The handle http://hdl.handle.net/1887/63240 holds various files of this Leiden University dissertation.

Author: Anguelova, G.V.
Title: Unravelling crossed wires: dysfunction in obstetric brachial plexus lesions in the light of intertwined effects of the peripheral and central nervous system
Issue Date: 2018-06-26
Increased brain activation during motor imagery suggests central abnormality in Neonatal Brachial Plexus Palsy


**Abstract**

Neonatal Brachial Plexus Palsy (NBPP) may lead to permanent impairment of arm function. As NBPP occurs when central motor programs develop, these may be ill-formed. We studied elbow flexion and motor imagery with fMRI to search for abnormal motor programming. We compared the cortical activity of adults with conservatively treated NBPP to that of healthy individuals stratified for hand dominance, using fMRI BOLD tasks of elbow flexion and motor imagery of flexion. Additionally, resting-state networks and regional gray matter volume were studied. Sixteen adult NBPP patients (seven men; median age 29 years) and sixteen healthy subjects (seven men, median age 27 years) participated. Cortical activation was significantly higher in patients during flexion imagery compared to healthy individuals and it increased with lesion extent and muscle weakness. The contralateral and ipsilateral premotor cortex, and the contralateral motor cortex showed stronger activity during imagined flexion in the right-handed NBPP subjects compared to healthy individuals. Activity patterns during actual flexion did not differ between groups. No differences in resting-state network connectivity or gray matter amount were found between the groups. NBPP affected imagined but not actual elbow flexion, suggesting an impairment of motor planning which would indicate abnormal motor programming in NBPP.

**Introduction**

Neonatal Brachial Plexus Palsy (NBPP) is a closed peripheral nerve traction injury that arises most commonly, but not exclusively, from shoulder dystocia during a difficult birth. Typically, shoulder and elbow flexion is impaired because of damage to the C5 and C6 spinal nerves. In more severe cases, extension and hand function are impaired as well. While mild nerve damage does not exclude a full recovery, severe damage can cause permanent impairment of arm function. A systematic literature search showed a residual deficit in 20 to 30% of cases.

Traction causes axonal loss of continuity with the end organ (e.g. the biceps muscle) followed by degeneration of the axon distal to the injury site (Wallerian degeneration). Even in severe nerve damage due to NBPP, there is usually no clear gap between the proximal and distal nerve ends. This is in contrast to adults with traumatic nerve lesions, and the difference is probably due to the smaller absolute size in infants. Instead, a ‘neuroma-in-continuity’ of the superior trunk is formed containing axons of which some cross the lesion site and enter empty basal laminal tubes. Functional recovery takes place over months to years and is hampered by several factors. The number of axons that successfully cross the lesion site is reduced with increasing severity of the nerve lesion. In addition, axons may connect with end organs differing from the original ones due to misrouting. This may disturb proprioceptive feedback, as well as motor firing patterns. Absent or inappropriate afferent input occurring at the age at which central motor programs are developed may inhibit the development of these programs. Neurophysiological evidence and clinical observations indicate that these programs are ill-formed in NBPP.

To assess central motor programming we investigated motor execution and imagery tasks with fMRI in conservatively treated NBPP adults. An expansion of motor cortical representation occurs not only at the onset of learning a new motor skill in healthy subjects, but also in patients following upper extremity injury and reconstruction. While a skill is being mastered, the degree of cortical representation and excitability decrease again. We used motor execution tasks to assess whether a central motor impairment in NBPP can be
linked to a different motor cortical representation compared to controls. With increasing practice motor tasks become automatic and require less planning effort. A decreased cortical activation has been found in the primary motor cortex contralateral to the attempted limb movement in paraplegics compared to healthy controls studied with motor imagery fMRI, which was attributed to an increased need for attention allocation. Therefore, to assess whether an increased planning effort contributes to the central motor impairment in NBPP we used imagery tasks. Accordingly, we expect that in the NBPP adults actual task execution does not require more central effort compared to controls, corresponding with a normal to decreased cortical activation, irrespective of muscle weakness, however planning of the movement does.

