Functional plasticity in the human motor system after transfer of intercostal nerves to the biceps muscle

M. Elschot[1,2], S. A. Rombouts[3,4], M. J. Malessy[5], C. A. Schimmelpenninck[3,6], M. J. van Osch[3,4], I. Toni[1], D. G. Norris[1,7], M. A. van Buchem[3], and P. F. Buur[1,3]

[1]Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, Netherlands, [2]Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands, [3]Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands, Leiden, Netherlands, [4]Leiden Institute for Brain and Cognition, Leiden University, Leiden, The Netherlands, Leiden, Netherlands, [5]Department of Neurosurgery, Leiden University Medical Center, Leiden, Netherlands, [6]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [7]Erwin L. Hahn Institute for Magnetic Resonance, University Duisburg-Essen, Essen, Germany, Essen, Germany

Introduction

It is well-established that the adult brain exhibits plasticity as a result of learning, or damage to either the central and/or peripheral nervous systems. Studies on stroke, for example, have reported that the function of the lesioned brain region can shift to neighboring areas [1]. It is also observed that after nerve deafferentiation the region that is deprived of sensory input is 'invaded' by the adjacent regions, thereby acquiring a new function [e.g. 2]. In this study, functional reorganization of the motor system is investigated in a unique group of patients that suffered a traumatic brachial plexus avulsion (BPA) which resulted in a complete loss of biceps function. Following their injury, the patients had undergone a surgical procedure in which part of the nerves innervating the intercostal muscles, which are involved in breathing and posture control, were transferred to the biceps in an attempt to (partially) restore its function [3]. After an initial phase in which (deep) breathing was necessary for biceps contraction, recovery proceeded to a state of volitional control, independent of breathing [4]. Here, the neural changes associated with the rewiring of the brain, leading to the shift from breathing-induced biceps contraction to voluntary movement, are explored using functional MRI with a simple motor paradigm involving real and imagined contraction of the biceps.

Methods

Subjects Patients who had undergone nerve transfer were recruited after approval by the ethical committee of the Leiden University Medical Center. Patients showing no recovery, that underwent additional surgery to improve biceps function, and those with neurological problems were excluded from the study. In total, fourteen patients (12 men, mean age 34, age range 22-52, mean biceps strength 3.5 on MRC scale) were scanned. These were individually age and sex-matched with fourteen control subjects (12 men, mean age 34, age range 23-50).

Task The paradigm consisted of a 2 x 2 factorial design with factors ARM (left/ right) and MOVEMENT (execution/imagery) plus a baseline condition. Conditions were indicated using letters for ARM ('L' and 'R') in different colors for MOVEMENT (green for execution, red for motor imagery). During execution, subjects had to press their lower arm upwards against a restraining belt which was placed to achieve isometric contraction without co-contraction of the triceps. During imagery subjects had to imagine performing the exact same task without actually moving. Stimulus blocks were presented in pseudo-randomized order and lasted 30 seconds. For each subject, 3 sessions of 10 minutes each were acquired.

Data acquisition Scanning was done at 3T using an eight-channel coil for signal reception. A multi-echo parallel-accelerated GE-EPI sequence was used for functional imaging, covering the whole brain (30 transverse slices, interleaved multi-slice acquisition, slice gap 10%, voxels 3.5 mm^3, FOV 224 mm, matrix 64 x 64, TE 9/23/36/50/63 ms, TR 2.6 s, flip angle 90°. Echoes were combined to a single data set using weighted summation [5]. High-resolution T_1-weighted images were acquired for anatomical reference using an MP-RAGE sequence. Task performance was monitored by means of recording electromyography using surface-electrode EMG on both biceps.

Data analysis Preprocessing and statistical analysis were done using SPM5 (Wellcome Department of Imaging Neuroscience, London, UK). As the affected arm differed between subjects, data of left-affected patients and their matched controls was flipped along the left-right dimension and data for all subjects was normalized to a symmetric version of the MNI template. First-level statistical images were entered into a 2x2x2 random-effects ANOVA with factors GROUP (patient/control) x ARM (healthy/affected) x MOVEMENT (execution/imagery).

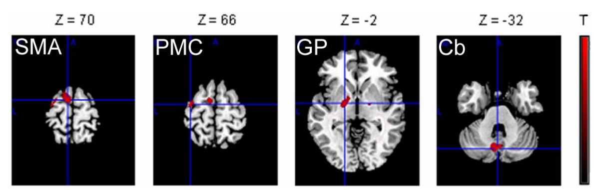

Fig. 1. Significant brain regions in between group contrast for motor execution > rest, patient > control group (p<0.001 uncorrected). Reverse contrast (control > patient group) shows no significant clusters.

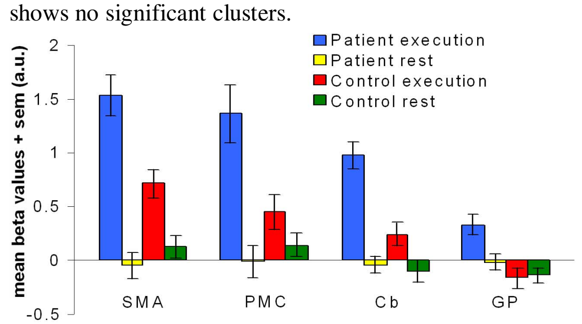

Fig. 2. Beta values for motor execution and rest for both patients and control group. While most areas are activated in both groups but stronger in patients, only the latter activate globus pallidus.

Results

Task performance as measured by EMG was equal for the two groups. Activation was found in expected brain regions for both patients and controls (p<0.05 whole brain FWE corrected). For execution, these included contralateral M1, premotor cortex (PMC), supplementary motor area (SMA) and ipsilateral cerebellum (Cb). Additionally, the patients showed activation in ipsilateral cerebellar vermis and bilateral globus pallidus (GP). For the imagery condition, SMA and middle frontal gyrus were activated in both groups. Significant between-group differences were only found for motor execution of the affected arm. Fig. 1 shows the significant areas for patients > control group, while the mean beta values for the task conditions are displayed in Fig. 2. For most regions, activation is present in both groups, but stronger in the patient group and, in the case of M1, shifted slightly medially. Globus pallidus is only activated in the patient group.

Discussion

The differences in brain activity between the patient group and healthy controls when performing biceps contraction are suggestive of cortical plasticity resulting from the peripheral rewiring. A medial shift of the M1 activation in the patient group might be indicative of involvement of the cortical area representing the respiratory muscles [6], which could be expected given the initial need to contract these muscles to achieve biceps contraction. Additionally, globus pallidus, which activates only in the patient group, has extensive inhibitory connections to the thalamus and basal ganglia and might be important for the breathing-independent biceps control by inhibiting the motor program for volitional breathing. These findings shed more light on the mechanisms responsible for reorganization of the healthy brain following peripheral nerve injury.

References

[1] Chen RLG, 2002, Neuroscience, 111(4): 761-73.
[2] Pons TP, 1991, Science, 252(5014): 1857-60.
[3] Malessy MJA, 1998, J Neurosurg 88: 266-71.
[4] Malessy MJA, 1993, Clin Neurol Neurosurg 95 Suppl: S95-102.
[5] Poser BA, 2006, Magn Reson Med, 55(6): 1227-35.
[6] McKay LC, 1995, J Appl Physiol 95(3): 1170-8.