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Sensory cortical re-mapping following upper-limb amputation and subsequent targeted reinnervation: A case report

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ABSTRACT

This case study demonstrates the change of sensory cortical representations of the residual parts of the arm in an individual who underwent a trans-humeral amputation and subsequent targeted reinnervation (TR). As a relatively new surgical technique, TR restores a direct neural connection from amputated sensorimotor nerves to specific target muscles. This method has been successfully applied to upper-limb and lower-limb amputees, and has shown effectiveness in regaining control signals via the newly re-innervated muscles. Correspondingly, recent study results have shown that motor representations for the missing limb move closer to their original locations following TR. Besides regaining motor control signals, TR also restores the sensation in the re-innervated skin areas. We therefore hypothesize that TR causes analogous cortical sensory remapping that may return closer to their original locations. In order to test this hypothesis, cortical activity in response to sensory-level electrical stimulation in different parts of the arm was studied longitudinally in one amputated individual before and up to 2 years after TR. Our results showed that 1) before TR, the cortical response to sensory electrical stimulation in the residual limb showed a diffuse bilateral pattern without a clear focus in either the time or spatial domain; and 2) 2 years after TR, the sensory map of the reinnervated median nerve reorganized, showing predominant activity over the contralateral S1 hand area as well as moderate activity over the ipsilateral S1. Therefore, this work provides new evidence for long-term sensory cortical plasticity in the human brain after TR.

1. Introduction

Changes in cortical mapping begin seconds after the loss of the limb and can continue to change years after the injury (Kaas et al., 1983; Merzenich et al., 1983; Merzenich and Jenkins, 1993). Previous studies have found that following upper extremity amputation, cortical sensory representations for the adjacent intact areas extend to cortical regions corresponding to the absent hand (Elbert et al., 1997; Grusser et al., 2001). Other studies have found that in human arm amputees, the cortical reorganization contralateral to the amputation spreads bilaterally to both hemispheres (Bjorkman et al., 2007a,b).

After immediate hand replantation and long-term hand transplants, hand function recovery has been reported to be associated with cortical reorganization. Although results related to motor cortical reorganization following repair are more readily available, few studies have reported sensory cortical reorganization on human subjects after nerve repair (Bjorkman et al., 2007a,b; Blume et al., 2014). In previous studies from Bjorkman et al. (2007a,b), sensory cortical remapping on one patient who underwent an immediate surgical hand replantation was reported. Twelve months after the surgery, the primary somatosensory cortex was found to reorganize with the activation pattern to be more bilateral compared to an able-bodied hand (Bjorkman et al., 2007a). Two years after the surgery, predominantly contralateral somatosensory cortex activation was reported (Bjorkman et al., 2007b). Similarly, animal studies reported that median nerve regeneration in adult owl monkeys showed the reestablishment of topographic representations for localized skin areas, although in a limited extent (Wall et al., 1986). These results provided evidence for reorganization of cortical sensory representation to a pattern closer to the 'intact' case after nerve repair.

As a relatively new surgical approach following amputation, targeted reinnervation (TR) provides a novel and fundamentally different way for nerve repair in that it denervates specific muscles and skin regions (Kuiken, 2003; Kuiken et al., 2004; Hijjawi et al., 2006), and then reinnervates them with the residual nerves of the amputated limb. After TR, the reinnervated muscles can act as a natural biological amplifier to enhance the efferent motor command signal, allowing for the control of a multi-degree of freedom myoelectric prosthesis. As

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compared to transplantation, TR is less costly, requires less time in hospital and for recovery, and can be applied to a wider amputee population (see a review for the comparison between transplantation and TR (Agnew et al., 2012)). It has been demonstrated that several months after TR, new functional connections between the nerves and muscles can be created, which restores motor function (Agnew et al., 2012). Correspondingly, a close to 'normal' motor cortical map for the missed limb related to motor task performance can be re-established (Chen et al., 2013). Besides recovery of motor function, TR also causes return of sensations of touch, pressure, vibration and temperature for the missing limb of the skin overlying reinnervated muscles (Kuiken et al., 2007a,b; Marasco et al., 2009). If indeed cortical restoration of original spatial maps is an important metric for the effectiveness of a restoration method, it will be of great importance to test whether TR successfully restores the sensory cortical representation as well. However, both short-term and long-term cortical changes in spatial mapping associated with TR-induced sensory recovery are still unknown. To answer this question, we used high-density electroencephalography (EEG) to identify and quantify cortical activity in response to stimulating the middle finger of the intact limb and the residual median nerve of the amputated limb in one session before and three sessions after targeted reinnervation surgery in an individual who underwent TR.

