CORTICOSPINAL EXCITABILITY OF TRUNK MUSCLES IN ANTICIPATORY POSTURAL ADJUSTMENTS

by

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Abstract

Objective: To investigate corticospinal excitability of trunk muscles during anticipatory postural adjustments (APAs) prior to a fast shoulder flexion task in an elderly and young cohort.

Methods: Twenty young healthy (20.3 ± 1.4 years) and 20 elderly adults (75.5 ± 4.8 years) completed questionnaires, balance and neurophysiological assessments. Participants underwent balance tasks on a force plate, which recorded their centre of pressure displacement. A recognition reaction time (RRT) paradigm was used where participants responded to a visual stimulus by flexing their shoulders bilaterally as fast as they could. Activity of bilateral anterior deltoid (AD) and erector spinae (ES) muscles were recorded using electromyography (EMG). Onset of AD and ES EMG was measured to represent RRT and APAs, respectively. Transcranial magnetic stimulation (TMS) was used to assess corticospinal excitability of the ES prior to the shoulder flexion task. Maximal voluntary contraction (MVC) of the ES was measured.

Results: The amplitude of ES motor evoked potentials (MEPs) was greater at 40ms than 50ms, and at 30ms than 40ms, prior to the onset of AD EMG in both cohorts. ES MEP amplitude at 40ms prior to the onset of AD EMG correlated with the onset of ES EMG in the elderly cohort only. A higher percentage of elderly individuals had delayed APA (75%) compared to young. Elderly participants showed greater postural sway during balance tasks.

Conclusions: Our findings outline the corticospinal excitability profile of trunk muscles during APAs in older adults, and suggest older adults have greater motor cortical involvement in APA function.

Acknowledgments

I would like to thank Dr Chloe Chiou for all her remarkable guidance and patience whilst supervising me throughout this project. Thank you to Dr Ned Jenkinson for his encouragement and support. I would also like to thank all the participants who volunteered and took part in this project. Finally, I would like to thank everyone who showed me endless support and encouragement to complete this project.

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List of Abbreviations

AD- Anterior Deltoid

AMT- Active motor threshold

ANOVA- Analysis of variance

AP- Anterial-posterior

APA- Anticipatory postural adjustment

CNS- Central nervous system

COM- Centre of mass

CoP- Centre of pressure

CPA- Compensatory postural adjustment

EMG- Electromyography

EQ-5D- EuroQol-5D

ES- Erector Spinae

FES-I- Falls efficacy scale – international

fMRI- Functional magnetic resonance imaging

IPAQ- International physical questionnaire – short form

M1- Motor cortex

MEP- Motor evoked potential

MET- Metabolic equivalent of task

ML- Medial-lateral

MVC- Maximal voluntary contraction

PET- Positron emission tomography

PMC- Pre motor cortex

rmsEMG- root-mean-square amplitude of background EMG

RRT- Recognition reaction time

RT- Reaction time

SD- Standard deviation

SEM- Standard error of the mean

SPSS- Statistical program for the social sciences

TES- Transcranial electrical stimulation

TMS- Transcranial magnetic stimulation

TrA- Transversus Abdominus

VAS- Visual analogue scale

1. Introduction

1.1. Trunk control and balance in older adults

Balance is considered a complex process in order to maintain or recover postural stability, and is thought to involve control from all levels of the central nervous system (CNS) (Herold et al. 2017). Postural control involves the ability to maintain one's centre of mass (COM) over the base of support, in response to perturbations (Hess, Woollacott and Shivitz, 2006). There are two main processes that are used to restore or maintain postural stability, anticipatory postural adjustments (APAs), and compensatory postural adjustments (CPAs). APAs occur prior to movements and are a feed forward process counteracting an expected perturbation (Bouisset and Zattara, 1990). It is considered as a first line of defence for postural control in anticipation of perturbations and has been observed whilst sitting, standing or walking (Aruin and Shiratori, 2003). On the contrary, CPAs are consequential responses to a postural perturbation, and therefore under the control of feedback mechanisms (Bigongiari et al. 2011). Unlike the absence of APAs that can be seen in neurological conditions such as Parkinson's disease (Bazalgette et al. 1986), it is thought that the APAs are delayed in elderly people, resulting in increased responses of the CPAs (Kanekar and Aruin, 2014). For example, in both self-paced voluntary shoulder movements (Woollacott & Manchester. 1993; Rogers, Kukulka and Soderberg, 1992) and in predictable external perturbations to the body (Kanekar and Aruin, 2014), activity of trunk and lower-limb muscles occurred later than that in anterior deltoid in older adults when compared to young adults, where their trunk and lower-limb muscles were activated prior the AD activation. Biomechanical studies using force platforms to measure centre of pressure (CoP) have shown that the

elderly relied more on CPAs when their APAs were delayed or impaired (Kanekar and Aruin, 2014). They also found smaller CoP displacements at the time of the perturbation were associated with delayed APAs in older adults, resulting in the need for larger CoP and COM displacements after the perturbation; suggesting a CPA mechanism.

Trunk muscles are involved in goal directed movements and postural adjustments. Evidence has shown that trunk muscles are activated prior to or at the same time as voluntary arm movements, and can be regarded as anticipatory if they occur from -100ms to +50ms of movement onset (Aruin and Latash, 1995). Studies have shown in healthy subjects an increased activity in erector spinae (ES) and in rectus abdominus during shoulder flexion and shoulder extension, respectively (Aruin and Latash, 1995). This finding suggests the effect of movement direction on APAs. However, this effect is less clear in the deep postural muscles, such as transversus abdominus (TrA), as studies showed that activity in the TrA preceded to activity in the anterior deltoid (AD) regardless of movement direction (Hodges and Richardson, 1997a). EMG activity of the trunk and lower-limb muscles has been shown to increase during CPA phases (following perturbation) in the elderly in a voluntary arm movement paradigm (Woollacott and Manchester, 1993; Rogers, Kukulka and Soderberg, 1992), and after external perturbations whilst also measuring the AD muscles in shoulder flexion (Kanekar and Aruin, 2014). This may be due to the delay in trunk and lower-limb muscles relative to the AD muscles, which in young adults were activated 50 to 200ms prior to the AD activation (Woollacott and Manchester, 1993; Rogers, Kukulka and Soderberg, 1992; Kanekar and Aruin, 2014).

One research question is whether delayed APAs of the trunk muscles are directly due to the aging process or whether it is due to slower movement velocities seen in the elderly. A slow arm movement has been associated with delayed onset of APAs in young adults, where it takes longer for the movement to occur and thus slower activation of APAs (Hodges and Richardson, 1997b). Research shows that older people have a slower reaction time and movement time compared to young adults when investigating agonist and antagonist muscles of the arm (Arnold et al, 2015), which could result in delayed APAs observed in the elderly. However, in another study, when the speed of the arm movement (velocity) was controlled for, onset of ES activity with respect to onset of AD activity were still later in older adults compared with young adults, suggesting the delayed onset of trunk muscles in older adults to be irrespective of movement speed (Woollacott and Manchester, 1993). This finding suggests that delayed APAs of the trunk muscles during the arm movements in the elderly might not be due to a decrease in movement velocities but changes in postural control with age.

1.2. Neural Control of trunk stability and balance

The neural control of APAs is still poorly understood. Early research suggested postural control to be a reflex in which the brainstem and spinal circuits play a major role (Sherrington, 1910). This position was supported by early research using decerebrate cats, where many postural reflexes were maintained even after the removal of higher cerebral function following decerebration (Sherrington, 1910). However, later work by Horak (1987) described postural control as a complex skill, involving organisation of senses by the whole CNS including the higher centres to control skeletal muscles. Jacobs and Horak's (2007) identified in a review of the

cortical involvement in postural responses, that postural responses appear to be part of a context-dependent (varying on task, environment, participants) and dynamic interaction between all levels of the neural axis. Due to varying characteristics i.e. height of participants, whether lower or upper extremities were being measured, what perturbations were delivered (velocity, direction) and the context (posture), studies vary in what is classified as short, medium and long latencies, thus general terms are used e.g. ‘initial’ and ‘late’ phases (Jacobs and Horaks, 2007). The evidence implies adjustments by cortical areas higher in the neural axis, are implied by longer latencies in the onset of postural responses compared to spinal stretch reflexes (Chan et al. 1979; Matthews. 1991). This long-loop latency is seen in the time difference between the tendon jerk reflex latency (the time signals need to travel the spinal cord) and the functional stretch reflex (FSR) latency (late response) (Chan et al. 1979). Further, an absence of FSR in those with cortical lesions, suggests the long central pathways involving the cortex play a role in the ‘late’ EMG response seen in humans (Chan et al. 1979). The idea that the CNS influences postural stability is thus supported by evidence of humans (Chan et al. 1979; Palmer, Downes and Ashby, 1996; Viallet et al. 1992) and animals (Bard, 1933) with cortical lesions having abnormal postural responses to perturbations.

The primary motor cortex (M1) is believed to play a key role in APAs, as lesions involving the M1, such as stroke (Pereira et al. 2014), are associated with disruptions of APAs in the contralateral muscles in a rapid arm abduction task (Palmer, Downes and Ashby, 1996), as well as in a bimanual load-lifting task (Viallet et al. 1992). In an experiment where patients with stroke were required to complete rapid forward stepping movements under simple or a choice reaction time conditions, those with

lesions at the premotor cortex (PMC) showed impairments to APAs, compared to age- and sex- matched healthy participants and those with spared PMC (Chang et al. 2010). This result suggests a vital role of the premotor cortex in selection and preparation of a movement (Chang et al. 2010).

Ageing brains demonstrate changes in structure and function, resulting in alterations in motor control (Papegaaij et al. 2014). A study investigating the effect of age on cortical control of upright stance using electroencephalography (EEG) showed the coherence between the M1 and postural muscles (tibialis anterior, gastrocnemius, rectus femoris, and biceps femoris) was greater post-perturbation when compared to pre-perturbation in the elderly cohort. The authors interpreted that the reduced efficiency of connection between the M1 and the postural muscles prior to the perturbation might cause impaired anticipatory postural control in older adults (Ozdemir et al. 2018). As the CNS restores and maintains posture through APAs and CPAs (Kanekar and Aruin, 2014), a resultant loss in postural control is associated with an increased number of falls, due to the relationship between balance, voluntary movements and posture (Rogers, Kukulka and Soderberg, 1992), however no direct correlation between impaired APAs and fall risk has been found. Rehabilitation processes for the elderly should focus on improving APA responses to external perturbations in order to improve postural control and balance (Santos et al. 2010).

1.3. Transcranial Magnetic Stimulation (TMS)

TMS is a non-invasive brain stimulation technique that can be used to investigate the function of corticospinal pathways via stimulation of the M1 (Barker, Jalinous and Freeston, 1985). TMS provides a pain-free, rapid and simple method as opposed to

the transcranial electrical stimulation (TES) to assess corticospinal excitability (Merton et al. 1982). Both TES and TMS can produce a muscle response known as a motor evoked potential (MEP), which can be recorded using EMG. By measuring the size and the latencies of the MEPs, researchers can quantify changes in corticospinal excitability in a resting muscle and in an active muscle.

1.4. Corticospinal Excitability

Changes in corticospinal excitability prior to voluntary movements have been investigated using a reaction time paradigm. Several studies reported increased corticospinal excitability between 50 to 120ms prior the voluntary movements, this time varies between the prime movers investigated; upper limb muscles including hand (Rossini et al. 1988; Chen et al. 1998) and forearm muscles (Leocani et al. 2000), and the lower limb muscles (Remaud, Bilodeau and Tremblay, 2014). Increased corticospinal excitability prior to the voluntary movements suggest motor cortical involvement in a voluntary movement. Research found warning signals to have an increased preparatory effect where the corticospinal excitability increased before an imperative stimulus was given, which resulted in a further increase in the corticospinal excitability, suggesting preparatory and initiation processes to be associated with corticospinal excitability (Kennefick, Maslovat and Carlsen, 2014).

Several lines of evidence have shown the feasibility to assess corticospinal excitability of trunk muscles (e.g. ES, TrA) using TMS (Nowicky et al. 2001; Chiou et al. 2014; Tsao, Galea and Hodges, 2008). The ES muscles are considered to play a mechanical role by extending the trunk to maintain COM within the base of support (Bergmark, 1989), in response to voluntary shoulder movements. Prior work has

shown increased muscle activity and amplitude of MEPs in the ES to counterbalance the torque induced by voluntarily holding the contralateral arm against different forces applied to the arm; this effect was observed in both standing and lying postures (Davey et al. 2002). Recent work has shown that corticospinal excitability of the ES was increased to a greater extent during a dynamic shoulder flexion task where APAs were required, compared with a static shoulder flexion task (with no APAs required) and a goal-directed voluntary trunk extension task in healthy adults (Chiou et al. 2016). The findings provide evidence of motor cortical involvement in APAs of the trunk muscles due to the increased corticospinal excitability seen as greater MEP amplitudes in the ES during movements requiring trunk stability. Furthermore, work has shown that corticospinal excitability of the ES starts to increase 40ms prior to a rapid shoulder flexion task (i.e. during APAs of the trunk) and the increased excitability was accompanied by reduced inhibition in M1 with no change in spinal excitability (Chiou et al., 2018). No change in spinal excitability suggests that postural adjustments are prepared prior to the movement onset in a feed forward manner, as they found across all time points the level of activity of the ES muscle was similar, therefore APAs are suggested to be mediated cortically (Choiu et al. 2018). These results again support the notion that APAs are modulated by the M1. Moreover, the authors did not observe the same effect in rectus abdominus during the shoulder flexion task, suggesting that motor cortical control of APAs is task-specific (Chiou et al., 2018), but not posture specific supporting Davey et al's (2002) work as they found similar excitability profiles in standing and lying.

