Supplementary Motor Cortical Changes Explored by Resting-State Functional Connectivity in Brachial Plexus Injury

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■ BACKGROUND: **Brachial plexus injury (BPI) is a serious peripheral nerve injury, and clinical outcomes are generally unsatisfactory. It has been reported that cortical plasticity could influence the restoration of motor function. However, the neurologic mechanism of BPI is unclear, which provides a basis for further investigation. The supplementary motor area (SMA) plays an important role in the regulation of motor function. This study aims to explore SMA—whole brain functional connectivity after deafferentation of the brachial plexus.**

■ METHODS: **Study subjects included 16 patients with BPI and 8 healthy volunteers. The seed region was defined by a block-design functional magnetic resonance imaging program that used unilateral imaginary hand grasp motion as a task stimulus. Next, the voxel—wise functional connectivity between the predefined region and the other regions of the brain was calculated.**

■ RESULTS: **We discovered decreased voxel—wise functional connectivity between the SMA and multiple brain regions, including precuneus, posterior cingulum cortex, and anterior cingulum cortex, that are closely associated with information integration or motor processing in patients with BPI.**

■ CONCLUSIONS: **Patients with BPI showed weakened functional connectivity between hand grasp—related areas and the SMA and multiple regions associated with motor processing or information integration. A clear image of the functional status of the brain after deafferentation was provided. On the basis of this discovery, a relationship between changes in neuroimaging measurements and clinical outcomes can be determined in future studies.**

INTRODUCTION

The brachial plexus is a network of nerve fibers formed from the 4 lower cervical roots and the first thoracic root (C5-T1). Treatment for brachial plexus injury (BPI) is challenging because of the complexity of the brachial plexus and the variability in injuries. Restoration of motor function is disappointing, especially for patients with complete brachial deafferentation—induced total brachial plexus root avulsion.[1] Some research on motor function after stroke found that the extent of cortical plasticity influences the prognosis.[2] Whether or not cortical reorganization also has a positive effect on motor recovery in patients with neural deafferentation is an interesting question. However, little research has explored the neurologic mechanism of BPI, which is the basis for further investigation.

Motor function is considered to be 1 of the most complicated physiologic processes in humans. The cortical projection for the upper extremity is located mainly in the primary motor cortex. It has been reported that regions responsible for injured limbs display weaker connections with the supplementary motor area (SMA).[3] However, the regulation of motor function is not restricted to only the connection between the SMA and primary motor cortex. Brain regions including putamen[4,5] and premotor cortex[6,7] are also involved in motor preparation and execution. Isolated imaging of the local functional connectivity (FC) between the SMA and primary motor cortex is inadequate to examine cortical plasticity after deafferentation.

Key words

- Brachial plexus injury
- voxel-wise functional connectivity
- Supplementary motor area

Abbreviations and Acronyms

BPI: Brachial plexus injury
DMN: Default mode network
FC: Functional connectivity
MRI: Magnetic resonance imaging
ROI: Region of interest
SMA: Supplementary motor area

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Since Biswal et al.[8] discovered that low-frequency fluctuations (<0.08 Hz) between regions in bilateral somatosensory cortices demonstrate high-level correlation, functional neuroimaging technology has been widely used to examine FC between distinct brain regions. It is believed that 2 cortical regions that have a high level of synchrony of low-frequency fluctuations of magnetic resonance imaging (MRI) time courses are likely to be functionally connected.[9,10] The method of calculating FC has been widely adopted in the exploration of interregional relationships. It is a noninvasive method and can be used to track global neurophysiologic changes in the brain.[11] It is also an ideal assessment of motor function after deafferentation of the brachial plexus on the whole-brain scale. The changes in connections between the SMA and the rest of the brain after deafferentation remain a fascinating topic. These changes form the basis for our investigation into motor function restoration.

MATERIALS AND METHODS

Participants

Study participants included 16 patients with BPI and 8 normal volunteers. All experimental procedures were carried out under the supervision of the Medical Ethical Committee of Huashan Hospital, and the Rights of Informed Consent were guaranteed. The patient group consisted of 8 male patients with right-side injury and 8 male patients with left-side injury. The patients underwent surgical treatment after their MRI scan. The diagnosis of BPI was determined by myelography, ultrasound, and electromyography. The diagnosis was confirmed by a subsequent surgical procedure with a direct view of the complete avulsion of the C5-T1 root. All patients were right-handed, and the age range was 20—52 years. The time interval between the injury and the functional MRI scan was 1—9 months. All participants had an intact cerebral cortex and denied neuropathic disorders.

