity, increased range of voluntary movement, synergistic patterns less evident (Gowland et al., 1995). None of the participants in the study were currently receiving any therapy addressing strength, balance or mobility.

Participants post-stroke scored significantly lower than controls in ambulatory balance as measured by the CB&M ($p < 0.01$). A lower score is indicative of decreased ambulatory balance at the level of independent walking in the community. The difference in balance self-efficacy, as measured by the ABC, a clinical measure of an individual's confidence in performing functional standing and walking tasks in the community, between participants post-stroke and controls did not reach significance ($p = 0.14$).

Pre-perturbation

Electrodermal activation

Participants post-stroke demonstrated significantly higher levels of electrodermal level ~~pre-perturbation EDA~~ than controls in both perturbation conditions (Fig. 2A, $p = 0.04$). There was a significant group x experience interaction ($p = 0.01$) in electrodermal level ~~pre-perturbation EDA~~ with participants post-stroke showing an increase in electrodermal level ~~pre-perturbation EDA~~ levels with experience in both conditions (Fig. 2A, $p < 0.01$), whereas the EDA did not change in controls in either condition.

Electromyography

Pre-perturbation, RMS EMG amplitude was significantly higher than quiet stance in the paretic medial gastrocnemius and soleus muscles of participants post-stroke during both self- and investigator-triggered perturbations (Fig. 3A, $p < 0.05$). This was not significant amongst the ankle plantarflexors of the control or non-paretic legs. Representative data from the paretic leg of a participant post-stroke and a healthy control during self-triggered perturbations (Fig. 4) show the pre-perturbation activation of the paretic plantarflexors is heightened compared to that of controls.

Pre-perturbation muscle activation of the control leg demonstrated modulation with condition. There was a significant group x condition interaction in the pre-perturbation activation of the medial gastrocnemius muscle ($p = 0.05$). That is, the control leg demonstrated significantly higher levels of pre-perturbation medial gastrocnemius activity during investigator-triggered than self-triggered perturbations (Fig. 3A, $p = 0.05$). This was not seen in the paretic or non-paretic legs of participants post-stroke.

There was a significant group x condition x experience interaction in the pre-perturbation activation of the soleus muscle ($p = 0.01$). Control participants had significant increases in the pre-perturbation soleus activity with experience during investigator-triggered perturbations (Fig. 3A, $p = 0.04$).

Post-perturbation responses

Electrodermal activation

Although there was a trend towards a group x condition x experience interaction for the ~~EDA~~ electrodermal response to perturbation ($p = 0.09$), pairwise comparisons revealed the ~~EDA~~ electrodermal response to perturbation was higher in participants post-stroke compared to controls during self-triggered perturbations (Fig. 2B, $p = 0.03$). Also during self-triggered perturbations, the ~~EDA~~ electrodermal response in controls tended to decrease in amplitude with experience (Fig. 2B, $p = 0.11$). Participants post-stroke demonstrated no change in the ~~EDA~~ electrodermal response to perturbation during either condition.

Electromyography

There were significant leg x condition x experience interactions for the post-perturbation responses in the medial gastrocnemius ($p = 0.02$) and soleus muscles ($p = 0.02$). In the paretic

MG response to perturbations, there was no significant difference between conditions during the initial perturbations, however, the paretic MG response was larger during final perturbations in the investigator-triggered compared to the self-triggered conditions ($p = 0.02$). There were no differences between conditions or with experience in the control and non-paretic MG muscles. The soleus response to perturbation in controls demonstrated a significant reduction in EMG during the investigator-triggered condition only ($p = 0.03$). The non-paretic soleus muscle response was higher during initial perturbations in the self- compared to the investigator-triggered conditions ($p = 0.05$), but was not significantly different between conditions during final perturbations.

Kinematics and kinetics

There was a main effect of condition on the peak COM displacement, with greater COM displacement observed during self-triggered compared to investigator-triggered conditions in both groups ($p = 0.04$) (Fig. 5A). This difference was not related to the pre-perturbation COM position as this was not significantly different between the self- and investigator-triggered conditions ($p = 0.60$). Independent of condition, controls demonstrated a faster peak COM velocity with experience (Fig. 5B, $p = 0.02$), which was not seen in participants post-stroke.

