Clinical Neurophysiology 131 (2020) 2829–2840

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Lateralized EEG mu power during action observation and motor imagery in typically developing children and children with unilateral Cerebral Palsy

Marijtje L.A. Jongsma [a,*,1], Bert Steenbergen [a,b], C. Marjolein Baas [a], Pauline B. Aarts [c], Clementina M. van Rijn [d,1]

[a] Behavioural Science Institute, Radboud University Nijmegen, the Netherlands
[b] CeDDR, Australian Catholic University, Melbourne, Australia
[c] Sint Maartenskliniek, Nijmegen, the Netherlands
[d] Donders Institute for Brain, Cognition, and Behaviour, Donders Centre for Cognition, Radboud University Nijmegen, the Netherlands

ARTICLE INFO

Article history:
Accepted 18 August 2020
Available online 13 October 2020

Keywords:
EEG
Mu rhythm
Alpha rhythm
Motor imagery
Action observation
Unilateral Cerebral Palsy

ABSTRACT

Objective: During motor execution (ME), mu power is diminished over the contralateral hemisphere and increased over the ipsilateral hemisphere, which has been associated with cortical activation of the contralateral motor areas and inhibition of the ipsilateral motor areas respectively. The influence of action observation (AO) and motor imagery (MI) on mu power is less clear, especially in children, and remains to be studied in children with unilateral cerebral palsy (uCP).
Methods: We determined mu power during ME, AO, and MI of 45 typically developing (TD) children and 15 children with uCP over both hemispheres, for each hand.
Results: In TD children, over the left hemisphere mu power was lowered during ME when the right hand was used. In line, over the right hemisphere mu power was lowered when the left hand was addressed. In addition, during AO and MI increased mu power was observed when the right hand was addressed. In children with uCP, over the spared hemisphere mu power was diminished during ME when the less-affected hand was used. However, over the lesioned hemisphere, no mu changes were observed.
Conclusions: The results of TD children fit the activation/inhibition model of mu power.
Significance: The results of children with uCP suggest that the lesioned hemisphere is unresponsive to the motor tasks.

1. Introduction

Action observation (AO), i.e. observing an action that is performed by another person, plays an important role in imitation learning since it appears to facilitate the acquisition of novel motor behaviors (Marshall and Meltzoff, 2011; Sarasso et al., 2015). Another covert approach for motor learning is motor imagery (MI) i.e. internally simulating a movement without the actual execution of that movement (Johnson, 2000; Mutsaarts et al., 2006). While it has been proposed that AO activates the motor cortex indirectly via the mirror neuron system (Marshall and Meltzoff, 2011; Sarasso et al., 2015), MI is understood to activate the cortical motor areas in a more direct manner (Jeannerod, 1994). In addition, when MI and AO are combined, the ability to activate the motor system has been found to be even more marked compared to MI and AO separately (Eaves et al., 2016; Scott et al., 2018).

An example of a commonly employed MI task is the Visual Guided Pointing Task (VGPT) in which the participant has to either perform or imagine a repetitive action by (imaginarily) moving the hand between a starting point and several target points (Smits-Engelsman and Wilson, 2013). Usually, the ability to perform MI is determined by comparing the correspondence between actual and imagined motor actions with respect to the movement duration of trials that vary in difficulty (Choudhury et al., 2007; Smits-Engelsman and Wilson, 2013). The difficulty of the trials is manipulated by varying the size of the target points. However,

* Corresponding author at: Radboud University Nijmegen, Faculty of Social Sciences, Behavioural Science Institute, Montessorilaan 3, P.O. Box 9104, 6500 HE Nijmegen, the Netherlands.

E-mail address: m.jongsma@donders.ru.nl (M.L.A. Jongsma).

[1] Contributed equally.

https://doi.org/10.1016/j.clinph.2020.08.022
1388-2457/

apart from the comparison of movement duration, the activation of the neural substrate involved in AO and MI can also be more directly studied, via changes observed in the electroencephalogram (EEG) (ter Horst et al., 2012, 2013).

In typically developing individuals, when examining the EEG recorded during movement related tasks, the mu rhythm is of particular interest (Pineda, 2005). The mu rhythm is closely related to alpha activity (8–13 Hz), but is more pronounced at electrode sites overlying the central cortices compared to the parietal cortices, with most dominant frequencies within the upper alpha range (10–13 Hz) (Marshall and Meltzoff, 2011; Pfurtscheller et al., 2008; Pineda, 2005; Pineda et al., 2000).

The Mu rhythm is proposed to reflect synchronized activity within the underlying thalamo-cortical circuits (Pfurtscheller, 2003). Desynchronized activity in this circuit points to cortical activation, and can be observed as a low power of the mu activity. This desynchronized activity can be observed just preceding and during the motor execution (ME) of goal directed behavior (Pineda, 2005). During a goal directed movement of the hand, a localized decrease of the mu power is commonly observed over the primary motor cortex of the contralateral hemisphere. Simultaneously, over the ipsilateral hemisphere, a more widespread increase of mu power can be seen over the central areas. This increase has been interpreted as active inhibition of the ipsilateral motor areas that are associated, but not involved in the task (for example to suppress mirrored or associated movements) (Duque et al., 2007; Nam et al., 2011; Pfurtscheller, 2003). This inhibition of associated movements is supposed to facilitate the activity in those specific cortical areas that are steering the refined goal directed movement (Klimesch et al., 2007; Suffczynski et al., 2001). Similarly, MI also influences the activity in the cortical motor areas, via an internal simulation of a ME (Johnson, 2000; Mutsaarts et al., 2006).

Apart from the indications that thalamo-cortical circuits are directly modulating the mu rhythm associated with ME and MI (Suffczynski et al., 2001), it has been proposed that the mu rhythm can also be modulated indirectly, via the prefrontal mirror neuron system (Braadbaart et al., 2013; Muthukumaraswamy et al., 2004; Pineda, 2005). Previous studies have reported that during AO, as during ME, a decrease of mu power can be observed (Fox et al., 2016; Muthukumaraswamy et al., 2004), probably via an influence of the mirror neuron system on the motor cortices (Braadbaart et al., 2013; Muthukumaraswamy et al., 2004; Pineda, 2005).

Although a clear lateralized change in mu power can be observed during ME, with lower mu power over the contralateral hemisphere compared to the ipsilateral hemisphere, it remains to be studied if mu power changes during AO and MI display a similar lateralized effect. Therefore, we determined the mu power during ME, AO and MI over the left and the right hemisphere and for the left and the right hand separately, and interpreted the results in terms of excitation/inhibition of the contra- and ipsilateral motor areas.

Another caveat in the literature is the direction of the observed changes in mu power. These changes are often described in terms of suppression and enhancement with respect to a baseline. However, a clear baseline is difficult to define and far from obvious, as multiple authors have pointed out (Brinkman et al., 2014; Hobson and Bishop, 2016; Tangwiriyasakul et al., 2013). Therefore, in the present paper we will study the mu power modulation comparing the hand under investigation with the other hand. We recorded the EEG over the left and right hemisphere, from frontal, central, and parietal areas.

First, we recorded the EEG from 45 typically developing (TD) children, to address the question whether during an AO and a combined MI-AO task, hemispheric differences in mu power can be observed, and interpreted the results in terms of excitation/inhibition of the associated contralateral and ipsilateral motor areas.

In addition to the measurements in TD children, we also studied the mu power in 15 children with unilateral cerebral palsy (uCP). Cerebral palsy (CP) is a group of non-progressive disorders related to movement and posture impairments (Rosenbaum et al., 2007). In uCP, the motor impairments are more marked on one side of the body due to a lesion in the contralateral hemisphere (Odding et al., 2006; Rosenbaum et al., 2007; WHO, 2001). It has been demonstrated that AO training shows promising results when used to improve motor performances of children with uCP (Buccino, 2014; Buccino et al., 2012). For example, Buccino et al. (2012) conducted a study in which children with uCP observed movie clips with daily activities, such as grasping and moving objects (experimental group), or movie clips with no motor content (control group), five times a week for three weeks in succession. After each session, both groups had to perform the movements which were shown to the experimental group. On these tasks, the experimental group performed better than the control group.

Other studies have examined whether MI might be suitable as an additional rehabilitation technique in e.g. adults recovering from stroke (see Nakano and Kodama (2017) for a comprehensive review). Indeed, MI training was shown to be beneficial in adult patients recovering from a stroke (Nakano and Kodama, 2017; Zimmermann-Schlatter et al., 2008) and studies on the effect of MI training in children with motor impairments are evolving with similar positive effects (Adams et al., 2017; Wilson et al., 2016, 2002). Extending these results, it has been proposed that MI training might also be beneficial as a rehabilitation technique in children with e.g. uCP (Buccino et al., 2012; Steenbergen et al., 2009). However, in previous studies from our group employing MI tasks, a diminished MI capacity in children with uCP was observed (Jongsma et al., 2016; Lust et al., 2016).

