The magnitude of the somatosensory cortical activity is related to the mobility and strength impairments seen in children with cerebral palsy

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The magnitude of the somatosensory cortical activity is related to the mobility and strength impairments seen in children with cerebral palsy. The noted disruption of thalamocortical connections and abnormalities in tactile sensory function has resulted in a new definition of cerebral palsy (CP) that recognizes the sensorimotor integration process as central to the motor impairments seen in these children. Despite this updated definition, the connection between a child’s motor impairments and somatosensory processing remains almost entirely unknown. In this investigation, we explored the relationship between the magnitude of neural activity within the somatosensory cortices, the strength of the ankle plantarflexors, and the gait spatiotemporal kinematics of a group of children with CP and a typically developing matched cohort. Our results revealed that the magnitude of somatosensory cortical activity in children with CP had a strong positive relationship with the ankle strength, step length, and walking speed. These results suggest that stronger activity within the somatosensory cortices in response to foot somatosensations was related to enhanced ankle plantarflexor strength and improved mobility in the children with CP. These results provide further support for the notion that children with CP exhibit, not only musculoskeletal deficits, but also somatosensory deficits that potentially contribute to their overall functional mobility and strength limitations.

magnetoencephalography; sensory; strength; gait; walking

CEREBRAL PALSY (CP) is one of the most prevalent and costly pediatric neurological impairments diagnosed in the United States (Christensen et al. 2014). A major therapeutic goal of the parents and children with CP is to improve and sustain mobility (Botos and Gericke 2003). To this end, a considerable amount of research funds that has been expended toward cataloging the various lower-extremity joint kinematic and kinetic deviations that are seen in the walking patterns of these children (Bell et al. 2002; Lin et al. 2000; Onley et al. 1990; Ounpuu et al. 1996; Riad et al. 2008). These efforts have largely assumed that the mobility deficiencies seen in children with CP primarily reside in the performance of the musculoskeletal machinery. Unfortunately, the outcomes of the treatment strategies that have followed this line of reasoning (i.e., surgery and flexibility and strength training) have been mixed and thus not clearly successful in improving mobility (Blumetti et al. 2012; Dreher et al. 2012; Pin et al. 2006; Taylor et al. 2013).

The revised definition of CP recognizes that the motor impairments seen in these children are at least partially a product of aberrant sensations and ability to interpret sensory information (Rosenbaum et al. 2007). This reclassification is supported by the numerous clinical reports of proprioception, stereognosis, and tactile discrimination deficits seen in children with CP (Auld et al. 2012; Clayton et al. 2003; Cooper et al. 1995; Goble et al. 2009; Robert et al. 2013; Sanger and Kukke 2007; Wingert et al. 2008). Several studies have begun to interrogate the potential relationship between the motor impairments and the sensory-processing deficits seen in children with CP. These studies have reported that the hand sensory discrimination deficits are linked with the child’s upper-extremity motor impairments (Krumlinde-Sundholm and Eliasson 2002; Sakzewski et al. 2010), prediction of grip forces (Gordon and Duff 1999; Gordon et al. 1999), and the likelihood that the child will learn a new upper-extremity motor skill (Robert et al. 2013). These outcomes clearly support the notion that the processing of somatosensations is an influential component of the motor performance of children with CP. Despite these novel insights, very few studies have examined the leg somatosensations in children with CP (Damiano et al. 2013; Wingert et al. 2009). These few investigations have shown that proprioceptive somatosensory deficits also persist for the lower extremities in children with CP. Furthermore, a recent study has shown that the hip joint proprioception deficits seen in children with CP that have a hemiplegic presentation may be related to their selection of a slower walking speed (Damiano et al. 2013). Further investigation of the lower-extremity somatosensations has the potential to shed light on how these aberrant somatosensations impact the mobility of children with CP.

