Reactivity of Sensorimotor Oscillations Is Altered in Children With Hemiplegic Cerebral Palsy: A Magnetoencephalographic Study

Elina Pihko,^{1*} Päivi Nevalainen,^{2,3} Selja Vaalto,^{4,5} Kristina Laaksonen,^{1,6} Helena Mäenpää,⁷ Leena Valanne,⁸ and Leena Lauronen³

¹Brain Research Unit, O.V. Lounasmaa Laboratory, Aalto University School of Science, Espoo, Finland

²BioMag Laboratory, HUS Medical Imaging Center, Helsinki University Central Hospital, Helsinki, Finland

³Department of Clinical Neurophysiology, Children's Hospital, Helsinki University Central Hospital and Helsinki University, Helsinki, Finland

⁴Department of Clinical Neurophysiology, HUS Medical Imaging Center, Helsinki University Central Hospital and Helsinki University, Helsinki, Finland

⁵Department of Clinical Neurophysiology, Faculty of Health Sciences, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

⁶Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland

⁷Department of Child Neurology, Children's Hospital, Helsinki University Central Hospital, Helsinki, Finland

⁸HUS Medical Imaging Center, Helsinki University, Helsinki, Finland

---

Abstract: Cerebral palsy (CP) is characterized by difficulty in control of movement and posture due to brain damage during early development. In addition, tactile discrimination deficits are prevalent in CP. To study the function of somatosensory and motor systems in CP, we compared the reactivity of sensorimotor cortical oscillations to median nerve stimulation in 12 hemiplegic CP children vs. 12 typically developing children using magnetoencephalography. We also determined the primary cortical somatosensory and motor representation areas of the affected hand in the CP children using somatosensory-evoked magnetic fields and navigated transcranial magnetic stimulation, respectively. We hypothesized that the reactivity of the sensorimotor oscillations in alpha (10 Hz) and beta (20 Hz) bands would be altered in CP and that the beta-band reactivity would depend on the individual pattern of motor representation. Accordingly, in children with CP, suppression and rebound of both oscillations after stimulation of the contralateral hand were smaller in the lesioned than intact hemisphere. Furthermore, in two of the three children with CP having ipsilateral motor representation, the beta- but not alpha-band modulations were absent in both hemispheres after affected hand stimulation suggesting abnormal sensorimotor network interactions in these individuals. The results are consistent

---

Contract grant sponsors: The Finnish Cultural Foundation, the Finnish Medical Foundation, the Foundation for Pediatric Research, the Arvo and Leena Ylppö Foundation, the Biomedicum Helsinki Foundation, the Jenny and Antti Wihuri Foundation, the Emil Aaltonen Foundation, Helsinki University Central Hospital research grants, and the aivoAALTO project grant from Aalto University.

*Correspondence to: Dr. Elina Pihko, Brain Research Unit, O.V. Lounasmaa Laboratory, Aalto University, PO Box 15100, 00076 Aalto, Finland. E-mail: elina.pihko@aalto.fi

Received for publication 10 April 2013; Revised 20 December 2013; Accepted 3 January 2014.

DOI 10.1002/hbm.22462

Published online 12 February 2014 in Wiley Online Library (wileyonlinelibrary.com).

with widespread alterations in information processing in the sensorimotor system and complement current understanding of sensorimotor network development after early brain insults. Precise knowledge of the functional sensorimotor network organization may be useful in tailoring individual rehabilitation for people with CP. *Hum Brain Mapp* 35:4105–4117, 2014. © 2014 Wiley Periodicals, Inc.

Key words: magnetoencephalography MEG; pediatric; somatosensory; transcranial magnetic stimulation TMS

INTRODUCTION

Cerebral palsy (CP), being one of the most common causes of chronic childhood disability, is a group of disorders that impair control of movement and posture due to damage to the developing brain. The underlying lesions can vary in location, extent, and timing of the insult. In a case where CP affects behaviorally only one side of the body (hemiplegic CP), these insults can lead to reorganization of the corticospinal motor pathways and result, for example, in ipsi- or bilateral motor cortical representation of the affected hand (Carr et al., 1993; Kesar et al., 2012; Staudt, 2010; Staudt et al., 2002, 2004, 2006a). However, in some cases, the corticospinal tracts in the lesioned (contralateral to the affected hand) hemisphere are sustained, even with very little remaining white matter (Staudt et al., 2006b). In addition to motor problems, tactile discrimination deficits are prevalent in individuals with CP (for a review see Clayton et al., 2003). In contrast to the motor system, the somatosensory representation remains in the lesioned hemisphere (i.e., contralateral to the affected hand) (Gerloff et al., 2006; Staudt et al., 2006a; Wilke et al., 2009). Nevertheless, bilateral abnormalities in functioning of the primary somatosensory cortices have been reported in children with hemiplegic CP (Nevalainen et al., 2012).

Abnormalities in functioning of the somatosensory cortex and its connections also influence the motor system. Thickbroom et al. (2001) argued that the dissociation of the laterality of the efferent corticospinal motor output and afferent somatosensory input might cause additional motor dysfunction due to an impairment of sensorimotor integration at the cortical level. It has further been suggested that in some cases the impairment of hand motor function might be caused by aberrant connections to or from the somatosensory cortex while corticospinal motor connections remain intact (Hoon et al., 2002). In line with the idea that the somatosensory system significantly contributes to motor symptoms in CP, sensory-level electric stimulation of the spastic limb can be used to improve the active and passive motion of the limb (Mäenpää et al., 2004). Furthermore, magnetoencephalographic (MEG) measurements showed in an 8-year-old child with hemiplegic CP that constraint-induced movement therapy increased specifically the activity of the contralateral somatosensory cortex supposedly as a result of increased sensory feedback from the affected limb (Sutcliffe et al., 2007).

The temporal and spatial details of human cortical sensorimotor functioning have been widely studied with MEG (Hari and Forss, 1999). A few recent MEG studies have also demonstrated diverse functional abnormalities of the somatosensory system in people with CP. In children with hemiplegic CP due to a subcortical brain lesion, MEG revealed bilateral alterations in evoked responses to electric stimulation of the median nerve, which included missing deflections, aberrant morphology, longer latencies, and lower amplitudes of some of the evoked responses within 100 ms from the stimulation (Nevalainen et al., 2012). In another study, six children with spastic CP (two hemiplegic, three diplegic, and one quadriplegic) had longer evoked response latencies to stimulation of the index fingers (Guo et al., 2012) than typically developing (TD) children. In four participants with spastic diplegic CP, Kurz and Wilson (2011) observed smaller amplitudes of the responses at 40 ms after tibial nerve stimulation than in age-matched controls.