**Materials And Methods**

**Subjects**
Sixteen adult NBPP patients and sixteen healthy subjects participated in the study. Patients were recruited from the Leiden University Medical Centre data base and were looked for nationwide with the help of the Dutch Erb’s Palsy Association. The minimum inclusion age was 18 years. Healthy individuals were matched to patients for sex, age (± 5 years) and handedness. Patients with NBPP had not undergone nerve surgical reconstruction of the brachial plexus or secondary surgery to improve elbow function. Further exclusion criteria were the presence of other relevant neurological diseases and MRI exclusion criteria such as claustrophobia and implanted devices. The protocol was approved by the Medical Ethics Committee of the Leiden University Medical Centre. All participants provided written informed consent.

**Lesion Extent**
Arm function of all patients was examined by an experienced brachial plexus surgeon (MJAM). Individual muscles were graded according to the Medical Research Council scale; active and passive range of motion was documented and the Mallet scale for shoulder function was assessed. Subsequently, motor function was tested to assess the extent of the NBPP lesion and subdivided in four groups: group 1 concerned C5 and C6 damage, with impaired shoulder abduction, exorotation, and elbow flexion. Group 2 concerned C5, C6, and C7 damage, clinically as group 1 with additional weakness of elbow, wrist and finger extension. Group 3 had C5 to C8 damage, clinically as group 2 with absence of extension function additionally. Group 4 had C5 to T11 damage, clinically as group 3 plus absent or minimal intrinsic hand muscle function.

**Motor tasks**
Motor execution tasks consisted of isometric biceps contraction, a task that even NBPP patients with a weak biceps muscle can perform; also, isometric contraction avoids MRI movement artefacts. Vacuum pillows were placed around both forearms to obtain immobilization of the forearm after air evacuation. The arm was further immobilized by a sandbag of 3.5 kilograms placed on top of the vacuum pillow. The forearms were positioned next to the body at a comfortable elbow flexion angle between 10º and 30º using cushions. The arm was supinated as far as possible without causing discomfort. Finally, a strap was placed over the middle of each forearm to prevent flexion. Subjects were instructed to lie still during the experiment. For the motor imagery task, subjects had to imagine rhythmically pushing their forearm against the strap at approximately 1 Hz. The flexion task consisted of actual isometric biceps contraction. Both tasks were performed for left and right arms separately.

Stimuli were presented using a computer running the Matlab-based PsychToolbox (The Mathworks Inc.) and were projected onto a screen visible through a mirror above the eyes of the subject. To indicate movement execution, green letters were used; for the imagery condition, red letters were used. The letters ‘L’ and ‘R’ indicated that the task should be performed using the left and right arm, respectively. Thirty second task blocks were presented in a random order intermixed with 30 second baseline blocks where a fixation cross was presented. To minimize effects of muscle fatigue, the sequence of blocks was split into three 10 minute sessions. Subjects were given rest between sessions until they indicated they were ready to continue. In all subjects this was within three minutes. The tasks were performed on two occasions: once to obtain electromyographic data and once to obtain fMRI data.

**Electromyography**
Subjects were trained with EMG feedback to perform the tasks before scanning. To do so, subjects were in supine position with their arms immobilized as
explained above. Surface self-adhesive EMG electrodes were placed on both the left and right biceps and triceps muscle belly and 0.5 cm distally. Subjects observed their EMG activity during the tasks on a screen. They were instructed to aim for activity in the agonist and reduce activity in the antagonist as much as possible during execution and not to activate both agonist and antagonist during imagery flexion. Responses were acquired using a band pass filter of 20 Hz - 2 kHz and recorded over a minimum of 100 s for each of the total four conditions (motor execution/motor imagery, right/left arm) using a Medelec Synergy EMG apparatus (Oxford Instruments, Abingdon, Oxfordshire, UK). Biceps EMG activity was not measured during MRI scanning.

fMRI data acquisition

Four brain scans were acquired: a T1-weighted anatomical scan, a high-resolution T2*-weighted scan, and T2*-weighted task-related and resting-state BOLD fMRI. Data were acquired at the Leiden University Medical Centre with a 3 Tesla Achieva scanner (Philips Medical Systems, Best, The Netherlands). An eight-channel head coil was used for all data collection.