Outcomes from diffusion tensor imaging (DTI) studies have identified that the poor somatosensations seen in children with CP are likely related to structural damage along the thalamocortical pathways (Hoon et al. 2009; Rose et al. 2007; Trivedi et al. 2008, 2010). These studies have also reported that the extent of the damage is correlated with the degree of impairment in the child’s upper-extremity somatosensation, overall muscular weakness, Gross Motor Function Classification Score (GMFCS), and deviations in the gait biomechanics (Hoon et al. 2009; Rose et al. 2007; Trivedi et al. 2008, 2010). These relationships imply that the structural damage along the
thalamocortical tracks may result in faulty processing by the somatosensory networks. Several magnetoencephalography (MEG) and electroencephalography (EEG) studies have further explored this possibility and have shown that the somatosensory-evoked potentials/fields for the hand, foot, and lips are diminished and in some cases latent in children with CP (Kulak et al. 2005, 2006; Kurz and Wilson 2011; Kurz et al. 2012; Riquelme and Montoya 2010; Teflioudi et al. 2011). In addition, it has been noted that these aberrant event-related potentials are correlated with the two-point tactile discrimination deficits seen in children with CP (Maitre et al. 2012). Altogether, these results support the notion that children with CP likely have uncharacteristic activity within the somatosensory cortices. Nevertheless, it remains relatively unknown whether the mobility impairments seen in children with CP might be related to uncharacteristic activation within the somatosensory cortices.

Our prior MEG experimental work has begun to address this knowledge gap. Initially, we applied tactile stimulation to the bottom of the foot and showed that the strength of the activity within the sensorimotor cortices was related to the precision of the ankle plantarflexion force production of children with CP (Kurz et al. 2014). Recognizing that the ankle plantarflexors play a major role in the control of gait (Winter 1983), we extended our prior experimental work to evaluate whether the abnormal neural activity within the somatosensory cortices is related to the strength of the ankle plantarflexors and the mobility impairments seen in children with CP.

MATERIALS AND METHODS

Participants. Eleven children with a diagnosis of either spastic diplegic or hemiplegia CP (age = 14.5 ± 0.7 yr) and a GMFCS score between I and III participated in this investigation. An additional 11 age-matched typically developing (TD) children (age = 14.1 ± 0.7 yr) served as a control group. The Institutional Review Board at the University of Nebraska Medical Center reviewed and approved this investigation. Informed consent was acquired from the parents, and the children assented to participate in the experiment.

Motor performance experimental methods. An isokinetic dynamometer (Biodex, Shirley, NY) was used to measure the maximum isometric torque generated by the ankle plantarflexors. The children were seated in an adjustable chair with their foot position on a pedal that was interfaced with the torque motor. The back of the chair was in an upright position, the knee was extended, and the ankle was in a neutral position. The voltage output from the torque motor was read by custom LabVIEW (National Instruments, Austin, TX) software and sampled at 1 kHz by a 14-bit National Instruments analog-to-digital converter. The amount of torque generated was graphically displayed on a large monitor as a single box that moved vertically depending on the amount of torque the child applied to the foot pedal apparatus. The largest isometric torque generated from two maximum plantarflexion contractions was used to establish the child’s maximum voluntary torque (MVT). The MVT was normalized by the child’s body mass for analysis.

Mobility was quantified by having the children walk at their preferred and fast-as-possible walking speeds across a mat that registered their digital footprints (Gaitrite, Sparta, NJ). The data collected from the mat were used to calculate the child’s walking velocity, step length, and cadence. Each child completed two trials at the respective speeds. The average preferred and fast-as-possible walking speeds were used in the analysis.

MEG experimental paradigm. The children were seated with their head positioned within the helmet of the whole-head 306-sensor Elekta MEG system (Helsinki, Finland), while a unilateral tactile stimulation was applied to the bottom of the foot at the first metatarsal using a small airbladder. Neuromagnetic responses were continuously sampled at 1 kHz. The data analysis epochs were a total duration of 1.2 s (−0.5 s to +0.7 s), with the onset of the mechanical stimulation defined as time 0.0 s, and the baseline defined as −0.5 s to 0.0 s. Artifact-free epochs were imaged using a linearly constrained minimum variance beamformer, which employs spatial filters in the time-frequency domain to calculate 3D images of the local power of neuronal current (Gross et al. 2001; Hillebrand et al. 2005; van Veen et al. 1997). The single images were derived from the cross-spectral densities of all combinations of MEG sensors and averaged over the 4–14-Hz time-frequency range. In principle, the beamformer operator generates a spatial filter that passes signals without attenuation from a region of interest, while suppressing activity in all other brain regions. The filter properties arise from the forward solution (lead field) for each location on a volumetric grid specified by input voxel space and from the MEG covariance matrix. Basically, for each voxel, a set of beamformer weights is determined, which amounts to each MEG sensor being allocated a sensitivity weighting for activity in the specific voxel. This set of beamformer weights is the spatial filter unique to the given voxel, and this procedure was iterated until such a filter was computed for each voxel in the brain. Activity in each voxel was then determined independently and sequentially to produce a 2.0 × 2.0 × 4.0-mm resolution volumetric map of electrical source activity for each of the ~135 artifact-free trials per participant. Following convention, noise-normalized maps of source strength were derived from these volumetric output images by dividing, on a voxel-by-voxel basis, the projected source power by the estimated amount of uncorrelated noise power projected through the beamformer weights (Hillebrand et al. 2005; van Veen et al. 1997). The functional images were transformed into a standardized space (Talairach and Tournoux 1988), and the amplitude of the peak voxel in the group-difference statistical parametric map (SPM) was extracted for each child. Complete details of the MEG experimental methods employed in this study are described in our recent paper (Kurz et al. 2014). As a secondary analysis, we extracted a virtual sensor time series representing the 4–14-Hz frequency range in each child from the peak voxel in the group-difference SPM and focused on the amplitude of the peak latency for each child within the initial 200 ms of the time series. We chose this window because it included the average peak latency in each group.