In addition to evoked activity, MEG can be used to study spontaneous cortical oscillations and their modulation to external stimulation. Spontaneous rhythmic oscillations appear in the sensorimotor cortical regions in the frequency bands around 10 and 20 Hz, referred to as alpha and beta bands, respectively. Both oscillations can be modulated by movement as well as by somatosensory stimulation. For example, stimulation of the median nerve leads to an initial poststimulus suppression (also called event-related desynchronization) of the oscillations (about 100–300 ms poststimulus) followed by a subsequent rebound (event-related synchronization) larger in amplitude than the prestimulus level (Della Penna et al., 2004; Salenius et al., 1997; Salmelin and Hari, 1994). Poststimulus suppression has been related to increased and the subsequent rebound to decreased excitability in cortical neuronal networks (Neuper and Pfurtscheller, 2001; Salmelin et al., 1995). Consistent with reduced motor cortex excitability during the beta rebound, motor-evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) after conditioning median nerve stimulation are reduced in amplitude at a time course that corresponds with the timing of the beta-band rebound (Chen et al., 1999).

We used whole-head MEG to measure whether the reactivity of sensorimotor oscillations to electric median nerve stimulation differ between children with spastic hemiplegic CP and in TD children. As somatosensory and motor

cortical representation may show distinct laterality in CP, we also localized the primary somatosensory (SI) and motor (MI) cortical areas in the CP children using somatosensory-evoked magnetic fields (SEFs) and navigated TMS (nTMS), respectively. We further hypothesized that changes in the hemisphere of motor control after early brain lesion would affect the pattern of reactivity of the sensorimotor oscillations in children with CP.

MATERIALS AND METHODS

Participants

The participants included 12 children diagnosed with spastic, hemiplegic CP (seven females and five males, age range from 11 to 17 years) and 12 age- and sex-matched TD participants (age range: 12–18). A child neurologist (author HM) recruited the participants from the Department of Child Neurology at the Helsinki University Central Hospital. Eight of the children in the CP group with only subcortical lesions had participated in an earlier study of somatosensory-evoked fields (Nevalainen et al., 2012). Four additional participants had lesions extending to the primary sensorimotor cortices [see Fig. 1 for magnetic resonance images (MRIs)]. In the CP group, the left hemisphere was lesioned in ten participants and the right hemisphere in two (see Table I for details of lesion types and locations). Four participants with CP were on antiepileptic medication: oxcarbazepine for Participants P2 and P6, and valproate for P3 and P4.

Since our CP participants included children with lesions in either the left or right hemisphere, each child in the TD group was assigned in the group analysis to have a “lesioned” hemisphere according to the matched CP participant’s side of damage. This was done in order to balance out any possible inherent differences in the functioning of the left and right hemispheres. Before participation, the experimental procedures were explained to the subjects and to their parent(s). All participants and one of their parents signed an informed consent. The Ethics committee of the Hospital district of Helsinki and Uusimaa approved the study protocol.

Behavioral Tests

An occupational therapist assessed the motor performance in individuals with CP with the Manual Ability Classification System (MACS), which ranks the bimanual ability of everyday life into five levels (1—minor difficulties in handling objects requiring fine motor control; 5—severe impairment; Eliasson et al., 2006). The tactile sensitivity was evaluated at the tip of digit II with Semmes-Weinstein monofilaments (scores 1–6: 6—normal, 4—diminished protective touch, and 1—no sensation).

Stimulation

Right and left median nerves were electrically stimulated in separate runs with 0.5-ms constant current pulses

with stimulation intensity just above the motor threshold. The interstimulus interval was 2 s.

MEG Recordings

MEG was recorded in the BioMag Laboratory in a magnetically shielded room (Euroshield, Finland) with a whole-scalp helmet-shaped sensor array consisting of 306 independent channels: 204 gradiometers and 102 magnetometers (Elekta Neuromag Vectorview, Elekta Oy, Helsinki, Finland). Only gradiometer data were used in analysis of the sensorimotor oscillations. The sampling rate was 987 Hz, and the measuring band pass from 0.03 to 320 Hz. Eye movements were recorded with two electrodes, one above the left and the other below the right eye canthi with a ground on the forehead. Periods with eye movements ($\pm 100 \mu\text{V}$ signal in the bipolar eye movement lead) were excluded from the oscillation amplitude curves. An individual Cartesian coordinate system was constructed for each participant by digitizing the preauricular points and nasion before the recordings. Four position indicator coils were attached to the head. In the beginning of both recording blocks, the coils were fed with excitation currents to determine the head position relative to the sensors. During the measurement, the participants sat comfortably watching a self-chosen video without sound.

MEG Analysis

For the MEG analysis, artifacts were first removed from the raw data with the spatiotemporal signal space separation method (Taulu and Simola, 2006) in MaxFilter® software (Elekta Neuromag®; Elekta Oy, Helsinki, Finland) using a correlation limit of 0.98 and a 4-s time window. Then, individual spectral content of the data was calculated for each subject from a 400-s period at the beginning of the raw data file (Graph software, Elekta). In addition, time–frequency representations (Morlet wavelets with steps of 1 Hz) were calculated to inspect the modulation of oscillations in different frequency bands (Brainstorm software, Tadel et al., 2011). For further analyses, we selected for each subject frequency bands around the visually-determined spectral peaks with a bandwidth of about 5 Hz for the alpha-band oscillations (range from 6–11 to 9–14 Hz) and about 10 Hz for the beta-band oscillations (range from 12–23 to 17–27 Hz). When two peaks were observed in the beta band, the chosen band covered both frequencies.

The reactivity of the sensorimotor oscillations in alpha and beta bands was analyzed using the temporal–spectral evolution method (Salmelin and Hari, 1994), where the data were first bandpass filtered through the individually chosen frequency bands, then rectified, and finally averaged, time-locked to the median nerve stimulation. In this way, the absolute amplitudes of the oscillation envelopes were in the same units (fT/cm) as the raw data and

Figure 1.

