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Associations between gait coordination, variability and motor cortex inhibition in young and older adults

Clayton W. Swanson[a], Brett W. Fling[a,b,*]

[a] Department of Health & Exercise Science, Colorado State University, Fort Collins, CO, USA
[b] Molecular, Cellular, and Integrative Neuroscience Program, Colorado State University, Fort Collins, CO, USA

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ABSTRACT

Interlimb coordination and gait performance diminish with age, posing a risk for gait-related injuries. Further, levels of inhibition within the motor cortex are significantly associated with coordination of the upper extremities in healthy aging, however, it is unknown if this same association exists for lower extremity control. To investigate the relationship between gait coordination and cortical inhibition we measured gait coordination via the phase coordination index and motor cortex inhibition via the cortical silent period in 14 young and 15 older adults. Gait coordination was reduced in older adults while walking at their self-selected pace, as was cortical inhibition, solely in the non-dominant motor cortex. Furthermore, young adults were better able to maintain lower extremity coordination and variability with reduced cortical inhibition, whereas older adults with increased cortical inhibition demonstrated better walking performance. These findings suggest a fundamental shift in the relationship between motor cortex inhibition and lower extremity control with age, similar to previous work demonstrating an age-related difference in the association between motor cortex inhibition with bimanual control.

1. Introduction

The ability to perform movements that involve interlimb coordination is fundamental to many tasks of daily living, including the manipulation of objects with our hands, standing up from a chair, walking, and climbing stairs (Fujiyama et al., 2012; James et al., 2017a; Penninx et al., 2000). Moreover, increasing age is associated with a lack of coordination, causing deficits in our ability to coordinate two limbs together to complete specific tasks. An ever-evolving body of literature indicates that walking incorporates a specific set of movements that involve both spatial and temporal coordination of the lower extremities, and that this interlimb coordination is vital to our ability to control both legs in time and space to ambulate effectively and safely (Brach et al., 2001; Brach et al., 2007; Hausdorff et al., 2001; James et al., 2017a; James et al., 2016).

Gait coordination is the ability to appropriately time left-right stepping patters within the construct of a stride during walking, commonly quantified using the phase coordination index (PCI) (James et al., 2017a; Kribus-Shmiel et al., 2018; Plotnik et al., 2007). Gait variability is typically defined as the kinetic stride-to-stride fluctuations of multiple gait cycles over a period of time and distance (Lord et al., 2011). Coordination and variability measures appear to distinguish gait limitations and are important factors associated with mobility performance (Brach et al., 2001; Brach et al., 2007; Cohen, 1992; Dingwell et al., 2017; James et al., 2016; Kang and Dingwell, 2008). Both coordination and variability are sensitive enough to discern between older individuals with and without mobility and cognitive impairments or as a predictor of future fall risk (Hausdorff et al., 1998; James et al., 2017a; Maki, 1997; Martin et al., 2013; Verghese et al., 2009). For instance, James et al. (2017a) assessed interlimb coordination within 127 older adults and demonstrated a significant association between impaired coordination and falls occurring within the prior year. Additionally, stride length and swing time variability was assessed in 597 individuals ≥70 years of age and exhibited the most meaningful predictor of both non-injurious and injurious falls when comparing gait speed, cadence and stride length to variability metrics of stride length and swing time (Verghese et al., 2009). Furthermore, variability metrics are associated with fall risk independently of individuals who have a cognizant fear of falling (Maki, 1997). While coordination has not been studied to the same extent as variability, both coordination and variability lack correlation to gait speed at self-selected walking speeds (Plotnik et al., 2013). Additionally, coordination and variability display

* Corresponding author at: Department of Health & Exercise Science, Colorado State University, 1582 Campus Delivery, Moby B -201A, Fort Collins, CO 80523, USA.

E-mail address: Brett.Fling@colostate.edu (B.W. Fling).

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a lack of association to each-other depicting distinct features of gait for healthy controls spanning ages between 20 and 85 and individuals with Parkinson's disease (Plotnik et al., 2007). While these studies are descriptive, the neural mechanisms that underlie both typical and atypical interlimb gait coordination remain unclear.

Conventionally, the neural control of gait has been described at the level of the spinal cord through the direction of central pattern generators. However, with the advancement of various neuroimaging techniques including transcranial magnetic stimulation (TMS), positron emission tomography, functional magnetic resonance imaging (fMRI), functional near infrared spectroscopy, electroencephalography, and single photon emission tomography our understanding of locomotor control has been further elucidated (Capaday et al., 1999; Christensen et al., 1999; Fukuyama et al., 1997; Gwin et al., 2011; Hamacher et al., 2015; Petersen et al., 2001; Petersen et al., 1998; Schubert et al., 1999; Schubert et al., 1997). These diverse techniques have revealed various degrees of cortical activation for individuals while actively walking. Furthermore, several groups have utilized TMS to demonstrate significant involvement of the corticospinal tract during walking cycles (Capaday et al., 1999; Nielsen, 2003; Schubert et al., 1997). For example, motor evoked potential (MEP) amplitude which indirectly measures glutamatergic activity in the cortex via monosynaptic projections to spinal motoneurons fluctuates during various parts of the gait cycle (Petersen et al., 1998). Specifically, MEPs of the soleus are increased during the stance phase and absent during the swing phase (Capaday et al., 1999; Petersen et al., 1998). Furthermore, inhibitory activity while walking has been assessed using TMS (Petersen et al., 2001). These findings demonstrate reduced muscle activity of activated leg muscles during the gait cycle, indicating the corticospinal contribution to muscle activity can be decreased via cortical inhibition. Therefore, it is plausible different aspects of bipedal gait may be controlled at various levels of the central nervous system. Further, neurochemical balance alters with age and may contribute to precise ambulatory control of the lower extremities similar to the cortical control of the upper extremities (Heuninckx et al., 2008).