In order to establish whether AO and MI in training programs for children with uCP would be suitable, a first step would be to determine whether the cortical motor system in children with uCP is capable to respond to AO and MI tasks. Because uCP results from the direct damage to the cerebral motor circuits, the mu rhythms arising from this circuitry might be affected as well. Therefore, we determined the mu rhythm during ME, AO and MI in children with uCP, with respect to both the intact and lesioned hemisphere. The EEG was recorded in a similar configuration as for the typically developing children. The data were collected to address the question whether in children with uCP hemispheric differences in mu power can be observed during AO and MI, and whether hemispheric differences in mu power can be observed when the less-affected or the affected hand is addressed. The results from this study might provide electrophysiological support for the use of specific AO and MI-AO training programs to (re)gain motor skills in children with e.g. uCP.

2. Methods

2.1. Participants

In the first study, a total of 60 typically developing children (TD) were recruited, all right-handed. The age of the children was between 5 and 12 years old. Children and their parents/legal guardians were approached via an information letter that was distributed at 5 primary schools. The work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The experiment was approved by the ethics committee ECSS (Ethics Committee Social Sciences) at the Radboud

University Nijmegen, the Netherlands (nr. ECG30062011). All children's parents/legal guardians signed a written informed consent letter. Participation in the study was voluntary, and all children received a small gift with a monetary value of five euros for taking part in the study.

In the second study, a total of 19 children with unilateral cerebral palsy (uCP) were recruited. The age of the children was between 8 and 18 years old. Children diagnosed with uCP and without an intellectual disability (i.e. IQ score <70), and normal or corrected to normal hearing and vision were approached via an informational letter that was distributed in two rehabilitation centers in the Netherlands to the children and their parents/legal guardians. The experiment was approved by the medical ethical committee region Arnhem-Nijmegen (CMO: NL 44687.000.13). All children's parents/legal guardians signed a written informed consent letter and all children over 12 years old signed a written informed consent letter before starting with the experiment. All children received the small gift.

2.2. The Visual Guided Pointing task

In both studies an adapted version of the Visual Guided Pointing Task (VGPT) was used (Spruijt et al., 2015). The task was presented on a touchscreen placed on a table in front of the child. Short video clips showed a hand performing the task from a first-person perspective. Different clips depicted easy and difficult trials performed by either a right or a left hand. Depending on the instruction – "pay attention to the video clip because you will be asked to repeat this task after the clip" for the AO condition, or "pay attention to the video clip and imagine that the hand you see is your own hand" for the MI-AO condition – the same stimulus material could be used and compared from both the AO condition and the MI conditions.

The stimulus composition was as follows: The touchscreen displayed five white target dots distributed within the shape of a half circle. At the bottom of the touchscreen a white circle marked the central starting position. A green "start" and a red "stop" button were displayed on the left and right side of the central starting point (see Fig. 1). The exact position of the start and stop button depended on whether a right- or left hand trial was presented. In right hand trials, the start button was depicted on the left side of the central starting point, whereas in left hand trials it was depicted on the right side. The distance between each of the target dots and the central starting point was 15 cm. Trials varied in difficulty: In easy trials, the target dots had a diameter of 20 mm whereas in difficult trials the diameter was 5 mm. Easy and difficult trials were presented in a semi random order. All trials started by touching the green start button with a touch pen, followed by a movement to the central starting point. From there, back and forth movements between the five target dots and the central dot were made by moving the touch pen over the screen. The trial would end after the last movement to the central starting point was made and the child touched the red "stop" button with the touch pen. The total time to perform a trial was determined by both the speed and the accuracy because the experiment was programmed in such a way that the trial did not end until all target dots were touched. In right hand trials, the target dots were approached from left to right, and in left hand trials the target dots were approached from right to left.

2.3. Task conditions

The tasks were presented in a fixed, for the children logical order, starting with the AO condition (look at the hand performing the task because you will be asked to do this task yourself afterwards), followed by the ME condition (please do the task the same way as you have observed before), ending with the MI condition (look at the hand performing the task and imagine it is your own hand you're looking at).

2.3.1. AO (Action Observation)

Video clips of a hand holding the touch pen and performing the task were projected on the touchscreen. Children were instructed to observe the hand closely because they had to perform the task in the same way. Video clips (lasting 20–30 sec each) consisted of recordings of two easy and two difficult trials, and were presented in a semi-random order for each hand. First, the four clips of the dominant hand / less-affected hand were presented, followed by four clips of non-dominant / affected hand. See Fig. 1A.

2.3.2. ME (Motor Execution)

The original layout of the target dots, central starting point, and start and stop buttons were presented as described above. Children were instructed to perform the task as demonstrated in the video clips of AO. First, the four trials for the dominant hand / less-affected hand were presented, next, the four trials for the non-dominant hand / affected hand were presented. See Fig. 1B.

2.3.3. MI (Motor Imagery)

The videos were projected on the touchscreen again. Children were instructed to imagine that the hand in the video was their own hand performing the task. Again, the dominant hand / less-affected hand clips were presented first, followed by the non-dominant hand / affected hand clips. See Fig. 1C.

2.4. Procedure

Data were collected at a quiet room, for the TD children at the child's school and for the uCP children at the child's center for rehabilitation. A mobile EEG lab was used. After the children arrived, they were seated at a table with the touchscreen. While the EEG cap was positioned on the child's head, they were given the opportunity to watch an animation film. Next, the experiment was explained to the child. At the start of the experiment, the children placed their hands next to the touchscreen. Before the start of the experiment, a 1 minute of eyes open followed by a 1 minute eyes closed resting EEG was recorded. Finally, the AO, ME, and MI tasks were presented. Recording the EEG signals lasted about 15 minutes.

2.5. EEG recording

EEG signals were recorded using a 32-channel actiCap system (MedCaT B.V. Netherlands) with a BrainAmp EEG amplifier. The electrodes were placed according to the international 10–20 system, with the ground electrode at the AFz position and the reference at the left mastoid bone. Eye movements were recorded by two electrodes; one placed below the right eye, and one placed lateral of the right eye. All impedances were kept below 20 kΩ. The signals were sampled at 1000 Hz, with high-pass and low-pass filters set at 0.1 Hz and 100 Hz. Data at the $F_{3/4}$, $C_{3/4,}$ and $P_{3/4}$ were further analyzed.

2.6. Data preprocessing

The analyses of the EEG signals were performed offline with BrainVision Analyzer 2.1 (Brain Products GmbH). The raw EEG signal was first re-referenced to linked mastoids. Then, a high-pass filter with a cutoff of 0.53 Hz and a low-pass filter with a cutoff of 40 Hz were applied. Of the EEG during rest, 20 consecutive epochs of 1024 ms from the eyes open and the eyes closed recording were analyzed. Epochs were corrected for eye movement artifacts by using the Gratton and Coles algorithm (Gratton et al., 1983). Next,

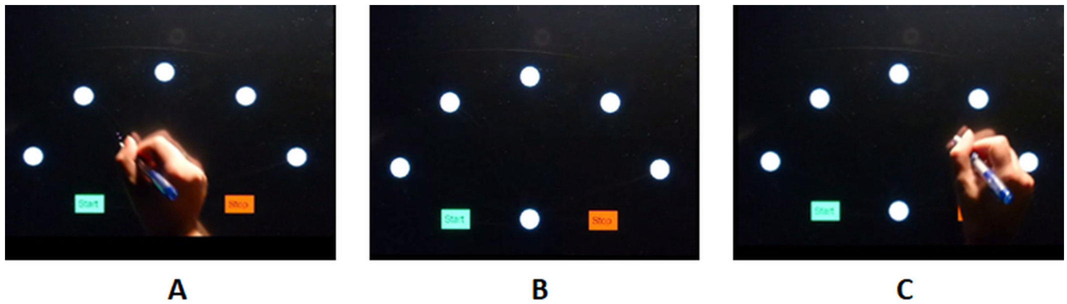

Fig. 1. Illustration of the Visual Guided Pointing Task (VGPT) as represented on the touchscreen. (A) Represents an action observation (AO) trial for the right hand, (B) represents a motor execution (ME) trial for the right hand, (C) represents a motor imagery (MI) trial for the right hand.

epochs were detrended and the epochs containing artifacts which exceeded an amplitude of 150 μV were excluded. For all AO, ME, and MI trials, the recording of each trial was segmented relative to the marker position into 10 epochs, each with a length of 1024 ms, starting 500 ms following the beginning of the task. Data were analyzed separately for the dominant / less-affected hand and for the non-dominant / affected hand. Fast Fourier Transformation (FFT) with a 10% Hanning window was performed (1 Hz resolution) to obtain the EEG power spectra. The spectra were averaged for each condition and each hand. The power (μV^2) of the mu peak, a fixed frequency at 10 Hz, was further analyzed.