Age-related changes in corticospinal excitability in older adults have been reported, where amplitudes of MEPs in hand muscles were reported to be smaller in older

adults than in young adults (Rozand et al. 2019). In addition, amplitudes of MEPs and H-reflex in tibialis anterior were smaller in the elderly than in the young adults during submaximal voluntary contractions, indicating age-related changes in neurophysiological function in both cortical and spinal circuits (Škarabot et al. 2019). Furthermore, a recent study has demonstrated a loss of discrete motor cortical organization between lumbar paraspinal and gluteus medius muscles in older adults with delayed APAs of gluteus medius during an arm abduction task compared with young adults with no delayed APAs (Smith and Fisher, 2018). The data suggests an association between changes in the M1 and altered APAs in the elderly. Changes in corticospinal excitability of prime-movers in older adults have been reported. Using a Go/No-Go reaction time paradigm a study showed a smaller increase in corticospinal excitability of a hand muscle prior to the movement in older adults than in young adults (Fujiyama, Tandonnet and Summers, 2011). On the contrary, a study using a simple reaction time paradigm found that older adults demonstrated a significant facilitation of MEPs in a small hand muscle preceding the imperative stimulus compared with young adults, albeit the timing of the facilitation of MEPs was similar between the age groups (Levin et al. 2011). The different findings may be due to different study paradigms employed but it also highlights the need for more research into age-related changes in neurophysiological function and postural control. Whether delays in APAs of the trunk muscles seen with ageing may be associated with changes in corticospinal excitability remains unknown and is the aim of this study.

1.5. Aim and Hypotheses

The aim of this project was to investigate corticospinal excitability of trunk muscles prior to a fast shoulder flexion task in an elderly cohort, compared with a young healthy cohort. We hypothesised that the increase in corticospinal excitability prior to the shoulder movement would be delayed in the elderly cohort, and that the delays seen in corticospinal excitability observed in the elderly cohort may correlate with the delayed APAs of the trunk muscles and reduced balance.

2. Methods

2.1 Ethics

Ethics were obtained through the appropriate University of Birmingham ethics committee before testing took place. Written informed consent was obtained from all participants prior to the experiment. Participants were made aware of their right to withdraw at any point throughout the study, with no explanation required.

2.2 Participants

Healthy, adult volunteers from two cohorts took part in this study, a young cohort (18-35 years, n = 26), and an elderly cohort (≥65 years, n = 28). The young participants were recruited from the University of Birmingham student body; the elderly participants were recruited through The University of Birmingham's 1000 Elderly mailing list. On arrival to the laboratory, participants were greeted, briefed about the study and asked to fill in the consent form and questionnaires; this included the Falls Efficacy Scale - International (FES-I), the International Physical Questionnaire-Short Form (IPAQ), and the EuroQol-5D (EQ-5D). FES-I is a 16-item questionnaire measuring individuals concerns or fears of falling (Yardley et al. 2005); IPAQ is a 9-item questionnaire measuring the amount of activity per week individuals spend on sitting, walking, taking part in moderate, and vigorous activity (Craig et al. 2003). The EQ-5D questionnaire measures individuals' quality of life, with concerns about their mobility, self-care, pain and discomfort, anxiety and depression, and usual activities, and their self-perceived health based on a visual analogue scale (VAS) between 0 (worst health possible) and 100 (best health possible) (Balestroni and Bertolotti, 2015). Participants were also asked to fill in the TMS safety questionnaire. They were

excluded from the neurophysiological assessment (details below) if they met the TMS exclusion criteria (Rossi et al. 2011) including a family history of epilepsy, concussion, pregnancy, metal implants in the brain, unexplained faints, cardiac pacemakers. Furthermore, participants who did not have visible motor evoked potentials (MEPs) in erector spinae (ES) (young: n=6; elderly: n=7) or were unable to tolerate the sensation of the TMS were also excluded (n=1). All recruited participants underwent the functionality testing, with 20 from each cohort further took part in the neurophysiological assessment (table 1).

	Mean	**SD**	**Range**
	Young(n=20)		
Age (years) **	20.25	1.41	19-23
Height (cm)	171.525	7.04	161-183
Weight (kg)	68.45	6.86	56-83
Motor Threshold (MT)	80.05	14.52	57-100
Intensity	96.06	17.42	68.4-120
Reaction Time (ms) **	205.2	25	161.5-243.7
	Elderly (n=20)		
Age (years) **	75.45	4.83	69-86
Height (cm)	169.4	10.94	150-193
Weight (kg)	64	16.25	40-110
Motor Threshold (MT)	81.15	16.99	50-100
Intensity	97.38	20.39	60-120
Reaction Time (ms) **	230.9	24.23	185.5-279.3

Table 1. Participant information of elderly and young who took part in both parts of the study

Intensity refers to the TMS intensity used for testing (1.2 x MT)

** = $p < 0.01$ between-group comparisons.

2.3 Instrumentation

Motion and force plate

Movement trajectory and CoP during the functionality testing were recorded using a 3D motion capture system (BTS Bioengineering S.p.A., Milano, Italy; SMART-Suite, SMART-DX6000) and a force platform (BTS Bioengineering S.p.A., Milano, Italy; BTS INFINI-T), respectively at a sampling rate of 250 Hz. Reflective markers were placed on the ulnar styloid process of bilateral wrists for the motion capture system to track arm movements.

Electromyography (EMG)

Muscle activity was recorded using surface EMG (Delsys® Bagnoli-2 EMG system). Electrodes (19.8 mm x 35mm) were placed over muscle bellies and in line with the approximate orientation of muscle fibres of bilateral ES at the 12^{th} thoracic vertebral level, and AD (figure 1). Reference electrodes were placed at the 7^{th} cervical vertebral level, and the elbow (olecranon) to reduce background noise. T12 was the chosen point for electrode positioning as ES muscle function in this area is predominantly concerned with postural adjustments to maintain the COM (Davey et al. 2002). The position was identified by palpation of the L4 (Lumbar vertebrae) and counting up from the level of the iliac crest. EMG signals were pre-amplified (1000x), and band-passed filtered between 20 and 450Hz before being sampled at 1 kHz by a micro 1401 (CED, Cambridge, UK). The data were acquired, stored, and analysed by Signal software (version 6, CED, Cambridge, UK).

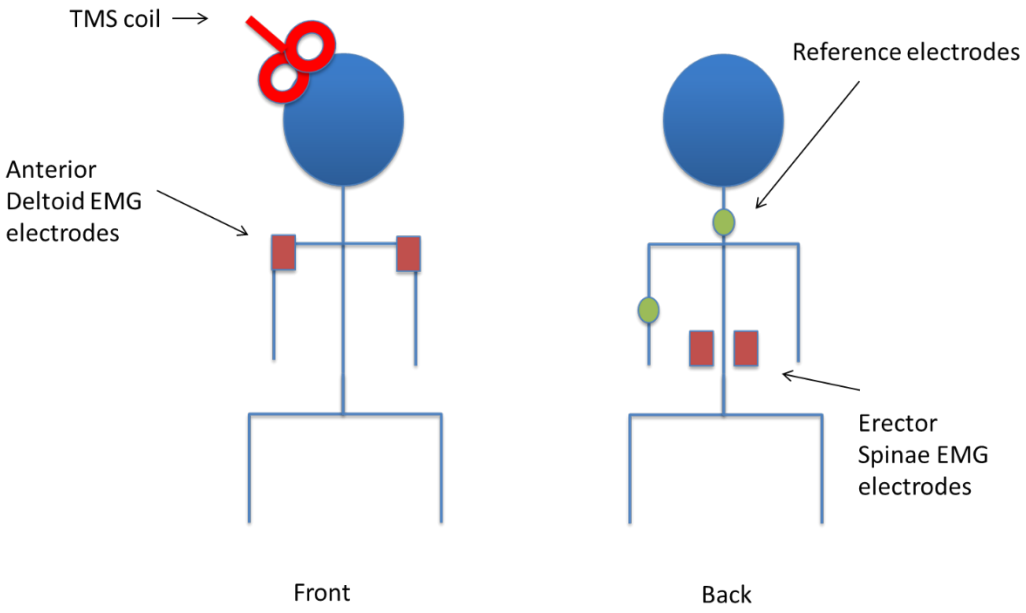


Figure 1. TMS set up and electrode placement

Transcranial magnetic stimulation (TMS) and motor evoked potentials (MEPs)

TMS was delivered over M1 using a Magstim 200^2 stimulator connected to a D70 Alpha (Coated) figure-of-eight coil (outside coil diameter: 18cm; The Magstim Company Ltd, UK), at a position that elicited maximal MEP of the contralateral ES (Chiou et al. 2018). For all participants, centre of the head (the vertex) was found through marking the intercept between the sagittal inion-nasion and lateral tragus-tragus lines and marked on their scalp with a marker pen. M1 was located relative to this point as approximately 2cm lateral and 2cm posterior to the vertex (O'Connell et al. 2007). The coil was moved around the M1 to find the site, which evoked reliable and maximal MEPs in the contralateral ES. This location was defined as the 'hotspot' and marked on the scalp to ensure repositioning of the coil throughout the experiment (similar in both groups; figure 2). The coil was held 45° to the midline with the handle pointing posteriorly to induce a current flow in the anteromedial direction

(Lazzaro et al. 2004). The procedure started from the hemisphere ipsilateral to the dominant arm, and if clear ES MEP responses were unable to be obtained then the same procedure was repeated on the other hemisphere. The hemisphere which gave reliable MEPs was then determined as the targeted hemisphere and the contralateral ES was the targeted muscle.

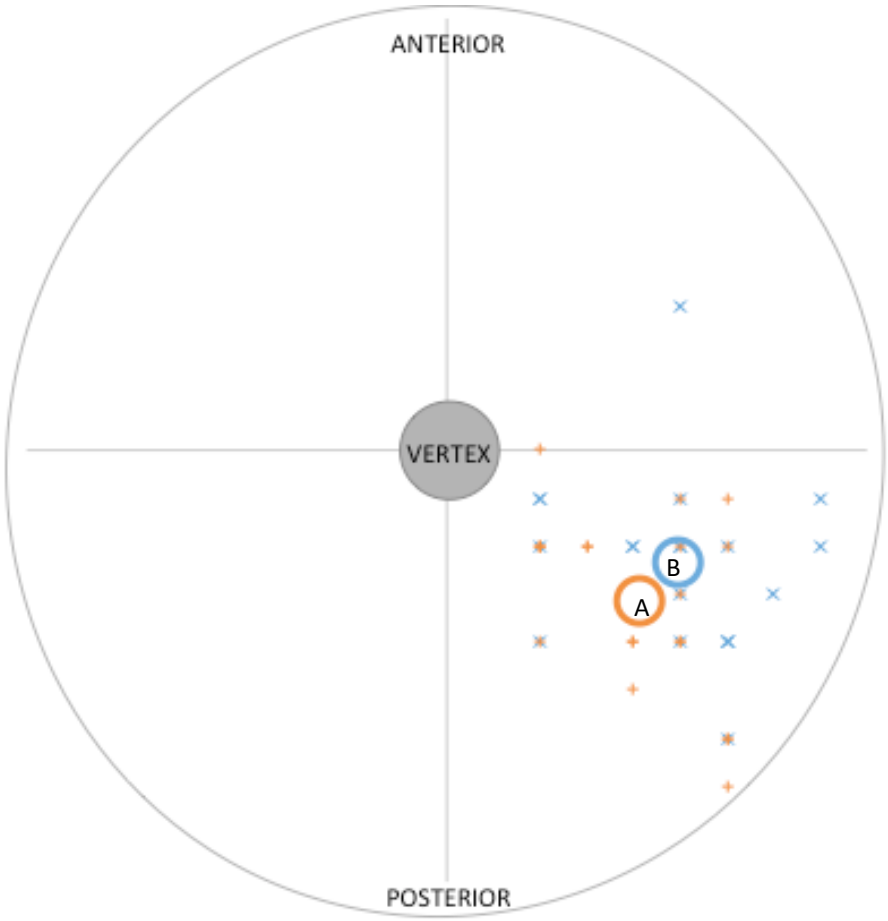


Figure 2. 'Hotspot' location of each participant (not hemisphere specific) (A) Elderly average spot (2cm lateral and 1.5cm posterior). (B) Young average spot (2.5cm lateral and 1cm posterior).

Active motor threshold (AMT) was assessed due to participants being seated in an upright position during testing, and was defined as the minimal stimulus intensity required to evoke visible MEPs (clear MEPs displayed on Signal) in at least 3/6 consecutive trials (Chiou et al. 2018; Chiou et al. 2016). Test intensity was set as 1.2

x the threshold intensity and used throughout the experiment (Cuypers, Thijs and Meesen, 2014). AMT and test intensity were similar in both elderly and young cohorts (table 1).

2.4 Experimental protocol

All participants undertook neurophysiological and functionality assessments on the same day. For the functionality assessments, participants were instructed to perform a number of balance tasks on the force plate. The tasks included: 1) feet shoulder width, 2) feet close, 3) tandem stand, and 4) one-leg stand (Figure 3). For the tandem stand and one-leg stand, participants were able to choose which foot to place forward and which foot to stand on that allowed them to stay the most stable. Each task was recorded for 30 seconds or until the participants lost balance. During the tasks, an experimenter was standing near the participants to ensure safety without providing assistance for the maintenance of balance. In addition to the

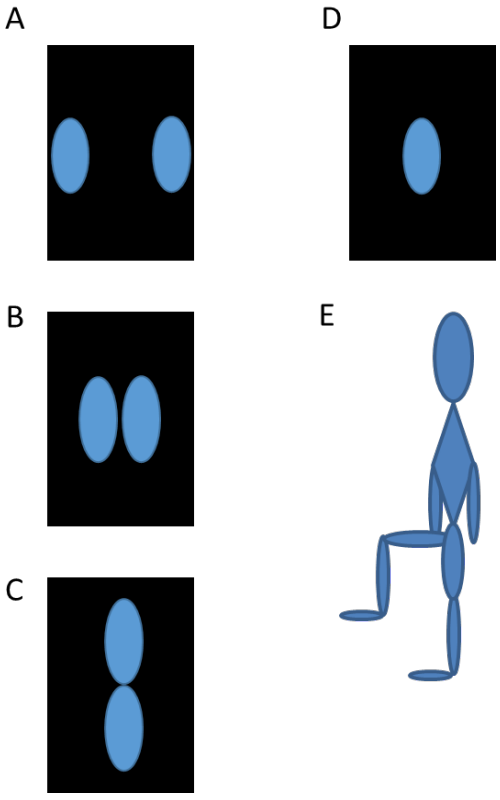


Figure 3. Balance tasks 1.4. (A) Feet shoulder width. (B) Feet closed. (C) Tandem stand. (D + E) One leg stand.