In the left column, coronal magnetic resonance images (MRIs) of the CP children show the brain lesions and the locations of the earliest SEF responses (white squares), the hemisphere from which the nTMS evoked motor responses to the affected hand (schematic coil), and the side of the affected hand (schematic hand). Furthermore, the latency and location of the earliest SEF response (white squares in the middle column) and the optimal representation area(s) for the APB muscle of the affected hand in nTMS (white circles in the right column) are shown on axial MRIs. Patients 1–4 have corticosubcortical brain lesions and no typical N20m or P35m SEF components were present in any of them, i.e., the SEF morphology was severely abnormal. However, the (earliest) elicited abnormal SEF response to stimulation of

the affected hand was localized to the contralateral hemisphere and there were no responses from the ipsilateral primary sensorimotor area. Of these children P1–P3 had ipsilateral and P4 had contralateral motor representation. Patients 5–12 had subcortical lesions and the early SEF morphology in all of them showed the normal N20m–P35m pattern, and at least one of these early SEF components could be modeled with an ECD (Nevalainen et al., 2012). Patient 5 had periventricular leukomalacia and contralateral motor representation of the affected hand. Patients 7–11 had a small periventricular infarction and bilateral motor representation of the affected hand. nTMS was not performed in Patients 6 and 12 who also had infarctions involving only subcortical structures.

TABLE I. Lesion characteristics (by MRI), motor (MACS), and tactile (touch = monofilament test) abilities, side of the motor cortex representation (by nTMS), normality/abnormality of SEFs and frequency of the maximal suppression and rebound of alpha- and beta-band oscillations in the lesioned hemisphere of participants with CP after contralateral stimulation

#	Side	MRI lesion			MACS	Touch	nTMS	MN SEF	Alpha	Alpha	Beta	Beta
		Type	Location ^a	Extent ^b					Supp	Reb	Supp	Reb
P1	Left	Infarction	SI/MI + subcx	3	3	np.	Ipsi	Major abn.	11	12	-	-
P2	Left	Infarction	SI/MI + subcx	3	3	4	Ipsi	Major abn.	8	8	13	14
P3	Right	Polymicrogyria	SI/MI + subcx	3	2	5	Ipsi	Major abn.	9	12	-	-
P4	Left	Infarction	SI/MI + subcx	3	np.	5	Contr	Major abn.	10	10	17	14
P5	Right	PVL	Subcx	3	3	6	Contr	Minor abn.	8	9	18	17
P6	Left	Infarction	Subcx	2	2	6	np.	Minor abn.	7	8	15	17
P7	Left	Infarction	Subcx	2	1	4	Bilat	Minor abn.	11	11	25	22
P8	Left	Porencephaly	Subcx	1	2	6	Bilat	Minor abn.	11	11	21	16
P9	Left	Infarction	Subcx	2	1	6	Bilat	Normal	9	11	21	22
P10	Left	Infarction	Subcx	1	1	6	Bilat	Normal	9	9	18	16
P11	Left	Infarction	Subcx	1	1	6	Bilat	Normal	10	10	19	14
P12	Left	Infarction	Subcx	1	1	6	np.	Normal	9	9	19	16

^aLesion location SI/MI involves somatosensory and/or motor cortex, Subcx includes subcortical structures (periventricular white matter in all subjects ± thalamus, brain stem, capsula interna); np. = not performed.

^bLesion extent: lesion Size 3 stands for an infarction of the whole middle cerebral artery (MCA) area or a corresponding size of some other type of lesion. Size 1 indicates only a spot type lesion. Manual Ability Classification System (MACS) scores (classified from 1 to 5: 1 signifies minor disability in fine hand motor function. In our patients the worst score was 3 indicating difficulties in performing everyday activities and dependence on environmental adjustments) and monofilament test (Touch) showing somatosensation (classified from 6 to 1: 6 = normal. In our patients the worst score was 4 = diminished protective touch sensation). MN SEF, somatosensory-evoked field to median nerve stimulation; Major abn., both major early SEF deflections (N20m–P35m) missing; Minor abn., one of the early deflections missing/too low in amplitude for dipole modelling; Normal, normal SEF.

evoked responses. The amplitude envelopes were calculated from all channels for each subject in the two frequency ranges, independently for left- and right-hand stimulation, and were low-pass filtered at 10 Hz. The channels with maximum suppression and rebound in hemispheres contra- and ipsilateral to the stimulated hand were chosen and peak amplitudes (relative to the baseline) and latencies for suppression and rebound of the oscillations were obtained. The peak value was taken into account only if the peak amplitude exceeded the noise level [2 standard deviation (SD) from the –500 ms to –100 ms prestimulus baseline].

The somatosensory representation area in the CP patients was determined by modeling the earliest detectable SEF component after median nerve stimulation with an equivalent current dipole (ECD) using a spherical head model based on individual anatomical MRIs. The location of the ECD was then superimposed on these individual MRI for visualization. For more details of the ECD modeling procedure, see Nevalainen et al. (2012).

Transcranial Magnetic Stimulation

Ten children with CP participated in the nTMS examination. For mapping the cortical representations of intrinsic hand muscles, we used nTMS (eXimia NBS; Nexstim, Hel-

sinki, Finland), which combines traditional TMS and neuronavigation (Ruohonen and Karhu, 2010). In nTMS, mapping is guided by individual MRIs and computational electric field display and each stimulation site is tagged to the MRI. As the mapping surface we chose three-dimensional (3D) surface rendering, in which sulci and gyri were easily identified. Single biphasic pulses were delivered with a Nexstim stimulator via a figure-of-eight-shaped coil.

MEPs were recorded from abductor pollicis brevis (APB) and abductor digiti minimi muscles by continuous electromyography (EMG; 9/10 subjects: Nexstim EMG system; 1/10 subjects: ME 6000; Mega Electronics, Kuopio, Finland). Muscle activity was monitored on-line and subjects were encouraged to avoid any muscle activation in the hands during the stimulation procedure. The EMG signals were sampled at 3 kHz (Nexstim EMG)/1 kHz (ME 6000), filtered (10–500 Hz in Nexstim EMG/ 8–500 Hz in ME 6000), amplified, and stored for off-line analyses.

First, the intact hemisphere was mapped in each subject. Stimulation intensity was adjusted individually according to MEP amplitudes. Intensity was increased if MEP amplitudes were generally <100 μ V and decreased if amplitudes were >1 mV. After determining the stimulation intensity, the intensity was kept constant to map the different cortical areas. Mapping started from the anatomical hand knob and continued point-by-point along precentral and

postcentral gyri as well as the gyri anterior to the precentral gyrus (distance between stimulation points 2–5 mm, direction of the induced current perpendicular to sulci, interstimulus interval ~5 s). The stimulation site producing continuously the highest peak-to-peak amplitudes in contralateral APB was determined and defined as the optimal representation area of contralateral APB. If short-latency ipsilateral MEPs were detected, the optimal representation area for ipsilateral APB was determined similarly.

Mapping of the lesioned hemisphere was performed in a manner similar to the intact hemisphere. If the patient had a corticosubcortical infarction, mapping was targeted to the remaining cortical areas around the affected cortex. Stimulation intensity was adjusted as in the mapping of the intact hemisphere and increased up to the maximum stimulator output if the MEPs could not be detected with lower intensities. The optimal representation area of contralateral and possible ipsilateral APB was also determined as in the intact hemisphere.