With respect to the TD children, only right-handed children were included in the study. In order to determine hand preference for writing, children were asked to write their name on a piece of paper. For the uCP children, children with an affected right hand and a lesioned left hemisphere, the electrode positions were inverted (i.e., F_3, C_3, and P_3 were redefined as F_4, C_4, and P_4, whereas F_4, C_4, and P_4 were redefined as F_3, C_3, and P_3). Thus, at group level, electrodes F_3, C_3, and P_3 were always located over the spared hemisphere and electrodes F_4, C_4, and P_4 were always located over the lesioned hemisphere, allowing a better comparison with the TD group.

2.7. Statistics

Data of the mu power was further analyzed using IBM SPSS Statistics 25 (www.ibm.com). We performed General Linear Models (GLMs), post-hoc GLMs, and paired samples t-tests where appropriate.

The data of the TD and of the uCP children were analyzed separately and patterns of changes were qualitatively compared.

With respect to the eyes open versus the eyes closed recordings, a 3-within repeated measures GLM analysis was performed. The within factors were recording (2 levels: eyes open, eyes closed), cortical area (3 levels: frontal (F), central (C), parietal (P)), and hemisphere (2 levels: left/spared hemisphere, right/lesioned hemisphere).

With respect to AO, ME, and MI condition, the mu power was analyzed with a 4-within repeated measures GLM analysis, with area (3 levels: frontal (F), central (C), parietal (P)), hemisphere (2 levels: left/spared hemisphere, right/lesioned hemisphere), hand (2 levels: right/less-affected hand, left/affected hand), and motor task (3 levels: AO, ME, MI) being the within subject variables. The results of this overall analysis are given in the appendix.

For the data of the TD and uCP children, this overall analysis showed several interaction effects with area (see the appendix for all the F, p, and η^2 values). Visual inspection of the spectra showed only mu power differences on the electrodes overlying the sensory motor cortex, both contra- and ipsilateral, therefore the $C_{3/4}$ electrodes were subsequently analyzed with a 3-within repeated measures GLM analysis. The within factors were hemisphere (2 levels: left/spared hemisphere, right/lesioned hemisphere), hand (2 levels: right/less-affected hand, left/affected hand), and task (3 levels: AO, ME, MI), and. Post-hoc analyses per hemisphere were performed when appropriate.

3. Results

3.1. Typically developing children

The recordings of 15 TD children showed excessive artefacts and/or missing data in one or more of the tasks and were therefore excluded. Complete data sets of 45 TD children (24 males; 21 females) were available for statistical analyses. The age of the included children ranged from 6 years and 2 months old to 12 years and 5 months old, with a mean age of 8 years and 9 months old. The mean time to complete the ME task was 14 seconds. No difference in completion time between hands was observed (ranges: right hand 8.5–25 s., left hand 8.3–26 s.).

3.1.1. The eyes open and eyes closed recordings.

Fig. 2a depicts the averaged power spectra of the eyes open and eyes closed recordings at the $F_{3/4}$, $C_{3/4}$, and $P_{3/4}$ electrode locations. In the mean spectrograms an alpha peak in the eyes closed recording can be seen with a maximum over the $P_{3/4}$ electrodes and a dominant peak frequency at 9 Hz. In the eyes open recording, a mu peak can be observed with a maximum over the $C_{3/4}$ electrodes and a dominant peak frequency at 10 Hz. We further analyzed the power of this 10 Hz frequency. Apart from a main effect of recording ($F_{(1,\ 44)} = 52.83$; $p < .001$; $\eta^2 = 0.546$) and a main effect of cortical area ($F_{(2,\ 43)} = 15.11$; $p < .001$; $\eta^2 = 0.413$), the 3-within repeated measures GLM analysis showed a recording * area interaction effect ($F_{(2,\ 43)} = 21.93$; $p < .001$; $\eta^2 = 0.505$) and a recording * area * hemisphere effect ($F_{(2,\ 43)} = 5.20$; $p = .009$; $\eta^2 = 0.195$). Post-hoc analyses per recording revealed for the eyes open recording no area or hemisphere effects (overall mean: 6.42 (SD 3.95) μV^2). However the eyes closed recording showed a main effect of area ($F_{(2,\ 43)} = 31.21$; $p < .001$; $\eta^2 = 0.415$) such that the power of 10 Hz frequency reached maximal values at posterior sites ($P_{3/4}$: 25.1 (SD 23.0) / 26.5 (SD 20.3) μV^2) compared to central ($C_{3/4}$: 15.2 (SD 11.0) / 14.1 (SD 8.48) μV^2) and frontal sites ($F_{3/4}$: 11.6 (SD 8.30) / 11.5 (SD 7.13) μV^2). The left panel in Fig. 2C depicts the mu power results of the eyes open and eyes closed recordings.

3.1.2. The AO, ME, and MI conditions.

Because the mu peak was most pronounced at central leads, and previous studies have focused predominantly on the central

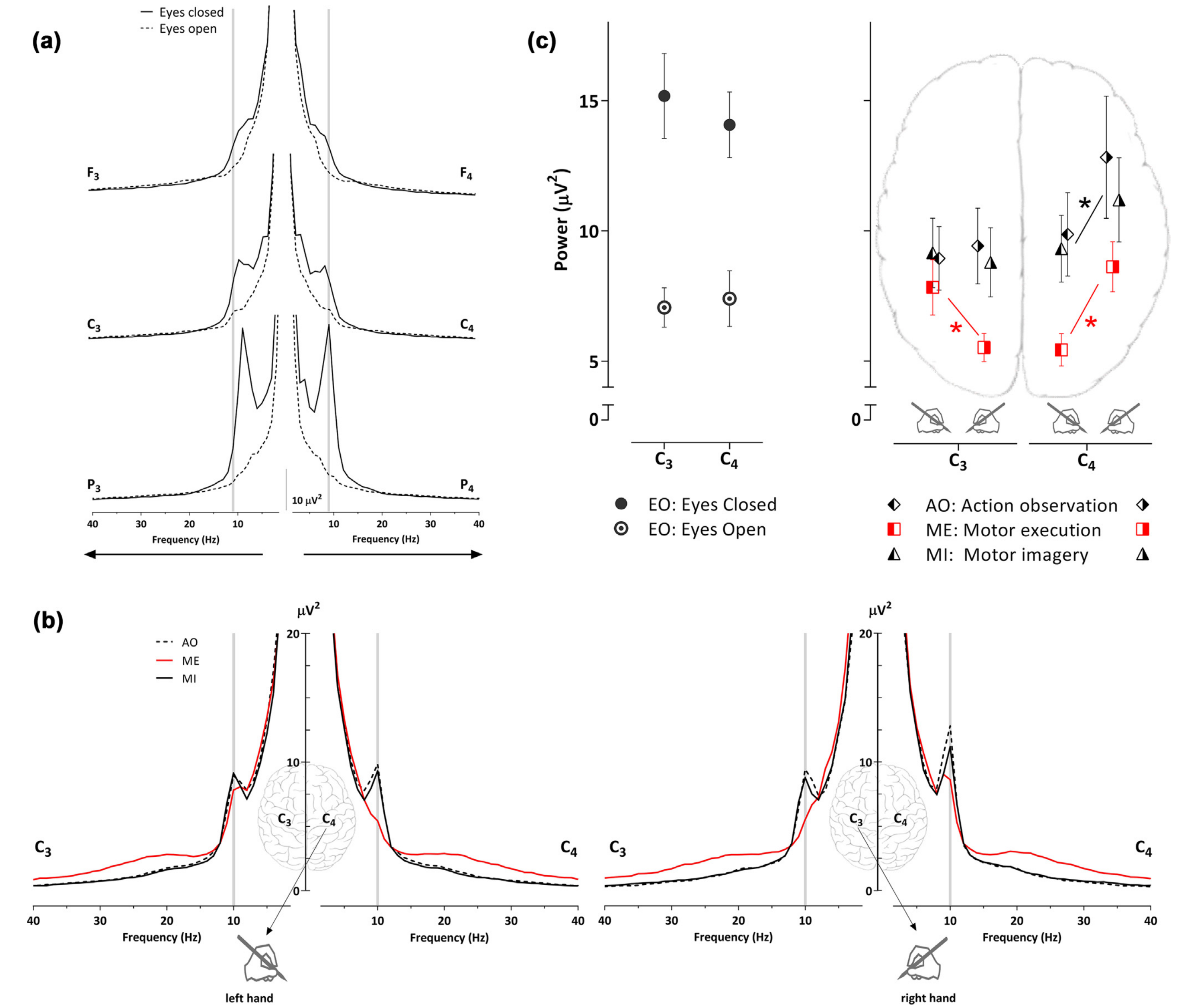

Fig. 2. The results of the typically developing (TD) children. Panel A shows the spectrograms of the EEGs measured during eyes open and eyes closed, at the frontal, central and parietal leads, and over the left and right hemisphere. Panel B shows the spectrograms measured over the left and right hemisphere during the action observation (AO), motor execution (ME), and motor imagery (MI) condition, at the central C_3 and C_4 leads only. Panel C shows for both the eyes open / eyes closed recordings (left) and all motor task conditions (right), the means and SEMs of the power of the 10 Hz peaks over the left and right hemisphere.

regions, the mu power at the central electrodes was further analyzed.