T1-weighted images were acquired with the following scan parameters: 140 transverse slices, voxel size = 1.17x1.17x1.2 mm, FOV = 224x177x168 mm, 192x152 matrix, flip angle = 8º, TR (repetition time)/TE (echo time) = 9.7/4.6 ms. T2*-weighted images were acquired with the following parameters: 84 transverse slices, voxel size = 1.96x2.01x2.00 mm, no slice gap, FOV = 220x220x168 mm, 112x109 matrix. For the task fMRI the whole brain was covered by acquiring 38 transverse slices, voxel size = 2.75x2.75x2.75 mm, 0.275 mm slice gap, 80x79 matrix, flip angle = 80º, TR/TE = 2200/30 ms. The resting-state fMRI parameters were equal to the task fMRI except for the slice gap which was 0.272 mm.

fMRI data preprocessing

fMRI data was preprocessed with FSL version 4.1.7 (Analysis Group, FMRIB, Oxford, UK). The following processing steps were applied: motion correction, removal of non-brain tissue, spatial smoothing using a Gaussian kernel of 8 mm full width at half maximum, grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor and high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with a 128 s cut-off). To register fMRI scans to standard space, functional scans of an individual were registered to the corresponding high-resolution T2*-weighted images, which were registered to the T1-weighted images, followed by registration to MNI-152 standard space (T1 standard brain averaged over 152 subjects; Montreal Neurological Institute, Montreal, QC, Canada) images. Preprocessed MRI data of patients with an affected left arm were mirrored with respect to the midsagittal plane. In this way the hemisphere corresponding with the affected arm was on the same (left) side for all patients and the right hemisphere corresponded with the unaffected arm. This was also done for the corresponding matched controls.

Data analysis – task fMRI

Data analysis was carried out in three steps: 1) calculating the mean cortical response per condition per person per task block, 2) combining the three task blocks, and 3) comparing NBPP patients and controls. This is described in detail below. For every subject, four regressors, one for each of the conditions, were modelled as square-wave functions with duration equal to that of the task block. The haemodynamic responses generated by each task condition were modelled by convolving these square-wave functions with a canonical haemodynamic response function. Each subject’s mean response for the three sessions was estimated with a second-level analysis (FSL FEAT version 5.98 Multi-level analysis) resulting in one contrast per person proceeding in the third-level analysis. Contrasts representing the difference between each task condition and baseline were calculated and compared between NBPP patients and healthy individuals with a mixed effects third-level analysis using FSL FEAT version 5.98. Additional to whole brain analysis, masking allowed to define the brain regions where cortical activity was expected and increased during the tasks. Masks were binary representations of the following regions of interest: 1) left and right motor cortex (area 4a and 4p) together, 2) left and right premotor cortex (area 6) together, which were selected from the Juelich Histological Atlas in FSL. Age, extent of the brachial plexus lesion and biceps strength were normalized and added as covariates in the statistical group model. When clinical notes described biceps strength as MRC scale 5, this was noted as 4.75. The cluster threshold was set at z=2.3 and the cluster corrected significance threshold at p=0.05. As arm dominance may change due to NBPP, results were stratified according to the subjects’ dominant side. Hand dominance was reported by the participants and corroborated
by observing with which hand they wrote. The 10 left-handed patients were compared at group level with the six healthy left-handed individuals and the six right-handed patients were compared with the remaining 10 healthy right-handed individuals. An additional comparison was performed between the domiant and non-dominant hemispheres in healthy individuals to ascertain the presence of activation differences due to arm dominance.

**Data analysis – EMG**

To exclude learning effects the first 50 seconds of the EMG signal for each of the four conditions (motor imagery/flexion, right/left arm) were excluded from analysis. The EMG signal was then rectified and the sum of values between 50 and 100 s of the recording was calculated. Differences in muscle activation between motor imagery and motor execution, and between the right and left arm, were tested with the non-parametric dependent samples Wilcoxon’s test. Differences between healthy individuals and patients were tested with the Mann-Whitney U test. SPSS Statistics 20.0 (Armonk, NY: IBM Corp.) was used for statistical testing with a significance threshold of 0.05.