Statistical analysis. Spearman rho rank-order correlations were used to determine the relationship between the amplitude of the peak voxel in the group-difference SPM, which was located in the medial wall of the contralateral postcentral gyrus and the respective behavioral measures. Spearman rho rank-order correlations were also used to determine the relationship between the virtual sensor peak amplitude, extracted from the peak voxel in the group-difference SPM, and the respective behavioral measures. The respective rank-order correlations were initially evaluated using the data collected from the entire group of participants. This was followed up by a separate analysis of the relationships that existed within the respective children with CP and TD control groups. Lastly, separate Wilcoxon matched pairs were used to determine whether there were differences between the children with CP and the TD children for the behavioral measures and the virtual sensor amplitude. All statistical analyses were performed with IBM SPSS Statistics Version 22, with α = 0.05.

RESULTS

MEG results. As reported in our companion manuscript (Kurz et al. 2014), the children with CP exhibited less 4–14-Hz activity in the medial wall of the contralateral postcentral gyrus (P < 0.05, cluster corrected), whereas TD children had increased neuronal discharges in this same brain area (P < 0.05, cluster corrected). This pattern of responses gave rise to a

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significant group effect ($P < 0.05$, cluster corrected) in this same region of the medial postcentral gyrus. These results indicated that the responsiveness of primary somatosensory cortices to the external afferent feedback was weaker and aberrant in the children with CP.

The virtual sensor extracted from the peak voxel within the medial postcentral gyrus cluster corroborated these results (Fig. 1). Critically, the peak amplitude of activity in this voxel (0–200 ms) was reduced by 43% in the children with CP and significantly differed from the TD children (CP = 0.07 ± 0.04 nAm; TD = 0.12 ± 0.05 nAm; $P = 0.02$). There was no significant difference in the latency of the peak amplitude (CP = 173 ± 26 ms; TD = 177 ± 23 ms; $P = 0.72$).

**Behavioral results.** The children with CP generated a lower maximum torque with the ankle plantarflexors compared with the TD children (Fig. 2; $P = 0.001$). For the measured gait variables, the children with CP had slower preferred (CP = 0.004) and fast-as-possible walking speeds ($P = 0.0001$) compared with the TD children (Fig. 3A). Furthermore, the TD children used a longer step length than the children with CP while walking at their preferred ($P = 0.03$) and fast-as-possible speeds (Fig. 3B; $P = 0.0001$). There were no differences in the cadence used at the respective walking speeds (Fig. 3C).

**Correlations with amplitude of peak voxel in the SPM.** For the entire group of children, there was a positive correlation between the amplitude of the peak voxel in the group-difference SPM and the torque generated by the ankle plantarflexors (rho = 0.40; $P = 0.04$). This implied that the participating children who had a greater amount of activity within the somatosensory cortices were likely able to generate a larger torque with the ankle plantarflexors. For the preferred walking speed, there was a positive correlation between the step length (rho = 0.38; $P = 0.04$) and the amplitude of the peak voxel in the group-difference SPM and a negative correlation between the cadence and the amplitude of the same peak voxel (rho = −0.38; $P = 0.04$). This suggests that children with a greater amount of somatosensory activity were more likely to use a longer step length and have a faster cadence while walking at their preferred pace. We also found that there was a positive correlation between the amplitude of the peak voxel in the group-difference SPM and the step length at the fast-as-possible walking speed (rho = 0.40; $P = 0.03$). This relationship suggests that the children who utilized a longer step length while walking fast also tended to have greater activity in the somatosensory cortices. All of the Spearman rho rank-order correlations between the amplitude of the peak voxel in the group-difference SPM and the behavioral data collected from all children are presented in Table 1.