Fig. 2b depicts the averaged power spectra of the AO, ME, and MI conditions at the $C_{3/4}$ electrode positions. The spectra of the frontal and parietal leads are shown in the appendix. Fig. 2c depicts for both hands the mu power results of the AO, ME, and MI conditions at the $C_{3/4}$ electrode positions.

Apart from a main condition effect ($F_{(2,\ 43)}$ = 4.97; p = .011; η^2 = 0.188) and a main hand effect ($F_{(1,\ 44)}$ = 5.23; p = .027; η^2 = 0.106), the 3-within repeated measures GLM analysis revealed a condition * hemisphere interaction ($F_{(2,\ 43)}$ = 5.65; p = .007; η^2 = 0.208) and a condition * hand interaction ($F_{(2,\ 43)}$ = 13.84; p < .000; η^2 = 0.392). Post-hoc, hemispheres were analyzed separately with a 2-within repeated measures GLM analyses, with hand (2 levels: right hand, left hand), and condition (3 levels: AO, ME, and MI) as within subject variables.

For the left hemisphere, apart from a main hand effect (F(1, 44) = 4.07; p = .050; η2 = 0.085) and a main condition effect (F (2, 43) = 5.00; p = .011; η2 = 0.189), a hand * condition interaction was observed (F(2, 43) = 3.41; p = .042; η2 = 0.137). For the AO condition, pairwise comparisons showed no difference between hands. For the ME condition, pairwise comparisons showed that the mu power was lower for the right hand than for the left hand (p < .05). For the MI condition, pairwise comparisons showed no difference between hands. For the right hemisphere, only a main hand effect (F(1, 44) = 21.36; p < .001; η2 = 0.327) and a main condition effect (F(2, 43) = 4.79; p = .013; η2 = 0.182) were observed, such that mu power was highest for the right hand in all conditions, and mu power was lower in the ME condition compared to the AO and MI condition. In all, these results show decreased mu power over the contralateral hemisphere during ME of either hand, suggesting cortical activation. In addition, increased mu power was

Table 1
Characteristics of the children with unilateral Cerebral Palsy (n = 15).

Characteristic	n	Mean	Range	SD
Gender				
Male	*5*			
Female	*10*			
Affected hand/hemisphere				
left hand/right hemisphere	*11*			
right hand/left hemisphere	*4*			
Age		*11 y 11 m*	*8 y 5 m – 17 y 10 m*	
MACS				
1	*3*			
2	*10*			
3	*2*			
B&B				
Less-affected hand		*59.6*	*47–84*	*11.1*
Affected hand		*30.8*	*2–51*	*13.4*
ABILH		*3.05*	*0.51–6.68*	*1.46*
COPM-P		*3.54*	*1.3–8.3*	*1.68*
COPM-S		*3.82*	*1.7–10*	*2.04*

Abbreviations: MACS, Manual Ability Classification System; B&B, Box and blocks test; ABILH-log, ABILHAND-kids (logits), a measure of manual ability for children with upper limb impairments; COPM-P/COPM-S, Canadian Occupational Performance Measure (P, performance; S, satisfaction). (See also Geerdink et al. (2013)).

observed over the ipsilateral hemisphere during AO and MI, but only when the dominant, right hand was under investigation.

3.2. Children with uCP

After artifact rejection, complete data sets of 15 children with uCP were available for statistical analyses. Four of these children had a lesion in the left hemisphere, therefore their data were inverted as described in the methods.

See table 1 for the characteristics of the children with uCP.

The mean time to complete the ME task was 12 seconds for the less-affected hand (range 7.1–16 s), and 16 seconds for the affected hand (range 8.9–25 s). The completion time for the affected hand was significantly longer than that of the less-affected hand (t (14) = 3.26, p = .006).

3.2.1. The rest conditions

Fig. 3a depicts the averaged power spectra for the rest conditions comparing the eyes open with the eyes closed condition at the $F_{3/4}$, $C_{3/4}$, and $P_{3/4}$ electrode locations. In accordance with the TD group, in children with uCP the alpha peak frequency has a higher power during the eyes closed condition than during the eyes open condition and is maximal over the $P_{3/4}$ electrodes.

As for the TD group, in the uCP group we further analyzed the power of the mu 10 Hz frequency. For the eyes open versus the eyes closed recordings, apart from a main effect of condition ($F_{(1, 14)} = 15.50$; $p = .001$; $\eta^2 = 0.525$) and a main effect of cortical area ($F_{(2, 13)} = 5.98$; $p = .014$; $\eta^2 = 0.479$), the 3-within repeated measures GLM analysis showed a condition * area interaction effect ($F_{(2, 13)} = 10.05$; $p = .002$; $\eta^2 = 0.607$). Post-hoc analyses per condition revealed no effects during the eyes open recording (overall mean 9.95 (SD 5.33) μV^2). However, the eyes closed recording showed a main effect of area ($F_{(2, 13)} = 7.08$; $p = .008$; $\eta^2 = 0.521$) such that the power of 10 Hz frequency reached maximal values at posterior sites ($P_{3/4}$: 29.3 (SD 25.2) and 26.2 (SD 19.8) μV^2) compared to central ($C_{3/4}$: 17.0 (SD 13.8) and 15.8 (SD 11.8) μV^2) and frontal sites ($F_{3/4}$: 12.7 (11.4) and 14.3 (SD 11.3) μV^2). The left panel of Fig. 3c depicts the mu power results of the eyes open and eyes closed recordings.

3.2.2. The AO, ME, and MI conditions

As for the TD group, in the uCP group we applied a 3-within repeated measures GLM analysis for $C_{3/4}$ electrode sites with hemisphere (2 levels: spared hemisphere, lesioned hemisphere), hand (2 levels: less-affected hand, affected hand), and condition (3 levels: AO, ME, MI). Fig. 3b depicts the averaged power spectra of the AO, ME, and MI conditions at the $C_{3/4}$ electrode positions for both hands. The spectra of the frontal and parietal leads are shown in the appendix. Fig. 3c depicts the mu power results of the rest conditions and of the AO, ME, and MI conditions at the $C_{3/4}$ electrode positions.

Apart from a main hemisphere effect ($F_{(1, 14)} = 9.06$; $p = .009$; $\eta^2 = 0.393$), the 3-within repeated measures GLM analysis revealed a condition * hemisphere interaction ($F_{(2, 13)} = 4.97$; $p = .025$; $\eta^2 = 0.433$). Thus, hemispheres were analyzed separately with a 2-within repeated measures GLM analyses, with hand (2 levels: less-affected hand, affected hand), and condition (3 levels: AO, ME, and MI) being the within subject variables.

For the spared hemisphere, apart from a main condition effect ($F(2, 13) = 5.07$; $p = .024$; $\eta^2 = 0.438$), a hand * condition interaction was observed ($F(2, 43) = 4.56$; $p = .032$; $\eta^2 = 0.413$). For the AO condition, pairwise comparisons showed no difference between hands. For the ME condition, pairwise comparisons showed that the mu power was lower for the less-affected hand than for the affected hand ($p < .05$). For the MI condition, pairwise comparisons showed no difference between hands. For the lesioned hemisphere, no main condition or hand effects were observed, and no hand*-condition effect was observed.

Thus, comparable to the TD group, in the children with uCP the spared hemisphere is activated during ME when the contralateral, less-affected hand is used (lower mu power) whereas the lesioned hemisphere is unresponsive to the motor tasks.

