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Cerebral plasticity after contralateral cervical nerve transfer in human by longitudinal PET evaluation

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ABSTRACT

Object: The treatment of brachial plexus avulsion injury remains a challenging problem. Admittedly, central nervous mechanisms play a significant role in the motor recovery of the paralyzed hand after peripheral nerve surgery. The present study aimed at investigating the relationship between cerebral reorganization and motor recovery after a unique peripheral crossing nerve transfer surgery in brachial plexus injury patients.
Methods: In the present study, two brachial plexus avulsion injury patients with were followed up for 4 years after contralateral C7 nerve transfer surgery. In the surgery, an intact nerve root from the intact limb was transferred to repair the injured nerves. One patient showed a good motor recovery in the paralyzed hand while the other showed relatively poor outcomes. In the longitudinal follow-up, 9 PET scans of the brain were conducted in both patients at regular intervals of every 6 months. A correlation analysis between cerebral glucose metabolism and flexion power of the paralyzed wrists and fingers was performed to investigate the involvement of brain reorganization during the process of motor recovery.
Results: The cerebral glucose metabolism in the corpus callosum, premotor cortex (Broadmann Area 6) and the precuneus were found positively correlated with the motor recovery of the paralyzed hand in Patient A ($P < .01$). Positive correlation between the cerebral glucose metabolism and the motor recovery of the paralyze hand was only present in the corpus callosum in Patient B ($P < .01$).
Conclusion: Corpus callosum, premotor cortex and precuneus were related with motor recovery after contralateral cervical nerve transfer surgery. The accumulating activation of these cortical regions potentially represented the recovery of high-order motor networks and may have facilitated the motor recovery.

1. Introduction

Peripheral nerve injuries resulting in sensory deafferentation and motor differentiation could cause a series of dysfunctions. Besides, it has been widely reported that the interruption of peripheral neural pathway has exerted influence on the finely-constructed cortical map. Peripheral nerve injuries trigger cerebral plasticity at multiple levels, including cortical and subcortical areas. Wang et al. reported that patients with definite reinnervation of muscle still suffered from poor hand motor function [1]. Meanwhile, another study pointed out those younger patients who do not have satisfied electrophysiological results still enjoyed good clinical outcome [2]. Multilevel cellular, chemical and functional changes from the fingertips to brain cortex were considered influencing factors of motor and sensory functions restoration after surgery [3]. With the support of evidence, the restoration of hand motor function is believed to share a close relationship with the remodeling of central nervous system rather than peripheral factors [4,5].

A previous study has already explored the central remodeling process in the sensorimotor cortex after peripheral nerve injury [6]. Our experimental study in rats revealed a striking dynamic process of interhemispheric plastic reorganization after contralateral C7 nerve (CC7) transfer surgery from the contralateral side to the injured forepaw [7]. Subsequently, we observed patients who suffered brachial plexus avulsion injury (BPAI) treated by

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CC7 transfer showed interhemispheric cortical reorganization which was indicated by PET scanning. Sensorimotor cortex, especially supplementary motor area (SMA) also impose a significant role in the process of the cortical reorganization [8]. This pattern of cortical reorganization made great contributions to the good functional recovery after surgery. However, based on the literature, the brain regions that benefit the sensorimotor recovery still remains an interesting topic for scholars.

To find the answer to this interesting topic, we performed longitudinal PET scans, which may contribute to a better understanding of cortical reorganization after CC7 transfer. In this work, two BPAI patients with CC7 transfer were recruited for long-term follow-up. One showed a good functional restoration of the paralyzed hand while the other proved to be relatively poor (as shown in Table 1). The EMG results and Tinel's sign determined the reinnervation of C7 in both of them after the surgery. The evaluation of longitudinal PET imaging of the two patients demonstrated the different central remodeling process following peripheral injury and neurotization.

2. Methods

2.1. Patient population

Two right-handed male patients aged 37 and 39 years old were recruited. The intervals between trauma and CC7 nerve transfer surgery were 3 months. Both of them had suffered from left C5-T1 nerve roots complete avulsion. Before surgery, the diagnosis was made by physical examination, electromyography (EMG) and ultrasound and confirmed by surgical exploration and intraoperative EMG. Both of them had an intact cerebral cortex and denied neuropathic disorders.