Our separate analysis of the data collected for the children with CP revealed that there was a strong positive correlation between the amplitude within the same peak voxel and the strength of the ankle plantarflexors (Fig. 4; $P = 0.02$). This implies that children with CP who generated larger ankle torques also tended to have greater activation within the somatosensory cortices to a peripheral tactile simulation applied to the bottom of the foot. The preferred (CP = 0.05; Fig. 2A) and fast-as-possible (Fig. 5E; $P = 0.03$) walking speeds of the children with CP were also moderately correlated with the amplitude of the peak voxel in the group-difference SPM. In addition, the step length (Fig. 5D; $P = 0.01$) at the fast-as-possible walking speed was strongly correlated with the amplitude of the same peak voxel. These combined results indicate that the mobility of the participating children with CP was strongly related to the amount of activity within somatosensory cortices. All of the Spearman rho rank-order correlations between the amplitude of the peak voxel in the group-difference SPM and the behavioral data collected from the children with CP are presented in Table 1.

For the data collected from the TD children, there was a moderate negative correlation between the cadence at the preferred walking speed and the amplitude of the peak voxel in the group-difference SPM (rho = −0.58; $P = 0.04$). This suggested that the TD children who utilized a faster cadence also tended to have greater activation within the somatosensory cortices. In addition, we found a strong negative correlation between the step width at the fast-as-possible walking speed and the amplitude of the same peak voxel (rho = −0.67; $P = 0.01$). This implied that the TD children who had greater activity within the somatosensory cortices also tended to use a

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**Fig. 1.** Group-averaged 4–14-Hz virtual sensor time series extracted from the peak voxel in the group-difference statistical parametric map. The virtual sensor for the typically developing children is represented by a solid line, whereas that for the children with cerebral palsy is shown with a dashed line. The application of the tactile simulation to the bottom of the foot occurs at 0 ms. The average time series clearly shows that the initial 200 ms of the time series was diminished in children with cerebral palsy compared with the typically developing children.

**Fig. 2.** Box plots of the ankle plantarflexion torques measured for the typically developing children and the children with cerebral palsy. The data are presented in quartiles, and the bold line on each box plot represents the median.
narrower step width. None of the other variables measured were significantly correlated with the amplitude of the peak voxel in the group-difference SPM. All of the Spearman rho rank-order correlations between the amplitude of the peak voxel and the behavioral data collected from the TD children are presented in Table 1.

Correlations with source amplitude of the virtual sensor. For the entire group of children, there was a strong positive correlation between the peak amplitude of the virtual sensor (0–200 ms), extracted from the peak voxel of the group-difference SPM, and the preferred walking velocity (rho = 0.66; P = 0.002). This implied that the participating children who had a larger somatosensory cortical response to the tactile stimulation tended to also walk at a faster speed. For the preferred walking speed, there was a positive correlation between the step length (rho = 0.47; P = 0.04) and the magnitude of the peak activity and a negative correlation between the step width and the magnitude of activity (rho = −0.61; P = 0.006). This suggests that the children with a larger somatosensory cortical response to the tactile stimulus were more likely to use a longer step length and would select a narrower step width while walking at their preferred speed. We also found that there was a negative correlation between the magnitude of peak activity and the step width for the fast-as-possible walking speed (rho = −0.46; P = 0.05). This relationship further implies that the selection of a step width during gait may be related to the amount of activity seen within somatosensory cortices after a tactile stimulation. None of the other variables were significantly correlated with the peak virtual sensor amplitude measured in the somatosensory cortices (0–200 ms) after a tactile stimulus was applied to the bottom of the foot. In addition, we were unable to find any correlations between the peak amplitude and the behavioral variables when the Spearman rho rank-order correlations were performed separately for the TD children and children with CP. All of the Spearman rho rank-order correlations between the virtual sensor peak amplitude, extracted from the peak voxel of the group-difference SPM, and the respective behavioral variables are presented in Table 2.