4. Discussion

In the present study, we measured the mu power of the EEG, during an eyes open and an eyes closed recording, and during an adapted VGPT task that consisted of an AO, ME, and MI condition. Moreover, since there are conflicting results in the literature regarding the movement related lateralization of the power of the mu peak, we particularly explored whether hemispheric differences in mu power were observed (Brinkman et al., 2014; Hobson and Bishop, 2016; Tangwiriyasakul et al., 2013). In addition, we compared, qualitatively, the results of typical developing (TD) children and children with unilateral cerebral palsy (uCP). As there is a lack of understanding of the lateralized mu effects associated with AO and MI, we will discuss our main findings within the framework of the proposed model of local excitation of the contralateral motor

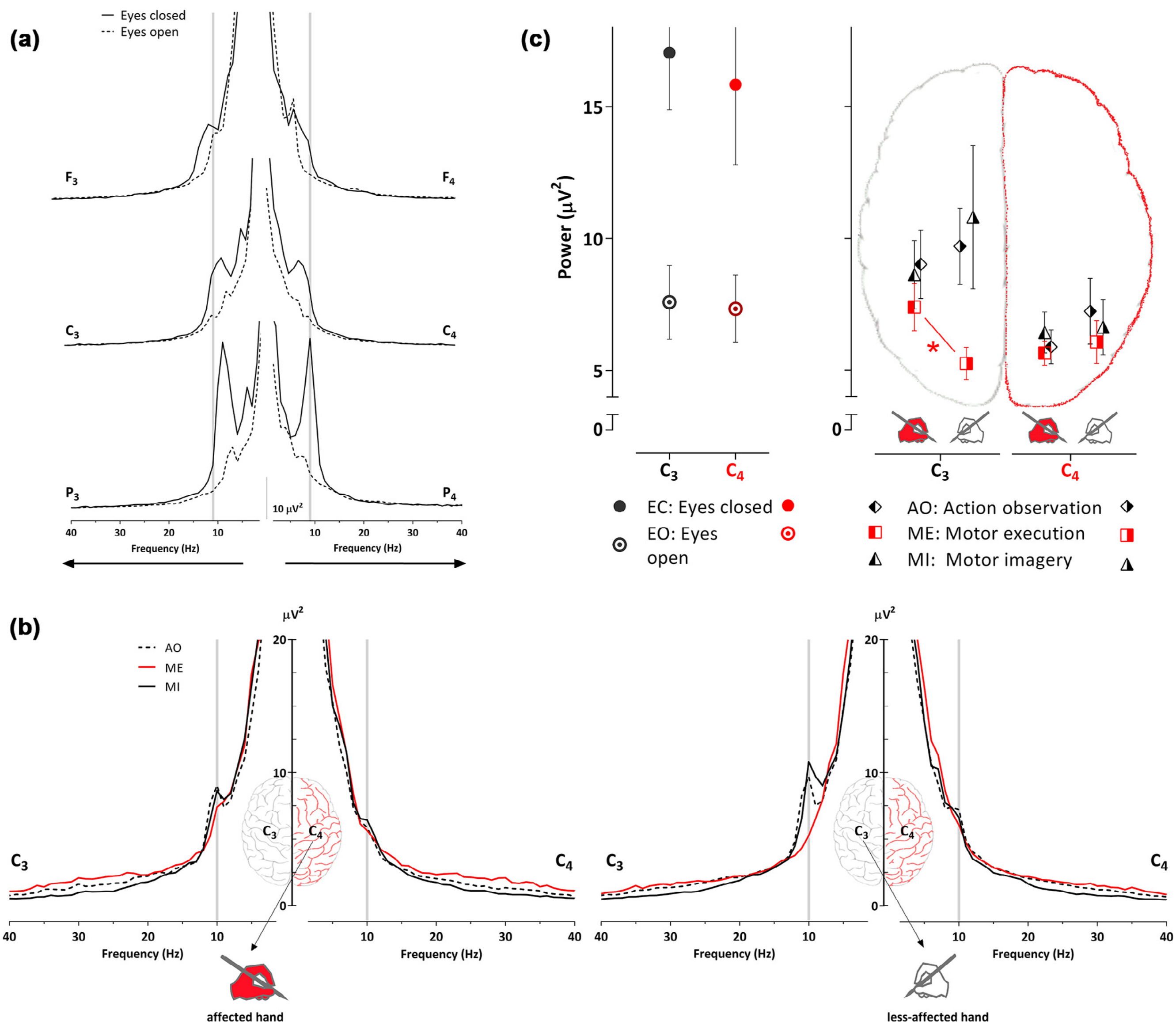

Fig. 3. The results of the children with unilateral Cerebral Palsy (uCP) are shown. Panel A shows the spectrograms of the EEGs measured during eyes open and eyes closed at the frontal, central and parietal leads, and over the left (spared) and right (lesioned) hemisphere. Panel B shows the spectrograms measured during the action observation (AO), motor execution (ME), and motor imagery (MI) condition, at the central C_3 and C_4 leads only. Panel C shows for both the eyes open / eyes closed recordings (left) and all motor task conditions (right), the means and SEMs of the power of the 10 Hz peaks over the left and right hemisphere.

areas and global inhibition of the associated ipsilateral motor areas. Finally, we will point to the clinical implications of our study.

Besides the AO, ME, and MI conditions, we measured the EEG during an eyes open and an eyes closed recording to evaluate the presence of the alpha and mu rhythm. These data were not used as a baseline for the AO, ME and MI conditions, since it remains debated whether such resting conditions provide a suitable baseline with respect to the experimental conditions (Brinkman et al., 2014; Hobson and Bishop, 2016; Tangwiriyasakul et al., 2013). In line with the literature, during the eyes open and the eyes closed recordings, the 10 Hz power was higher during eyes closed compared to eyes open recording in both groups of children. The clear difference between the eyes open and eyes closed recordings was maximal over the parietal electrodes. Indeed, ever since the first published recording of the human EEG, it is commonly observed that during eyes closed the power of the classical alpha band (8–12 Hz) is maximal over the posterior sites (Berger, 1929). The mu rhythm, although within the same frequency range as the alpha rhythm, is distinctly different from the alpha rhythm because it is more pronounced over central electrode sites instead of over the posterior sites. Moreover, where alpha power is especially sensitive to the eyes open versus eyes closed contrast, the mu power is more sensitive to motor related tasks, as will be discussed below. In addition, it is worth to note that during the eyes open and eyes closed recordings, no central mu power differences were found between the hemispheres, for neither the TD group, nor for the group of children with uCP.

At the central electrodes, we measured the mu power during ME, AO, and MI for each hemisphere and for each hand separately and in the next paragraphs we will interpret the results in terms of excitation and inhibition in the motor circuits of the two hemispheres.

In the TD group, for the ME condition we found a hand difference in the mu power over both the left and right hemisphere, such