**Data analysis – resting-state**

Standard group independent component analysis (ICA) was carried out using probabilistic ICA as implemented in FSL MELODIC version 3.10. Default group ICA processing steps were applied to the individual preprocessed and normalized data sets: masking out non-brain voxels, voxel-wise mean centering of the data, and normalization of the voxel-wise variance based on all data sets. Subsequently, data sets from the healthy individuals were concatenated in time to create a 1D voxel time course file, which was then projected into a 25-dimensional subspace using principal component analysis. Next, the data set was decomposed into 25 sets of independent vectors which describe signal variation across the temporal (time courses) and spatial (maps) domains by optimizing for non-Gaussian spatial source distributions using the FastICA algorithm. The values of the resulting estimated component maps were divided by the standard deviation of the residual noise and set at a probability threshold of $p > 0.5$ by fitting a Gaussian/Gamma mixture model to the histogram of intensity values.

Subject-specific statistical maps were created to test for differences between NBPP and healthy groups in the identified components with a dual regression procedure. In short, multiple linear regression of the $z$-threshold group ICA maps against the preprocessed individual 4D resampled data sets yielded a subject specific time course for each component separately. Next, multiple linear regression of these time courses was carried out against the pre-processed individual 4D data sets in the standard space resolution of 2 mm. This resulted in subject specific $z$-maps for each of the 25 components.

Statistical difference was assessed non-parametrically using the FSL’s randomise tool version 2.8 with 5000 permutations. Besides modeling regressors for each of the two groups, additional regressors describing age, lesion extent and biceps strength were added, corresponding to the task fMRI model. For each resting-state network, the resulting statistical maps were threshold-free cluster enhancement corrected for family-wise errors using a threshold of $p \leq 0.05$ and controlled for the local false discovery rate at a threshold of $q \leq 0.05$.

**Data analysis – gray matter regional volumes**

Voxel-based morphometry analysis was run on the acquired T1-weighted data sets, carried out with FSL tools. First, structural images were brain-extracted and gray matter-segmented before being registered to the MNI 152 standard space using non-linear registration. The resulting images were flipped and averaged along the x-axis to create a left-right symmetric, study-specific gray matter template. Second, all native gray matter images were non-linearly registered to this study-specific template and modulated to correct for local expansion (or contraction) due to the non-linear component of the spatial transformation. The modulated gray matter images were then smoothed with an isotropic Gaussian kernel with a sigma of 3 mm. Finally, statistical difference was assessed using the FSL’s randomise tool version 2.8 as described for resting-state data analysis except for false discovery rate correction.

**Results**

Characteristics of the groups are shown in Table 1. Sixteen adult NBPP patients (seven men, median (25th-75th percentile) age 29 (22-41) years, six right-handed) and sixteen healthy subjects (seven men, median (25th-75th percentile) age 27 (23-41) years, 10 right-handed) participated in the study. There were four patients in group 1, nine in group 2, two in group 3, and one in group 4.
Task fMRI

During the motor imagery flexion task cortical activation was significantly \((z>2.3, p<0.05)\) increased in NBPP patients compared to healthy individuals. Comparison of the whole brain showed increased cortical activation during motor imagery flexion of the affected arm in right- (Fig. 1a) and left-handed (Fig. 1b) NBPP patients compared to healthy individuals. Increasing lesion extent and decreasing biceps muscle force were associated with a higher cortical activation in these groups. During the imagery flexion of the healthy arm, there was increased activation only in right-handed NBPP patients, (Fig. 1c) with a similar effect of lesion extent and biceps muscle force on cortical activation as for the affected arm, as well as decreasing age. Region of interest masks, the areas where cortical activation may be expected in healthy individuals, showed that during motor imagery flexion of the affected arm the following regions were more activated in the right-handed NBPP subjects than in healthy individuals: the contralateral premotor cortex, ipsilateral premotor cortex and the contralateral motor cortex. During motor imagery flexion of the healthy arm the contralateral premotor cortex and ipsilateral premotor cortex were more activated in the right-handed NBPP subjects than in healthy individuals. No differences were found between the two groups during execution of the flexion task. There were no significant differences in cortical activation within healthy individuals between the dominant and the non-dominant hemispheres.

