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Illusory movements prevent cortical disruption caused by immobilization

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ABSTRACT

Enforced limb disuse strongly disrupts the cortical networks that are involved in sensorimotor activities. This disruption causes a cortical reorganization that may be functionally maladaptive. In this study, we used functional magnetic resonance imaging (fMRI) to investigate whether it is possible to prevent this reorganization by compensating for the lack of actual kinesthetic perception with illusory movements induced by "neuromimetic" proprio-tactile feedback that is artificially delivered during immobilization. Sixteen healthy volunteers were equipped for five days with full-hand ortheses that prevented them from performing finger and hand movements but allowed for kinesthetic and tactile sensations. Eight participants received a twice-daily proprio-tactile treatment consisting of the perception of kinesthetic sensations resembling those felt during actual movements generated by miniature vibrators set in the ortheses at the finger and wrist levels. Eight untreated participants received no stimulation. The effects of hand immobilization and treatment were assessed by fMRI during a calibrated voluntary hand movement task and hand tactile stimulation before cast placement and immediately after cast removal. We found that the sensorimotor network was preserved in subjects who underwent this treatment during hand immobilization, while the sensorimotor network of untreated subjects was significantly altered. These findings suggest that sensory feedback and associated movement perception may counteract disuse-induced cortical plastic changes through recruitment of a large part of the cortical network used for actual performed movement. The possibility of guiding cortical plasticity with proprioceptive augmented feedback is potentially relevant for rehabilitation efforts.

Introduction

Human and animal studies have led to the concept of use-dependent plasticity, according to which neuroplastic changes dependent on environmental requirements such as learning or pathological conditions may occur in cortical organization of an adult nervous system (Granert et al., 2011; Kaas et al., 1983; Ungerleider et al., 2002). Cortical rearrangement that encodes the kinematic parameters of a practiced movement has been observed after only 30 min of repetitive finger movements (Classen et al., 1998), or following long-lasting learning of skilled motor activities in musicians (Elbert et al., 1995) or blind Braille readers (Pascual-Leone et al., 2005). Functional remapping also appears as a consequence of sensory or motor restriction, following cortical or spinal cord injury (Topka et al., 1991), limb amputation (Chen et al., 1998; Giraux et al., 2001), hand dystonia (Rosenkranz et al., 2009) or peripheral deafferentation (Rossini et al., 1996; Tinazzi et al., 1998). Few studies have explored the cortical effects of transient enforced non-use of a limb caused by serious sprain or a fracture requiring a cast for several weeks. Transcranial Magnetic Stimulation (TMS) studies on patients with limb fractures reached contradictory conclusions, finding that the corticomotor representation of the immobilized limb muscle either decreased (Liepert et al., 1995) or remained unchanged, with variable effects on motor-evoked potentials amplitude (Facchini et al., 2002; Lundbye-Jensen and Nielsen, 2008; Zanette et al., 1997, 2004). Structural changes were also recently shown in the contralateral primary motor cortex of patients with writer's cramp after four weeks of hand immobilization (Granert et al., 2011). Using a voxel-based-morphometry method, they observed a decrease in the grey matter along with a concurrent decrease in cortical excitability, as attested by patients' responses to TMS. Interestingly, subsequently increasing these patients' hand activity for eight weeks sufficed to reverse the effects of immobilization, resulting in opposite changes in both the regional grey matter and motor hand area excitability. As mentioned by these authors "this activity-driven bi-directional plasticity" is functionally relevant since structural changes are mirrored by changes in regional excitability. Data recently published by Langer et al. (2012) support consistently these results. In a study involving the use of similar methods on subjects with various upper limb injuries requiring two weeks of immobilization, these authors found that the cortical thickness in the contralateral primary motor and sensory areas decreased as well as the fractional anisotropy of contralateral corticospinal

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tract. In addition, they established that these changes were associated with a skill transfer from the right injured to the left intact hand.

Thus while neural plasticity can be viewed as an adaptive mechanism of the nervous system for learning or to compensate for brain damage, it can be functionally maladaptive following periods of disuse by inducing motor disorders that are liable to delay recovery. By disrupting the action/perception loop, limb immobilization not only makes action impossible but also prevents the brain from receiving kinesthetic information from the peripheral part of the body involved. Based on the observation that vibration can induce illusory sensations of movement (Goodwin et al., 1972; Roll and Vedel, 1982) and activate the corresponding motor areas (Duclos et al., 2007; Kavounoudias et al., 2008; Naito and Ehrsson, 2001; Naito et al., 1999; Romaiguere et al., 2003), we wondered whether it is possible to use plasticity to prevent corticomotor disruption during transient limb immobilization by providing augmented proprio-tactile feedback during this period. The results of various studies (Naito and Ehrsson, 2001; Naito et al., 1999; Romaiguere et al., 2003) have shown that applying vibratory stimulation evokes similar patterns of cerebral activation to those evoked by an actual movement, especially in contralateral sensorimotor cortex (S1M1), bilateral supplementary motor area (SMA), dorsal premotor (PMd), posterior parietal and cingulate cortices. Interestingly, Romaiguere et al. (2003) reported that these activations disappeared in the premotor and cingulate cortices and that they were substantially reduced in the contralateral S1M1 and the bilateral SMA when two antagonist wrist muscles were stimulated at the same vibration frequency known to activate muscle spindle endings without giving rise to any illusory sensations of movement. Naito et al. (1999) have also established that when purely tactile 10-Hz or 220-Hz vibration is applied to a subject's wrist without inducing any kinesthetic sensations, no cortical motor activation occurs. On the contrary, by contrasting a vibration-induced illusory movement condition versus a pure tactile vibration condition, these authors showed that kinesthetic illusions are specifically associated with primary motor cortex, SMA, PMd and cingulate cortex activations.