Although the peak APCOP displacement demonstrated a trend towards a leg x condition x experience interaction ($p = 0.10$), the peak APCOP displacement of the paretic leg was significantly lower than controls in both conditions (Fig. 6A, $p < 0.05$). During self-triggered perturbations, controls significantly increased the peak APCOP displacement with experience of repeated perturbations ($p = 0.02$), however, there was no significant difference between conditions or with experience in the peak APCOP displacement in the paretic and non-paretic legs.

There was a significant leg x condition x experience interaction in peak APCOP velocity ($p = 0.05$). The peak APCOP velocity of the paretic leg was slower compared to controls and the non-paretic leg (Fig. 6B, $p < 0.01$) during the self-triggered condition. In controls, the peak APCOP velocity in response to initial perturbations was significantly faster during investigator-triggered perturbations ($p < 0.01$), but there was no significant difference between conditions in the final perturbations. In contrast, the APCOP velocity in the non-paretic leg showed no difference between conditions in response to initial perturbations, however, during final perturbations the APCOP velocity response was faster in the investigator-triggered than in the self-triggered condition ($p = 0.02$). In the paretic leg, final perturbations showed faster APCOP velocity in response to investigator-triggered compared to self-triggered conditions ($p = 0.02$). The observations of APCOP displacement and velocity are not explained by the percent weight-bearing prior to perturbation as post-hoc analysis revealed no significant differences for participants post-stroke (self-triggered, $54.0 \pm 5.3\%$, investigator-triggered, $51.6 \pm 5.0\%$) or controls (self-triggered, $46.0 \pm 2.7\%$, investigator-triggered, $49.8 \pm 2.2\%$, $p = 0.82$).

Discussion

This study compared the level of physiological arousal and the postural control strategy adopted by participants post-stroke and age-matched controls during conditions of repeated self-triggered and investigator-triggered external perturbations. Regardless of condition, participants post-stroke demonstrated higher anticipatory levels of physiological arousal than controls. In both conditions, levels of physiological arousal in anticipation of the perturbation increased with experience of repeated trials in participants post-stroke, whereas controls demonstrated low levels of anticipatory arousal that did not change with experience. In contrast, knowledge of the

perturbation timing resulted in a decrease in peak physiological arousal response to perturbations over repeated trials in controls whereas there was no change in participants post-stroke. Controls demonstrated increased APCOP displacement with repeated trials in the self-triggered condition whereas participants post-stroke did not. Examination of levels of physiological arousal and postural control strategies of controls revealed evidence of habituation in response to self-triggered perturbations, whereas this was not seen in participants post-stroke.

Physiological arousal while experiencing perturbations

This study is the first to show that physiological arousal during external perturbations is heightened following stroke and demonstrates a lack of habituation of heightened anticipatory arousal with experience of repeated perturbations, even when the timing of the perturbation is known. In this paradigm, the magnitude and direction of the perturbation were known and therefore were predictable (only the exact timing of the investigator-triggered perturbations was not known). Knowledge of the timing of the perturbation has been shown to inform the postural strategy adopted during perturbations (Badke et al. 1987; Cordo and Nashner 1982; Santos et al. 2010a and 2010b). We anticipated that the arousal of participants post-stroke would be higher than controls. However, we also anticipated the arousal associated with certainty of the timing of the perturbation would be less during self-triggered perturbations with evidence of habituation in both groups, as has previously been shown in healthy subjects (Sibley et al. 2008; Sibley et al. 2010). Our results show that, despite having knowledge of the perturbation characteristics (direction and magnitude) and the additional control of timing, participants post-stroke demonstrated higher levels of physiological arousal than controls in both conditions, and a lack of habituation over repeated trials. This suggests that participants with stroke do not exhibit the same learning response as controls do with the self-triggered repeated external perturbations used during this experiment. This may be related to participants' post-stroke perception of threat to balance, regardless

of being able to control the timing of the perturbation. In contrast, the physiological arousal in response to perturbation depended on the knowledge of perturbation timing only in controls. During the self-triggered condition only, a habituation of the physiological arousal response to perturbation was observed in control participants but not in participants post-stroke. These findings of modulation of the physiological arousal in controls are in agreement with previous observations in healthy subjects demonstrating habituation of physiological arousal response during conditions of minimal threat (perturbations experienced while standing on a low-height platform), but not during higher-threat conditions of perturbations experienced while standing on an elevated platform (Sibley et al. 2010).

