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NEUROPLASTICITY OF PREHENSILE NEURAL NETWORKS AFTER QUADRIPLEGIA

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Abstract—Targeting cortical neuroplasticity through rehabilitation-based practice is believed to enhance functional recovery after spinal cord injury (SCI). While prehensile performance is severely disturbed after C6–C7 SCI, subjects with tetraplegia can learn a compensatory passive prehension using the *tenodesis* effect. During tenodesis, an active wrist extension triggers a passive flexion of the fingers allowing grasping. We investigated whether motor imagery training could promote activity-dependent neuroplasticity and improve prehensile tenodesis performance. SCI participants ($n = 6$) and healthy participants (HP, $n = 6$) took part in a repeated measurement design. After an extended baseline period of 3 weeks including repeated magnetoencephalography (MEG) measurements, MI training was embedded within the classical course of physiotherapy for 5 additional weeks (three sessions per week). An immediate MEG post-test and a follow-up at 2 months were performed. Before MI training, compensatory activations and recruitment of deafferented cortical regions characterized the cortical activity during actual and imagined prehension in SCI participants. After MI training, MEG data yielded reduced compensatory activations. Cortical recruitment became similar to that in HP. Behavioral analysis evidenced decreased movement variability suggesting motor learning of tenodesis. Data suggest that MI training participated to reverse compensatory neuroplasticity in SCI participants, and promoted the integration of new upper limb prehensile coordination in the neural networks functionally dedicated to the control of healthy prehension before injury.

Key words: magnetoencephalography, rehabilitation, spinal cord injury, cortical plasticity, motor imagery.

INTRODUCTION

Spinal cord injury (SCI) is the traumatic disruption of the neural pathways between the brain and the peripheral effectors. Extensive cortical reorganizations occur due to neuroplasticity after SCI (for a review, see Kokotilo et al., 2009). Transcranial magnetic stimulation studies evidenced higher levels of corticospinal excitability in muscles innervated above the level of injury (Levy et al., 1990; Topka et al., 1991; Streletz et al., 1995). Brain imaging studies provided evidence that disconnected brain regions became progressively re-assigned to the control of spared movements represented in adjacent sites of the cortical homunculus (Bruehlmeier et al., 1998; Lotze et al., 1999a; Curt et al., 2002; Mikulis et al., 2002). Overall, cortical neuroplasticity after SCI may contribute to "*maximize output*" to the unaffected muscles (for a review, see Nardone et al., 2013). Jurkiewicz et al. (2007) reported that concentration of activations within the primary motor cortex and decreased activity within secondary brain motor regions during wrist extensions correlated with functional recovery during the first year post-injury (see also Green et al., 1999). Targeting cortical neuroplasticity through rehabilitation-based practice may thus lead to better understand recovery processes after complete SCI.

Activity-dependent neuroplasticity inspired the development of rehabilitation strategies after SCI (for review, see Dunlop, 2008; Harvey et al., 2009). These foremost involve physical practice (PP)-based training (*e.g.*, physiotherapy, robot-assisted motor training). Interestingly, motor imagery (MI, the mental representation of an action without engaging in its actual execution) represents an "*emerging avenue*" to CNS stimulation after SCI (Dunlop, 2008). A large body of neuroscience research provided evidence that MI and PP are functionally equivalent neural processes, *i.e.,* both tasks engage overlapping structures within the brain motor network underlying actual motor preparation and execution (Decety et al., 1994; Jeannerod, 1994; Porro et al., 1996; Lotze et al.,

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Abbreviations: ERD, event-related desynchronization; ERS, event-related synchronization; HP, healthy participant; KVIQ, Kinesthetic and Visual Imagery Questionnaire; MEG, magnetoencephalography; MI, motor imagery; MRI, magnetic resonance imaging; MT, movement time; MV, movement variability; SAM, Synthetic Aperture Magnetometry; SCI, spinal cord injury; TP, tenodesis prehension.