EMG, resting-state and gray matter

Median (25th-75th percentile) biceps activation (sum of samples) is shown in Table 2 with the corresponding \(p\)-values. During motor execution triceps co-contraction was higher in patients compared to controls only in the affected arm (patients 105(77-250)mV, controls 63(27-79)mV, \(p<0.001\)) and not in the unaffected one (patients 50(35-89)mV, controls 60(31-144)mV, \(p=0.918\)), corresponding with the biceps activity findings for that task: affected arm (\(p=0.034\)), unaffected one (\(p=0.759\)). There were no significant differences in the resting-state networks or the amount of gray matter between NBPP and healthy individuals.

Discussion

The main finding of this study is that NBPP patients showed more cortical activity than healthy individuals during motor imagery flexion of the affected arm. The increase was found in cortical premotor areas of both hemispheres, as well as in contralateral motor areas in right-handed NBPP patients. The findings were not restricted to the affected arm, but also account for the healthy arm, where cortical premotor areas were also more activated in right-handed NBPP patients than in controls. Additionally, higher cortical activation was associated with an increasing lesion extent and a decreasing biceps muscle force. The motor imagery findings contrast with results of the actual flexion task, during which no increase of cortical activation in NBPP patients was seen.

The EMG feedback training was included to ensure that the motor imagery tasks were executed as intended namely, a higher biceps EMG activation during motor execution than during the imagery motor task. The lack of EMG differences between the healthy side in patients and healthy individuals both during motor imagery and execution, show that patients were able to perform the different tasks appropriately. There was one unexpected EMG difference though: a higher biceps activity was recorded in the patients’ affected arm during motor execution suggesting that more muscle effort was necessary to achieve the same task with the affected arm than with the healthy one. The increased triceps co-contraction during motor execution which was only observed in the affected arm in NBPP patients may be due to misrouting.

We did not find significant differences in the resting-state networks between NBPP and healthy individuals. Resting-state fMRI may reflect ongoing functional communication between brain regions during rest, e.g. long term motor training may significantly increase resting-state activity within primary motor regions. Functional connections of resting-state networks tend to be strongly related to structural white matter connections. Accordingly, our findings may not be explained by differences in connectivity. In addition, we did not find any differences in gray matter volume.

Motor imagery

To put our findings into perspective, we will compare NBPP with some
other developmental and acquired neurological disorders. During motor imagery the representation of a given motor act is internally rehearsed within working memory without any overt motor output. It comprises two parts: a representation of the body, and a representation of the goal of the action. Several factors are probably necessary to form a body representation during early development; these are: proprioceptive feedback from the affected as well as the healthy limb, and visual feedback, which can be obtained from observing others (mirror neurons) or possibly the affected limb in NBPP. The influence of all three factors may be enhanced by increased use or diminished by disuse of the limb.

In spinal cord lesions, enhanced activation and recruitment of additional cortical regions has been reported, findings reminiscent of the present study. A principal difference with NBPP is however that traumatic spinal cord lesions are usually acquired later in life when motor program development is complete. A higher contralateral cortical activation was found in amputees during imagined hand movements compared to healthy subjects, but again the lesion is acquired later in life. A reduced somatosensory cortical representation area has been reported in patients with limb aplasia or dysmelia.

Contralateral cortical activation was found varying from reduced to equal to that of the healthy side during a motor task, and no activation was found during an imagery motor task. However, the applicability of these findings is uncertain: the study concerned only two patients and activation was absent with the imagery task protocol in two healthy subjects.

How can the increased cortical activity during motor imagery in NBPP be interpreted?

Motor imagery has been linked to action planning. Our findings suggest that in NBPP patients an increased central effort is required for action planning, which increases with lesion extent and muscle weakness. When a motor task is learned, the task initially requires full attentional control. With practice the tasks become automatic and require less central effort. With this in mind, the motor imagery in NBPP resembles a newly learned task, requiring much attention. In paraplegics, a similar increased need for attention allocation was suggested as well.