Postural control of external perturbations

Examination of postural control surrounding the initial perturbations, specifically, revealed that the anticipatory plantarflexor muscle activation in participants post-stroke (in either leg) was not significantly different whether the external perturbation is self-triggered or investigator-triggered, whereas, there was suggestion of modulation of levels of pre-perturbation muscle activation in controls depending on the trigger condition. This suggests that participants post-stroke had an increased perception of postural threat more so than controls, in anticipation of the external perturbation, regardless of trigger-condition, used in this paradigm.

The movement of the APCOP of both the paretic and the non-paretic leg in response to repeated perturbations is not indicative of habituation with repeated perturbations when timing of the perturbation is self-triggered. There is a suggestion that with increased experience, the non-paretic soleus muscle demonstrated increased levels of anticipatory muscle activation regardless of condition and that repeated exposure to self-triggered perturbations tended to result in higher levels of pre-perturbation muscle activation in both paretic plantarflexor muscles. In contrast to

participants post-stroke, control subjects demonstrated a decrease in anticipatory plantarflexor muscle activity together with an increase in peak APCOP forward displacement with repeated perturbations during the self-triggered condition only. This habituation to self-triggered perturbations suggests that control participants became more comfortable with the addition of knowledge of timing of the perturbation, consistent with the reduction in ~~EDA~~ electrodermal response (Figure 2B). Anticipatory increases in activation of muscles which are able to dampen the displacement effect of an expected perturbation are scaled to an individual's perception of their ability to withstand the perturbation (Brown and Frank 1997; Horak et al. 1989; Jacobs and Horak 2007; Santos et al. 2010a). This may further reflect an increased perception of threat to standing balance during external perturbations in participants post-stroke more so than age-matched controls and additionally suggests that control and knowledge of timing of perturbations in participants post-stroke further facilitates the use of anticipatory paretic muscle activation. Participants post-stroke have been shown previously to use a co-contraction strategy about the ankle to maintain standing balance when anticipating external perturbations (Pollock et al., 2015). Measurement of other postural muscles which would be able to resist an anterior perturbation (e.g. hip extensors) may further contribute to understanding of the use of anticipatory postural control strategies in people post-stroke.

In the paretic and non-paretic leg of participants post-stroke, a decreased APCOP velocity in response to perturbation was evident during self-triggered perturbations compared to investigator-triggered perturbations. This decrease in APCOP velocity with the addition of knowledge of timing is suggestive of an increase in anticipatory muscle activation associated with this condition. Particularly with increased experience, the paretic leg demonstrates a tendency towards increased levels of activation of the plantarflexor muscles in anticipation of

self-triggered perturbations. Interestingly, there is some suggestion that as participants post-stroke tended to employ a strategy of increased anticipatory muscle activation with increased knowledge of anticipated perturbations, there was a decrease in the reliance on the reactionary aspect of the postural strategy used. Prior knowledge of direction and timing of a perturbation has also been shown to improve the timing of gastrocnemius muscle burst onset and temporal coordination with other muscles of the paretic leg during anteriorly-directed perturbations (Badke et al. 1987), suggesting that attentional variables may be a critical source of information for preprogrammed postural reactions. In the current study, it is possible that improved timing and coordination of lower extremity muscle activation associated with increased control of timing in participants post-stroke may have resulted in decreased overall amplitude of muscle activation required to respond to the perturbation.

Clinical relevance

As decreased balance confidence has been suggested to influence the risk of falls more so than many physical measures of balance post-stroke (Pang and Eng 2008; Salbach et al. 2006; Schmid et al. 2012), it is tempting to suggest that the heightened level of physiological arousal noted in participants post-stroke in the current study which lacks modulation between conditions is a result of decreased balance confidence in participants post-stroke specifically. However, the differences in arousal behaviour between participants following stroke and controls were seen despite relatively small differences in balance confidence measured by the ABC scale in each group. This finding suggests the need to use a separate measure of state-related changes in arousal such as EDA to detect these changes with stroke as physiological arousal may be influenced by a variety of factors including a range of emotional and attentional demands.