Magnetic Resonance Image

The MRIs were obtained with a 3-T unit (Philips Intera Achieva, Amsterdam, the Netherlands) from all participants with CP. An experienced neuroradiologist performed the structural analysis from T2-weighted axial and coronal images (slice thickness 3 mm) and axial fluid-attenuated inversion recovery images (4 mm). The side, extent (cortico-subcortical involving SI and/or MI or pure subcortical), and type (arterial infarction or developmental) were determined (Table I). T1-weighted 3D images were used for MEG-MRI integration and navigation in nTMS.

Statistics

The MEG variables were tested for normal distribution with Shapiro–Wilks test and additionally for skewness and kurtosis. In the case of non-normal distribution (amplitudes and beta-band peak frequencies), the data were analyzed with the nonparametric Wilcoxon signed-rank test and Mann–Whitney *U* test. Latencies were normally distributed and analyzed with mixed analysis of variance (ANOVA; GLM; IBM Statistics SPSS 20).

RESULTS

Primary Somatosensory and Motor Representation in Children With CP

Of the 12 children with CP, in two the motor representation of the affected hand was in the contralateral hemisphere, in five the motor representation was bilateral, and in three ipsilateral, as shown by nTMS (Table I and Fig. 1). The SEFs to median nerve stimulation showed that somatosensory representation was contralateral in all children

with CP. Even in the three children with ipsilateral motor representation (P1–P3), no somatosensory responses were detected in the ipsilateral SI. Although the normal early SEFs with latencies of 20–30 ms were abnormal (longer latency or abnormal morphology) or missing in these three children, the earliest activation (albeit later than the normal 20–30-ms responses) was localized in the contralateral (lesioned) hemisphere (Fig. 1).

Behavioral Tests and Motor Representation

The behavioral scores were obtained in 10/12 CP children; one child (P1) did not undergo the sensitivity assessment and another one (P4) the manual ability test. The manual ability scores (MACS) were the worst (gr 3) in the two CP children with ipsilateral motor representation (P1 and P2); however, one child with contralateral representation also had score 3 (P5, Table I). The scores on sensory abilities had the same tendency: Three children (P2–P4) with corticosubcortical lesions (and very abnormal early SEFs) had lowered scores (4 and 5). Additionally, one child with bilateral motor representation, minor SEF abnormality, and a subcortical lesion (P7, Table I) had score 4. Generally, children with corticosubcortical lesions, including the children with ipsilateral hand motor representation, had lower scores than children with pure subcortical lesions.

Modulation of the Sensorimotor Oscillations With Respect to Motor Representation Pattern

In general, both the TD children and the children with CP showed clear oscillatory activity over the central sensorimotor areas in the alpha and beta frequency bands. Figure 2A,B shows the recorded sensorimotor oscillations from one CP and one TD child and how the alpha- and beta-band oscillations were modified after the stimulation (Fig. 2C). In the ipsilateral hemisphere, the modulation amplitudes were in some cases low. A modulation (suppression or rebound) was considered to be present if the peak amplitude was either lower than or exceeded the ± 2 SD noise level. For group analysis, if modulation was not detected, its value was set to 0 fT/cm.

At the individual level, the alpha-band modulations were detected in the contralateral hemisphere to stimulation of both hands in all CP children as well as all TD children. Also ipsilateral modulations in alpha-band were detected in all subjects except for one CP child (P2). In contrast, in two of the three CP children with ipsilateral motor representation of the affected hand (P1 and P3), neither the beta-band suppression nor rebound was reliably detected in the contralateral (lesioned) or ipsilateral (intact) hemisphere after stimulation of the affected hand though alpha-band modulation was present in both hemispheres. In both of them, stimulation of the unaffected hand modulated the beta-band oscillation in both contralateral (intact)

Figure 2.

(A) Raw data from one gradiometer channel over the sensorimotor area of the lesioned hemisphere to stimulation of the contralateral median nerve in one child with CP (left column) and in one with typical development (TD) (right). The vertical lines show stimulation onset every 2 s. (B) One epoch from the upper curve is shown in more detail. Note how the oscillations are suppressed after the stimulation. (C) Strength of the alpha (solid line) and beta-band (dashed line) oscillations for the same

participants, averaged over all epochs. The time scales in (B) and (C) are the same. The vertical line indicates the time of the median nerve stimulation. Curves under the baseline show suppression of the rhythmic activity compared with the baseline level, followed by subsequent rebound over the baseline level. The suppression is robust in both frequency bands, but the alpha-band rebound is not seen on these measurement channels.

as well as ipsilateral (lesioned) hemisphere. In the third CP child (P2) with ipsilateral motor representations, the beta-band modulation was detected contralaterally to stimulation of both the affected and unaffected hands, but the beta oscillations in the lesioned hemisphere occurred at very low frequencies (13 and 14 Hz for suppression and rebound, respectively, compared with 24 and 18 Hz in the intact hemisphere). In this child, stimulation of the unaffected hand induced suppression and rebound in both alpha and beta bands in the contralateral, intact hemisphere, but neither alpha- nor beta-band modulations in the ipsilateral (lesioned) hemisphere. Stimulation of the affected hand induced alpha-band modulations bilaterally but no beta-band modulation in the intact, ipsilateral hemisphere. Additionally, in one TD child the beta-band suppression was not detected after contralateral stimulation in either hemisphere and the rebound was not detected in one hemisphere. The beta-band modulations (suppression and rebound in both hemispheres) were thus present in all but the three CP children (P1–P3) and one TD child.

Comparison of Sensorimotor Oscillations in CP vs. TD Children

The peak latencies of the beta-band suppression and rebound in the contralateral hemisphere were 294 ± 13 and

818 ± 35 ms [mean $\pm$ standard error of the mean (SEM)], respectively. Latencies of the alpha-band suppression and rebound were significantly longer (407 ± 16 and $1,154 \pm 43$ ms) than those for the beta-band modulation (mixed ANOVA; group: CP/TD $\times$ hemisphere: lesioned/intact $\times$ frequency: alpha/beta $\times$ modulation type: suppression/rebound, main effect for frequency $F(1,18) = 64.3$, $P < 0.001$), in line with earlier findings (Salenius et al., 1997; Salmelin et al., 1995). There were no significant differences in modulation latencies between the CP and TD children.