DISCUSSION

This investigation explored the relationship between cortical activity within the somatosensory cortices and the lower-extremity motor performance of children with CP. Our results indicated that the amplitude of activity in the neural populations representing the foot in the somatosensory cortices is related to mobility and strength.
sory cortices have a diminished response to tactile stimulation in children with CP. Our results suggest that stronger activity within the somatosensory cortices in response to tactile stimulation of the foot is potentially related to enhanced ankle plantarflexor strength and improved mobility in the children with CP. These results are innovative because they show that aberrant activity within somatosensory cortices is likely related to the lower-extremity motor performance of children with CP. These results provide new support for the definition of CP that was put forth by Rosenbaum and colleagues (2007) that classified CP as having disturbances of sensation that affect movement.

The children with CP walked slower than the TD children at their preferred and fast-as-possible walking speeds. In addition, the children with CP had a shorter step length but a similar cadence as the TD children for both of the walking speeds investigated. Our experimental work suggests that these noted mobility differences may partly be a product of the strength of neural activity within the somatosensory cortices to somatosensations on the bottom of the foot. The experimental paradigm used in this investigation used a small airbladder to stimulate the foot mechanoreceptors. These receptors were chosen because they provide important sensory information about the temporal and spatial application of the pressures that are applied to the bottom of the foot during gait (Perry et al. 2001). We suggest that children with CP who display less activity within the somatosensory cortices after stimulation of these mechanoreceptors may have less certainty about the plantar pressures they experience during gait. This potential link implies that the slower walking speeds seen in the children with CP may represent a more cautious gait that is partly due to uncertainties about the peripheral somatosensations.
Prior DTI studies have shown that damage to the thalamocortical tracts is related to the somatosensory impairments seen in children with CP (Hoon et al. 2009; Rose et al. 2007; Trivedi et al. 2008, 2010). These results suggest that the abnormal activity within somatosensory cortices reported here may have been instigated by perinatal damage to the thalamocortical tracts. Potentially, this damage may alter the signal-to-noise ratio in such a way that the threshold for activation of the somatosensory cortices becomes uncharacteristic and perhaps unresponsive to important peripheral feedback. A prior study has shown that the functional connectivity of the white matter fiber tracts can be improved in children with CP after an intensive therapeutic protocol (Trivedi et al. 2008). This suggests that the net effect of structural damage along the thalamocortical tracts may be somewhat reversible, which may improve neural activity within the somatosensory cortices.

The results of this exploratory study have provided unique information, but they fall short of showing that the strength of somatosensory activity predicts the strength and mobility problems seen in children with CP. The reason that we are cautious in making this conjecture is because it is just as likely that the motor impairments seen in children with CP (i.e., cocontractions, spasticity, and poor selective muscular control) also played a role in the noted mobility and strength impairments. Therefore, it is more likely that the motor control problems seen in children with CP related to poor sensorimotor integration, rather than a purely sensory or motor deficiency. Additionally, we suspect that the reduced strength of somatosensory cortical activity may be related to the lack of physical activity reported in children with CP. Support for this premise is based on the plethora of experiments that have shown that somatosensory cortical activity and architecture are use dependent.

Although our experimental results are insightful, the broader clinical question is how the noted somatosensory processing deficits seen in children with CP can be overcome. This is especially salient because the outcomes from prior animal and human studies have established well that the somatosensory cortices play an integral role in the learning of new motor skills (Pavlides et al. 1993; Robert et al. 2013; Sakamoto et al. 1989; Vidoni et al. 2010). Behavioral results from a previous investigation have suggested that somatosensations are recalibrated after practicing a new motor skill (Ostry et al. 2010). On the basis of these results, we suspect that increased practice with the impaired limb may result in enhanced neural activity within the sensorimotor networks of children with CP. Similar concepts have already infiltrated the constraint-induced movement paradigms, which are being used to improve motor function of the hand (Uswatte and Taub 2013). Testing these therapeutic concepts would be laudable and may have the potential to alter the treatment strategies that are currently being used to improve the mobility and lower-extremity strength of children with CP.

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CORTICAL ACTIVITY IS RELATED TO MOBILITY AND STRENGTH