Changes in attention, cognitive effort, or emotional arousal have been shown to influence physiological arousal levels (Critchley et al. 2000). It has also been shown that regardless of the nature of the stimuli (valence) physiological arousal can modulate postural control (Horslen and Carpenter 2011). In the current study, although anticipatory level of physiological arousal did not significantly differentiate between trigger conditions with experience in participants post-stroke, levels of anticipatory and reactive muscle activation may suggest an influence of the trigger condition on adaptation of the postural strategy to repeated external perturbations. The addition of self-initiated external perturbations has been shown to result in a gradual increase in negative cortical potentials prior to perturbations (suggested to indicate a change in postural central set) and lessened the peak amplitude of negative cortical potentials post-perturbation (suggested to be associated with postural error detection) (Mochizuki et al. 2008). Within the brain, control of predictable threatening stimuli has been shown to decrease levels of activity in the ventromedial prefrontal cortex and hippocampus, areas of a neural circuit important in modulation of emotional reaction, however, the modulation of physiological arousal that occurred with control of predictable threatening stimuli in the same study was similar to that of additional areas of the prefrontal cortex (Wood et al. 2015). In the current study, it is possible that heightened physiological arousal, associated with established perceptions of balance ability in participants post-stroke, exerts an initial influence on the general tonic state of postural muscle activation (including postural muscles about the hip and knee not measured within the current study) as is suggested by the limited movement of the APCOP of the paretic leg specifically. However, the rise in physiological arousal with continued exposure to perturbations may be more reflective of heightened attentional focus or vigilance with experience of repeated perturbations and the continued effort of the participant post-stroke to adapt their postural control (anticipatory

versus reactive postural strategy) appropriately to the trigger-condition. The findings of the current study suggest that although physiological arousal likely influences the tonic components of postural control (Horlsen and Carpenter 2011), further conscious or sub-conscious processing of conditions surrounding the anticipated perturbation may influence the postural strategy adopted by people with stroke over continued exposure. This suggests a further component of complexity to the influence of physiological arousal and cortical control on postural reactions during external perturbations which pose a threat to standing balance.

Importantly, although with experience there was some suggestion of an altered motor control strategy employed between conditions in participants post-stroke, the increasing level of anticipatory physiological arousal that lacked modulation between conditions, may have influenced the overall lack of habituation noted in the APCOP response to the external stimuli even under conditions of self-triggered perturbations. Further understanding of this relationship may prove important to the retraining of postural reactions to external perturbations in people following stroke as evidence of habituation is commonly an indicator of motor skill acquisition and may require longer to obtain or be demonstrated differently following stroke.

Detailed understanding of autonomic dysfunction secondary to stroke is limited by a lack of neuroimaging of structures such as the supranuclear autonomic nuclei. Therefore, we cannot comment on the effects of stroke on this central pathway. Instead, we may be showing the effects of stroke on the individual's perception of threat imposed by the external perturbations, thereby impacting levels of physiological arousal.

Conclusion

This is the first report offering insight into the ANS responses accompanying postural control responses to external perturbations in people post-stroke. Participants post-stroke demonstrated increased physiological arousal in anticipation of a perturbation regardless of experiencing repeated self- or investigator-triggered perturbations. The postural control strategy, as described by the APCOP displacement and velocity and the plantarflexor muscle activity, together with the ~~EDA~~ electrodermal response to perturbations, is suggestive of habituation to self-triggered perturbations in controls but not in participants post-stroke. However, the postural strategy of participants post-stroke demonstrated modulation of APCOP parameters and plantarflexor muscles between conditions after experiencing repeated perturbations, which suggests an influence of the addition of knowledge of timing on the adaptation of the postural strategy.

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Table 1 Participant characteristics

	Age (yrs)	Sex (m/f)	Post onset (yrs)	Paretic side (R/L)	CMSA * (0-7)	CB&M (0-96)	ABC (100%)
Stroke	66.2 ± 9.2	8m /2f	6.6 ± 3.6	5 R / 5L	3(IQR 3-6)	31.9 ± 23.8	83.0 ± 17.6
Control	68.0 ± 8.2	7m / 3f	n/a	n/a	n/a	80.9 ± 7.8	93.0 ± 6.7

*Chedoke McMaster Stroke Assessment (CMSA) reported as median and interquartile range.

Note: Community Balance & Mobility Scale (CB&M), Activities-specific Balance Confidence Scale (ABC).