In children with CP, suppression and rebound of both alpha- and beta-band oscillations to contralateral stimulation were smaller in the lesioned than intact hemisphere (Fig. 3, Table II, Wilcoxon signed-rank test, alpha suppression $P = 0.003$; alpha rebound, $P = 0.01$; beta suppression $P = 0.005$; beta rebound $P = 0.006$). As this analysis was carried out blind to the TMS results regarding the side of the motor representation, we later reanalyzed the data without the three subjects with ipsilateral motor representation, and found essentially the same results. No hemisphere differences, however, were revealed in the TD children (Table II).

Comparison of the modulation amplitudes between contra- and ipsilateral hemispheres showed that, in both hemispheres of the TD children, both alpha- and beta-band suppression and rebound (except for alpha-band

Figure 3.

Strengths (relative to the baseline) of suppression and rebound of alpha- and beta-band MEG rhythms to contralateral median nerve stimulation in the lesioned and intact hemispheres in children with CP (left) and in TD children. The horizontal lines denote median values, boxes include 50% of the data points, whiskers show data range without outliers, which are shown by the spheres. **indicates $P \leq 0.01$.

rebound in the “intact” hemisphere) were smaller to ipsilateral than contralateral stimulation (Wilcoxon signed-rank test, Table II). In children with CP, alpha and beta suppression and rebound were smaller to ipsilateral than contralateral stimulation only in the intact hemisphere. In their lesioned hemisphere, there were no differences between the modulation amplitudes to ipsi- and contralat-

eral stimulation. The modulation amplitudes to ipsilateral stimulation did not differ between the lesioned and the intact hemisphere, either in TD or CP children.

The beta band was clearly divided into two separate sub-bands: the frequency of the peak suppression in the beta band was higher than the frequency of the subsequent rebound. This difference can be seen from the time-frequency representations of one CP and one TD child (Fig. 4). The median frequency averaged over both hemispheres for suppression was 21 Hz and for rebound 18.5 Hz in the TD group. The difference was statistically significant for the TD children in both hemispheres (Wilcoxon signed-rank test, “lesioned” $P = 0.003$; “intact” $P = 0.03$) but not for the CP group (Fig. 5, Table I). Generally, in the lesioned hemisphere, the frequencies for both suppression and rebound in the beta band tended to be lower in the CP children than in the TD children (Mann-Whitney test, difference for beta rebound $P = 0.09$, median TD 18.0 Hz, CP 16.0 Hz; beta suppression $P = 0.03$, TD 21.0 Hz, CP 18.5 Hz).

DISCUSSION

By recording with MEG the modulation of the alpha- and beta-band sensorimotor oscillations to median nerve stimulation, we tested whether the reactivity of the ongoing primary sensorimotor cortical activity in children with hemiplegic CP differs between the lesioned vs. intact hemisphere or in comparison with TD children. In children with CP, suppression and rebound of both frequency bands to contralateral stimulation were smaller in the lesioned than intact hemisphere, whereas there were no differences between the hemispheres in the TD children. In addition, in the TD children and in the intact hemisphere of the CP children, the suppression and rebound were stronger to the contra- than ipsilateral stimulation,

TABLE II. Absolute peak amplitudes [fT/cm; mean (SEM)] of suppression and rebound to contra- and ipsilateral stimulation in the two frequency bands and hemispheres

Hemisphere	Contralateral				Ipsilateral			
	Alpha band		Beta band		Alpha band		Beta band	
	Suppression	Rebound	Suppression	Rebound	Suppression	Rebound	Suppression	Rebound
CP								
Lesioned	4.40 (1.24)	2.05 (0.33)	3.31 (0.89)	2.29 (0.68)	2.76 (0.68)	1.71 (0.42)	2.18 (0.53)	1.7 (0.39)
Intact	10.65 (3.0)	3.86 (0.7)	6.32 (1.39)	6.35 (1.28)	4.08 (1.63)**	1.83 (0.33)**	2.30 (0.49)**	1.86 (0.36)**
TD								
Lesioned	8.63 (2.02)	2.90 (0.93)	5.72 (1.44)	5.81 (1.41)	4.83 (1.32)**	1.49 (0.38)*	2.91 (0.74)*	1.93 (0.52)**
Intact	11.29 (3.37)	2.78 (0.77)	7.53 (2.13)	4.33 (0.89)	5.48 (1.54)*	2.76 (0.76)	3.09 (0.75)*	2.64 (0.71)*

Stars denote significant difference of the ipsilateral value from the corresponding contralateral one,

*is $P < 0.05$, **is $P < 0.01$,

Wilcoxon signed-rank test, not corrected for multiple comparisons. Note that in children with CP the ipsilateral values do not differ from the contralateral ones in the lesioned hemisphere.

Figure 4.

Baseline-corrected (−500/−100 ms) time–frequency representations from one channel over the central sensorimotor area in the intact hemisphere in one child with CP (left) and in one TD child (right). Bluish colors indicate suppression and the warm colors rebound. The red arrows show maximum suppression, and the black arrows maximum rebound in the beta band. Note also the clear suppression and rebound in alpha band in these

individuals. The stimulus artifact is reflected around 0 ms in higher frequencies. The increase in 4–5 Hz power around 100 ms reflects the somatosensory response to median nerve stimulation. Color scales show power. Note that the scales for the CP and TD child differ as the figure is not designed for quantitative comparison.

whereas there was no difference between the amplitudes in the lesioned hemisphere of the CP children.

The smaller suppression and rebound of the alpha- and beta-band sensorimotor oscillations to contralateral sensory stimulation in the lesioned vs. intact hemisphere of the CP children could be due to diminished thalamocortical sensory connections (Hoon et al., 2002; Lee et al., 2005) and/or subsequent aberrant functioning of cortical sensorimotor networks. In three subjects (P1–P3) the normal early SEF response sequence (N20m–P35m) to median nerve stimulation was missing and in one subject (P4), though the first SEF was detected already at 22 ms, its morphology was abnormal. Despite the abnormal early SEFs, oscillations in alpha band were modified also in these four subjects. At least in these four subjects, however, the abnormal conduction of sensory information to SI could have directly led to reduced alpha modulations in the lesioned hemisphere. On the contrary, in an earlier study including a subgroup of these same CP children with only subcortical lesions (P5–P12), the early-latency SEFs (N20m–P35m) did not differ between the lesioned and intact hemispheres, though the SEF responses following the N20m (with latencies of 25–60 ms) showed some bilateral alterations as compared with the TD children (Nevalainen et al., 2012). As these later deflections are more likely to reflect the activation of local cortical networks after the initial arrival of thalamocortical input to the cortex, which is reflected in the early 20-ms response (Allison et al., 1989; Jones et al., 2007), the differences between the modulations in lesioned and intact hemispheres in these

subjects might at least partly be due to aberrant cortical processing.