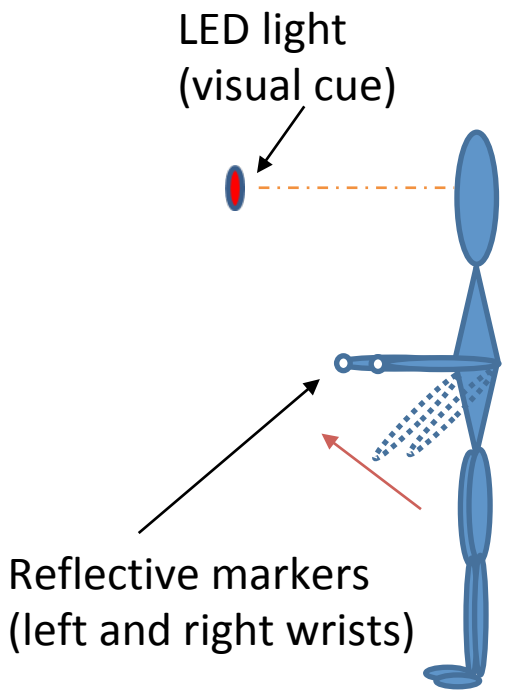


Figure 4. Protocol of task 5 (RT) in response to LED light in front of participants at eye level

balance tasks, participants were asked to raise arms bilaterally as fast as they can but keep their body as stable as they can in response to an LED light placed ~1m in front of them at eye level (Figure 4). A verbal warning signal, ‘Ready’ was given to all participants prior to the LED light, which was controlled by a button press. The interval between the verbal warning signal and the visual cue was unfixed. The task was repeated 10 times.

For the neurophysiological assessments, participants were required to go through a series of tasks including baseline measurements, reaction time, main trial and maximal voluntary contractions. Ten MEPs were recorded as baseline MEPs whilst participants were seated upright with arms by their side. A seated position was chosen due to our preliminary data (n=6) showing no significant differences in the timing of increasing corticospinal excitability of the ES between a seated or standing position in young healthy adults. This finding is in line with previous research showing no differences in corticospinal excitability as well as in spinal excitability between different postures, such as between standing or lying (Chiou et al. 2018), and between standing and seated positions (Hortobágyi et al. 2018).

Recognition reaction time (RRT) was tested following the baseline measurements. It consisted of two conditions: 1) light, and 2) TMS noise. Participants were instructed to flex bilateral shoulders to 90° as fast as they could only when the light came on, and to not respond (arms kept by their side with no movement) during the TMS noise condition. This was to remove reaction to auditory cues, isolating and controlling for response to visual cue only (Chiou et al. 2018) as it has been found that auditory reaction time is faster than visual reaction time by 47miliseconds (Shelton and Kumar, 2010). A verbal warning signal, ‘Ready’ was given to all participants prior to

the LED light, which was controlled by a button press. The interval between the warning signal and the LED light was unfixed, varying between 1-3 seconds.

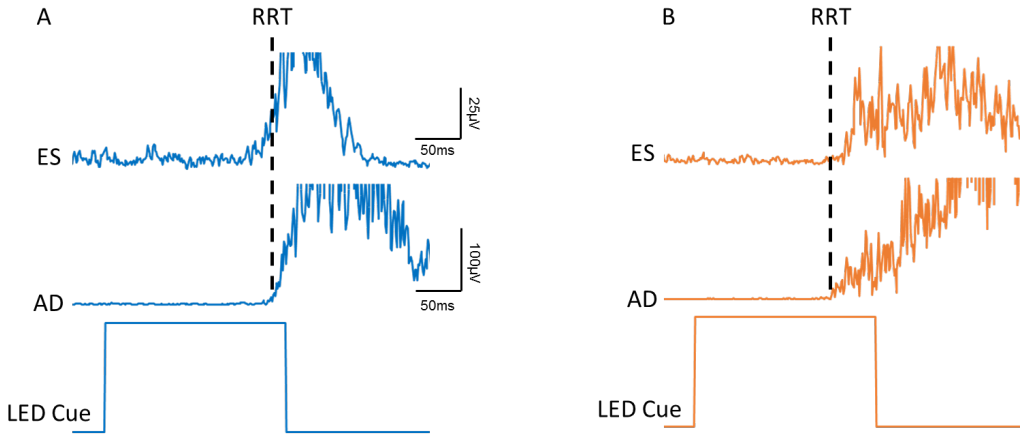


Figure 5. Recognition Reaction Time (RRT) in young and elderly. (A) Young. (B) Elderly.

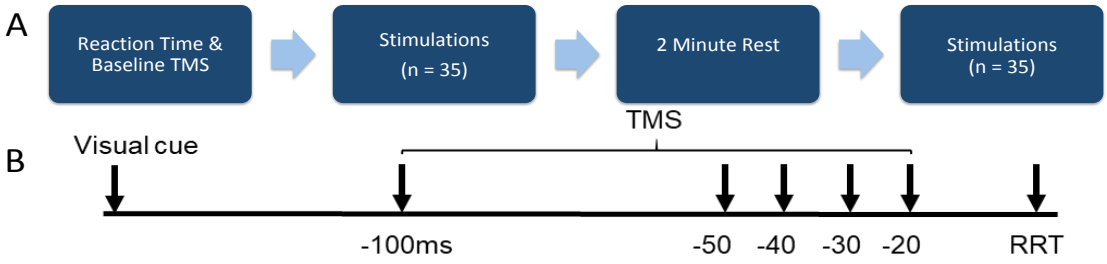


Figure 6. (A) Experimental procedures. (B) TMS paradigm. RRT: recognition reaction time

Each condition was repeated 10 times and their order was randomised to ensure that the participants were unable to predict which condition was coming next. Ten trials obtained from the cue only condition were averaged and an RRT was determined visually at which AD EMG rose significantly above the baseline for all participants (figure 5). This data was then used to calibrate the timing of the stimuli for the main task for each individual.The main task was divided into two halves, as it was too demanding for the individual to perform all 70 trials at once. The experimental conditions consisted of 7 states: cue only (no stimulation), TMS only (no visual cue),

a cue with TMS prior to the RRT at 100ms, 50ms, 40ms, 30ms, and 20ms prior RT (Figure 6). The 7 states were randomised, with 5 trials for each condition in each block (35 trials in one block x 2 blocks = 70 trials in total). The participants were instructed to move their arms only when they saw the LED light flash and ignore the noise of the TMS (figure 7). A warning signal 'Ready' was given each trial regardless of whether there was a visual cue or not for consistency. In situations where participants reacted to the warning signal or the TMS noise, they were required to complete additional stimulations to ensure enough data was collected.

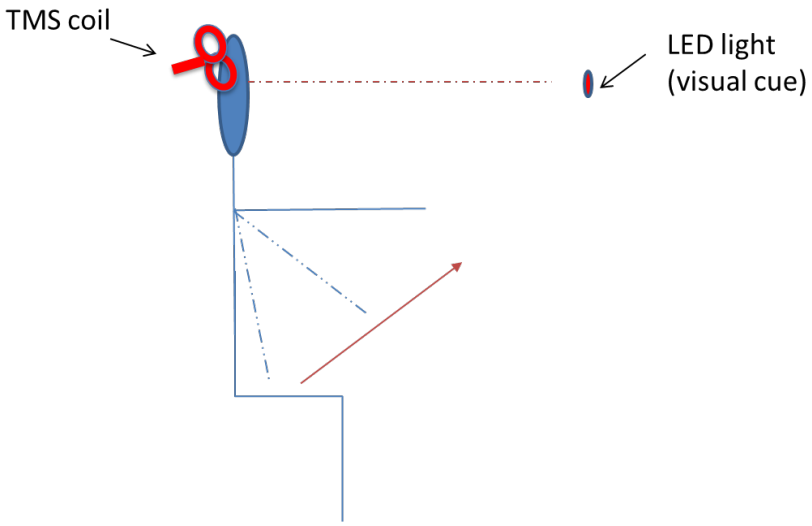


Figure 7. TMS experimental set up for main trials

Three brief maximal voluntary contractions (MVCs) of the ES were recorded whilst participants were lying face down on a massage table. This was achieved with one experimenter applying resistance at the scapula whilst the participant lifted their chest off the table by pushing against the resistance. Breaks were given between each contraction.

2.5 Data analysis

The FES-I questionnaire was analysed through a sum of the total score of all 16 answers, giving a result between 16 and 64. The IPAQ was analysed through use of a formula equating the MET (metabolic equivalents) minutes of each score of walking (3.3 x minutes per week), moderate activity (4 x minutes per week), and vigorous activity (8 x minutes per week), referring to the amount of oxygen consumed e.g 1MET = at rest. EQ-5D was analysed by categorising answers into 'problem' or 'no problem'; score 1 was categorised as no problem and score 2 and above was categorised as problem. Their EQ-VAS (visual analogue scale) score was taken from the visual analogue scale (0-100; 0 indicating poor health, 100 indicating good health), indicating their self-rated wellness on the day.

MATLAB software (MATLAB_R2017b; The MathWorks, Inc., Natick, Massachusetts, United States) was used for offline processing of kinetic and kinematic data. All data were low-pass filtered using a Butterworth filter with a cut-off frequency of 4Hz. For the kinematic data, onset of the arm movements was defined visually as when one of the wrist markers moved (coordination of the marker changed in y-axis). For the kinetic data, maximum trajectory of CoP and sway (variation of CoP) in anterial-posterior (AP) direction and in medial-lateral direction (ML), sway area, and sway velocity were calculated using MATLAB codes.

EMG data were first visually inspected to remove trials without a visible MEP, a failure to respond, and incorrect responses i.e. to TMS only states. Frames where ES or AD activity were present before the stimulation were also removed. Reaction time was measured manually frame-by-frame from the rectified EMG traces. It was

determined where the AD or ES EMG rose above more than 3 standard deviation (SD) of the mean pre-stimulus EMG level (Chiou et al. 2018). Data were reorganised into relative time points (-100ms, 85ms, 70ms, 60ms, 50ms, 40ms, 30ms, and 20ms) for each participant due to RT varying throughout the trials. This was done through analysing the data and measuring the MEP latency of each frame, shown in figure 8. However, 20ms was not included in the stats or graphs due to few frames being valid at that time point across both groups. Signal scripts were also used to calculate peak-to-peak amplitude of MEPs and root-mean-square amplitude of background EMG (rmsEMG) in a 100ms window prior to the stimulation from unrectified EMG traces. Rectified EMG was used to measure reaction time by identifying visually the point where the activity increased above the pre-stimulus line.

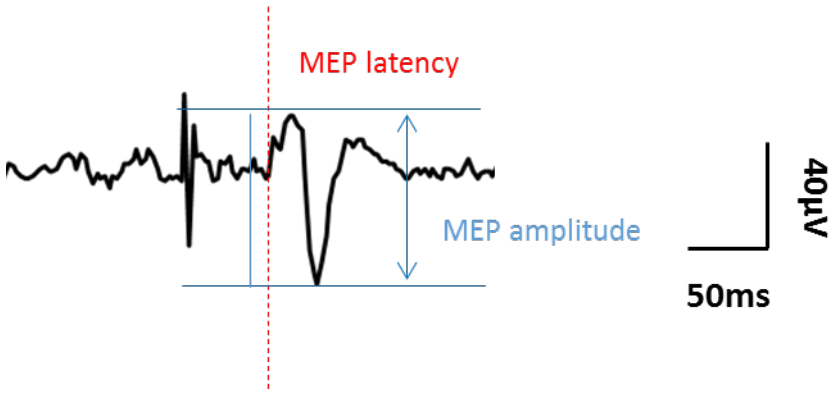


Figure 8. MEP trace displaying how amplitude and latency were measured

2.6 Statistical analysis

Statistical Program for the Social Sciences (SPSS v.23, IBM Corp, Armonk, NY, USA) was used to perform statistical analysis. Normal distribution was tested by the Shapiro-Wilk test. If data failed the normality test, non-parametric tests were applied;

if sphericity assumption failed for repeated ANOVAs, Greenhouse-Geisser corrections were applied. For continuous data (IPAQ-MET, EQ-VAS, CoP variables, RT), independent t tests or Mann-Whitney U tests (for non-parametric tests) were used to examine between-group differences (young vs. elderly cohort). For discrete data (IPAQ, EQ-5D; FES-I), Chi-square tests were employed for between-group comparisons. To determine changes in ES MEPs along the course of time in the APA window and whether this was different between groups, a mixed-model repeated measure ANOVA was applied to examine any effect of time (-100ms, 85ms, 70ms, 60ms, 50ms, 40ms, 30ms, TMS alone) and an interaction between group and time. Within-subjects contrasts post-hoc tests were used where appropriate. To characterise the relationship of MEPs with APAs and reaction time (onset of ES and AD EMG), Pearson correlation analysis was used. Significance was set at $p < 0.05$, with Bonferroni correction to adjust for multiple comparisons. Group data are presented as mean±SD in the text and mean±SEM in figures.

3. Results

3.1. Questionnaires

Results of the IPAQ questionnaire demonstrated that the younger cohort on average per week had a higher MET output (5705.9 ± 5228.5METs) than the elderly cohort (3266.5 ± 2705.5METs; $t(48) = -2.1$, $p = 0.041$; figure 8). There were more young adults categorised as high level of activity than older adults. Between group differences were seen in amount of activity per week, where the young cohort showed higher levels of activity in the IPAQ questionnaire, $\chi^2(2, n = 50) = 10.52$, $p = 0.005$.

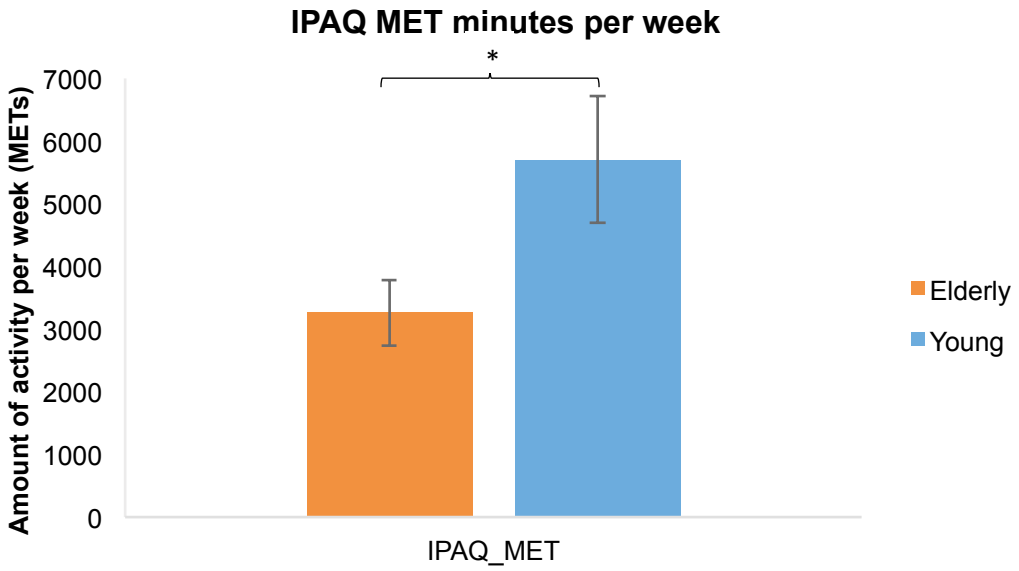


Figure 9. Mean MET output per week in elderly and young.

