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Children with cerebral palsy have altered oscillatory activity in the motor and visual cortices during a knee motor task

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ABSTRACT

The neuroimaging literature on cerebral palsy (CP) has predominantly focused on identifying structural aberrations within the white matter (e.g., fiber track integrity), with very few studies examining neural activity within the key networks that serve the production of motor actions. The current investigation used high-density magnetoencephalography to begin to fill this knowledge gap by quantifying the temporal dynamics of the alpha and beta cortical oscillations in children with CP (age = 15.5 ± 3 years; GMFCS levels II–III) and typically developing (TD) children (age = 14.1 ± 3 years) during a goal-directed isometric target-matching task using the knee joint. Advanced beamforming methods were used to image the cortical oscillations during the movement planning and execution stages. Compared with the TD children, our results showed that the children with CP had stronger alpha and beta event-related desynchronization (ERD) within the primary motor cortices, premotor area, inferior parietal lobule, and inferior frontal gyrus during the motor planning stage. Differences in beta ERD amplitude extended through the motor execution stage within the supplementary motor area and premotor cortices, and a stronger alpha ERD was detected in the anterior cingulate. Interestingly, our results also indicated that alpha and beta oscillations were weaker in the children with CP within the occipital cortices and visual MT area during movement execution. These altered alpha and beta oscillations were accompanied by slower reaction times and substantial target matching errors in the children with CP. We also identified that the strength of the alpha and beta ERDs during the motor planning and execution stages were correlated with the motor performance. Lastly, our regression analyses suggested that the beta ERD within visual areas during motor execution primarily predicted the amount of motor errors. Overall, these data suggest that uncharacteristic alpha and beta oscillations within visuomotor cortical networks play a prominent role in the atypical motor actions exhibited by children with CP.

1. Introduction

Cerebral palsy (CP) is the most prevalent pediatric neurologic impairment diagnosed in the United States (Christensen et al., 2014). Damage to the periventricular white matter areas during birth, or shortly after, is the most common cause (Bax et al., 2005). This damage reduces the fidelity of information that is transmitted along the thalamocortical and corticospinal tracts (Hoon et al., 2009), which of course results in a wide variation of sensorimotor impairments. Such variability in the nature and severity of impairments is an inherent characteristic of patients diagnosed with the CP umbrella term. Over 90% of these children have musculoskeletal impairments that result in slower and less coordinated motor actions (Abel and Damiano, 1996; Johnson et al., 1997; Norlin and Odenrick, 1986). These observations have fueled the original belief that the motor aberrations seen in children with CP primarily originated in the musculoskeletal machinery (Pin et al., 2006; Moreau et al., 2012; Blumetti et al., 2012; Dreher et al., 2012; Taylor et al., 2013). However, this hypothesis has been significantly challenged in recent years, as it is becoming widely recognized that the white matter damage seen in these children likely impacts activity within the key brain networks that are involved in processing sensory information and the production of motor actions (cf.

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Cramer et al., 2011; Graham et al., 2016). Understanding how the perinatal brain injuries found in children with CP may affect brain function in these key networks is crucial for advancing our understanding of the basic neurophysiology that underlies CP.

Data from electroencephalography (EEG), magnetoencephalography (MEG) and invasive electrocorticography (ECoG) experiments have shown that the cortical oscillatory activity in the beta range (15–30 Hz) decreases prior to the onset of movement, and that this decrease is largely sustained throughout the movement (Jurkiewicz et al., 2006; Miller et al., 2007; Wilson et al., 2010; Tzagarakis et al., 2010; Wilson et al., 2011; Wilson et al., 2014; Tzagarakis et al., 2015; Grent-'t-Jong et al., 2014; Heinrichs-Graham et al., 2014; Kurz et al., 2016). This response is typically referred to as the beta event-related desynchronization (ERD) and it involves bilateral neural activity across sensorimotor cortices, with the strongest maxima contralateral to the effector producing the motor action, which is consistent with the somatotopic/motortopic organization of the pre/post-central gyri. Additional areas of concurrent beta ERD activity often include the premotor area, supplementary motor area (SMA), parietal cortices and mid-cingulate. While these previous studies have advanced our understanding of how the healthy brain produces motor actions, we still have a limited understanding of the nature of these cortical oscillations in children with CP.