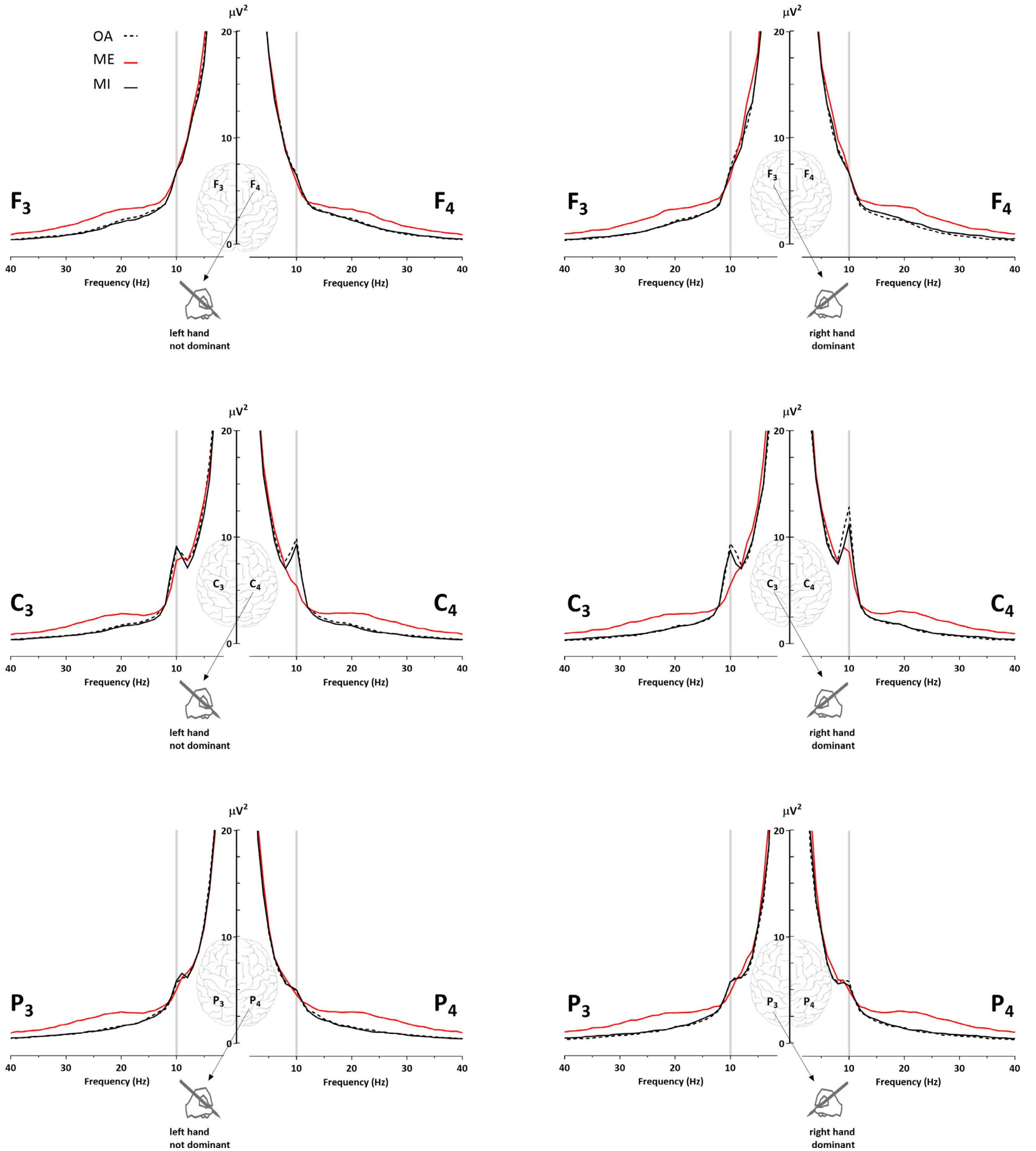

Fig. A1. The grand average spectrograms of the EEGs of the typically developing children (TD), for the left and right frontal ($F_{3/4}$), central ($C_{3/4}$), and parietal ($P_{3/4}$) areas, for the tree tasks: action observation (AO), motor execution (ME) and motor imagery (MI). Frequency (Hz) is plotted on the x-axes (NB: left x-axes are mirrored); power (μV^2) is plotted on the y-axes. The panels on the left show the data for the left hand, the panels on the right show the data for the right hand.

that the mu power was lower when the contralateral hand was used compared to the ipsilateral hand. This is in line with earlier studies that demonstrated that ME results in a marked lateralized mu effect with lower mu power over the contralateral hemisphere (Muthukumaraswamy et al., 2004; Nam et al., 2011; Pfurtscheller et al., 2008). Most studies concerned with mu power during motor tasks describe the data as a decrease of the mu power which points to cortical activation (Francuz and Zapala, 2011; Hobson and Bishop, 2016; Jeannerod, 1994). In addition, some studies have also reported an increased mu power which points to cortical inhibition. For example, Jensen and Mazaheri (2010) suggested that an increase in 10 Hz power might reflect an active inhibition of non-task related areas. Similarly, Haegens et al., (2010) described an increase of the 10 Hz power in a sensorimotor task over the

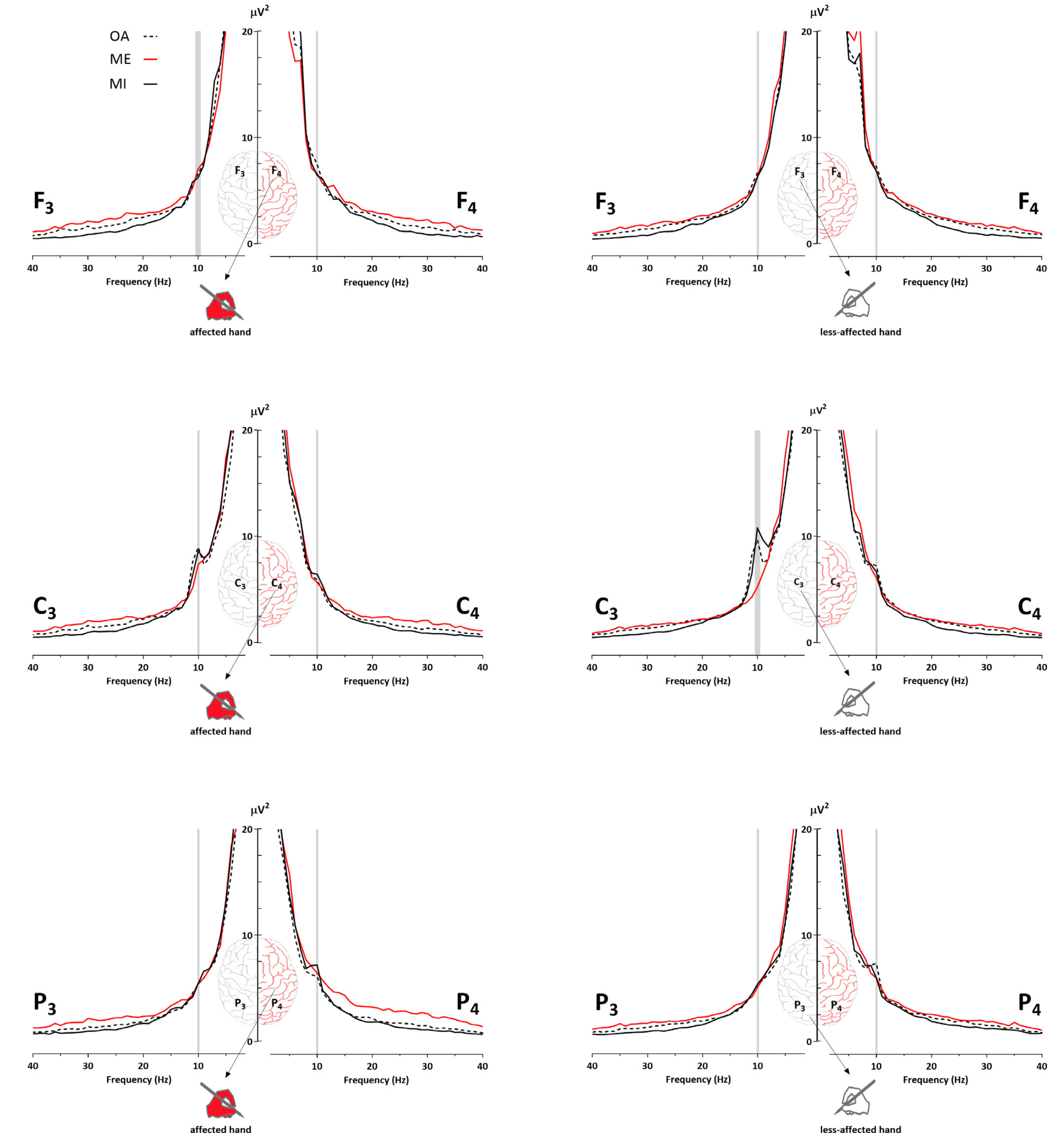

Fig. A2. The grand average spectrograms of the EEGs of the children with unilateral Cerebral Palsy (uCP), for the left and right frontal ($F_{3/4}$), central ($C_{3/4}$) and parietal areas ($P_{3/4}$), for the tree tasks action observation (AO), motor execution (ME) and motor imagery (MI). Frequency (Hz) is plotted on the x-axes (NB: left x-axes are mirrored); power (μV^2) is plotted on the y-axes. The panels on the left show the data for the affected hand, the panels on the right show the data for the less-affected hand.

ipsilateral hemisphere. Active inhibition of the ipsilateral hemisphere is beneficial during ME tasks to prevent associated movements. Because no reliable baseline value for the mu power can be determined, we describe and interpret the mu power results in terms of hemispheric differences. Thus, during ME, the contralateral hemisphere is more activated than the ipsilateral hemisphere. Similarly, mu and alpha power changes have been interpreted as contralateral desynchronization dominance reflecting excitation and ipsilateral synchronization dominance reflecting inhibition (Jensen and Mazaheri, 2010; Nam et al., 2011).

In TD children, this lateralized mu power difference was observed over both hemispheres during ME. However, in the group of children with uCP this power difference was only observed over the spared hemisphere. This result suggests a regular involvement of the spared hemisphere when executing a goal directed movement with the less-affected hand.

With respect to the AO and MI conditions, in the group of TD children the left hemisphere showed no changes in mu power, whereas over the right hemisphere mu power was higher when the dominant hand was addressed compared to the non-dominant hand. Although most EEG studies have investigated AO and MI effects with respect to only the dominant hand (Braadbaart et al., 2013; Frenkel-Toledo et al., 2013; Muthukumaraswamy et al., 2004), or neglected the dominance of the hand (Nam et al., 2011; Willems et al, 2009), others determined the AO and MI capacity for the dominant and non-dominant hand separately and reported a mirrored effect (Brinkman et al., 2014; Pfurtscheller et al., 2008; Willems et al., 2009). It has been reported that AO leads in general to a bilateral effect on the mu power, as the mirror neuron system is understood to be bilaterally activated (Muthukumaraswamy et al., 2004). In contrast, for MI tasks hemispheric differences of mu power have been reported (Nam et al., 2011). Our observation of a marked AO and MI effect over only the right hemisphere, suggests that during AO and MI of especially the dominant hand, the ipsilateral hemisphere is involved in inhibiting the associated motor programs. Possibly, more marked inhibition is needed for the dominant hand because of the higher familiarity with writing motions used in this task.