Furthermore, at the individual level, we hypothesized that in children with CP the side of cortical motor representation of the affected hand would affect the pattern of reactivity of the sensorimotor oscillations. Our results indicate that this was true for the most severe cases when the early lesion included, in addition to subcortical areas, also part of the neocortex and the motor representation was relocated to the hemisphere ipsilateral to the affected hand. Previously Gerloff et al. (2006) showed, using TMS and MEG, that in patients with similar early dichotomy of motor and somatosensory representations of paretic hand to ipsi- and contralateral hemispheres, respectively, the corticomuscular coherence in the beta band occurred between the EMG from muscles in the affected hand and the ipsilateral, intact M1. In our subjects with ipsilateral motor representation, the beta-band oscillations in the lesioned hemisphere did not show normal reactivity. In two of the three CP children with ipsilateral motor representation of the affected hand, the nTMS, SEFs, and modulation of oscillations jointly indicate a dissociation of somatosensory and motor representations. In these two subjects (P1 and P3), neither beta-band suppression nor rebound to stimulation of the affected hand was detected in either the contra- or ipsilateral sensorimotor area. However, the alpha-band modulation was detected in both hemispheres. First, these results suggest that the sensorimotor alpha and beta modulations at least partly rely on different neural networks. Furthermore, the lack of beta

Figure 5.

Frequencies of the beta-band suppression and rebound in the CP children (left) and TD children (right) in the lesioned and intact hemispheres.

modulation in the ipsilateral hemisphere, where nTMS elicited motor responses in the affected hand, may reflect the aberrant network properties, specifically the inability of somatosensory afferent flow (via the opposite hemisphere) to influence excitability of the motor cortex controlling the affected hand.

Generally in line with previous results, ipsilateral stimulation induced smaller suppression and rebound than contralateral stimulation in both hemispheres of TD children and in the intact hemisphere of the children with CP (Cheyne et al., 2003; Gaetz et al., 2010; Salenius et al., 1997; Salmelin and Hari, 1994). Interestingly, in the lesioned hemisphere of children with CP, effects of stimulation of ipsi- and contralateral hands on the oscillations were similar. The contralateral modulations are mediated/initiated by direct thalamocortical afferents, whereas the route to the ipsilateral sensorimotor cortex is likely to be more complex. Sensorimotor cortices in both hemispheres belong to the same functional resting-state network (Biswal et al., 1995; Fox and Raichle, 2007). Further, electrophysiological and functional MRI results have shown that unilateral stimulation activates in the ipsilateral hemisphere, in addition to the secondary somatosensory cortex, also SI, specifically area 2 (e.g., Hari and Forss, 1999; Hlushchuk and Hari, 2006; Iwamura, 2000). The most plausible route from periphery to the ipsilateral sensorimotor cortex is through the intact contralateral hemisphere via the corpus callosum. If this is the case, it is possible that the relative preservation of modulation to ipsilateral

stimulation (compared to diminished modulation to contralateral stimulation) reflects activation of different (and intact) neuronal population by the ipsilateral stimulation.

The neural architecture of the sensorimotor oscillations and of their reactivity is complex and not completely understood. Traditionally, movement-related reactivity of the alpha band has been attributed to the postcentral (somatosensory) gyrus, while also the precentral (motor) cortex contributes to beta-band oscillations (Pfurtscheller et al., 1996; Salmelin and Hari, 1994; Salmelin et al., 1995). Recent work has suggested the involvement of several independent neural generators for oscillations in both frequency bands. In monkeys studied with intracortical local field potential and single unit recordings, the beta-band oscillation power was strongest in SI, but the intrinsic rhythmicity was most prevalent for the pyramidal tract output cells in the primary motor cortex (Witham and Baker, 2007). In human recordings with cortical depth electrodes, suppression of both frequency bands during preparation and execution of a self-paced movement was seen in all three subjects in both pre- and postcentral gyri (Szurhaj et al., 2003). Modeling the activity of the primary somatosensory cortex suggested that alpha- and beta-band oscillations could, theoretically, both be generated in the SI cortex (Jones et al., 2009). Accordingly, in MEG experiments, SI was responsive to 23-Hz vibrotactile stimulation showing evoked oscillations (steady state response) in phase synchrony with the stimulation (Bardouille and Ross, 2008; Nangini et al., 2006). Furthermore, the beta-band oscillation is modulated not only by voluntary movements, but also by electric or tactile stimulation of the hand (Cheyne et al., 2003; Della Penna et al., 2004; Gaetz and Cheyne, 2006; Hari et al., 1997; Laaksonen et al., 2012; Salenius et al., 1997) or by anticipation of a tactile event (Van Ede et al., 2010, 2011; Van Ede and Maris, 2013). When purely tactile stimulation was used to modulate the oscillations, the suppression in alpha band and rebound in beta band were localized to somatosensory and motor cortices, respectively (Cheyne et al., 2003). However, as both primary motor and somatosensory cortices seem to be able to generate oscillations in alpha and beta bands, the modulations measured with MEG probably reflect complex interactions in the sensorimotor networks including both motor and somatosensory cortices.

As further evidence of the complexity of the underlying mechanisms of oscillations, suppression, and rebound of sensorimotor beta band have been localized to different areas. While both alpha- and beta-band suppressions to tactile brush stimulation were localized to contralateral SI, beta rebound was localized to primary motor cortex (Gaetz and Cheyne, 2006). Also, movement-related suppression of both alpha and beta bands were localized to the postcentral and beta rebound to the precentral gyrus (Jurkiewicz et al., 2006). Beta rebound has further been associated with motor cortex, because it is dampened by motor cortex activation due to movement execution, observation, or motor imagery (Hari et al., 1997; Salenius et al., 1997; Schnitzler

et al., 1997). In line with these findings, TMS studies support the relationship of reduced motor cortex excitability during the beta rebound (Abbruzzese et al., 2001; Chen et al., 1998, 1999; Mäki and Ilmoniemi, 2010).

The diversity of the functional role of the oscillations and their modulations is further suggested by studies showing distinct reactivities in the beta band such that maximal postmovement synchronization (rebound) in one band was found in parallel with desynchronization (suppression) in another beta band (Pfurtscheller et al., 1997). In a study of the effect of action observation on sensorimotor oscillations, the largest rebound was in the lower (13–18 Hz) beta band (Avanzini et al., 2012). Our result showing higher frequencies for the suppression vs. rebound in the beta band of the TD children supports this notion of several functional subcomponents of the oscillations and their modulation. In the CP group, the suppression and rebound frequencies did not differ, probably as a consequence of the tendency to generally lower beta frequencies in the CP group, as was also suggested previously for children with hemiparetic CP (Kulak et al., 2005).