Neuroimaging studies of children with CP have historically focused on identifying structural aberrations within the white matter, with very limited attention toward understanding the altered neurophysiology of brain networks serving the production of motor actions (Carr et al., 1993; Maegaki et al., 1999; Staudt et al., 2002; Vandermeeren et al., 2003a; Vandermeeren et al., 2003b; Hoon et al., 2009; Holstrom et al., 2010). However, we have recently begun to address this substantial knowledge gap through the use of MEG imaging in children with CP. This work has shown that the beta ERD response is significantly stronger in the sensorimotor cortices of children with CP during the planning of knee extension movements (Kurz et al., 2014). These findings imply that the impaired leg motor actions seen in children with CP may be partially related to the inability to formulate a motor plan that predicts the ideal muscle synergies for achieving a motor goal. In the current investigation, we further interrogate the neurophysiology of motor control in children with CP by quantifying the strength of the cortical oscillations during a goal-directed, visuomotor, target-matching task that was performed with the knee joint. We chose a task requiring visuomotor transformations because visual feedback is critical to constructing an accurate motor plan, yet the role of visuomotor processing in CP-related movement abnormalities is completely unknown. Prior experimental work has shown that visual information processed in the occipital cortices is not only used for stimulus discrimination, but is also critical to online motor performance and may actually modulate the strength of the neural activity in motor areas during visuomotor tasks (Ledberg et al., 2007; Strigaro et al., 2015). Our primary hypothesis was that children with CP would have uncharacteristic beta oscillations relative to typically developing (TD) children in sensorimotor and occipital cortices during the planning and motor execution stages of the visuomotor target-matching task. Furthermore, we hypothesized that these altered beta oscillations would be correlated with reductions in movement accuracy in children with CP.

2. Materials and methods

2.1. Subjects

The Institutional Review Board at the University of Nebraska Medical Center reviewed and approved the protocol for this investigation. Thirteen children with CP that had a spastic diplegic presentation (age = 15.5 ± 3 years; 8 males; GMFCS levels II–III) and 15 typically developing children (age = 14.1 ± 3 years; 8 males) with no neurological or musculoskeletal impairments participated in this investigation. The children with CP were excluded if they had an orthopedic surgery or anti-spasticity treatments within the last 6-months or if the child had too low of cognition to follow directions. All of the parents provided written consent that their child could participate in the investigation and the children assented. None of the participating children had visible white or grey matter lesions that would have affected the integrity of the cortical surface in neural areas of interest (i.e., motor system, occipital, and inferior frontal gyrus). In addition, the participating children were not on any medication and did not have visual processing impairments.

2.2. MEG data acquisition and experimental paradigm

Neuromagnetic responses were sampled continuously at 1 kHz with an acquisition bandwidth of 0.1–330 Hz using an Elekta MEG system (Helsinki, Finland) with 306 magnetic sensors, including 204 planar gradiometers and 102 magnetometers. All recordings were conducted in a one-layer magnetically-shielded room with active shielding engaged for advanced environmental noise compensation. During data acquisition, the children were monitored via real-time audio-video feeds from inside the shielded room. A custom built head stabilization device that consisted of a series of inflatable airbags that surrounded the sides of the head and filled the void between the head and MEG dewar was worn for all data collections. This system stabilized the head and reduced the probability of any large head movements occurring during the data collections.

The children were seated upright in a magnetically silent chair during the experiment. A custom-built magnetically silent force transducer was developed for this investigation to measure the isometric knee extension forces generated by the children (Fig. 1A). This device consisted of a 20 × 10 cm airbladder that was inflated to 317 kPa, and fixed to the anterior portion of the lower leg just proximal to the lateral malleoli. A thermoplastic shell encased the outer portion of the airbladder and was secured to the chair with ridged strappings. Changes in the pressure of the airbag as the child generated an isometric contraction were quantified by an air pressure sensor (Phidgets Inc., Calgary, Alberta, CA) and were subsequently converted into units of force.

The experimental paradigm involved the child generating an isometric knee extension force that matched target forces that varied between 5 and 30% of the child's maximum isometric knee extension force across trials. The step size between the respective targets was one unit of force. The target force was visually displayed as a box and the force generated by the child was shown as a smaller box that was animated vertically, based on the isometric force generated (Fig. 1B). The children were instructed to match the presented targets as fast and as accurately as possible. The distinct target forces were presented in a

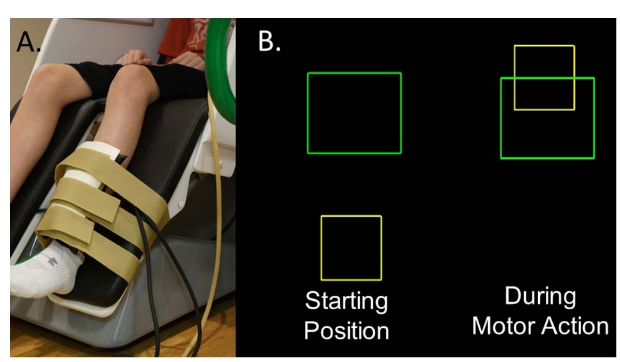

Fig. 1. A) Depiction of the custom-built pneumatic force transducer that is positioned just proximal to the lateral malleolus of the child. B) The isometric knee extension force generated by the child animates the yellow box to ascend vertically to match the green target box. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)