With respect to the children with uCP, a different pattern was observed compared to the TD children. In children with uCP, the lesioned hemisphere appeared to be unresponsive to all motor tasks, independent of whether the less-affected hand or the affected hand was addressed. More specifically, the mu power was lower over the lesioned hemisphere compared to the mu power over the spared hemisphere, and no differences between ME, AO, and MI were observed over this hemisphere. Apart from being unresponsive to the motor task, the lesioned hemisphere especially seems to lack the capacity to increase the mu power and might therefore lack the capacity to functionally inhibit motor programs, which is needed for a coordinated control of goal directed motor behavior. This lack in capacity to generate mu activity contrasts the capacity to generate the classic increase in alpha activity over the posterior sites during the eyes closed condition. Thus, this incapacity seems to be specific for the mu rhythm and related to the motor areas.

The lack of motor activation in children with uCP is well known and most therapies are aimed to increase motor activation. However, the disruptive effect of a lack of inhibitory control during motor actions is clinically apparent in the form of e.g. the occurrence of mirror movements and associated movements in many children with uCP (Klingels et al., 2016), as well as in patients with lesions of the prefrontal cortex (Brass et al., 2003). In general, inhibition has long been known to be a key concept in motor behavior because any successful goal directed behavior depends on it: in order to successfully execute a movement you should be able to simultaneously suppress associated but irrelevant movements (Dillon and Pizzagalli, 2007). To increase the hand capacity and hand performance of children with uCP, multiple effective rehabilitation approaches have been developed (Novak et al., 2019). For example, the results of a Cochrane review by Hoare et al. (2019) support both Constraint Induced Movement Therapy (CIMT) and bimanual training (BiT) programs. While the specific characteristics of children who would benefit either from CIMT or from BiT are not (yet) clear, this Cochrane review implies to base the choice for the specific intervention on clinical reasoning by the therapist led by child- and family-centered goals (Hoare et al, 2019). The current study suggests a decreased ability of the lesioned hemisphere to actively inhibit the cortical motor areas, independent of the used hand. Thus, training schedules that put an emphasis on the coordinated use of both hands, as in BiT, might be preferred because they help to establish better control in neural synchronization and desynchronization of the involved thalamo-cortical circuits during meaningful goal directed bimanual movements. Interestingly, in their study, Gordon et al., (2011) proposed that bimanual training leads to a more marked improvement with respect to the ability to perform self-determined goals compared to CIMT. However, how the mu rhythm responds during bilateral tasks remains to be studied.

Noteworthy, most EEG studies on AO and MI report the data in one-sided terms of mu suppression which is associated with cortical activation (Francuz and Zapala, 2011; Hobson and Bishop, 2016; Jeannerod, 1994). However, increases in mu power associated with active inhibition are commonly ignored.

The data from the current study suggest that in uCP, the lesioned hemisphere lacks the ability to respond to the motor tasks suggesting a decreased ability to actively inhibit the motor system, and even its ability to be activated during motor execution might be compromised. Therefore, children with uCP seem to rely on their spared hemisphere to control their motor behavior, whether they use the less-affected or affected hand.

Study limitation

Our results display similar mu power effects for the AO and MI condition. It seems that the applied design is not suitable to distinguish between AO and MI. Indeed, both the AO and MI condition used the same stimulus material and only differed with respect to the instruction.

In addition, to be able to vividly engage in MI, it is necessary to have access to pre-existing complex motor programs that are associated with the imagined movement. The creation of such complex motor programs like writing, however, depends on training and automatization of this behavior (Davidson and Wolpert, 2005). We therefore argue that the children in our study were able to actively engage in MI during the AO and MI conditions when the dominant hand was involved due to the activation of previously learned motor programs, but less so when the non-dominant hand was involved.

We were only able to obtain a complete data set from 15 children with uCP. Thus, the sample size of this group was small and highly divers with respect to e.g. etiology and remaining hand capacity of the affected hand. However, including enough participants from special populations, like children with uCP, is commonly challenging.

Final conclusions of this explorative study

For TD children the lateralization of the mu power during AO and MI, being higher over the ipsilateral hemisphere than that over the contralateral hemisphere, fits in the view of active inhibition of overt movements.

In children with uCP the mu power over the lesioned hemisphere did not show any response to the motor tasks, independent of the hand under investigation. Moreover, AO and MI resulted in higher mu power over the spared hemisphere compared to the lesioned hemisphere, independent of the hand being used. These results suggest that children with uCP rely on the spared hemisphere for the inhibitory control of motor behavior, for both the less-affected and for the affected hand.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors wish to thank the Sint Maartenskliniek, Nijmegen and the Roessingh Centre for Rehabilitation Enschede for their contribution to this project. In addition, all participating children and their parents and the schools involved in this project are greatly acknowledged. Special thanks should be given to Dalina Delfing and Anja Roubos for their enthusiastic contributions to this project. This work was supported by the Netherlands Scientific Research NWO Brain and Cognition program project nr: 433-09-215.

Appendix A

The results of the 4-within GLM with repeated measures for typically developing (TD) children.

Apart from a main condition effect ($F_{(2,\ 43)}$ = 4.42; p = .018; η^2 = 0.171) and a main area effect ($F_{(2,\ 43)}$ = 9.55; p < .001; η^2 = 0.308), the 4-within repeated measures GLM analysis revealed several significant 2-, 3-, and 4-way interactions: a condition * area interaction ($F_{(4,\ 41)}$ = 2.75; p = .041; η^2 = 0.212); a condition * hemisphere interaction ($F_{(2,\ 43)}$ = 4.57; p < .016; η^2 = 0.175); an area * hemisphere interaction ($F_{(2,\ 43)}$ = 33.23; p < .001; η^2 = 0.608); a condition * area * hemisphere interaction ($F_{(4,\ 41)}$ = 15.11; p = .015; η^2 = 0.256); a condition * hand interaction ($F_{(2,\ 43)}$ = 13.16; p < .001; η^2 = 0.380); a condition * area * hand interaction ($F_{(4,\ 41)}$ = 6.79; p < .001; η^2 = 0.399); a condition * hemisphere * hand interaction ($F_{(2,\ 43)}$ = 3.70; p = .033; η^2 = 0.147); an area * hemisphere * hand interaction ($F_{(2,\ 43)}$ = 5.46; p = .008; η^2 = 0.203); a condition * area * hemisphere * hand interaction ($F_{(4,\ 41)}$ = 5.15; p = .002; η^2 = 0.335). The data are provided in Supplementary file: Jongsma_Mu power_raw data for open access.xlsx. See Fig. A1 for a graphical representation of the full spectograms.

The results of the 4-within GLM with repeated measures for children with unilateral CP.

The 4-within repeated measures GLM analysis revealed several significant 2 and 3-way interactions: an area * hemisphere interaction ($F_{(2,\ 13)}$ = 6.16; p = .013; η^2 = 0.486) and a condition * area * hemisphere interaction ($F_{(4,\ 11)}$ = 3.82; p = .035; η^2 = 0.581). The data set is provided in Supplementary file: Jongsma_Mu power_raw data for open access.xlsx. See Fig. A2 for a graphical representation of the full spectograms.

Appendix B. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2020.08.022.