2. Methods

2.1. Subject

A 24-year-old, right hand dominant male, who sustained a traumatic injury and a left trans-humeral amputation in July 2007, was recruited for this study. The subject has used a prosthesis since October of 2007. He wears it for several hours a day and uses it to help him hold objects, fold clothes, drive and open letters. Initially post-operation, he reported that he had some phantom limb sensation. However, when we recruited him in 2008, he said that the phantom limb pain was gone, and that he only occasionally experienced phantom limb sensation and that this was not bothersome to him. The first set of experimental data were collected in August 2008, 1 week before his targeted reinnervation (TR) surgery. As shown in Fig. 1, during the TR surgery, the median nerve was transferred to the medial head of the biceps; the distal radial nerve was transferred to the lateral head of the triceps; and the ulnar nerve was transferred to the motor reinnervation point of the brachialis. Subcutaneous fat was removed over the biceps and triceps to increase the EMG signal magnitude for subsequent myoelectric control. The fat removal denervated some of overlying skin enabling hand afferents to reinnervate the participant's skin after several months. When this section of skin was touched after reinnervation occurred, he felt his missing hand. Post-TR, three sets of data were collected in January and July of 2009 and June 2010.

To verify the reliability of our experimental protocol and data processing, we also recruited one age-matched able-bodied right hand dominant control participant (age: 24 years old). Two sets of data were collected in the able-bodied control participant on March 23rd, 2010 and April 13th, 2010.

All studies were approved by the Institutional Review Board of Northwestern University and in compliance with the principles of the Declaration of Helsinki with written consent provided by the participants prior to participation.

2.2. Experimental protocol

In each of the participants, we first searched for the stimulation site and intensity using constant current square-wave pulses that were delivered by a Compex II stimulator (Compex Medical SA, Ecutens, Switzerland) with pulse width at 0.3 ms long, and interstimulus interval at 200 ms. When determining the stimulation site, we searched for the location where the subject felt the most focused sensation of one of the four fingers. Then, the intensity was set to the highest amplitude that the participant could tolerate without losing focus or causing discomfort, pain, or detectable muscle contractions. The amputee subject reported the strongest and most focused sensation of the tip of his missing middle finger when stimulating the reinnervated median nerve site, although also with faint sensation of his thumb and elbow. As reference, we also recorded somatosensory-evoked potentials (SEPs) while stimulating the tip of his middle finger from the intact side. For each site, 2000–3000 trials of SEPs were recorded in 2 or 3 blocks of 1000, with at least 5 min of resting time between each block. During all of the experiments, the amputee participant remained relaxed and tried to avoid eye movements. The middle finger from the

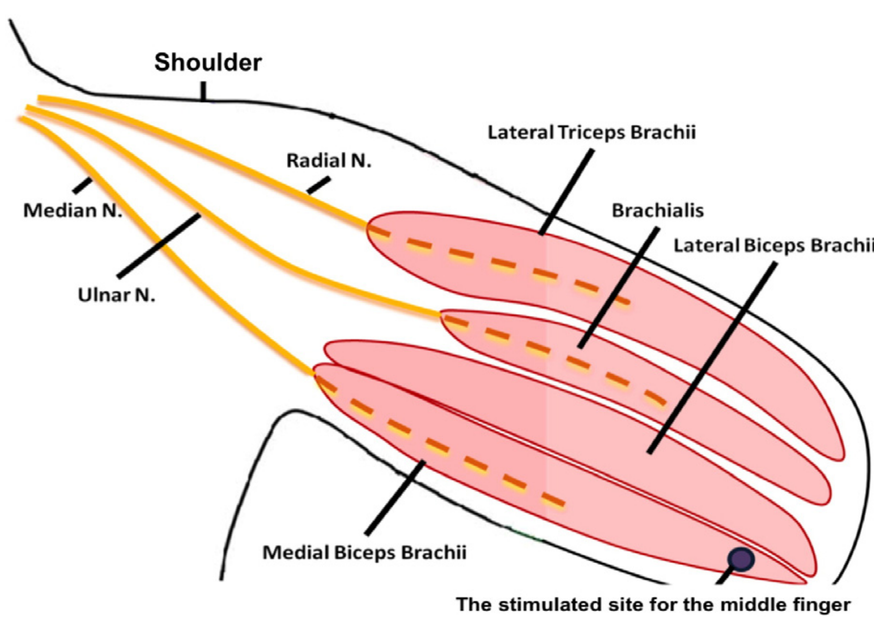

Fig. 1. Schematic of the targeted reinnervation (TR) procedure for the amputee subject.