There were no significant differences in cortical activation within healthy individuals between the dominant and non-dominant hemispheres, suggesting that effects in the patient group cannot be attributed to normal variations due to hand dominance. Yang and colleagues found that in children with right NBPP only 17% preferred to use their right upper limb for overall movements in contrast to 90% in the general population and 93% in children with left NBPP. The significant differences we found only in the right-handed patients may suggest that switching hand dominance may represent a strategy to reduce central effort.

The role of ipsilateral activation

In addition to the contralateral cortical activation, we also found significantly stronger ipsilateral cortical activation in the premotor areas during motor imagery flexion of the affected arm in NBPP patients compared to healthy individuals. Increased ipsilateral cortical activation has also been found in arm amputees who lost the arm in childhood. There are several explanations for our findings, in line with other studies: first, ipsilateral activation is unintentional, representing increased use of the healthy arm to increase stability and compensate for the loss of affected arm function. Second, these findings might reflect central fatigue, which may cause bilateral activation: during repetitive unilateral limb movement the muscles of the contralateral limb may show increased EMG-activity, and more so as the movement requires greater effort. These findings fit with the concept that motor imagery in NBPP requires much effort. Finally, a third explanation holds that pre-existing cortical connections with the ipsilateral hemisphere are either disinhibited or strengthened. A similar explanation has been proposed for mirror movements observed in children with cerebral palsy.

The role of the healthy arm

Besides increased cortical activity during imagery flexion of the affected arm in patients, we also found such an effect during imagery flexion of the healthy arm in the right-handed patients. Performing a unilateral task can be associated with bilateral cortical activity, applying to both sensory and motor activation. In view of our findings, it is plausible that the healthy arm compensating for the loss of function of the affected arm led to the increased cortical activation. In amputees, movements of the intact hand also showed increased cortical activity.
in the former sensorimotor hand territory of the affected hand. Accordingly, inclusion of intact hand engagement in rehabilitation has been suggested. This view corresponds with the framework of neural representation formation where formation depends on sensory input from the healthy limb.

**Motor execution**

We did not find any cortical activation differences between NBPP patients and healthy individuals during the actual flexion task. Apparently, in the adult NBPP patients we have studied, central pathways involved in elbow flexion recovered enough to result in a normal degree of activation. As said, cortical representation expands at the onset of learning a new motor skill and decreases when the skill is mastered. Impaired central motor programming in children with NBPP is supported by neurophysiological evidence and clinical observations. Our results suggest three possibilities: firstly, in children with NBPP motor cortical representation is expanded but decreases in time due to motor learning. Secondly, because motor execution is essentially a combination of planning and actual execution, the increased cortical activity during planning masks decreased cortical activity during pure execution. A decreased contralateral cortical activation has been found in the primary motor cortex during attempted movement in paraplegics compared to healthy controls. Thirdly, cortical activity in patients is increased to the level of healthy subjects due to higher biceps muscle activity in patients, suggested by the training session EMG recording.

**Limitations and consequences**

We did not measure biceps EMG activity during MRI scanning, so it remains possible that the tasks were carried out differently during scanning than intended. However, we feel that having an EMG-guided practice session was valuable as a quality control distinguishing motor execution and imagery. Another limitation might be that the NBPP population was heterogeneous in severity of the lesion, which may have affected our findings. However, in all patients at least a C5, C6 lesion was involved, affecting the biceps muscle as the main agonist of flexion, the focus of this study. In conclusion, motor imagery of elbow flexion in NBPP involves increased cortical activation. The increased activity points to an increased need for task attention, which in turn is probably caused by an interplay of motor and sensory components and the time of the lesion. It is unknown to what extent this central phenomenon affects daily functioning, and also to which extent it influences the ability to train arm function. Future studies should elucidate the role of the central nervous system in NBPP in more detail, focusing on a possibly shifting role over time. Effects of training focusing not only on the affected but also the healthy arm also deserve further study.

**Acknowledgements**

We thank Z.V. Angelov for his assistance with Matlab, B. Klaassens with data processing and F. Erthal for pointing out some valuable references to us.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
References

Table 1. Demographic details of the subjects with Neonatal Brachial Plexus Palsy (NBPP) (P1 – P17) and the healthy individuals (C1 – C17). Lesion extent groups: 1. C5 and C6 roots, 2. C5, C6 and C7, 3. C5 – C8 and 4. C5 – Th1. Degree of recovery assessed using MRC scale for muscle strength (0 = no movement observed, 5 = normal muscle contraction).