In conclusion, in accordance with previous studies (e.g., Staudt et al., 2002, 2004, 2006a; Wilke et al., 2009), we observed several different patterns of sensorimotor representation in children with hemiplegic CP. The present study extends the earlier knowledge gained with MEG of aberrant functioning of the sensorimotor system by indicating that reactivity of sensorimotor oscillations to sensory stimulation is dependent on these individual representation patterns of sensorimotor system (i.e., ipsi vs. contra/bilateral motor representation). At the group level, we further showed that, even though somatosensory representation of the affected hand remained in the contralateral, lesioned hemisphere in the children with CP, somatosensory processing in the lesioned hemisphere deviated from that in the intact hemisphere: the reactivity of both alpha- and beta-band sensorimotor cortical oscillations to contralateral median nerve stimulation in children with CP was reduced in the lesioned hemisphere. This finding agrees with observed motor and sensory deficits and with increasing knowledge of the role of the aberrant somatosensory system enhancing the motor problems in hemiplegic CP. Future studies on the cortical mechanism are needed to help to plan improved ways of rehabilitation.

ACKNOWLEDGMENTS

We thank Riitta Hari for useful discussions.

REFERENCES

- Abbruzzese G, Marchese R, Buccolieri A, Gasparetto B, Trompetto C (2001): Abnormalities of sensorimotor integration in focal dystonia: A transcranial magnetic stimulation study. *Brain* 124: 537–545.
- Allison T, McCarthy G, Wood CC, Darcey TM, Spencer DD, Williamson PD (1989): Human cortical potentials evoked by stimulation of the median nerve. I. Cytoarchitectonic areas generating short-latency activity. *J Neurophysiol* 62: 694–710.
- Avanzini P, Fabbri-Destro M, Dalla Volta R, Daprati E, Rizzolatti G, Cantalupo G (2012): The dynamics of sensorimotor cortical oscillations during the observation of hand movements: An EEG study. *PLoS One* 7:e37534.
- Bardouille T, Ross B (2008): MEG imaging of sensorimotor areas using inter-trial coherence in vibrotactile steady-state responses. *Neuroimage* 42:323–331.
- Biswal B, Yetkin FZ, Haughton VM, Hyde JS (1995): Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med* 34:537–541.
- Carr LJ, Harrison L, Evans AL, Stephens JA (1993): Patterns of central motor reorganization in hemiplegic cerebral palsy. *Brain* 116:1223–1247.
- Chen R, Corwell B, Hallett M (1999): Modulation of motor cortex excitability by median nerve and digit stimulation. *Exp Brain Res* 129:77–86.
- Chen R, Yaseen Z, Cohen LG, Hallett M (1998): Time course of corticospinal excitability in reaction time and self-paced movements. *Ann Neurol* 44:317–325.
- Cheyne D, Gaetz W, Garnero L, Lachaux J-P, Ducorps A, Schwartz D, Varela FJ (2003): Neuromagnetic imaging of cortical oscillations accompanying tactile stimulation. *Brain Res Cogn Brain Res* 17:599–611.
- Clayton K, Fleming JM, Copley J (2003): Behavioral responses to tactile stimuli in children with cerebral palsy. *Phys Occup Ther Pediatr* 23:43–62.
- Della Penna S, Torquati K, Pizzella V, Babiloni C, Franciotti R, Rossini PM, Romani GL (2004): Temporal dynamics of alpha and beta rhythms in human SI and SII after galvanic median nerve stimulation. A MEG study. *Neuroimage* 22: 1438–1446.
- Eliasson A-C, Krumlinde-Sundholm L, Rösblad B, Beckung E, Arner M, Öhrvall A-M, Rosenbaum P (2006): The Manual Ability Classification System (MACS) for children with cerebral palsy: Scale development and evidence of validity and reliability. *Dev Med Child Neurol* 48:549–554.
- Fox MD, Raichle ME (2007): Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci* 8:700–711.
- Gaetz W, Cheyne D (2006): Localization of sensorimotor cortical rhythms induced by tactile stimulation using spatially filtered MEG. *Neuroimage* 30:899–908.
- Gaetz W, MacDonald M, Cheyne D, Snead OC (2010): Neuromagnetic imaging of movement-related cortical oscillations in children and adults: Age predicts post-movement beta rebound. *Neuroimage* 51:792–807.
- Gerloff C, Braun C, Staudt M, Hegner YL, Dichgans J, Krügeloh-Mann I (2006): Coherent corticomuscular oscillations originate from primary motor cortex: Evidence from patients with early brain lesions. *Hum Brain Mapp* 27:789–798.
- Guo X, Xiang J, Mun-Bryce S, Bryce M, Huang S, Huo X, Wang Y, Rose D, Degrauw T, Gartner K, Song T, Schmit J, Vargus-Adams J (2012): Aberrant high-gamma oscillations in the somatosensory cortex of children with cerebral palsy: A meg study. *Brain Dev* 34:576–583.