** = p < 0.05*

We found that the elderly cohort had a significantly higher percentage of individuals with a fear of falling in the FES-I questionnaire (42.3%) compared with the young group who had no fear of falling (0%; $\chi^2(1, n = 50) = 13.02$, $p < 0.001$). Older adults had more concerns of pain and discomfort compared with young adults ($\chi^2(2, n=50) = 9.64$, $p = 0.008$; figure 9).

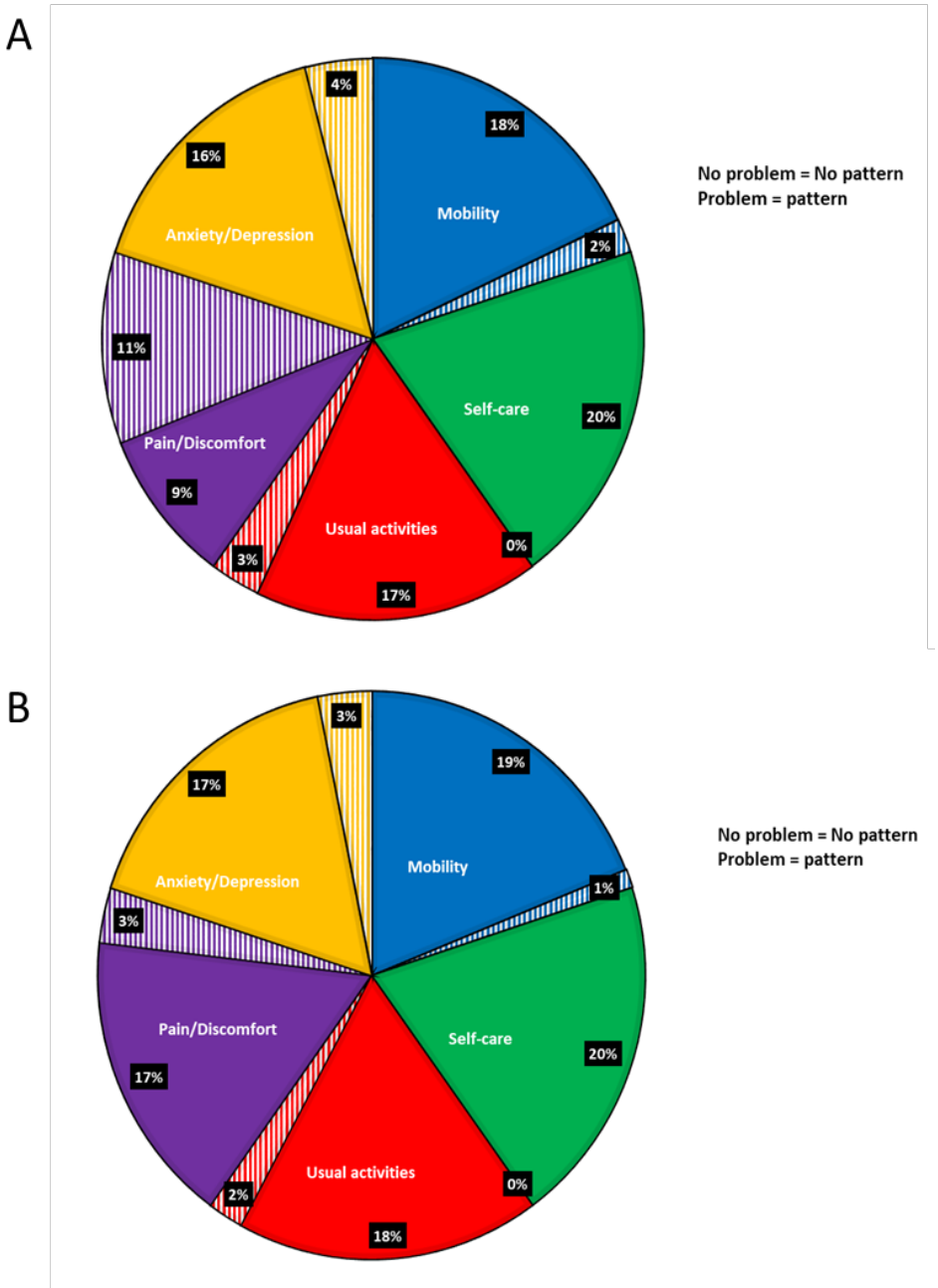


Figure 10. Problem vs no problem determined through EQ-5D-5L Questionnaire (A) Elderly. (B) Young.

Results showed that there was no difference in EQ-VAS values between elderly (87.44 ± 11.1) and young groups (85.54 ± 9.44; t(47) = .64; p = 0.523), suggesting that they subjectively viewed their health to be at the same level.

3.2. Functionality tests: Balance assessment

Significant differences were seen for the tandem stand in anteroposterior sway with the elderly cohort showing greater variations in CoP displacement (0.71 ± .39cm) compared to the young cohort (.42 ± .17cm; t(35.5) = 3.47, p = 0.001). Significant differences were also seen for mediolateral sway where elderly showed a greater variations in CoP displacement (.63 ± .18) than young (.38 ± .11cm; t(50) = 6.01, p < 0.001). Elderly displayed a greater movement of CoP for area (8.9 ± 8.85cm^2) than the young cohort (3.08 ± 1.88cm^2; t(28.73) = 3.47, p = 0.002; figure 10).

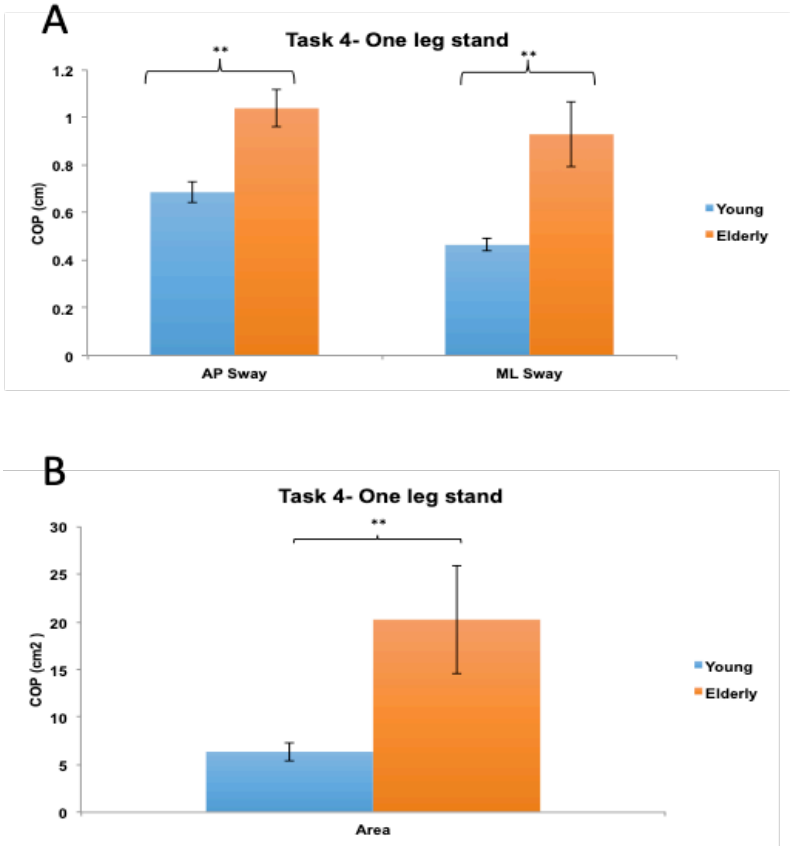
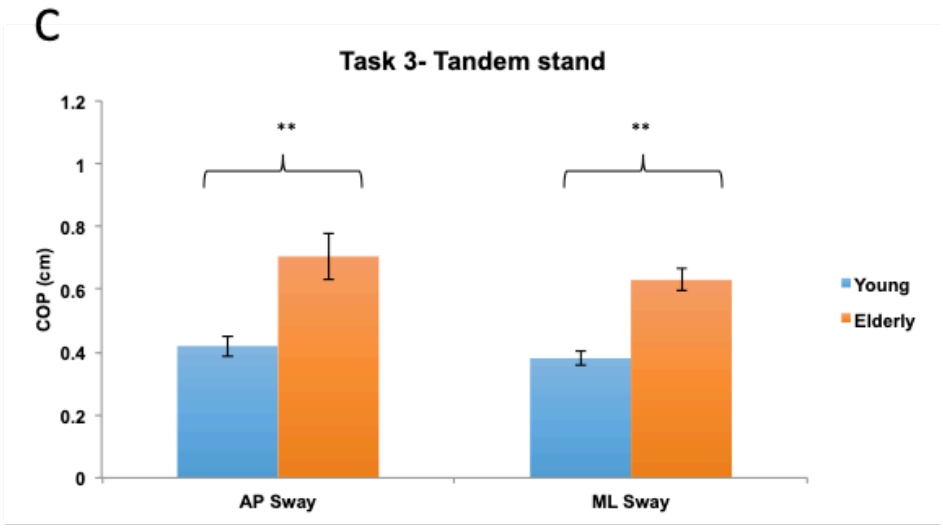


Figure 11. Task 3-Tandem stand. (A) Mean anteroposterior sway and mediolateral sway between elderly and young. (B) Mean sway area between elderly and young.

*** = p < 0.01*

Significant differences were seen for one leg stand in anteroposterior sway with the elderly cohort displaying larger variations in CoP displacement (1.04 ± .404cm) than the young cohort (.69 ± .22cm; $t(39.38) = 3.88$, $p < 0.001$). Along with elderly showing higher variations in CoP displacement in mediolateral sway (.93 ± .71cm) than the young cohort (.47 ± 0.13cm; $t(49) = 3.23$, $p = 0.002$). CoP area was also shown to be greater in the elderly cohort (20.25 ± 28.93cm^2) than the young cohort (6.35 ± 5.01cm^2; $t(26.56) = 2.412$, $p = 0.023$; figure 11).



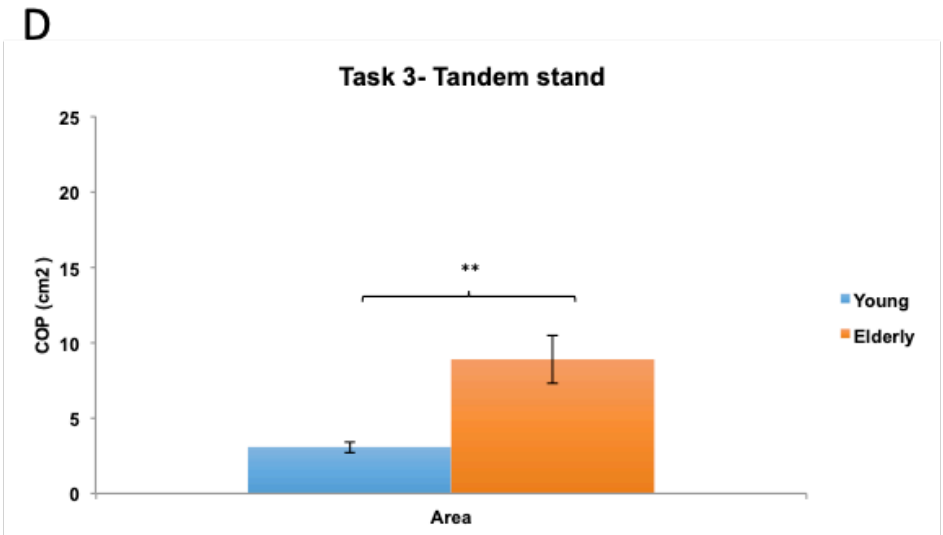


Figure 12. Task 4- one leg stand. (C) Mean anteroposterior sway and mediolateral sway between elderly and young. (D) Mean sway area between elderly and young.

*** = p < 0.01*

CoP velocity during the fast shoulder flexion task was faster in the young cohort (11.73 ± 5.48cm/s) than in the elderly cohort (8.83 ± 2.56cm/s; t(33.74) = -2.409, p = 0.022; figure 12). This result may suggest that the young cohort was more confident than the elderly cohort in moving their body in order to generate required momentum for the fast, voluntary arm movement.

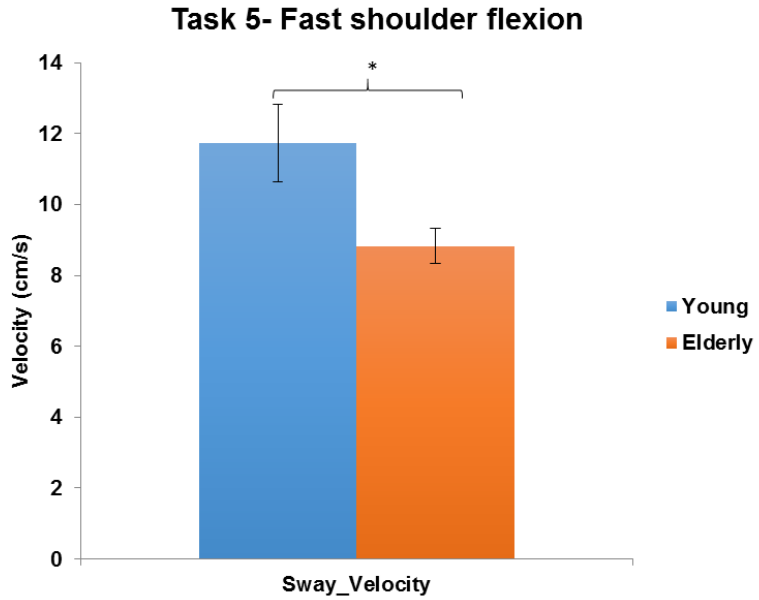


Figure 13. Task 5- Fast shoulder flexion. Rapid arm movement in response to LED light. Mean sway velocity between elderly and young.

