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Recovery function of somatosensory evoked brain response in patients with carpal tunnel syndrome: A magnetoencephalographic study

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HIGHLIGHTS

- The N20m component to paired median nerve stimulation recovered earlier in CTS patients than controls.
- Distance of N20m equivalent current dipoles to first and middle finger stimulation was shorter in CTS than controls.
- CTS is associated with disinhibition and abnormality of somatotopic organization in primary somatosensory cortex.

ABSTRACT

Objective: The recovery function of somatosensory evoked magnetic fields (SEFs) was recorded to investigate excitatory and inhibitory balance in the somatosensory cortex of patients with carpal tunnel syndrome.
Methods: SEFs were recorded in patients and controls. Recordings were taken following median nerve stimulation with single and double pulses with interstimulus intervals of 10–200 ms. The root mean square for the N20m component following the second stimulation was analyzed. SEFs following stimulation of the first and middle digits were also recorded and the location for the equivalent current dipoles was estimated in three-dimensional planes.
Results: Distances on the vertical axis between the equivalent current dipoles for the first and third digits were shorter in patients than in control participants. The root mean square for the N20m recovered earlier in patients compared to controls; this was statistically significant at an interstimulus interval of 10 ms. There was no relationship between N20m recovery and the equivalent current dipole location in the primary somatosensory cortex.
Conclusions: Carpal tunnel syndrome was associated with functional disinhibition and destruction of the somatotopic organization in the primary somatosensory cortex.
Significance: Disinhibitory changes might induce a maladaptation of the central nervous system relating to pain.

1. Introduction

Brain plasticity refers to the brain's ability to reorganize itself throughout life, which can occur according to peripheral and central conditions (Pascual-Leone et al., 2005). For example, plastic

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changes in the brain have been observed following peripheral lesions (Mohanty et al., 2015; Navarro et al., 2007), as well as lesions in the central nervous system (Isa and Nishimura, 2014; Nudo, 2007). These changes can be adaptive or maladaptive, but the outcome cannot be predicted based on the location of the primary lesion (Nava and Röder, 2011). Adaptive changes result in behavioral developments such as gaining knowledge, skills, and adaptation to physical disability caused by injury or diseases (Kujala and Näätänen, 2010). On the other hand, maladaptive changes have been found to induce distortion in mental and physical balance, which can cause abnormal sensation, movement, and behavior (Baliki et al., 2011; Johnston, 2004; Nava and Röder, 2011).

The hand area occupies a relatively large area in the primary sensorimotor cortex compared to other parts of the body. For this reason, it has been a target for investigations of brain plasticity in experimental (Jenkins et al., 1990; Merzenich and Jenkins, 1993; Spengler et al., 1995) and clinical studies (Dhond et al., 2012; Maeda et al., 2013; Napadow et al., 2007). As reviewed by Lundborg (2000, 2003), the reorganization of peripheral anatomical and functional structures following hand surgery would not be possible without brain plasticity.

One of the most common peripheral neuropathies is carpal tunnel syndrome (CTS), which is caused by entrapment of the median nerve at the wrist. Motor consequences of CTS include weakness with wasting of intrinsic hand muscles that are innervated by the median nerve. Sensory symptoms include paresthesia in the median nerve territory, and pain that is sometimes unbearable in the early and chronic stages of CTS (Middleton and Anakwe, 2014). Based on what is known about plasticity, CTS should be accompanied by plastic changes in the brain (Lundborg, 2000, 2003). Although structural changes in the brains of patients with CTS have indeed been reported (Dhond et al., 2012; Maeda et al., 2013; Napadow et al., 2007), functional neural changes have yet to be uncovered. We hypothesized that functional changes in the central nervous system could be another aspect of the pathophysiology of peripheral nerve lesions, and that brain function in patients with CTS might give us biological information related to treatment outcomes. Recent advances in imaging techniques, such as functional magnetic resonance imaging, have enabled us to visualize structural and hemodynamic functional changes in the human brain (Maeda et al., 2013; Napadow et al., 2007). Magnetoencephalography (MEG) has also been a powerful tool to investigate neural activity, with high temporal resolution and reliability for source estimation (Maeda et al., 2013; Pizzella et al., 2014).