References

Adams ILJ, Smits-Engelsman B, Lust JM, Wilson PH, Steenbergen B. Feasibility of motor imagery training for children with developmental coordination disorder – a pilot study. Front Psychol 2017;8(1271).
Berger H. Über das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr 1929;87(1):527–70.
Braadbaart L, Williams JH, Waiter GD. Do mirror neuron areas mediate mu rhythm suppression during imitation and action observation?. Int J Psychophysiol 2013;89(1):99–105.
Brass M, Derrfuss J, Matthes-von Cramon G, von Cramon DY. Imitative response tendencies in patients with frontal brain lesions. Neuropsychology 2003;17(2):265–71.
Brinkman L, Stolk A, Dijkerman HC, de Lange FP, Toni I. Distinct roles for alpha- and beta-band oscillations during mental simulation of goal-directed actions. J Neurosci 2014;34(44):14783–92.
Buccino G. Action observation treatment: a novel tool in neurorehabilitation. Philos Trans R Soc Lond B Biol Sci 2014;369(1644):20130185.
Buccino G, Arisi D, Gough P, Aprile D, Ferri C, Serotti L, et al. Improving upper limb motor functions through action observation treatment: a pilot study in children with cerebral palsy. Dev Med Child Neurol 2012;54(9):822–8.
Choudhury S, Charman T, Bird V, Blakemore SJ. Development of action representation during adolescence. Neuropsychologia 2007;45(2):255–62.
Davidson PR, Wolpert DM. Widespread access to predictive models in the motor system: a short review. J Neural Eng 2005;2(3):S313–9.
Dillon DG, Pizzagalli DA. Inhibition of action, thought, and emotion: a selective neurobiological review. Appl Prev Psychol 2007;12(3):99–114.
Duque J, Murase N, Celnik P, Hummel F, Harris-Love M, Mazzocchio R, et al. Intermanual Differences in movement-related interhemispheric inhibition. J Cogn Neurosci 2007;19(2):204–13.
Eaves DL, Riach M, Holmes PS, Wright DJ. Motor imagery during action observation: a brief review of evidence, theory and future research opportunities. Front Neurosci 2016;10:514.
Fox NA, Bakermans-Kranenburg MJ, Yoo KH, Bowman LC, Cannon EN, Vanderwert RE, et al. Assessing human mirror activity with EEG mu rhythm: A meta-analysis. Psychol Bull 2016;142(3):291–313.
Francuz P, Zapala D. The suppression of the mu rhythm during the creation of imagery representation of movement. Neurosci Lett 2011;495(1):39–43.
Frenkel-Toledo S, Bentin S, Perry A, Liebermann DG, Soroker N. Dynamics of the EEG power in the frequency and spatial domains during observation and execution of manual movements. Brain Res 2013;1509:43–57.
Geerdink Y, Aarts P, Geurts A. Motor learning curve and long-term effectiveness of modified constraint-induced movement therapy in children with unilateral cerebral palsy: a randomized controlled trial. Res Dev Disabil 2013;34:923–31.
Gordon AM, Hung Y-C, Brandoa M, Ferre CL, Kuo H-C, Friel K, et al. Bimanual training and constraint-induced movement therapy in children with hemiplegic cerebral palsy: a randomized trial. Neurorehab Neural Rep 2011;25(8):692–702.
Gratton G, Coles MG, Donchin E. A new method for off-line removal of ocular artifact. Electroencephalogr Clin Neurophysiol 1983;55(4):468–84.
Haegens S, Osipova D, Oostenveld R, Jensen O. Somatosensory working memory performance in humans depends on both engagement and disengagement of regions in a distributed network. Hum Brain Mapp 2010;31(1):26–35.
Hoare BJ, Wallen MA, Thorley MN, Jackman ML, Carey LM, Imms C. Constraint-induced movement therapy in children with unilateral cerebral palsy. Cochrane Database Syst Rev 2019;4(4):CD004149.
Hobson HM, Bishop DVM. Mu suppression - A good measure of the human mirror neuron system?. Cortex 2016;82:290–310.
Jeannerod M. The representing brain: Neural correlates of motor intention and imagery. Behav Brain Sci 1994;17(2):187–202.
Jensen O, Mazaheri A. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. Front Hum Neurosci 2010;4:186.
Johnson SH. Thinking ahead: the case for motor imagery in prospective judgements of prehension. Cognition 2000;74(1):33–70.
Jongsma ML, Baas CM, Sangen AF, Aarts PB, van der Lubbe RH, Meulenbroek RG, et al. Children with unilateral cerebral palsy show diminished implicit motor imagery with the affected hand. Dev Med Child Neurol 2016;58(3):277–84.
Klimesch W, Sauseng P, Hanslmayr S. EEG alpha oscillations: the inhibition-timing hypothesis. Brain Res Rev 2007;53(1):63–88.
Klingels K, Jaspers E, Staudt M, Guzzetta A, Mailleux L, Ortibus E, et al. Do mirror movements relate to hand function and timing of the brain lesion in children with unilateral cerebral palsy?. Dev Med Child Neurol 2016;58(7):735–42.
Lust JM, Wilson PH, Steenbergen B. Motor imagery difficulties in children with Cerebral Palsy: A specific or general deficit?. Res Dev Disabil 2016;57:102–11.
Marshall PJ, Meltzoff AN. Neural mirroring systems: exploring the EEG mu rhythm in human infancy. Dev Cogn Neurosci 2011;1(2):110–23.
Muthukumaraswamy SD, Johnson BW, McNair NA. Mu rhythm modulation during observation of an object-directed grasp. Brain Res Cogn Brain Res 2004;19(2):195–201.
Mutsaarts M, Steenbergen B, Bekkering H. Anticipatory planning deficits and task context effects in hemiparetic cerebral palsy. Exp Brain Res 2006;172(2):151–62.
Nakano H, Kodama T. Motor imagery and action observation as effective tools for physical therapy. Neurol Phys Therapy 2017. https://doi.org/10.5772/67519.
Nam CS, Jeon Y, Kim YJ, Lee I, Park K. Movement imagery-related lateralization of event-related (de)synchronization (ERD/ERS): motor-imagery duration effects. Clin Neurophysiol 2011;122(3):567–77.
Novak I, Morgan C, Fahey M, Finch-Edmunson M, Galea C, Hines A, et al. State of the evodence traffic lights 2019: systematic review of interventions for preventing and treating children with cerebral palsy. Curr Neurol Neuresci 2019;20(3). https://doi.org/10.1007/s11910-020-1022-z.
Odding E, Roebroeck ME, Stam HJ. The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil Rehabil 2006;28(4):183–91.
Pfurtscheller G. Induced oscillations in the alpha band: functional meaning. Epilepsia 2003;44(s12):2–8.
Pfurtscheller G, Scherer R, Muller-Putz GR, Lopes da Silva FH. Short-lived brain state after cued motor imagery in naive subjects. Eur J Neurosci 2008;28(7):1419–26.
Pineda JA. The functional significance of mu rhythms: translating "seeing" and "hearing" into "doing". Brain Res Brain Res Rev 2005;50(1):57–68.
Pineda JA, Allison BZ, Vankov A. The effects of self-movement, observation, and imagination on mu rhythms and readiness potentials (RP's): toward a brain-computer interface (BCI). IEEE Trans Rehabil Eng 2000;8(2):219–22.
Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, et al. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl 2007;109:8–14.
Sarasso E, Gemma M, Agosta F, Filippi M, Gatti R. Action observation training to improve motor function recovery: a systematic review. Arch Physiother 2015;5:14.

Scott M, Taylor S, Chesterton P, Vogt S, Eaves DL. Motor imagery during action observation increases eccentric hamstring force: an acute non-physical intervention. Disabil Rehabil 2018;40(12):1443–51.
Smits-Engelsman BC, Wilson PH. Age-related changes in motor imagery from early childhood to adulthood: probing the internal representation of speed-accuracy trade-offs. Hum Mov Sci 2013;32(5):1151–62.
Spruijt S, van der Kamp J, Steenbergen B. Current insights in the development of children's motor imagery ability. Front Psychol 2015;6:787.
Steenbergen B, Craje C, Nilsen DM, Gordon AM. Motor imagery training in hemiplegic cerebral palsy: a potentially useful therapeutic tool for rehabilitation. Dev Med Child Neurol 2009;51(9):690–6.
Suffczynski P, Kalitzin S, Pfurtscheller G, Lopes da Silva FH. Computational model of thalamo-cortical networks: dynamical control of alpha rhythms in relation to focal attention. Int J Psychophysiol 2001;43(1):25–40.
Tangwiriyasakul C, Verhagen R, van Putten MJ, Rutten WL. Importance of baseline in event-related desynchronization during a combination task of motor imagery and motor observation. J Neural Eng 2013;10(2) 026009.
ter Horst AC, Jongsma ML, Janssen LK, van Lier R, Steenbergen B. Different mental rotation strategies reflected in the rotation related negativity. Psychophysiology 2012;49(4):566–73.
ter Horst AC, van Lier R, Steenbergen B. Mental rotation strategies reflected in event-related (de)synchronization of alpha and mu power. Psychophysiology 2013;50(9):858–63.
WHO, 2001. International Classification of Functioning, Disability and Health (ICF). Retrieved from http://apps.who.int/classifications/icfbrowser/.
Willems RM, Toni I, Hagoort P, Casasanto D. Body-specific motor imagery of hand actions: neural evidence from right- and left-handers. Front Hum Neurosci 2009;3:39.
Wilson PH, Adams IL, Caeyenberghs K, Thomas P, Smits-Engelsman B, Steenbergen B. Motor imagery training enhances motor skill in children with DCD: A replication study. Res Dev Disabil 2016;57:54–62.
Wilson PH, Thomas PR, Maruff P. Motor imagery training ameliorates motor clumsiness in children. J Child Neurol 2002;17(7):491–8.
Zimmermann-Schlatter A, Schuster C, Puhan MA, Siekierka E, Steurer J. Efficacy of motor imagery in post-stroke rehabilitation: a systematic review. J Neuroeng Rehabil 2008;5:8.