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (y)</th>
<th>Sex</th>
<th>MRC biceps</th>
<th>Affected arm</th>
<th>Lesion extent group</th>
<th>Dominant hand</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>21</td>
<td>F</td>
<td>5</td>
<td>L</td>
<td>2</td>
<td>R</td>
</tr>
<tr>
<td>P2</td>
<td>21</td>
<td>F</td>
<td>-</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>P3</td>
<td>29</td>
<td>F</td>
<td>4</td>
<td>R</td>
<td>1</td>
<td>R</td>
</tr>
<tr>
<td>P4</td>
<td>23</td>
<td>F</td>
<td>4</td>
<td>R</td>
<td>1</td>
<td>L</td>
</tr>
<tr>
<td>P5</td>
<td>35</td>
<td>F</td>
<td>5</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>P6</td>
<td>43</td>
<td>F</td>
<td>5</td>
<td>R</td>
<td>3</td>
<td>L</td>
</tr>
<tr>
<td>P7</td>
<td>29</td>
<td>M</td>
<td>5</td>
<td>R</td>
<td>4</td>
<td>L</td>
</tr>
<tr>
<td>P8</td>
<td>21</td>
<td>M</td>
<td>5</td>
<td>L</td>
<td>1</td>
<td>R</td>
</tr>
<tr>
<td>P9</td>
<td>53</td>
<td>F</td>
<td>4</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>P10</td>
<td>30</td>
<td>F</td>
<td>3</td>
<td>R</td>
<td>2</td>
<td>R</td>
</tr>
<tr>
<td>P11</td>
<td>24</td>
<td>M</td>
<td>5</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>P12</td>
<td>28</td>
<td>M</td>
<td>3</td>
<td>R</td>
<td>1</td>
<td>L</td>
</tr>
<tr>
<td>P13</td>
<td>64</td>
<td>F</td>
<td>5</td>
<td>L</td>
<td>2</td>
<td>R</td>
</tr>
<tr>
<td>P14</td>
<td>64</td>
<td>M</td>
<td>3</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>P15</td>
<td>22</td>
<td>M</td>
<td>5</td>
<td>L</td>
<td>3</td>
<td>R</td>
</tr>
<tr>
<td>P16</td>
<td>24</td>
<td>M</td>
<td>4</td>
<td>R</td>
<td>2</td>
<td>L</td>
</tr>
</tbody>
</table>

Table 2. Median (25th-75th percentile) biceps activation (sum of samples, in mV) during the EMG training session.

<table>
<thead>
<tr>
<th></th>
<th>NBPP patients</th>
<th>Healthy individuals</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imagery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected arm</td>
<td>27 (20-44)</td>
<td>30 (11-38)</td>
<td>0.822</td>
</tr>
<tr>
<td>Unaffected arm</td>
<td>22 (9-43)</td>
<td>10 (7-79)</td>
<td>0.142</td>
</tr>
<tr>
<td>Execution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected arm</td>
<td>153 (102-346)</td>
<td>105 (46-148)</td>
<td>0.034</td>
</tr>
<tr>
<td>Unaffected arm</td>
<td>115 (62-160)</td>
<td>102 (57-143)</td>
<td>0.759</td>
</tr>
</tbody>
</table>

L – left, R – right, M – male, F – female, y – years

NBPP - Neonatal Brachial Plexus Palsy
Figure 1. Increased cortical activation during the imagery flexion of a. the affected arm in right-handed Neonatal Brachial Plexus Palsy (NBPP) patients, b. the affected arm in left-handed NBPP patients, and c. the healthy arm in right-handed NBPP patients compared to healthy individuals. The red area shows $z>2.3$, $p<0.05$, corrected. The crossing of the green lines indicates the maximal voxel: a. $x=134$, $y=90$, $z=132$; b. $x=54$, $y=132$, $z=72$; c. $x=42$, $y=84$, $z=124$ in MNI-coordinates.