With advancing age, there are multi-faceted declines in motor performance as well as changes in cortical inhibition (Fling et al., 2012; Hermans et al., 2018; Hortobagyi et al., 2006; Oliviero et al., 2006; Papegaaij et al., 2014; Peinemann et al., 2001; Pitcher et al., 2003). Transcranial magnetic stimulation (TMS) offers a non-invasive method of studying the biochemical properties of the motor cortex believed to reflect both excitation via glutamatergic activity and inhibition via gamma-aminobutyric acid (GABA) or GABA-ergic cortical circuits (Bhandari et al., 2016; Cash et al., 2017; Di Lazzaro et al., 2000; Kujirai et al., 1993; Lazzaro et al., 1998; Ziemann et al., 1996a, 1996b). The cortical silent period (cSP) is a common method of assessing GABA-ergic circuits, and is specifically thought to assess $GABA_B$ and the inhibitory properties of corticospinal neurons (Werhahn et al., 1999). The cSP refers to an interruption of an ongoing voluntary muscle contraction initiated by a TMS stimuli used to assess upper and lower motor neurons within the corticospinal tract stemming from a particular region of interest within the motor cortex. Although, the mechanisms of an induced silent period via TMS are not fully understood, it is widely agreed upon that the initial part (first ~50 ms) of a silent period corresponds to spinal contributions and the remaining portion of the silent period is of cortical origin (Christie and Kamen, 2014; Roick et al., 1993; Säisänen et al., 2008; Taylor et al., 1997; Triggs et al., 1993; Uncini et al., 1993; Wilson et al., 1993; Wolters et al., 2008; Ziemann et al., 1996a, 1996b). However, the silent period has also been claimed to be entirely of cortical origin generated from the primary motor cortex (Roick et al., 1993; Säisänen et al., 2008; Schnitzler and Benecke, 1994). While a vast body of literature exists demonstrating the associations between motor cortex inhibition, upper extremity control, and the effects of healthy aging (Fling and Seidler, 2012; Fujiyama et al., 2009; Fujiyama et al., 2012; Oliviero et al., 2006), there remains a substantial lack of knowledge regarding how cortical inhibition is associated with lower extremity coordination and gait variability.

The purpose of this study was to evaluate the effects of healthy aging on gait coordination and its associations to motor cortex inhibition. Testing was conducted on two separate days for both healthy young (YA) and older adults (OA); day one incorporated wireless inertial sensors used to collect spatiotemporal, variability, and bilateral interlimb coordination measures of gait during a 6-minute walk test (6MWT) and, on a separate day, participants underwent TMS to assess the cSP of both the dominant and non-dominant leg regions of the primary motor cortices, respectively. We hypothesized that healthy older individuals would have a significantly increased PCI and a significantly shorter cSP compared to their younger counterparts. Finally, we hypothesized that PCI would be significantly correlated with cSP duration in OA, demonstrating a similar association between motor cortex inhibition and lower extremity coordination to those typically observed with the upper extremities during bimanual movements (Boisgontier and Swinnen, 2015; Fling and Seidler, 2012; Fujiyama et al., 2009).

2. Methods

2.1. Participants

Twenty-nine healthy adults participated in the study; 14 young participants (6 females; age range, 20–31 years; mean age, 24.4 ± 3.6 years) and 15 older participants (6 females; age range, 65–83 years; mean age 72.3 ± 5.7 years). All participants were able to ambulate independently with no acute fall history (prior 6 months) and had no diagnosed neuromuscular, neurodegenerative, cognitive, orthopedic, or other comorbidities that would impact their gait or risk of TMS. All subjects were either screened in-person or over the phone, once eligibility was determined participants were scheduled for two separate visits within ten days of each other. In addition, prior to enrollment, all subjects were required to score greater than or equal to 27 on the Mini Mental State Exam (MMSE) (YA; MMSE score range, 28–30 years; mean score 28.43 ± 0.76; OA; MMSE score range, 27–30 years; mean score 28.87 ± 0.92) (Tombaugh and McIntyre, 1992). This study was performed in accordance with the Declaration of Helsinki and approved by the Colorado State University Institutional Review Board (#17-7053H), all participants provided written informed consent prior to participating.

2.2. Procedures

Participants had two testing sessions which were separated by > 24 h and < 10 days apart. Testing sessions included an instrumented assessment of gait and TMS testing. To complete the instrumented assessment, six wireless inertial sensors were positioned on each foot, around the posterior pelvis at the level of L5, on the sternum, and around each wrist (Mancini et al., 2011). All sensors were attached to the body using Velcro and elastic straps. Sensors were fit tight enough to limit unwanted sensor movement without being uncomfortable for the participant.

2.2.1. Gait assessment

Instrumented assessment of gait was conducted using the 6MWT at the participants' natural, self-selected walking pace. Participants were asked to walk back and fourth down a well-lit hallway of 30 m in length. The walkway was marked at each end with visible tape to indicated where participants should turn around, tape was used instead of a cone to mimic a natural turn and minimize distraction. While walking participants were asked to maintain a forward gaze and to not communicate with the tester for the duration of the trial.

2.2.2. Cortical silent period (cSP) assessment

Subjects were seated in an adjustable upright chair with their legs