Data Acquisition

For scanning, participants lay supine in the head coil of a GE Signa VH/i 3-tesla scanner (GE Healthcare, Shanghai, China). The participants' heads were fixed with the help of foam pillows and a belt over the forehead to minimize head movements. The gradient echo planar imaging sequence parameters used for acquisition of the functional images were as follows: repetition time = 2000 ms; echo time = 35 ms; flip angle = 90°; field of view = 240 × 240 mm; acquisition matrix = 64 × 64; and voxel resolution = 3.75 × 3.75 × 5 mm. Each volume had 33 slices. When the structural images were collected, we used a three-dimensional spoiled gradient-recalled acquisition sequence. We acquired 1-mm-thick axial sections. The parameters were as follows: repetition time = 1000 ms; echo time = 5 ms; flip angle = 200°; interslice space = 0 mm; field of view = 240 × 240 mm; acquisition matrix = 256 × 256; and number of excitations = 1.

Experimental Paradigm

A resting-state MRI scan was first scheduled for all participants. The participants were required to avoid any structural thinking. Next, a 400-second-long MRI scan was arranged for all participants. In addition to the resting-state MRI scan, we arranged a task for the healthy participants. The participants were instructed to imagine completing a hand grasping motion characterized by repeated flexion and extension of the 5 fingers. In the imagery task, the participants were required to follow instructions and repeat the imaginary movement in their minds. The block of imaginary hand grasps lasted for 30 seconds, alternating with 30-second rest periods. The participants were required to keep calm during the rest period and to avoid unnecessary movements during the scan. The participants had to relax their bodies completely with no tactile muscle contraction. The right-hand and left-hand imaginary tasks were completed in 2 separate sessions. Data from the 2 motor imagery tasks were used for region of interest (ROI) definition. All participants underwent the MRI scan with eyes closed.

Preprocessing Procedures

After collecting the data, we used SPM8 software (Wellcome Department of Imaging Neuroscience, University College London, London, United Kingdom) implemented in MATLAB version 2010b (MathWorks, Natick, Massachusetts, USA) to analyze the MRI images. We also used the Data Processing Assistant for Resting-State fMRI: Advanced Edition (DPARSFA; C.-G. Yan and Y.-F. Zang, State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, China). Standard image preprocessing was carried out as follows. The first 10 time points were removed. Images from each participant were realigned and corrected for slice timing. The T1-weighted structural image was normalized to a Montreal Neurological Institute template. Next, the functional image volumes were normalized with the parameters derived from the structural volume. These images were subsequently smoothed with a Gaussian kernel of 6 mm. The linear trend from each session was removed. We set a range of 0.01—0.08 Hz for the temporal band-pass filter to obtain low-frequency fluctuations, which were considered to reflect spontaneous neuronal activity. The covariance with signals from cerebrospinal fluid, white matter, whole brain, and 6 parameters obtained by rigid body head motion correction[12,13] were also regressed out.

Localization of ROIs

The healthy participants were required to complete 2 motor imagery tasks in a block design experiment with alternating 30-second stimuli onset and 30-second rest blocks. During the onset stage, participants were asked to perform an imaginary left-hand or right-hand grasp motion. Both tasks led to activation in the SMA.

Using the general linear model, the activated area in the SMA was detected with a threshold of $P < 0.01$ and extracted as an ROI. The left-hand and right-hand imaginary motion task triggered different activated areas in cerebral cortex, which were defined as 2 different ROIs. The peak point of each ROI was listed as follows: 12, −4, 64 for left-hand imaginary task and −4, 10, 46 for right-hand imaginary task.

Voxel-Wise FC

After we acquired the ROI derived from the block-design results, we calculated correlation coefficients between the average time course of the seed region and time courses of all other voxels in the brain. The ROI determined by the right-hand imaginary motion task was applied to the patients with right-side BPI, and the ROI from the