In the present study, we used MEG to investigate changes in somatosensory neural function in patients with CTS. One recent study has suggested that the balance between excitatory and inhibitory neural functions plays an important role in brain plasticity, and that inhibitory neurons are involved in regulating neural network activity (Froemke, 2015). While excitatory responses to stimulation have been conventionally investigated by evoked cortical responses, specific recording techniques of evoked cortical responses, namely the recovery function, have enabled inhibitory neural function to be assessed (Goto et al., 2015; Hoshiyama and Kakigi, 2002, 2001). Therefore, we recorded somatosensory evoked cortical magnetic fields (SEFs) following median nerve stimulation, focusing on excitatory and inhibitory function in the primary somatosensory cortex (SI). To our knowledge, this has not previously been investigated. To elucidate the inhibitory function in the SI, we analyzed the recovery function of SEFs following paired stimulation of the median nerve.

2. Methods

Two experimental protocols to record SEFs were used. First, SEFs were recorded following sensory stimulation of the first and third digits in the affected side of patients with CTS and the right side of control participants. Second, recovery function of SEFs was recorded following median nerve stimulation in the affected side of patients with CTS and the right side of control participants.

2.1. Participants

Eleven patients with CTS (5 male and 6 female; mean age 66.8 ± 10.4 (SD) years) and 21 age-matched healthy controls (12 male and 9 female; mean age 68.0 ± 7.4 years) participated in the study. The diagnosis of CTS was based on a history of dysesthesias in the distribution of the median nerve and a positive provocative test (Iwatsuki et al., 2014). Patients were first treated conservatively with splinting, medication, and/or intra-carpal tunnel steroid injection. To confirm the diagnosis, nerve conduction studies were carried out. Eight patients had bilateral CTS, two patients had CTS on the right side, and one patient had CTS on the left. Patients with symptoms regarding other nerves or with history of psychological or neurological disorders were excluded from the study. Control participants had neither clinical symptoms nor history of peripheral or central neurological diseases, and the median sensory nerve conduction between the third digit and the right wrist was normal. Informed consent was obtained from all participants prior to the study, and the study was approved by the Ethics Review Committee of the Faculty of Medicine, Nagoya University, Aichi, Japan.

2.2. SEFs following finger stimulation

The first and third digits were separately stimulated using pairs of ring electrodes. Stimulus electrodes were placed around the base (cathode) and interphalangeal joint (anode) of the first digit, and the proximal (cathode) and distal (anode) of the third digit. Square wave pulses, with a duration of 0.2 ms and an intensity of 1.5 times the sensory threshold for each participant, were delivered at 2 Hz on one of the fingers of one hand in random order. Both hands were tested for the patients and the right hand only was tested for the control participants.

2.3. Recovery function

Our method to assess the recovery function of SEF has been described in previous studies (Hoshiyama and Kakigi, 2002, 2001; Goto et al., 2015). The median nerve was stimulated at the wrist using square wave pulses with a duration of 0.2 ms, and with a supra-motor threshold that evoked a slight twitch of the thenar muscle with each stimulus. Single or double pulses with interstimulus intervals (ISIs) of 10, 40, 80 or 200 ms were delivered randomly. The interval between the single or double stimulation was 0.75 s.

2.4. Magnetoencephalography recording

MEG signals were recorded in a magnetically shielded room using a whole-head MEG system (PQ-1160C, Yokogawa Electric Co., Japan) with a liquid helium recycler (HCS-MEG1, FTI, Japan). The MEG system included 160-channel axial-type first-order gradiometers with a 50 mm long baseline detection coil. The gradiometers were arranged in a uniformly distributed array on a helmet-type dewar. The sampling frequency was 5000 Hz and an initial bandpass filter was between 0.3 and 2000 Hz.

MEG signals were recorded for 0.5 s from the onset of the electrical stimulus in each stimulus condition. Epochs with MEG signals more than 3pT were automatically rejected. A total of 150 epochs for each stimulus condition were collected and averaged for the final analysis.