- Hari R, Forss N (1999): Magnetoencephalography in the study of human somatosensory cortical processing. *Phil Trans R Soc Lond B Biol Sci* 354:1145–1154.
- Hari R, Salmelin R, Mäkelä J, Salenius S, Helle M (1997): Magnetoencephalographic cortical rhythms. *Int J Psychophysiol* 26:51–62.
- Hoon AH, Lawrie WT, Melhem ER, Reinhardt EM, Van Zijl PCM, Solaiyappan M, Jiang H, Johnston MV, Mori S (2002): Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. *Neurology* 59:752–756.
- Hlushchuk Y, Hari R (2006): Transient suppression of ipsilateral primary somatosensory cortex during tactile finger stimulation. *J Neurosci* 26:5819–5824.
- Iwamura Y (2000): Bilateral receptive field neurons and callosal connections in the somatosensory cortex. *Phil Trans R Soc Lond B* 355:267–273.
- Jones SR, Pritchett DL, Sikora M, Stufflebeam SM, Hämäläinen M, Moore CI (2009): Quantitative analysis and biophysically realistic neural modeling of the MEG mu rhythm: Rhythmogenesis and modulation of sensory-evoked responses. *J Neurophysiol* 102:3554–3572.
- Jones SR, Pritchett DL, Stufflebeam SM, Hämäläinen M, Moore CI (2007): Neural correlates of tactile detection: A combined magnetoencephalography and biophysically based computational modeling study. *J Neurosci* 27:10751–10764.
- Jurkiewicz MT, Gaetz WC, Bostan AC, Cheyne D (2006): Post-movement beta rebound is generated in motor cortex: Evidence from neuromagnetic recordings. *Neuroimage* 32:1281–1289.
- Kesar TM, Sawaki L, Burdette JH, Cabrera MN, Kolaski K, Smith BP, O'Shea TM, Koman LA, Wittenberg GF (2012): Motor cortical functional geometry in cerebral palsy and its relationship to disability. *Clin Neurophysiol* 123:1383–1390.
- Kulak W, Sobaniec W, Bockowski L (2005): EEG spectral analysis and coherence in children with hemiparetic cerebral palsy. *Med Sci Monit* 11:CR449–CR455.
- Kurz MJ, Wilson TW (2011): Neuromagnetic activity in the somatosensory cortices of children with cerebral palsy. *Neurosci Lett* 490:1–5.
- Laaksonen K, Kirveskari E, Mäkelä J, Kaste M, Mustanoja S, Nummenmaa L, Tatlisumak T, Forss N (2012): Effect of afferent input on motor cortex excitability during stroke recovery. *Clin Neurophysiol* 123:2429–2436.
- Lee S-K, Kim DI, Kim J, Kim DJ, Kim HD, Kim DS, Mori S (2005): Diffusion-tensor MR imaging and fiber tractography: A new method of describing aberrant fiber connections in developmental CNS anomalies. *Radiographics* 25:53–65.
- Mäenpää H, Jaakkola R, Sandström M, Airi T, Von Wendt L (2004): Electrostimulation at sensory level improves function of the upper extremities in children with cerebral palsy: A pilot study. *Dev Med Child Neurol* 46:84–90.
- Mäki H, Ilmoniemi RJ (2010): EEG oscillations and magnetically evoked motor potentials reflect motor system excitability in overlapping neuronal populations. *Clin Neurophysiol* 121:492–501.
- Nangini C, Ross B, Tam F, Graham SJ (2006): Magnetoencephalographic study of vibrotactile evoked transient and steady-state responses in human somatosensory cortex. *Neuroimage* 33:252–262.
- Neuper C, Pfurtscheller G (2001): Event-related dynamics of cortical rhythms: Frequency-specific features and functional correlates. *Int J Psychophysiol* 43:41–58.
- Nevalainen P, Pihko E, Mäenpää H, Valanne L, Nummenmaa L, Lauronen L (2012): Bilateral alterations in somatosensory cortical processing in hemiplegic cerebral palsy. *Dev Med Child Neurol* 54:361–367.
- Pfurtscheller G, Stancák A, Edlinger G (1997): On the existence of different types of central beta rhythms below 30 Hz. *Electroencephalogr Clin Neurophysiol* 102:316–325.
- Pfurtscheller G, Stancák A, Neuper C (1996): Post-movement beta synchronization. A correlate of an idling motor area? *Electroencephalogr Clin Neurophysiol* 98:281–293.
- Ruohonen J, Karhu J (2010): Navigated transcranial magnetic stimulation. *Neurophysiol Clin* 40:7–17.
- Salenius S, Schnitzler A, Salmelin R, Jousmäki V, Hari R (1997): Modulation of human cortical rolandic rhythms during natural sensorimotor tasks. *Neuroimage* 5:221–228.
- Salmelin R, Hari R (1994): Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. *Neuroscience* 60:537–550.
- Salmelin R, Hämäläinen M, Kajola M, Hari R (1995): Functional segregation of movement-related rhythmic activity in the human brain. *Neuroimage* 237–243.
- Schnitzler A, Salenius S, Salmelin R, Jousmäki V, Hari R (1997): Involvement of primary motor cortex in motor imagery: A neuromagnetic study. *Neuroimage* 6:201–208.
- Staudt M (2010): Reorganization after pre- and perinatal brain lesions. *J Anat* 217:469–474.
- Staudt M, Braun C, Gerloff C, Erb M, Grodd W, Krägeloh-Mann I (2006a): Developing somatosensory projections bypass periventricular brain lesions. *Neurology* 67:522–525.
- Staudt M, Erb M, Braun C, Gerloff C, Grodd W, Krägeloh-Mann I (2006b): Extensive peri-lesional connectivity in congenital hemiparesis. *Neurology* 66:771.
- Staudt M, Gerloff C, Grodd W, Holthausen H, Niemann G, Krägeloh-Mann I (2004): Reorganization in congenital hemiparesis acquired at different gestational ages. *Ann Neurol* 56:854–863.
- Staudt M, Grodd W, Gerloff C, Erb M, Stitz J, Krägeloh-Mann I (2002): Two types of ipsilateral reorganization in congenital hemiparesis: A TMS and fMRI study. *Brain* 125:2222–2237.
- Sutcliffe TL, Gaetz WC, Logan WJ, Cheyne DO, Fehlings DL (2007): Cortical reorganization after modified constraint-induced movement therapy in pediatric hemiplegic cerebral palsy. *J Child Neurol* 22:1281–1287.
- Szurhaj W, Derambure P, Labyt E, Cassim F, Bourriez J-L, Isnard J, Guieu J-D, Mauguière F (2003): Basic mechanisms of central rhythms reactivity to preparation and execution of a voluntary movement: A stereoelectroencephalographic study. *Clin Neurophysiol* 114:107–119.
- Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM (2011): Brainstorm: A user-friendly application for MEG/EEG analysis. *Comput Intell Neurosci* 2011:1–13.
- Taulu S, Simola J (2006): Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. *Phys Med Biol* 51:1759–1768.
- Thickbroom GW, Byrnes ML, Archer SA, Nagarajan L, Mastaglia FL (2001): Differences in sensory and motor cortical

- organization following brain injury early in life. *Ann Neurol* 49:320–327.
- Van Ede F, De Lange F, Jensen O, Maris E (2011): Orienting attention to an upcoming tactile event involves a spatially and temporally specific modulation of sensorimotor alpha- and beta-band oscillations. *J Neurosci* 31:2016–2024.
- Van Ede F, Jensen O, Maris E (2010): Tactile expectation modulates pre-stimulus β -band oscillations in human sensorimotor cortex. *Neuroimage* 51:867–876.
- Van Ede F, Maris E (2013): Somatosensory demands modulate muscular beta oscillations, independent of motor demands. *J Neurosci* 33:10849–10857.
- Wilke M, Staudt M, Juenger H, Grodd W, Braun C, Krägeloh-Mann I (2009): Somatosensory system in two types of motor reorganization in congenital hemiparesis: topography and function. *Hum Brain Mapp* 30:776–788.
- Witham CL, Baker SN (2007): Network oscillations and intrinsic spiking rhythmicity do not covary in monkey sensorimotor areas. *J Physiol* 580:801–814.