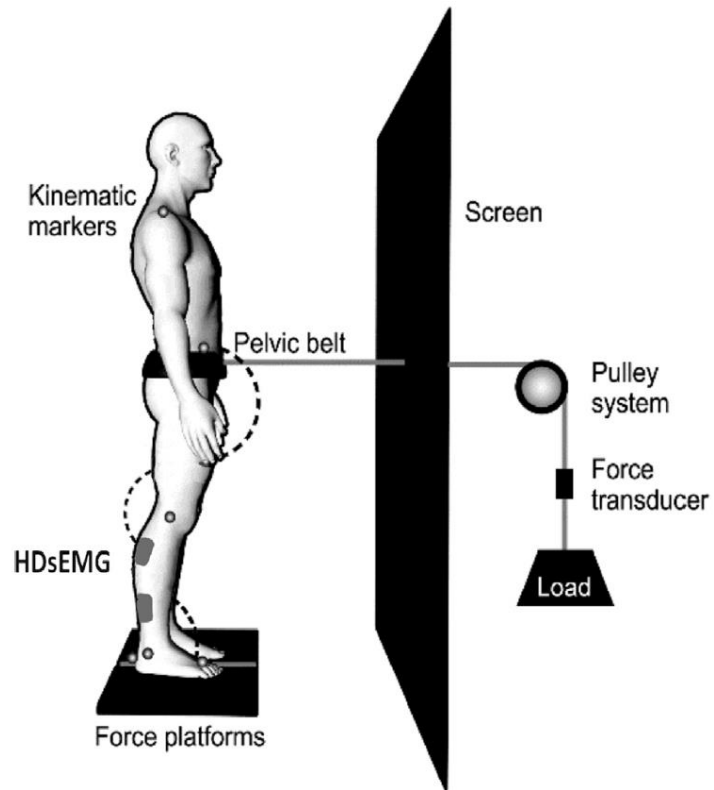


Figure 1. Experimental set-up. Participants stood with each foot on a separate force platform. Anteriorly-directed external loads of 2% body mass were dropped by a cable and pulley system attached to a belt around the participants' pelvis. Ten loads were released with investigator-triggered behind the screen or self-triggered with an electromagnet suspending the load.

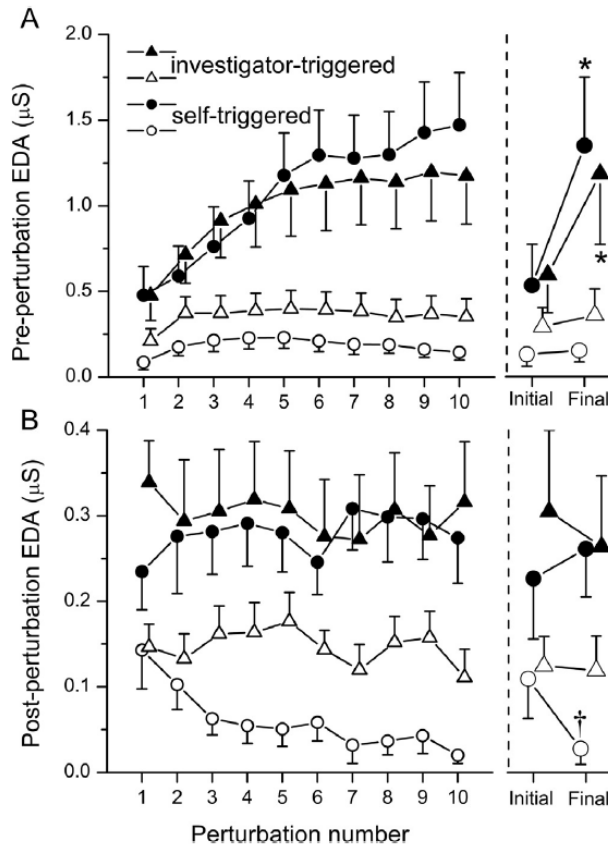


Figure 2. Electrodermal activation (EDA) prior to perturbation (A) and following perturbation (B) during self- (circles) and investigator-triggered (triangles) external perturbations in participants post-stroke (closed symbols) and controls (open symbols). In the right panels, the means of the first two (Initial) and the last two perturbations (Final) for each curve on the left are presented. In pre-perturbation (A), participants post-stroke demonstrated both significantly higher overall levels of EDA than controls ($p=0.04$) and an increase in the EDA with experience in both perturbation conditions. Post-perturbation (B), the EDA was lower with experience in controls only during self-triggered perturbations ($p=0.03$).

* $p<0.05$ and † $p=0.11$ denote EDA changes with experience of repeated perturbations for participants post-stroke and controls, respectively. Data are mean \pm SE.