2.2. Surgical procedure

In both cases, the entire trajectories of the left brachial plexuses were exposed. Definite diagnosis of total avulsion of spinal nerves from C5 through T1 was confirmed during the surgical exploration.

A complete CC7 transfer surgery [9,10] was divided into two stages with an interval of 8 months. The first stage of the operation was performed at 3 months after BPAI in both patients. At the first stage, the contralateral (right side) C7 nerve was cut off at the distal end of the trunk. The vascularized ulnar nerve on the paralyzed side (left side) was cut off at the wrist level. Then, the ulnar nerve was used as graft to coaptate with the CC7 nerve through the anterior cervical subcutaneous route. At the second stage of CC7 nerve transfer, the ulnar nerve on the paralyzed side was cut off at the axillary level and coaptated with the proximal median nerve to restore flexion function of the wrist and fingers. The PET scans were performed in both patients pre-operatively and every 6 months after the second stage of the surgery. The follow-up duration was 53 months totally in both patients.

2.3. Clinical evaluation

Both patients were followed up for more than 4 years (at an interval of 6 months). The flexion power of the wrist and fingers were assessed according to the Medical Research Council muscle strength grading system, with a scale ranging from M0 to M5. The nerve regeneration was evaluated by EMG. At each follow-up visit, clinical assessment, EMG test and PET scan were performed.

2.4. PET studies

During the PET scan, the subject's head was fixed to the scanner bed with a headband, with eyes covered and ears plugged.

2.5. PET scans

The PET scans were performed with a Siemens Biograph 64 PET/CT (Simens, Germany) in three-dimensional (3D) mode. This scanner acquires 63 slices with an interslice spacing of 2.43 mm. Totally, the PET scanner had axial view of 15.5 cm with no interplane dead space, ensuring the coverage of the brain from the vertex to the lower cerebellum. The PET cerebral glucose metabolism (CGM) scan started 30 min after an intravenous bolus injection of 5 mCi of ^{18}F-FDG. In addition, a 10-min emission scan was conducted for attenuation correction. Hanning filters were used, providing a transaxial and axial cut-off frequency of 0.5. No arterial blood sampling was performed.

2.6. Analysis of CGM data

Preprocessing of imaging data were performed by SPM 5 toolbox (including Wellcome Department of Cognitive Neurology, Institute of Neurology, University College of London) program implemented in the Matlab (Mathworks, Inc.). Prior to statistical analysis, all images were spatially normalized into the Montreal Neurological Institute (Chemnitz et al.) (McGill University) standard template to remove the inter-subject anatomic variability. The Affine transformation was conducted to determine the 12 optimal parameters used to register the brain on the template. Subtle differences between the transformed image and the template were removed with the application of the nonlinear registration method in which the weighted sum of the predefined smooth basis functions was applied in discrete cosine transformation. Spatially normalized images were smoothed by convolution based on an isotropic gaussian kernel with 10-mm FWHM. The smoothing aimed at increasing the signal-to-noise ratio as

Table 1
Demographics and clinical materials of 2 brachial plexus avulsion patients before and after contralateral C7 nerve transfer.

Time Course	Muscle power		Movement Patten	
	Patient A	Patient B	Patient A	Patient B
Pre-operation	M0	M0	None	None
Stage I of the operation	M0	M0	None	None
Stage II of the operation	M0	M0	None	None
6 months after the 2nd operation	M0	M0	None	None
12 months after the 2nd operation	M1	M0	Associate Movement	None
18 months after the 2nd operation	M2	M1	Associate Movement	Associate Movement
24 months after the 2nd operation	M3	M1	Associate Movement	Associate Movement
30 months after the 2nd operation	M3+	M1	Independent Movement	Associate Movement
36 months after the 2nd operation	M3+	M2	Independent Movement	Associate Movement
42 months after the 2nd operation	M4	M2	Independent Movement	Associate Movement

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