** = p < 0.05*

No significant differences were seen in standing with feet shoulder width or standing with feet close between the young or elderly cohort.

3.2.1. Comparisons between functionality tests and questionnaires

There were no correlations between the measures of postural sway during the balance tasks and the physical activity level measured in number of MET minutes per week (all p values > 0.05). In addition, we did not find differences in the measures of postural sway during the balance tasks between the older participants with and

without a fear of falling measured in the FES-I questionnaire (all p values > 0.05). Furthermore, postural sway was not different between the older participants who reported problems with pain and discomfort and those who did not (all p values > 0.05).

3.3. Anticipatory Postural Adjustments

3.3.1. Reaction Time

Significant differences were seen between the two cohorts for ES onset and AD onset. ES onset was slower in the elderly (235 ± 30ms) compared to the young cohort (202 ± 27ms; t(38) = 3.58, p = 0.001). AD onset was also slower in the elderly cohort (231 ± 24ms) compared to the young cohort (205 ± 25ms; t(38) = 3.3, p = 0.002; figure 13). However, no significant differences were seen in the difference in the ES onset with respect to the AD onset between the young cohort (-3 ± 12ms) and the elderly cohort (4 ± 16ms; t(38) = 1.479, p = .147).

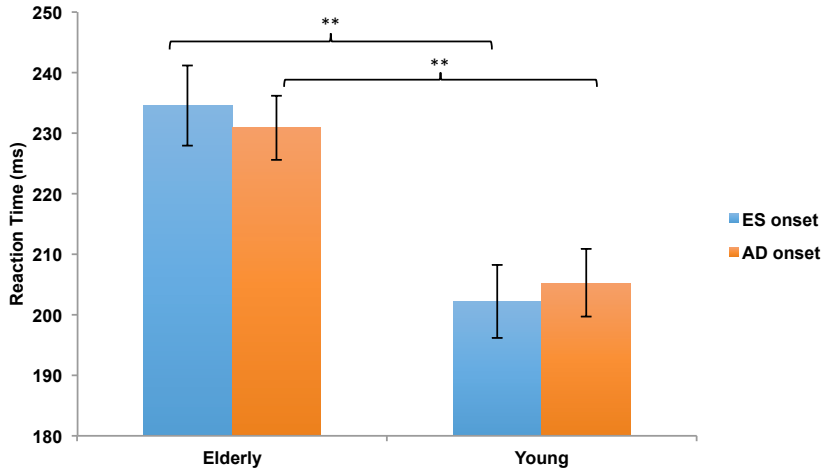


Figure 14. Mean reaction time displayed as ES onset and AD onset between elderly and young participants.

*** = p < 0.01*

Within the elderly cohort there were a higher percentage of individuals with a delayed APA (i.e. ES onset was later than AD onset) in comparison with the young cohort($\chi^2(1,) = 6.47$; $p = 0.011$; figure 14).

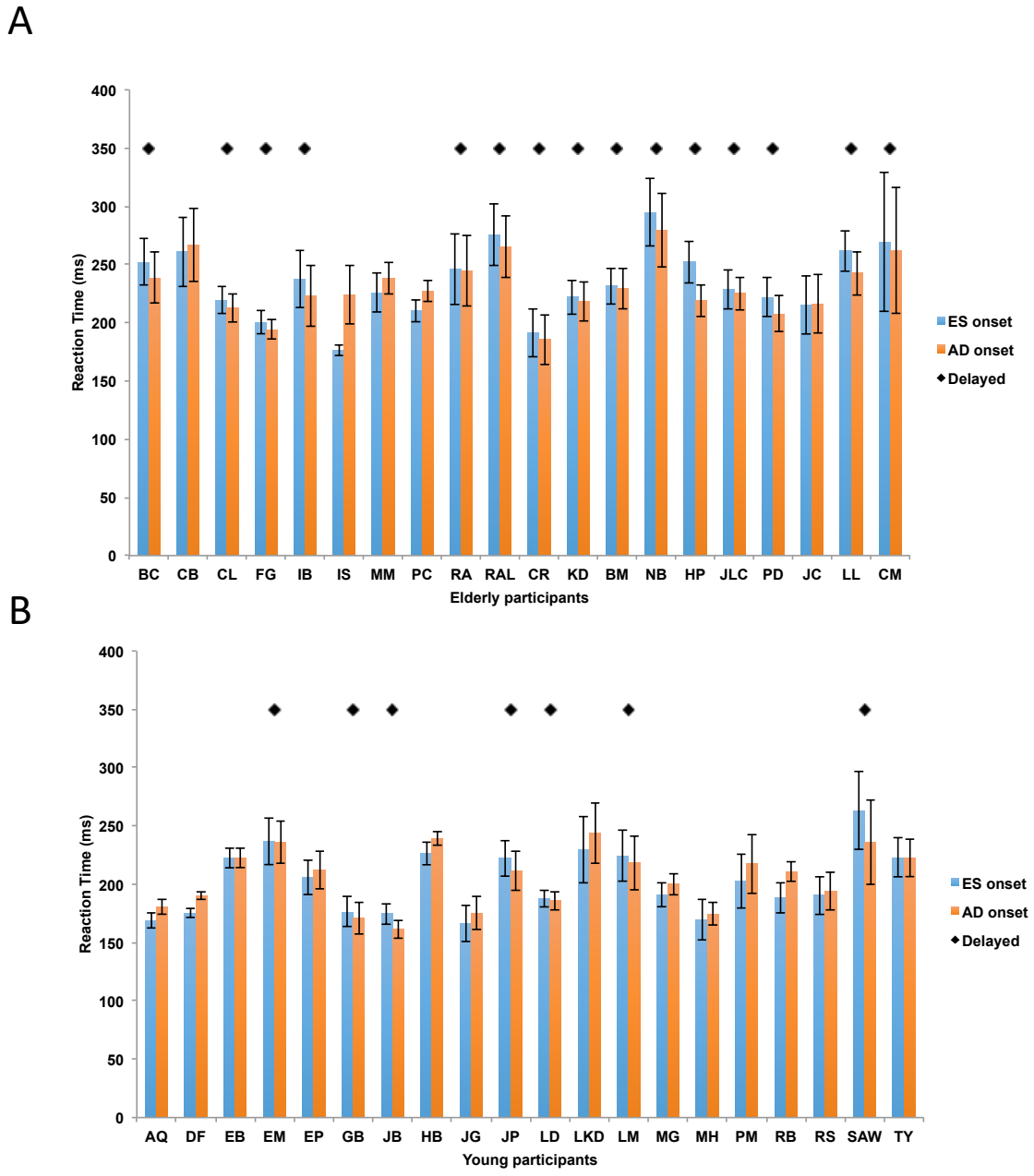


Figure 15. Reaction time. Individual ES and AD onset with markers indicating a delayed APA (ES onset). (A) Elderly participants. (B) Young participants. X-axis represents individual participant's initials.

3.3.2. Erector Spinae MEP

Figure 15 shows raw traces of ES MEPs recorded in a representative elderly participant. Note that MEP amplitudes are increased at the time point close to the reaction time. A mixed model repeated measures ANOVA showed a main effect of time in ES MEPs ($F(2.04, 56.98) = 12.1$, $p < 0.001$). However, there was no interaction between time and group in ES MEPs. Post-hoc tests revealed that the amplitude of ES MEP was greater at 40ms than at 50ms prior to the onset of AD in both young and elderly participants. The amplitude of ES MEP was greater at 30ms than 40ms prior to the onset of AD in both groups (figure 16). There was no difference between other time points.

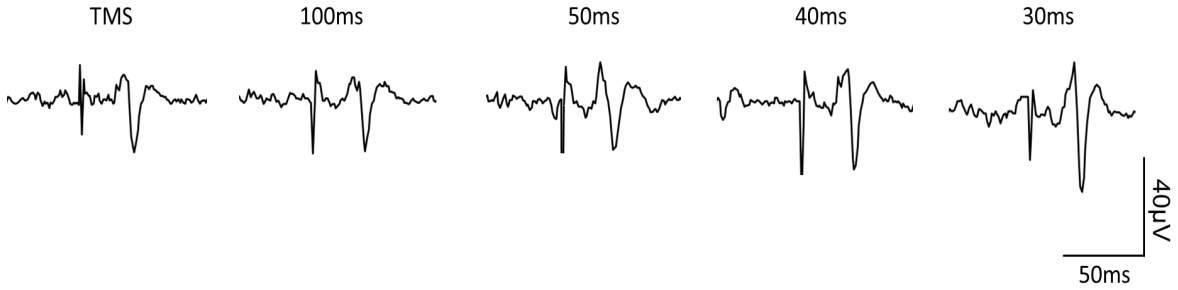


Figure 16. Raw traces of ES MEP at -100, 50, 40, 30ms and TMS only in an elderly participant.

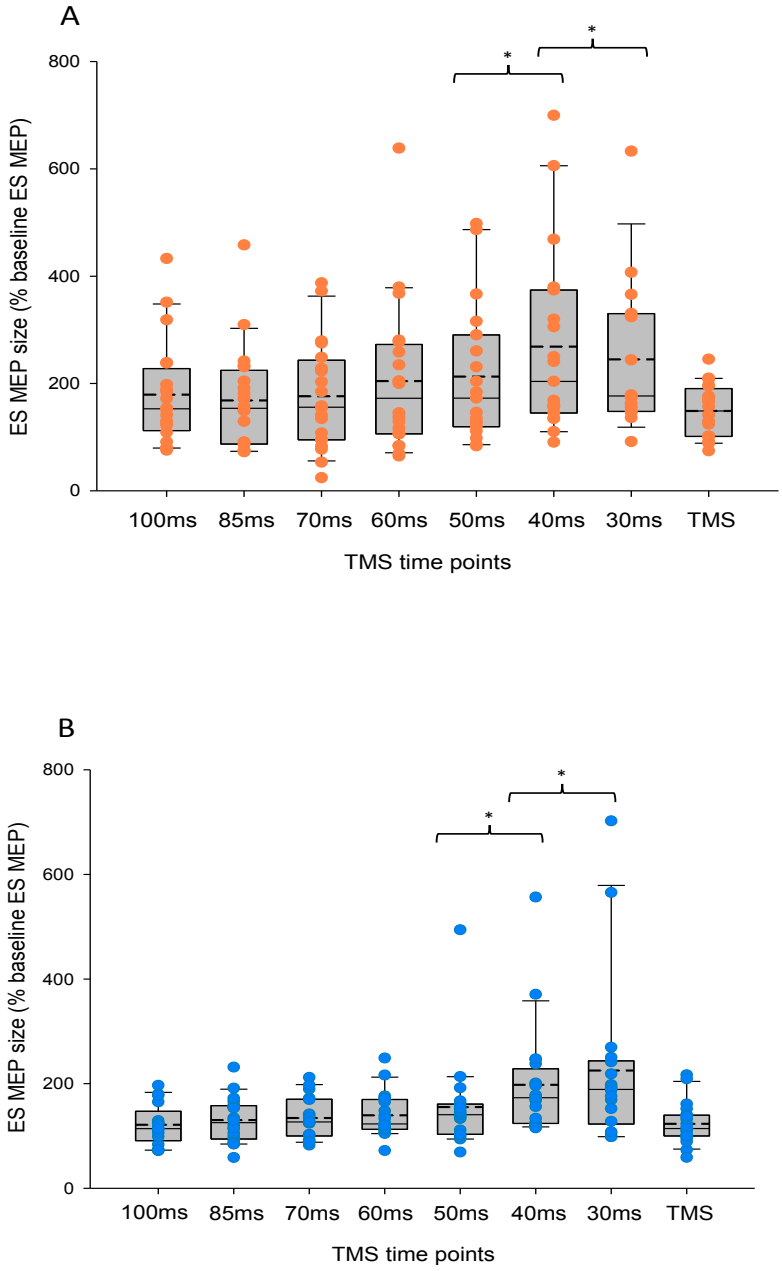


Figure 17. Individual data showing variance and mean (black dotted line) ES MEP amplitude as a percentage of the baseline ES MEP for elderly (A) and young (B) between the various TMS time points prior to reaction = p < 0.05*

The solid boxes indicate the interquartile range and the solid line indicates the median.

Amplitudes of ES MEPs were greater during the TMS only condition than during the baseline in both elderly (TMS; .085 ± .05; Baseline; .069 ± .056; t(19) = -3.52, p =

0.002) and young participants (TMS; .126 ± .084; Baseline; .099 ± .057; t(19) = -2.65, p = 0.016). Additionally, there was a significant difference in the baseline ES MEPs between the elderly cohort (.069± .056mV) and the young cohort (.099 ± .057; U= 118, p = .027); the elderly cohort had smaller ES MEPs at the baseline compared with the young cohort. However, we found that the averaged amplitude of ES MEP across time points showed a tendency to be larger in the elderly participants (207.1 ± 111.14) than in the young participants (158.1 ± 60.24; t(29.28) = 1.73, p = 0.094).

Peasron's correlation coefficient analysis showed that ES MEP at 40ms correlated with ES onset in the elderly cohort (r = -.714, p = 0.001), as well as at 30ms (r = -.695, p = 0.004; figure 17A, B); however, this was not found in the young cohort (figure 18C, D). The results indicate that older participants who had a slower ES onset also showed a smaller MEP amplitude prior the reaction time. We noticed some outliers in the data set (outside 95% confidence interval), and therefore a sub-analysis without the outliers was performed (40ms; n=17; 30ms; n=14). Results were in keeping with the main findings; correlations were found between ES MEP at 40ms correlated with the ES onset (r = -.502, p = .04), and between ES MEP at 30ms with the ES onset (r = -.680, p = .008).