Specific patterns of stimulation were therefore designed using a "proprioceptive model" (Roll et al., 2009) to generate "neuromimetic" vibration sequences giving rise to muscle and tactile afferent firing patterns mimicking those recorded during actual movements. Kinesthetic and tactile sensations were elicited via miniature vibrators inserted into a full-hand orthesis preventing subjects from performing right hand movements. Half of the subjects were exposed daily to these virtual hand movements, whereas the other half was not. Using fMR imaging methods, we assessed the effects of hand immobilization by comparing the activations occurring in the sensorimotor network of these two groups of subjects during a voluntary hand movement task and during a tactile finger stimulation, before placing the orthesis and immediately after its removal. We hypothesized that giving subjects the realistic feeling that their limbs were moving while wearing the cast by artificially inducing proprio-tactile inputs would compensate for the lack of natural feedback and might help to preserve the underlying cortical structures.

Materials and methods

Participants

Sixteen healthy, right-handed volunteers (10 women, 6 men, mean age: 28 years, range: 22–35 years) gave their written informed consent to participate in the fMRI experiments, which were approved by the local ethics committee. None of the subjects had fMRI contraindications.

Orthesis and "proprio-tactile treatment"

Thermoformed ortheses covering each subject's right hand up to the mid-forearm level were made to measure by a physiotherapist. They fitted each subject's hand and were designed to be as comfortable as possible. They were equipped with three miniature vibrators and a tactile matrix (Fig. 1A). Muscle proprioceptive vibrators (DC motors with eccentric masses 4 cm long and 1.5 cm in diameter) were embedded in specific places so that they lay against the skin covering the tendons of the wrist extensor and flexor muscles and the finger flexor muscles at the metacarpophalangeal joint level; they served to elicit single and combined illusory hand movements (Fig. 1B). The vibrotactile matrix consisted of a soft trapezoid array that included 10 circular flat microvibrators (1 cm in diameter and 0.2 cm deep) covered with a hypoallergenic film. Microvibrators were placed inside the matrix such that they would superficially stimulate the skin covering the entire inner surface of the 4 fingers of each subject's right hand. To prevent skin irritation, a protective medical fabric was set between each subject's skin and the orthesis.

In all the participants, the ortheses were locked into place early in the morning on Monday and were removed on Friday evening, just

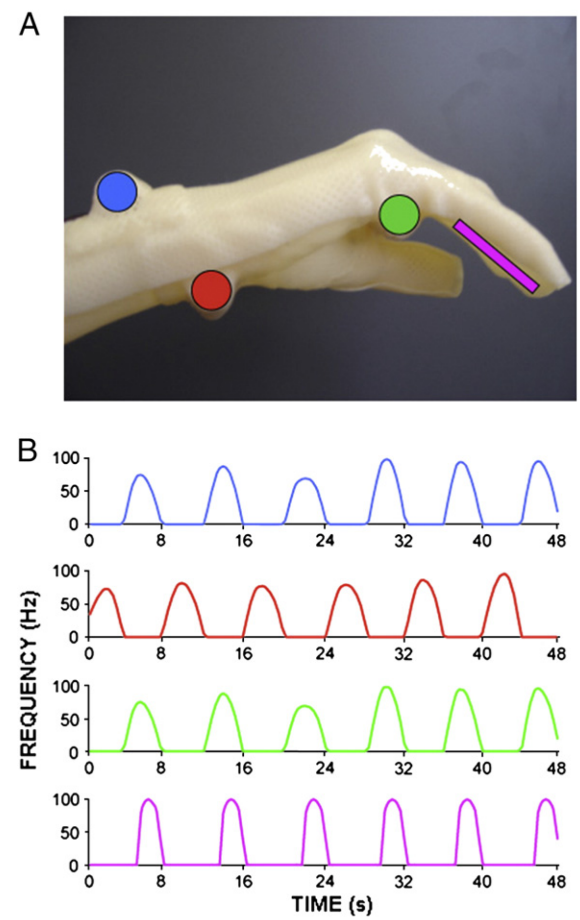

Fig. 1. Sensory feedback orthesis (A). Each subject wore a custom-made hand orthesis that included three miniature vibrators that were inserted so that they lay against the skin covering the tendons of the extensor (blue circle) and flexor (red circle) muscles of the wrist and those of the finger flexors (green circle) and one tactile matrix (purple bar), set over the skin on the inside of the subject's phalanxes apart from the thumb. (B) Examples of frequency variations as a function of time for each type of stimulation. In treated participants, these four types of stimulation were delivered either alone or in combination, giving six patterns of vibration that were applied to elicit the following single and combined illusory hand movement perceptions and one single superficial skin stimulation. All seven patterns were delivered randomly six times. Blue trace: wrist flexion, red trace: wrist extension, red and green traces: wrist and finger extension, purple trace: superficial skin stimulation, blue and red traces: alternate wrist flexion and extension, red, green and purple traces: wrist and finger extension combined with finger stimulation. The vibration patterns were generated and applied using a "proprioceptive model" described in the Materials and methods section.