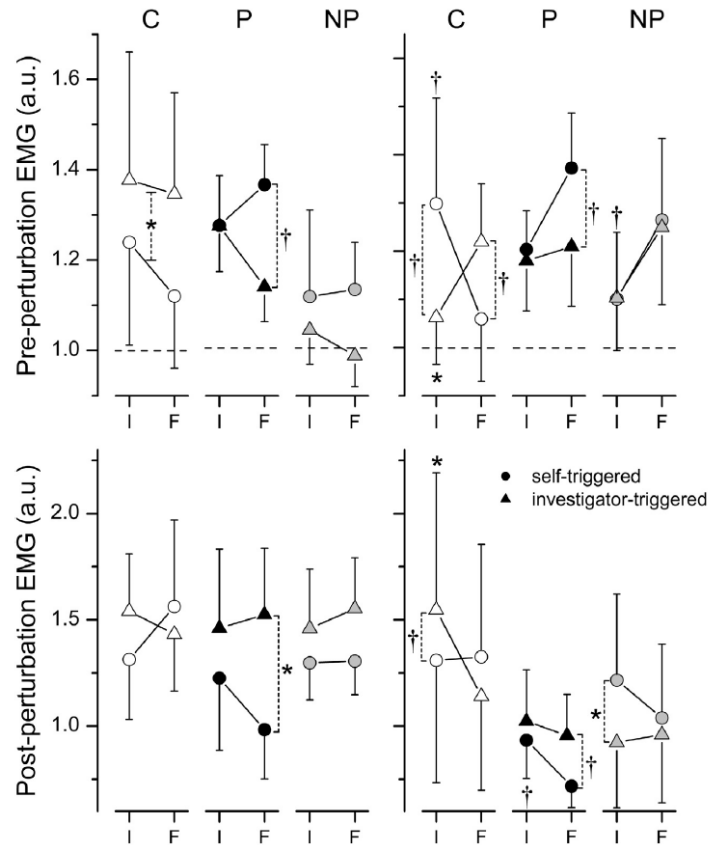


Figure 3. RMS EMG amplitude of the medial gastrocnemius (MG) and soleus (SOL) muscles for control (open symbols), paretic (black symbols) and non-paretic (grey symbols) legs during self-triggered (circles) and investigator-triggered perturbations (triangles) with experience of repeated perturbations (initial (I), final (F)). A) Pre-perturbation represented as a change from baseline quiet stance prior to any perturbations (dotted horizontal line). B) Post-perturbation represented as a change of RMS EMG amplitude from pre- to post-perturbation.

* $p < 0.05$ and † $p < 0.1$ denote significant comparisons. Symbols placed above or below the initial perturbation are for I vs. F comparison in each condition (self- or investigator triggered).

Brackets with symbols are for comparisons between conditions at each time point (initial or final). Data are mean \pm SE.

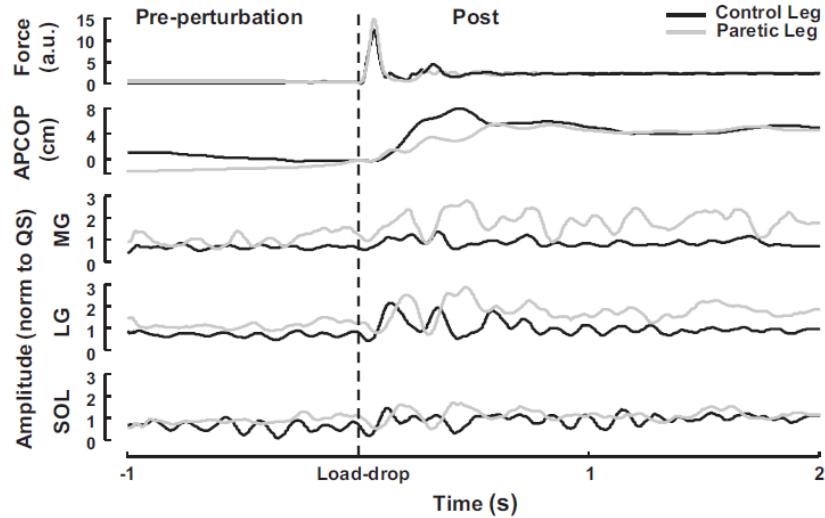


Figure 4. Responses to a single self-triggered perturbation in a participant post-stroke (paretic leg, gray) and a control subject (black). From top: force, representing application of load drop, anterior-posterior centre of pressure (APCOP) displacement, muscle activation amplitude, normalized to baseline quiet stance (QS) for medial and lateral gastrocnemius (MG, LG) and soleus (SOL). Note the higher pre-perturbation muscle activation and the smaller peak APCOP displacement in the paretic leg than control leg.