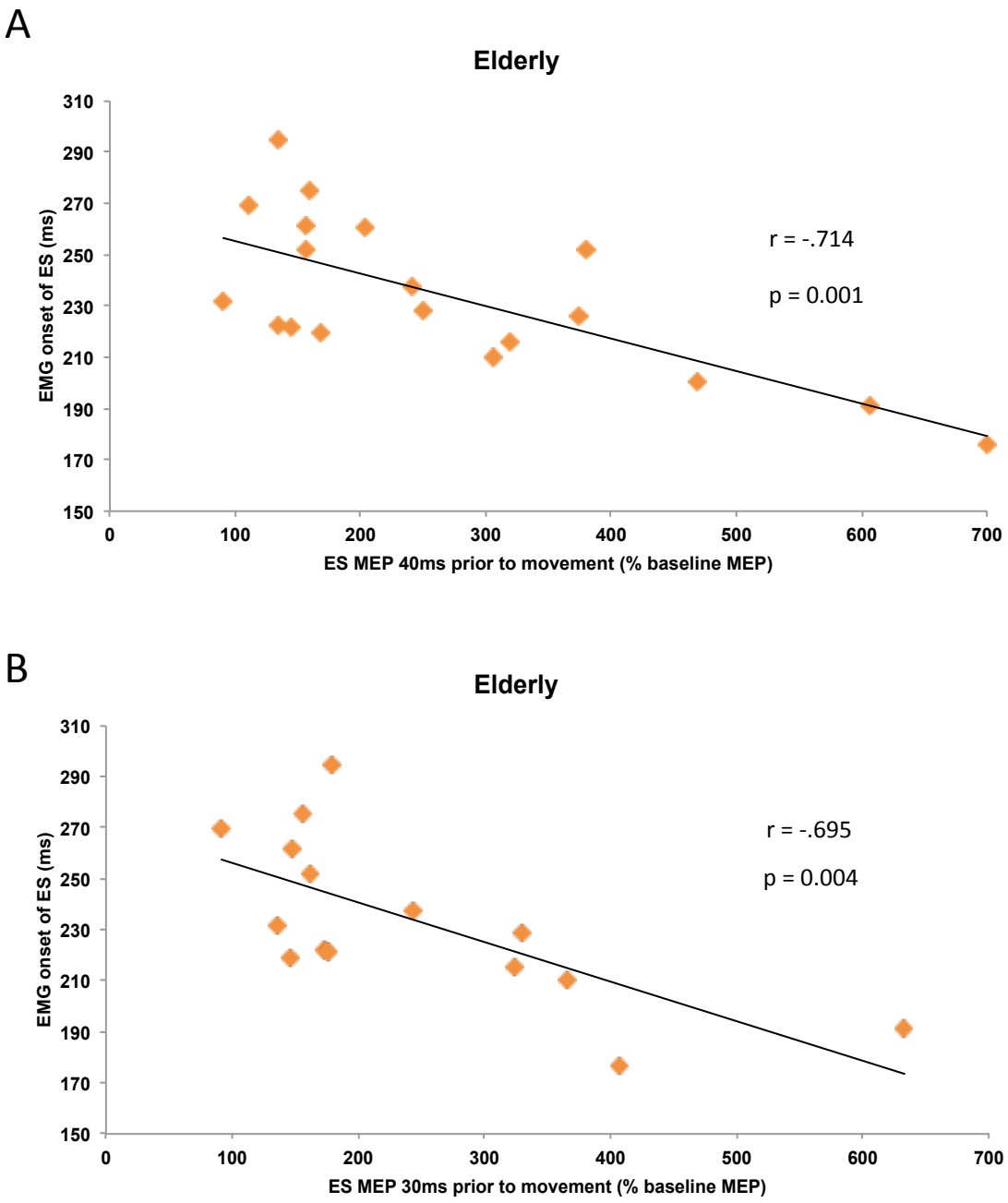


Figure 18. Correlation between ES MEP prior to movement (ms) as a percentage of baseline MEP. (A) Elderly MEP 40ms prior to movement. (B) Elderly MEP 30ms prior to movement.

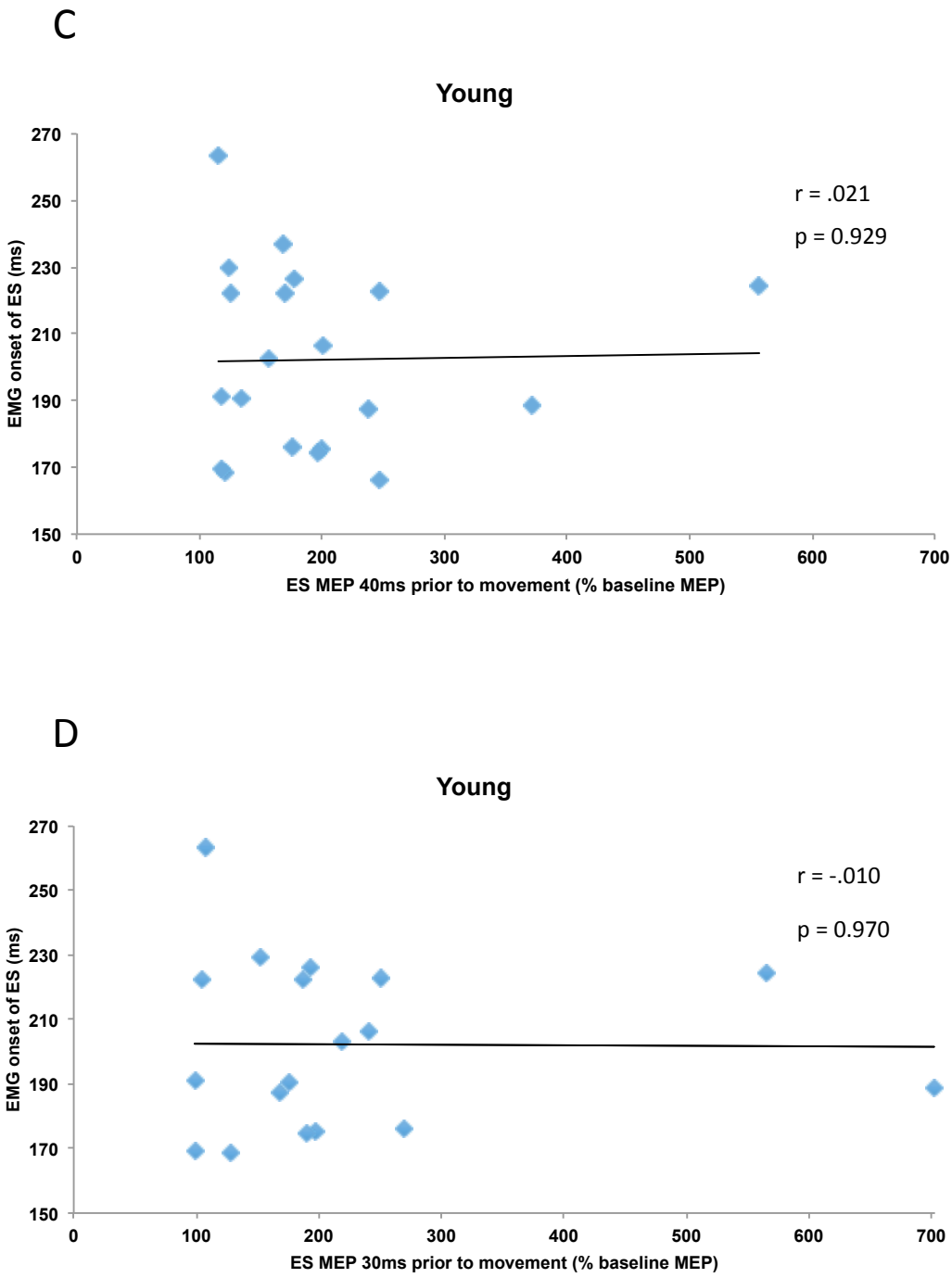


Figure 19. Correlation between ES MEP prior to movement (ms) as a percentage of baseline MEP. (C) Young MEP 40ms prior to movement. (D) Young MEP 30ms prior to movement.

3.3.3. Erector Spinae EMG

No differences in ES EMG were found between the age groups across all time points ($F(3.24, 84.35) = 1.4$, $p = 0.249$; figure 19). Further, ES MVCs were greater in the young cohort (.12 ± .04mV) than in the elderly cohort (.06 ± .03mV; $t(32.66) = -5.197$, $p < 0.001$).

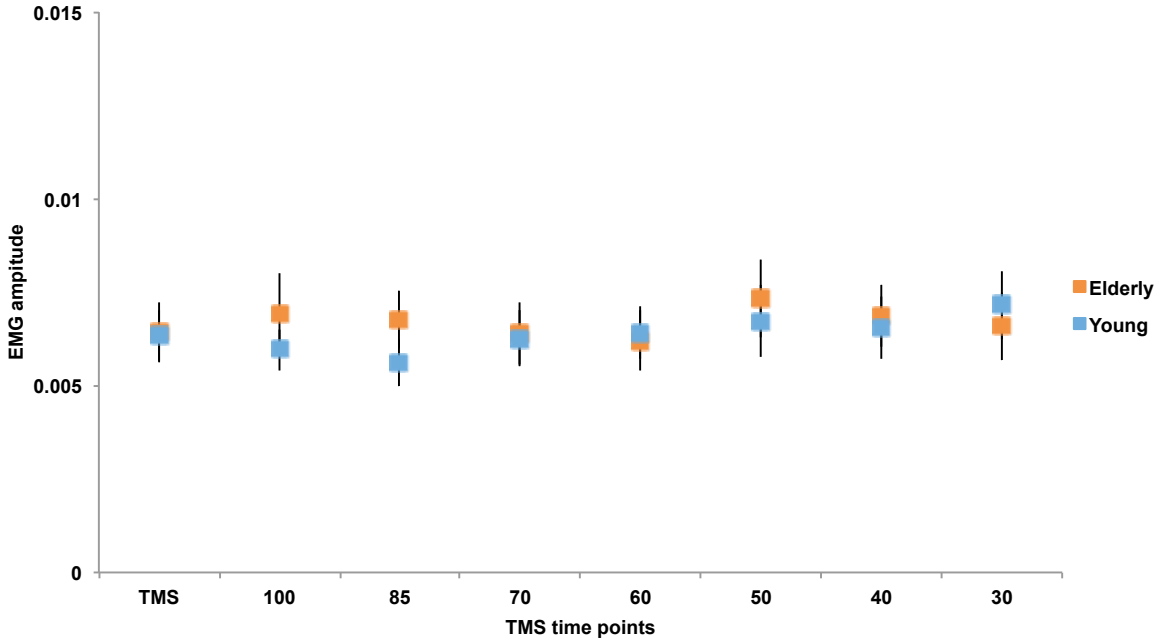


Figure 20. Mean raw EMG response of ES muscles at various time points of TMS relative to RT between elderly and young

Error bars indicate SEM and no significant difference between elderly and young.

4. Discussion

4.1. Major Findings

Our findings demonstrate that corticospinal excitability of the ES increases 40ms prior to the onset of the shoulder flexion task whilst in a seated position in both young and elderly participants. Although a delay in ES activation was seen in the elderly cohort during the fast shoulder flexion task, the timing of increased corticospinal excitability of the ES was not delayed, which is against our hypothesis. However, a tendency of greater amplitudes of ES MEPs was noted in the elderly participants compared to the young participants. In the elderly participants amplitudes of ES MEPs correlated with the onset of ES activity, indicating that older people having greater corticospinal excitability to the ES before moving the shoulders showed earlier activation of the ES, therefore smaller delays in APAs (muscle onset of AD and ES were closer). Our results may suggest age-related changes in motor cortical involvement, in the modulation of APAs of trunk muscles during a self-initiated perturbation task.

Prior work has shown increased corticospinal excitability of a prime-mover from 50 to 120ms prior to voluntary limb movements in young adults (Rossini et al. 1988; Chen et al. 1998; Leocani et al, 2000; Remaud, Bilodeau and Tremblay, 2014). There are few studies investigating changes in the corticospinal excitability of a non-prime mover involved in voluntary movements (Chiou et al. 2018; Aruin and Latash, 2014). Trunk muscles are activated prior to or concurrent with fast voluntary arm movements to maintain postural equilibrium as well as to assist voluntary arm movements, occurring from -100ms to +50ms of movement onset (Aruin and Latash, 1995).

Corticospinal excitability of the trunk muscles, specifically the ES muscles, have been shown to increase ~40ms prior the fast voluntary arm movements when the young healthy adults were in standing and in lying positions (Chiou et al. 2018). Our results are in line with these findings as our young participants showed increased corticospinal excitability at 40ms prior to the shoulder flexion task in seated position. Our findings support the notion that increased corticospinal excitability of the ES is hardwired to limb movement, and independent from postures. Another area of research has suggested APAs are required more so for voluntary movements rather than primarily trunk stability. A study looked into the activation of various trunk muscles when reaching in different directions, and found that ipsilateral muscles are associated with movement direction and showed greatest activation in comparison to contralateral muscles (Stamenkovic and Stapely, 2016). Their findings suggest that direction-dependent activity of the trunk muscles was involved in the initiation of a voluntary movement task during the preparatory phase as opposed to postural control. Our findings however, focused on the ES muscle activity contralateral to the shoulder muscles measured in reaction time, and saw contralateral ES muscle activation to precede AD onset during rapid arm movements, suggesting an APA strategy for postural control due to the contralateral muscles providing a stabilising mechanism during movement whilst initiation of movement may occur through activation of both ipsilateral and contralateral muscles.

Activation of the AD muscle preceding activation of the ES muscle was observed in majority of the elderly participants (75%). Due to the shoulder movement occurring prior to the trunk muscle activation it suggests a delayed APA of the trunk muscles, supported by previous research which suggests, it may be delayed if activation

doesn't occur before or at the same time as movement onset (Aruin and Latash, 1995). This finding is in keeping with previous findings showing delays in activation of ES with respect to activation of contralateral AD during self-paced voluntary movements in older adults, where ES activation occurred after AD activation when ES and AD onsets were measured in respect to the light onset (Woollacott and Manchester, 1993).It is important to note the age-related changes in postural control were seen as a delay in APAs rather than an absence (Kanekar and Aruin, 2014). While the onset of ES muscle was delayed with respect to the onset of contralateral AD muscle in our elderly cohort, we did not observe a delay in timing of increasing corticospinal excitability of the ES as hypothesised. Conversely, we found that in the elderly cohort the excitability was increased at 40ms prior to the onset of the AD, which was the same as that in the young cohort. Our findings are in keeping with a previous study showing that the timing of increasing corticospinal excitability of abductor pollicis brevis prior to reaction time of a fast thumb flexion task was similar between young and elderly participants, whereas the reaction time was slower in the elderly than in the young participants (Levin et al. 2011). An intriguing question is: "what could be the cause of delayed activation of ES muscle in the elderly if their corticospinal excitability was increased at the same timing as the young adult?" We were unable to measure H-reflex in this present study due to the trunk muscles being multi-innervated. However, prior work investigating changes in H-reflexes in soleus in seated position during fast voluntary arm movements showed that H-reflex amplitudes were consistent along the time course prior to the onset of the arm movements in both young and old adults (Hortobágyi et al., 2018). Furthermore, the same authors found that the H-reflex was suppressed before the arm movement in

the older adults, whereas it was facilitated in the young adults, suggesting lower spinal excitability before the execution of the shoulder movement in the older adults. However, we found that the elderly showed a tendency to have larger ES MEP amplitudes prior to the shoulder movement compared with the young participants. Since MEPs can be influenced by both motor cortical and spinal excitability, we speculate that there is a greater motor cortical contribution to the ES in the elderly participants compared with young participants for postural control.

