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Relationship between sensorimotor cortical activation as assessed by functional near infrared spectroscopy and lower extremity motor coordination in bilateral cerebral palsy

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ABSTRACT

Background: Evaluation of task-evoked cortical responses during movement has been limited in individuals with bilateral cerebral palsy (CP), despite documented alterations in brain structure/function and deficits in motor control.
Objective: To systematically evaluate cortical activity associated with lower extremity tasks, and relate activation parameters to clinical measures in CP.
Methods: 28 ambulatory participants (14 with bilateral CP and 14 with typical development) completed five motor tasks (non-dominant ankle dorsiflexion, hip flexion and leg cycling as well as bilateral dorsiflexion and cycling) in a block design while their sensorimotor cortex was monitored using functional near infrared spectroscopy (fNIRS), in addition to laboratory and clinical measures of performance.
Results: Main effects for group and task were found for extent of fNIRS activation (number of active channels; $p < 0.001$ and $p = 0.010$, respectively), magnitude of activation (sum of beta values; $p < 0.001$ for both), and number of active muscles ($p = 0.001$ and $p < 0.001$, respectively), but no group by task interactions. Collectively, subgroups with CP and especially those with greater impairments, showed higher extent and magnitude of cortical sensorimotor activation as well as higher amounts of concurrent activity in muscles not required for task performance. Magnitude of fNIRS activation during non-dominant dorsiflexion correlated with validated measures of selective control ($r = -0.60$, $p = 0.03$), as well as mobility and daily activity ($r = -0.55$, $p = 0.04$ and $r = -0.52$, $p = 0.05$, respectively) and self-reported gait function ($r = -0.68$, $p = 0.01$) in those with CP.
Conclusions: The association between higher activity in the sensorimotor cortex and decreased selectivity in cortical organization suggests a potential neural mechanism of motor deficits and target for intervention.

1. Introduction

Cerebral palsy (CP) is the most prevalent child-onset motor disorder and is caused by a non-progressive brain injury early in life (Graham et al., 2016; Sanger et al., 2006). In the case of bilateral lower extremity motor impairment, substantial research has been done in describing and quantifying motor behavior. It has been shown that this population demonstrates difficulty with selective voluntary motor control (Sanger et al., 2006; Fowler & Goldberg, 2009), manifesting as atypical synergistic movements within and across limbs (Fowler et al., 2009; Thelen et al., 2003). Studies have demonstrated greater difficulty with isolated distal movements compared to proximal movements (Fowler et al., 2010; Lim, 2015), increased co-contraction across joints (Chen et al., 2003), and impaired reciprocal activation (Chen et al., 2003).

Damage to the sensorimotor cortex and the corticospinal pathways are postulated to be a primary contributor to impaired selective voluntary motor control (Fowler et al., 2009; Cahill-Rowley & Rose, 2014; Sukal-Moulton et al., 2014a), with sensory cortex responses to external stimuli (Wingert et al., 2010; Kurz et al., 2014a) or sensory pathways (Hoon Jr. et al., 2009) in particular being implicated in bilateral CP.

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Transcranial magnetic stimulation (TMS) and magnetic resonance imaging (MRI) investigations in unilateral CP have indicated the capacity of the less damaged hemisphere to maintain ipsilateral projections in order to influence control of the paretic arm in unilateral CP (Eyre et al., 2007; Vandermeeren et al., 2009). In contrast, far less data have been reported in bilateral CP. Using TMS, a lateral shift in the location of motor representations, or "hot spots", for individual lower extremity segments was shown (Kesar et al., 2012; Maegaki et al., 1999), in addition to overlapping and sometimes bilaterally projecting cortico-muscular connections to upper and lower extremities (Wittenberg, 2009). One child with bilateral, asymmetrical CP showed a large area of fMRI cortical activation during an ankle dorsiflexion task (Phillips et al., 2007).

Brain imaging techniques enable researchers to decipher the mechanisms by which alterations in sensory and motor pathways may affect underlying lower extremity motor control in CP, with MRI having the greatest potential to evaluate both superficial and deeper brain structures (Wingert et al., 2010; Hilderly et al., 2016). However, with MRI, researchers are often limited to either structural or resting state connectivity measures (Burton et al., 2009), or small amplitude mostly single joint movements in supine during functional imaging measures (Phillips et al., 2007; Hilderly et al., 2016). Furthermore, obtaining high quality images is not always possible in children with CP due to exaggerated startle responses and/or involuntary movements which become increasingly more problematic in children with greater degrees of neurological involvement. Mobile brain imaging techniques such as functional near infrared spectroscopy (fNIRS) move with the head and body, allowing for the study of a wide range of motor tasks in a more naturalistic setting and in a broader clinical population.