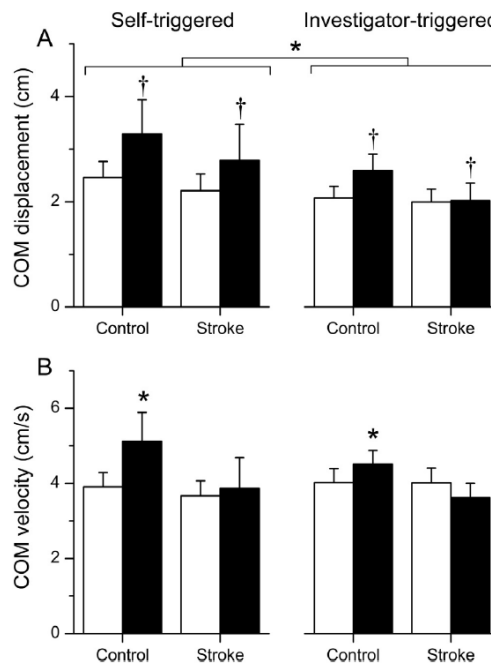


Figure 5. Peak centre of mass (COM) forward displacement (A) and velocity (B) during self-triggered (left) and investigator-triggered (right) external perturbations in participants post-stroke

and controls with open bars being initial responses and filled bars being final responses. Independent of group and experience, the COM displacement in response to the perturbation was significantly higher during self-triggered perturbations than investigator-triggered perturbations and tended to increase with experience. Independent of condition, controls demonstrated a faster peak COM velocity with experience.

* $p < 0.05$ and † $p < 0.1$ denote changes in COM displacement and velocity with experience of repeated perturbations or between conditions where comparisons pairs are indicated with brackets. Data are mean \pm SE.

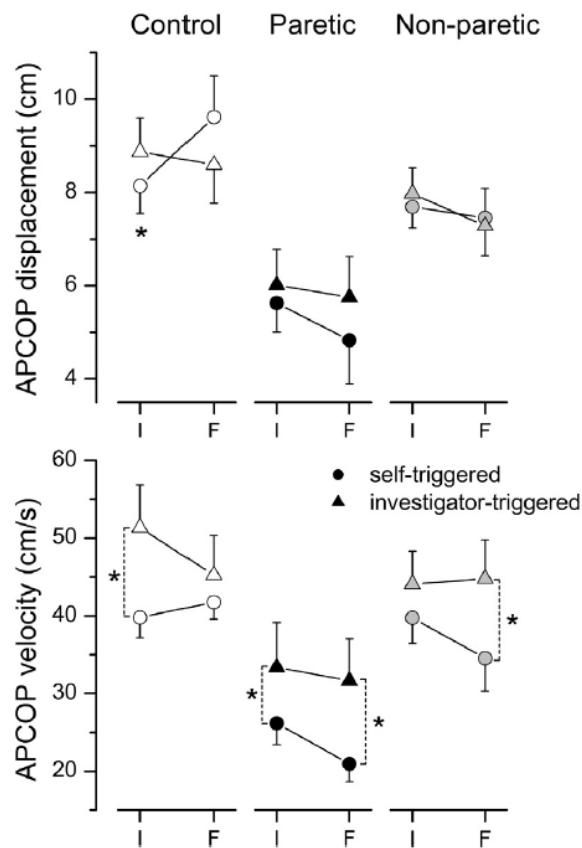


Figure 6. Anterior-posterior centre of pressure (APCOP) forward displacement (top) and velocity (bottom) for control (open symbols), paretic (black symbols) and non-paretic (grey symbols) legs during self-triggered (circles) and investigator-triggered perturbations (triangles) with experience of repeated perturbations (initial (I), final (F)). The paretic leg has less APCOP displacement and slower APCOP velocity than control (during both conditions) and non-paretic legs (during self-triggered condition).

* $p < 0.05$ denotes significant comparison. Symbol placed below the initial perturbation is for I vs. F comparison in self-triggered condition. Brackets with symbols are for comparisons between conditions at each time point (initial or final). Data are mean \pm SE.