We found a negative correlation between the onset of ES activation and the amplitude of ES MEPs at 40ms prior to the reaction time in the elderly cohort, indicating that those with lower corticospinal excitability to ES prior to the shoulder movement had greater delays in the onset of ES activation, hence greater delays in APAs of the trunk. As this was only seen in the elderly cohort it may suggest that elderly participants need a bigger response/more activation of neurons than the young to trigger a postural response. Another explanation could be that older adults tend to tune the corticospinal excitability in advance to better coordinate with postural muscles. Similar results were reported in Levin et al.'s (2011) work, which demonstrated a greater facilitation of corticospinal excitability of the thumb muscles prior to the thumb flexion task in the older adults compared with the young adults. Evidence from a functional MRI (fMRI) study has suggested a compensatory strategy of hyper-activation with increasing age, where additional and subcortical areas increased in activation in older adults when compared with young whilst taking part in a simple motor task (Mattay et al. 2002). Other research has found a relationship of brain structure and function with declines in motor performance, a study investigated the age-related changes in interhemispheric effects during a preparatory phase of a

bimanual task (Fujiyama et al. 2016). They found that age-related changes in the brains structure (i.e. white matter microstructure) had furthering effects on neurophysiological function, displayed in the declined performance of a bimanual coordination task. This idea lends support the aforementioned point where elderly may recruit more areas and neurons at the cortical level to compensate for the altered neurophysiological function in order to initiate the voluntary movement.

4.2. Other Findings

Our results showed larger CoP displacements during the tandem stand and one leg stand in the elderly cohort compared with the young cohort, indicating greater postural sway and poor balance in the elderly. The elderly cohort also displayed a higher percentage of participants to have a fear of falling and problems of pain and discomfort compared with young participants. These may influence balance control in the elderly people as biomechanical components are thought to involve limitations from pain, range of motion restrictions, and muscles strength and endurance (Horak, 1987). Research has shown evidence for this component with respect to gravity and the support surface. A previous study investigated the risk factors associated with falling in the elderly cohort during a one-year follow up study, and found various factors related to falls including abnormalities of balance and gait, and foot problems (Tinetti, Speechlev and Ginter; 1988). Their findings suggest that feet as the base of support play a vital role in postural equilibrium and thus balance. Although we did not see a correlation between neurophysiological measures and postural sway, other studies have shown changes in the CNS associated with motor performance. Prior work using fMRI has shown reduced lateralisation of the M1 activation during a dominant index-thumb tapping task in older adults, suggesting that they tend to

recruit more brain regions (i.e. increased activation of bilateral hemispheres) to produce the same motor performance (Naccarato et al. 2006). This study supports the findings of a previous PET (positron emission tomography) study showing differences in brain activation between low and high performing older adults during a memory and recall task (Cabeza et al. 2002). Older adults who recruited a similar brain network to the younger cohort showed reduced performance, whereas those who displayed bilateral activation of the brain had similar performance to the young cohort (Cabeza et al. 2002). Therefore, it may be that age-related declines in cognitive and motor performance are associated with a lack of reorganization of networks within the brain, and that the reorganization seen are to compensate for the age-related neural decline. In our case, increased facilitation of the corticospinal excitability may be the evidence of the reorganisation in the elderly cohort to maintain postural control.

4.3. Clinical Relevance

Previous research has shown the impairment of APAs and postural control in various populations, including the elderly (Woollacott and Manchester, 1993), stroke patients (Pereira et al. 2014), Parkinson's disease (Bazalgette et al. 1986), and those with lower back pain (Chiou et al. 2014). An increased number of falls have been associated with a loss of postural control (Roger, Kukulka and Soderberg, 1992), suggesting the vital role of postural control in the elderly population. Our findings support the evidence of impaired APAs in the elderly, and thus along with previous research may imply the effect of postural control on the wider population.

Our results suggest the tendency of older adults to increase motor cortical excitability to a greater extent before the arm movements in order to maintain the right postural strategy, i.e. APAs. These findings highlight the role of the M1 in postural control and balance, therefore targeting the M1 may be considered as part of training for improved postural control and balance. As our results displayed no difference in the timing of increased corticospinal excitability between the young and older adults, the tendency seen in older adults to greater increase motor cortical excitability could suggest the importance of improving the activation onset of APAs. Our research may support the suggestions of previous work where APAs can be improved through short term training i.e. a simple ball throwing exercise (Aruin et al. 2015). They took measurements of EMG activity of leg and trunk muscles during externally induced and self-initiated (bilateral arm flexion) before and after a single session of the ball throwing exercise, whilst stood on a force platform. They found improvements in APAs (earlier onset of anticipatory activity) of leg and trunk muscles prior to both self-perturbed and external perturbations following the single session (Aruin et al. 2015). Differing from conventional balance and strengthening exercises, the ball throwing exercise requires motor planning, and adjustments to external factors (perturbation). Previous research highlights the interaction of APAs and CPAs, and the benefits of improving APAs during external perturbations in order to improve postural control and balance (Santos et al. 2010). The M1 and the premotor cortex are involved in motor planning (Dum and Strick, 2002), which may explain the effect of ball-throwing exercises for improved APAs.

We found the elderly cohort displayed worse balance than the young cohort, although not correlating with their tendency to have a higher percentage of delayed

APAs (AD onset preceded ES onset), it could be suggested improving both balance and APAs individually would have an overall effect on performance and quality of life.

4.4. Limitations

Reaction time was an estimation of recognition reaction time therefore it was possible some participants responded to the noise of the TMS rather than the LED light. Due to a TMS induced delay in a simple reaction time task (Ziemann et al. 1997), variation was accounted for by including a warm up trial where participants were able to practice in order to recognise the correct moment and cue to react to. This was controlled for further by visual analysis of each frame and adjustments of the timing of the TMS pulses relative to the individuals' reaction time. Due to the noise of TMS, it should be noted some participants may have responded to the noise as a cue, rather than the visual cue. This was controlled for by visual analysis and removal of those with EMG activity of the ES muscles prior to TMS stimulation, as it has been found auditory reaction time is faster than visual reaction time (Shelton and Kumar, 2010). Fatigue could also be suggested as a limitation factor, however regular breaks were offered and there were no complaints of fatigue during or after the experiment.

4.5. Future Directions

Biomechanical studies have previously shown changes in leg joint angle to display a hip-ankle strategy during shoulder flexion, and an ankle-strategy during shoulder extension in a study where anticipatory increase in ES muscle activity was only seen in healthy young subjects when completing shoulder flexion (Aruin and Latash, 1995). It has been proposed there are three strategies within motor coordination; ankle strategy occurring due to small perturbations on a flat, wide surface, hip

strategy when perturbations are larger and on a narrow surface, and a stepping strategy when perturbations are large or fast (Horak, 1987). Although our research did not measure these strategies it could be relevant to incorporate these measurements in future work as previous research has supported the stepping strategy by investigating compensatory stepping in response to unpredictable postural perturbations (Mcllroy and Maki, 1996). They found the elderly were twice as likely to regain stability through additional steps in a compensatory manner, which were frequently directed to preserve lateral stability, which was not seen as often in the young cohort.

Previous research into the stepping strategy found that the elderly cohort use CPAs more to account for their delayed APAs (Aruin and Latash, 1995). Our study focused on APAs in the elderly cohort; however, future studies could also focus on CPAs, which are suggested to occur from 50 to 350ms after movement onset (Bigongiari et al. 2011; Santos et al. 2010). It has been suggested that age-related alterations are seen in CPAs as opposed to APAs (Claudino, dos Santos and Santos, 2013) providing evidence of the importance of CPAs in postural control and their impact on the elderly population.

Another possibility of an age-related delay in APAs may stem from spinal excitability. Evidence suggests the organisation of APAs to occur at a supraspinal level (Hortobágyi et al. 2018), and there to be an age-related change in spinal excitability due to the delay in APAs in older adults shown in previous research resulting in more compensatory strategies (Kanekar and Aruin, 2014; Aruin and Latash, 1995). Corticospinal excitability is a combination of the motor cortical excitability and spinal excitability. Measures of the motor cortex (e.g. intracortical inhibition) and spinal

excitability (cervicomedullary evoked potentials) are needed to reveal underlying mechanisms.

4.6. Conclusion

We demonstrate a delay in APA of the ES during the fast shoulder flexion task in the elderly and that correlates with increased facilitation of corticospinal excitability of the ES prior to the shoulder movement, with no delay in timing of increasing the excitability. Our findings provide further evidence for corticospinal contribution to postural control and highlights the importance of targeting corticospinal function for improved postural control in the elderly. This may have implications for a wide population since impaired postural control is seen in ageing as well as many other clinical conditions.

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Birmingham B15 2TT
United Kingdom

Dr Chloe Chiou
[redacted]

UNIVERSITY OF BIRMINGHAM

CORTICAL CONTROL OF POSTURAL RESPONSES TO TRUNK MUSCLES

Participant Information Sheet

Thank you for taking time to read this information sheet. We would like to invite you to join a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Trunk muscles are activated to stabilize the body when the arms or legs are moved (postural responses) and also to allow movements of the trunk (voluntary movements

such as bending forwards or backwards). Although the nervous system ultimately controls all of these responses, we are uncertain as to how these different responses are co-ordinated by the motor cortical areas of the brain.

Therefore, the purpose of the study is to investigate cortical control of trunk muscles during postural responses of the trunk. The study will provide further insights into the pathways controlling trunk muscles in healthy adults as well as helping us understand the dysfunction observed in both of these types of responses in patient populations (e.g. with low back pain).

Why have I been chosen?

We are asking you to think about joining this study because you can act as a healthy control subject and have no problems with your postural control.

Do I have to take part?

No. It is entirely up to you. If you would like to take part, you will be asked to sign a consent form. Even after you have signed this consent form and agreed to join the study, you are free to withdraw from the study at any time.

What will happen to me if I take part?

Once you have decided to take part in this study, you will be asked to come to the neurophysiological laboratory at University of Birmingham, where a member of our research team will discuss the study with you and answer any questions you may have. If you are still happy to take part, we will ask you to sign the consent form.

There are two parts in the study and you can do one or both of them. In order to record the electrical activity from the muscles (electromyography) and movements from your torso, small sticky surface electrode and reflective markers will be stuck to the skin overlying the trunk (front and back), neck and arms. In order to assess your balance, you will be asked to do some balance tasks on a force plate (measuring instrument). You will need to answer some questionnaires that will be asking you about your concern of the possibility of falling, your daily activities, and your health. You will be also taken basic information (e.g. date of birth, body height, body weight).

Part one. We will investigate the way the brain is involved in controlling postural adjustment of the trunk in response to arm movements. You will sit in an upright position and you will be asked to lift your both arms voluntarily a number of times. At the same time, we will activate the nervous system by a small magnetic stimulus to the nerves in the brain. These stimuli will be applied using a safe and painless investigative procedure called transcranial magnetic stimulation (TMS). We will also record the speed with which you move your arms.

Part two. We will monitor changes in your postural control every 6 months for up to 3 years. The assessments will be similar to the part one.

The relation between the stimulus and the electrical activity in the muscle as well as the balance will be analysed by computer. Each part will take no longer than 2 hours and if you choose to do more than one part we will do them on separate occasions at a time convenient to you.

What is the drug or procedure that is being tested?

There are no drugs being tested in this study and no new treatments. This study is simply looking at how the movement pathways to your trunk muscles affect postural adjustment. All testing protocols have been in use for many years.

What are the side effects of any treatment received when taking part?

There are no treatments given as part of this testing.

What are the possible disadvantages and risks of taking part?

The assessment techniques are safe and non-invasive and there are no known risks from having these test performed under strict safety guidelines. All tests will be performed within your limits of tolerance.

What are the possible benefits of taking part?

There are no clear benefits of taking part. However, this research may lead to knowledge into how the brain and nervous system control trunk muscles.

What if new information becomes available?

Any new information derived through this study will be made available to all of the subjects should they request this.

Will my taking part in this study be kept confidential?

Any information you give us will be kept confidential. If the study is published in a book or scientific journal, no individual will be identified in any way.

What will happen to the results of the research study?

The results of the study will be analysed by the research team and presented at neuroscience, neurological and other health care conferences and published in scientific journals. No individual subject will be identified in any report or presentation arising from the research.

Who is organising and funding the research?

The study will be run by a research team based at University of Birmingham and funded by University of Birmingham.

Who has reviewed the study?

This study has been approved by the University of Birmingham Ethical Review Committee.

Contact for further information about this study.

If you are unsure about this study and would like to consider further before you make your decision, please take your time to do so. You may ask for further information by telephoning [redacted]. The person to speak to, who is responsible for the study, is Dr Chloe Chiou. Alternatively, you can email us at [redacted]

Criteria for exclusion.

You CANNOT take part in this study if you:

1) Have any metal implants or an artificial cardiac pacemaker.

2) Have a history of epilepsy (fits or seizures) or a family history of epilepsy.

3) Have a history of brain damage (or neurosurgery), neurological or psychiatric disorders.

4) Are currently on antidepressants or other neuromodulatory drugs.

5) Are a child younger than 18.

6) Are (or think you may be) pregnant.

TMS Safety Questionnaire

If you agree to take part in this study, please answer the following questions. The information you provide is for screening purposes only and will be kept completely confidential.

Please tick the following information where it is applies to you:

Gender: O male O female O prefer not to say O non-binary

Dominant Hand: O left O right

Fluent English Speaker: O yes O no

Age (please specify) ___ yrs.