FNIRS is a non-invasive neuroimaging method that uses low-levels of red to near-infrared light to measure task-evoked changes in oxygenated and deoxygenated hemoglobin (Hb) concentrations on the cortical surface. These measurements are made by placing a head cap containing light emitters and detectors on the scalp overlying specific brain regions, which allows recording of optical density measures that are converted to relative changes in Hb concentrations, specifically increases in oxygenated hemoglobin (HbO) and decreases in deoxygenated hemoglobin (HbR) during functional tasks. This technology has been used with healthy adults during a number of motor tasks including stepping (Huppert et al., 2013; Koenraadt et al., 2014), gait (Miyai et al., 2001; Miyai et al., 2003; Suzuki et al., 2008), and balance tasks (Karim et al., 2013; Karim et al., 2012).

In unilateral CP, fNIRS has been used to assess brain activation during hand movements (Tian et al., 2008; Tian et al., 2010; Khan et al., 2010; Decampos et al., 2016), and to evaluate pre-frontal cortical activation in bilateral CP during a throwing task (Chaudhary et al., 2014). With respect to the lower extremity, one study evaluated fNIRS activation during gait in four children with bilateral CP compared to eight children with typical development (TD). The results showed higher levels of activation across sensorimotor and superior parietal lobules and greater variability in gait patterns in CP (Kurz et al., 2014b). Because of the small sample size, a direct correlation between cortical activity and gait variability was seen only with combined data from both groups. Understanding the relationship between increased brain activation and specific motor control deficits in CP is challenging when measured during a complex task such as gait, which involves coordination of multiple joints, reciprocal activity across legs, as well as dynamic postural control, all of which may be impaired in CP.

The goal of the current study was to systematically evaluate cortical activity and potential neural mechanisms associated with a range of simple to incrementally more complex lower extremity tasks including distal (ankle dorsiflexion) and proximal (hip flexion) single joint movements, coordinated unilateral and bilateral multi-joint tasks (single and bilateral cycling), and synchronous (bilateral dorsiflexion) as well as reciprocal (bilateral cycling) tasks performed in an upright position. FNIRS measures were related to clinical scales and simultaneous lower limb electromyography (EMG) measures to elucidate potential neural mechanisms underlying functional and performance differences. Our primary hypothesis was that individuals with CP would demonstrate higher magnitude and more widespread extent of brain activation (Kurz et al., 2014b) that would be related to a greater degree of task performance impairment as measured by EMG, a lower extremity selective motor control test and clinical scales assessing gait function, mobility and daily activity. Secondary hypotheses included: 1) a dominant hemisphere would still be identifiable in all groups contralateral to the dominant lower limb as indicated by group differences in an activation laterality index, even though the brain injury in CP is considered bilateral; 2) the center of activity would be more laterally located in CP compared to TD for unilateral tasks due to the high prevalence of midline brain injuries in the patient group and reorganization that may consequently occur more laterally (Maegaki et al., 1999); and 3) contrasts between tasks (unilateral, bilateral, single joint, multiple joint) would reveal differential responses across groups with respect to relative task difficulty due to underlying differences in motor coordination.

2. Materials and methods

2.1. Participants

A total of 28 participants completed the study, including 14 (5 males) with bilateral CP, GMFCS Levels I–III, and 14 (9 males) age-matched with TD. Participants were included if they were at least 5 years old, able to understand and follow simple directions for performing a repetitive task, and agreed to not drink caffeine or alcohol for 24 h before assessments to avoid associated alterations in blood flow dynamics. Exclusion criteria included any health condition or diagnosis other than CP that would affect the ability to maintain attention or move a body part repetitively for short periods of time, surgery within a year, or botulinum toxin injections within 6 months. The study was approved by the Institutional Review Board of the National Institutes of Health Clinical Center (protocol #13-CC-0110) and all participants (or their parents, as applicable) completed informed consent and assent.

A complete history and physical examination was performed by a pediatric physiatrist, followed by a number of standardized clinical assessments for those with CP, including the Gross Motor Function Classification System (GMFCS) (Palisano et al., 2008) and Hypertonia Assessment Tool (HAT) (Jethwa et al., 2010). Furthermore, the Selective Control Assessment of the Lower Extremity (SCALE) (Fowler et al., 2009), AbilLOCO (Caty et al., 2008), and PEDI-CAT (version 2.5) (Haley et al., 2005) were completed for correlation to fNIRS and electromyography (EMG) activity. The SCALE evaluates the ability to move each joint of the lower extremity independently, with each of 5 joints receiving a score of 0, 1, or 2 (best). For example, the SCALE score at the ankle involves dorsiflexing, plantarflexing, and then dorsiflexing the ankle again to a timed count, while the examiner observes for movement occurring at other joints on that limb or on the opposite leg. Parents of or adult participants with CP completed the AbilLOCO questionnaire about difficulty performing ambulation tasks and the PEDI-CAT which yields summary scores for Mobility and Daily Activity, with higher scores indicating greater function. A structural magnetic resonance image (MRI, T1 and T2 weighted) was completed on each participant, and evaluated by a neuroradiologist to provide more information about the type and extent of brain injuries to aid in interpretation of NIRS data. The Edinburg Handedness Inventory was completed by all participants with an additional question about lower extremity preferences to determine which leg to test.

2.2. Setup

Setup for each participant included placement of the fNIRS optodes (CW6, TechEn, Milford, MA) on the scalp regions that overlay the