	Yes	***No***
Have you ever suffered from any neurological or psychiatric conditions?		
If YES please give details (nature of condition, duration, current medication, etc)		
Have you ever suffered from epilepsy, febrile convulsions in infancy or had recurrent fainting spells?		
Does anyone in your immediate or distant family suffer from epilepsy?		
If YES please state your relationship to the affected		

family member.		
Do you suffer from migraine?		
Have you ever undergone a neurosurgical procedure (including eye surgery)?		
Do you currently have any of the following fitted to your body?		
Cochlear implant		
Heart pacemaker		
Medication pump		
Surgical clips		
Did you ever suffer from brain injury or brain trauma?		
Did you ever lose consciousness or fainted?		
Do you suffer any chronic skin disorders?		
If YES (to either of the three Q above) please give details:		
Are you currently taking any unprescribed or prescribed medication?		
If YES please give details:		

	Yes	*No*
Are you currently undergoing anti-malarial treatment?		
Have you drunk more than 3 units of alcohol in the last 24 hours?		
Have you drunk alcohol already today?		
Have you had more than one cup of coffee, tea, or other sources of caffeine, in the last hour?		
Have you used recreational drugs in the last 24 hours?		
Did you have very little sleep last night?		
Have you ever participated in a TDCS/TMS experiment before?		
If yes please indicate when was the last time you participated in a TDCS/TACS or TMS study?		
Have you participated in more than 1 TMS, TDCS or TACS experiment in the last 6 months?		
Please also tell us how you felt during and after the experiment.		

I confirm that the above information is accurate to the best of my knowledge.

Name in capital letters:	
Signature:	**Date:**
This form has been verified by (Staff only): Print Name: Signature:	**Date:**

PAGE 2 OF 2

Participant Consent Form **Participant code:**

Please circle the following answers that apply to you:

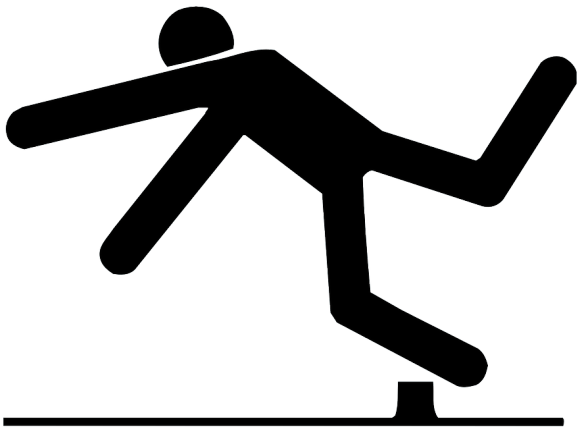
Have you read the information sheet?	YES	NO
Have you had an opportunity to ask questions and discuss	YES	NO
Have you received satisfactory answers to your questions?	YES	NO
Have you received enough information about the study?	YES	NO
Have you completed the screening questionnaire?	YES	NO
Who have you spoken to?	Name: Prof / Dr / Mr / Mrs / Miss /	
Do you understand that your are free to leave the study: • at any time?	YES	NO

I confirm that I have read the consent form and have completed the above questionnaire. The nature, purpose and possible consequences of the procedures have been explained. I understand that I may withdraw from the study at any time. I confirm that I have been through the safety screening procedures, and that I am happy to participate in this study.

Please note: All data arising from this study will be held and used in accordance with the Data Protection Act (1984). The results if the study will not be made available in a way which could reveal the identity of individuals.

Name in capital letters:	
Signature:	**Date:**
Researcher witness: Print Name: Signature:	**Date:**

UNIVERSITY OF BIRMINGHAM





Are you interested in knowing how the brain controls posture and how your age can affect your postural control?

We are carrying out a research study to investigate how the brain communicates with the postural muscles and how our age might affect the communications.

We would like to recruit healthy participants aged between 18 and 80 years

We will ask you to do some simple movements using your arms. We will evaluate your trunk muscle activity, reaction time, and balance.

The study will last approximately 2 hours at University of Birmingham, School of Sport, Exercise, and Rehabilitation Sciences building. Cost for transportation will be covered.

If you would like further information about the study, please speak to Dr Chloe Chiou on [redacted]. Alternatively you can email us at [redacted]

Thank you!

Recruiting participants from the 1000 Elders database

In the first instance we will advertise your study on our website and contact elders via email, if this does not generate a sufficient response we will then look at providing contact details for members who you can then contact directly (maximum 30 per request).

Please complete and return the fields below and provide us with your:

- Participant Information Sheet
- Any other documents that are relevant to your study

Project Principal Investigator: Dr Chloe Chiou

School/Institute/Department: School of Sport, Exercise, and Rehabilitation Sciences

Researcher conducting the study *(if different from the PI):* Dr Chloe Chiou and Miss Rebecca Rowland

Email Address *(to which volunteers can reply)***:**

Contact telephone number *(which volunteers can call)***:**

Name of project/study: age-related changes in postural control and balance

Start date: 1st November 2018

End date: 30th September 2019

Ethics approval details *(Reference number and approving committee)***: ERN_17-1541AP4 approved by UoB Ethics Committee (09/07/2018).**

Reason for no ethical approval:

Who are you looking to recruit? *(Please include number of participants you are looking to recruit, gender, age range)***: We are looking to recruit 20 healthy adults aged above 65 years to take part in our study.**

Please provide a short paragraph to advertise your study. This will be used in communications such as a newsletters and our *website* *(This should be no longer than 150 words, should include a brief description of your study, outline who you are looking to recruit, give a brief overview of the involvement required, and should be understandable to a general audience – please see example below*)**:**

Researchers in the School of Sport, Exercise, and Rehabilitation Sciences would like to know how the brain communicates with the postural muscles and how our age might affect the communications

We will ask you to do some simple movements using your arms and evaluate your trunk muscle activity, reaction time and balance assessed. We will activate the nervous system by a small magnetic stimulus to the nerves in the brain. These stimuli will be applied using a safe and painless investigative procedure called transcranial magnetic stimulation (TMS).

The study will last approximately 2 hours at University of Birmingham, School of Sport, Exercise, and Rehabilitation Sciences building. Cost for transportation will be covered.

If you would like further information about the study, please speak to Dr Chloe Chiou on . Alternatively you can email us at

Please note that making an enquiry does not commit you to taking part.

Please outline how you will feed back the results of your study to the volunteers who take part (*We have had complaints in the past that the elders are not informed of research results, and are not thanked for their time, so we insist that some consideration is given to how this will be achieved)***:**

We will send a short summary to document findings of the study to the volunteers once the study is complete and data analysis is finished. We will also disseminate our findings in the Agewell event.

It is important to note:

- Contact Information given/collected is strictly confidential and is for your use only, please do not pass any information on to other researchers.
- Please keep all information gathered in a password-protected electronic file.
- Do not print files containing personal information collected from the research volunteers.
- If you need to send a group email to your research participants, please ensure all email addresses are contained within the 'BCC' field so they are not disclosed to others.
- Any issues contacting the elders (e.g. contact info is out of date, or they want to be removed from the database etc.) should be forwarded to the 1000 Elders Database Administrator 1000Elders@contacts.bham.ac.uk

Example advert

Volunteers needed for a study of the effects of sitting time

Researchers in the School of Sport, Exercise and Rehabilitation Sciences would like to know how older people's bodies and minds respond to physical inactivity.

You will be asked to visit our research facility in the old Queen Elizabeth Hospital on four occasions. The first visit will be a familiarisation visit and will last 1 hour; the remaining 3 visits will last 6 hours each. During these longer visits, you will be asked to sit for different periods of time. Before and after the sitting we will ask you to do some simple tests of muscle function and tests of thinking and memory.

If you are aged 70 years or over and think you might be interested, please contact Dr Smith directly by telephoning [redacted] or via e-mail to [redacted] for more information.

Please note that making an enquiry does not commit you to taking part. All travel expenses will be refunded.

FES-I

Now we would like to ask some questions about how concerned you are about the possibility of falling. Please reply thinking about how you usually do the activity. If you currently don't do the activity (e.g. if someone does your shopping for you), please answer to show whether you think you would be concerned about falling IF you did the activity. For each of the following activities, please tick the box which is closest to your own opinion to show how concerned you are that you might fall if you did this activity.

		Not at all concerned 1	*Somewhat concerned 2*	*Fairly concerned 3*	*Very concerned 4*
1	Cleaning the house (e.g. sweep, vacuum or dust)	*1* ☐	*2* ☐	*3* ☐	*4* ☐
2	Getting dressed or undressed	*1* ☐	*2* ☐	*3* ☐	*4* ☐
3	Preparing simple meals	*1* ☐	*2* ☐	*3* ☐	*4* ☐
4	Taking a bath or shower	*1* ☐	*2* ☐	*3* ☐	*4* ☐
5	Going to the shop	*1* ☐	*2* ☐	*3* ☐	*4* ☐
6	Getting in or out of a chair	*1* ☐	*2* ☐	*3* ☐	*4* ☐
7	Going up or down stairs	*1* ☐	*2* ☐	*3* ☐	*4* ☐
8	Walking around in the neighbourhood	*1* ☐	*2* ☐	*3* ☐	*4* ☐
9	Reaching for something above your head or on the ground	*1* ☐	*2* ☐	*3* ☐	*4* ☐
10	Going to answer the telephone before it stops ringing	*1* ☐	*2* ☐	*3* ☐	*4* ☐
11	Walking on a slippery surface (e.g. wet or icy)	*1* ☐	*2* ☐	*3* ☐	*4* ☐
12	Visiting a friend or relative	*1* ☐	*2* ☐	*3* ☐	*4* ☐
13	Walking in a place with crowds	*1* ☐	*2* ☐	*3* ☐	*4* ☐
14	Walking on an uneven surface (e.g. rocky ground, poorly maintained pavement)	*1* ☐	*2* ☐	*3* ☐	*4* ☐
15	Walking up or down a slope	*1* ☐	*2* ☐	*3* ☐	*4* ☐
16	Going out to a social event (e.g. religious service, family gathering or club meeting)	*1* ☐	*2* ☐	*3* ☐	*4* ☐

FES-I: Prof Lucy Yardley and Prof Chris Todd

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRES

IPAQ: SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health-related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken in 12 countries (14 sites) across 6 continents during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages. IPAQ is suitable for use in regional, national and international monitoring and surveillance systems and for use in research projects and public health program planning and evaluation. International collaboration on IPAQ is on-going and an international prevalence study is under development.

Using IPAQ

Worldwide use of the IPAQ instruments for monitoring and research purposes is encouraged.

It is strongly recommended, to ensure data quality and comparability and to facilitate the development of an international database on health-related physical activity, that

- no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments,
- if additional questions on physical activity are needed they should follow the IPAQ items,
- translations are undertaken using the prescribed back translation methods (see website)
- new translated versions of IPAQ be made available to others via the web site to avoid duplication of effort and different versions in the same language,
- a copy of IPAQ data from representative samples at national, state or regional level be provided to the IPAQ data storage center for future collaborative use (with permission) by those who contribute.

More Information

Two scientific publications presenting the methods and the pooled results from the IPAQ reliability and validity study are due out in 2002.

More detailed information on the IPAQ process, the research methods used in the development of the IPAQ instruments, the use of IPAQ, the published papers and abstracts and the on-going international collaboration is available on the IPAQ web-site.

www.ipaq.ki.se

This is the final SHORT LAST 7 DAYS SELF-ADMINISTERED version of IPAQ from the 2000/01 Reliability and Validity Study. Completed May 2001.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

IPAQ: SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS

NOTE: EXAMPLES OF ACTIVITIES MAY BE REPLACED BY CULTURALLY RELEVANT EXAMPLES WITH THE SAME METS VALUES (SEE AINSWORTH *ET AL*., 2000).

This is the final SHORT LAST 7 DAYS SELF-ADMINISTERED version of IPAQ from the 2000/01 Reliability and Validity Study. Completed May 2001.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. This is part of a large study being conducted in many countries around the world. Your answers will help us to understand how active we are compared with people in other countries.

The questions are about the time you spent being physically active in the last 7 days. They include questions about activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Your answers are important.

Please answer each question even if you do not consider yourself to be an active person.

THANK YOU FOR PARTICIPATING.

In answering the following questions,

- **vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder that normal.

- **moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder that normal.

This is the final SHORT LAST 7 DAYS SELF-ADMINISTERED version of IPAQ from the 2000/01 Reliability and Validity Study. Completed May 2001.

Participant ID: _____

1a. During the last 7 days, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling,?

Think about *only* those physical activities that you did for at least 10 minutes at a time.

_____ **days per week** ⇨

or

☐ **none**

1b. How much time in total did you usually spend on one of those days doing vigorous physical activities*?*

_____ **hours** _____ **minutes**

2a. Again, think *only* about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week** ⇨

or

☐ **none**

2b. How much time in total did you usually spend on one of those days doing moderate physical activities*?*

_____ **hours** _____ **minutes**

3a. During the last 7 days, on how many days did you **walk** for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure.

_____ **days per week** ⇨

or

☐ **none**

3b. How much time in total did you usually spend walking on one of those days *?*

_____ **hours** _____ **minutes**

The last question is about the time you spent sitting on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.

4. During the last 7 days, how much time in total did you usually spend *sitting* on a **week day?**

____ **hours** _____ **minutes**

This is the end of questionnaire, thank you for participating.

This is the final SHORT LAST 7 DAYS SELF-ADMINISTERED version of IPAQ from the 2000/01 Reliability and Validity Study. Completed May 2001.



Patient Details
Subject Identifiction Number:

Subject Initials:

Date:

Health Questionnaire

English version for the UK

UK (English) v.2 © 2009 EuroQol Group. EQ-5D™ is a trade mark of the EuroQol Group

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

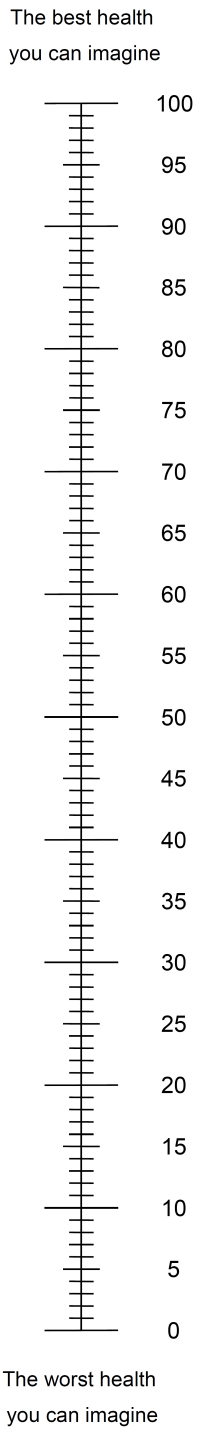
ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

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- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



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