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1999b; Ehrsson et al., 2003; Lotze and Halsband, 2006; Szameitat et al., 2007a,b; Guillot et al., 2012a; Burianova et al., 2013; Hétu et al., 2013). Activation intensities during MI are usually reduced by 30-50% as compared to PP (Porro et al., 1996; Lotze and Halsband, 2006; Munzert et al., 2009). Nonetheless, MI elicits sufficient CNS activation to stimulate cerebral neuroplasticity, thereby promoting motor learning and increased muscle performance in healthy participants (HP Pascual-Leone et al., 1995; Ranganathan et al., 2004). Functional equivalence between PP and MI is preserved for spared actions after complete SCI (Lacourse et al., 1999; Di Rienzo et al., 2013, 2014), and Cramer et al. (2007) provided evidence that SCI participants benefited from MI training to learn actions executed with muscles retaining a voluntary control.

Human prehension involves reaching and grasping objects within the haptic space (van de Kamp and Zaal, 2007). This function is severely disturbed after cervical SCI (Harvey, 1996; Snoek et al., 2004, 2008). According to the surgical classification of Giens (McDowell et al., 1986), finger and forearm muscles are paralyzed from the C6/C7 level. Accordingly, how can C6/C7 quadriplegic SCI participants achieve manual prehension in spite of finger and forearm muscle paralysis? SCI participants must learn a different pattern of prehension through extensive rehabilitation. Voluntary control of shoulder muscles is preserved, while active elbow and wrist extension remain possible due to residual control of the *triceps brachii* and *extensors carpi radialis*. Arm and hand positions during reaching can be controlled by proximal shoulder muscles while grasping is achieved with the tenodesis effect, *i.e.,* an active extension of the wrist triggering a passive flexion of the fingers (Harvey et al., 2001; Mateo et al., 2013). Tenodesis prehension (TP) is thus a compensatory prehension that requires a new motor program (*e.g.*, Mateo et al., 2013). Recent findings provided evidence that MI training improved the kinematic parameters of TP after cervical SCI, particularly movement speed and accuracy (Grangeon et al., 2010, 2012). MI was assumed to stimulate activity-dependent neuroplasticity. Grangeon et al. (2012) nonetheless underlined that their results were to be replicated on larger sample of SCI participants.

Prehension is controlled by a widespread cortical network involving frontal, parietal and occipital associative cortices interacting with primary somatosensory and motor structures (Jeannerod et al., 1995; Rizzolatti et al., 1996; Binkofski et al., 1998; Kuhtz-Buschbeck et al., 2001; Grafton, 2010). Whether similar neural networks underpin TP in C6/C7 quadriplegic participants is a first interest. A second issue relates the effect of MI training on TP, and the associated effects on the neural networks controlling PP and MI of prehension. Also, previous studies reporting the preservation of functional equivalence between MI and PP after SCI foremost involved *simple* motor sequences which could be easily physically executed (Lacourse et al., 1999; Sabbah et al., 2002; Di Rienzo et al., 2013). However, Olsson (2012) showed reduced recruitment of the motor system during MI of *complex* motor sequences that were impossible to perform after SCI. Olsson (2012) argued that the lack of PP due to chronic deafferentation and deefferentation led to the degradation of complex motor representations. Whether C6/C7 quadriplegic participants are able to achieve MI of TP with a high degree of functional equivalence in spite of the complexity of this skill is a final issue of interest. Using magnetoencephalography (MEG), we examined the effect of 5 weeks of MI training on TP performance in C6/C7 SCI participants. MI was integrated to the course of physiotherapy. MEG afforded investigation of cortical activity underlying actual and imagined TP.

EXPERIMENTAL PROCEDURES

Participants

SCI participants ($n = 6$) (five right handed, two females) were recruited from the Henri Gabrielle hospital (St Genis Laval, France) over a 1-year period of inclusion. Inclusion criteria were: (*i*) age range 18–55 years, (*ii*) SCI at the C6/C7 level eliciting complete motor deficit according to the American Spinal Injury Association (ASIA) impairment scale (Maynard et al., 1997), (*iii*) post-traumatic period superior to 6 months (*i.e.*, corresponding to the spontaneous motor recovery plateau; Waters et al., 1993; Yakura, 1996). Exclusion criteria were: (*i*) non-stabilized hypertension or pathological dysfunction of the autonomic nervous system, (*ii*) cerebral damage and/or cognitive deficit, (*iii*) elbow or shoulder joint amplitude restriction, upper limb para osteo-arthropathy, (*iv*) simultaneous inclusion to another study, and (*v*) presence of metallic objects within the body (*e.g.* pacemaker, auditory device or brace) incompatible with MEG or functional magnetic resonance imaging (fMRI) recordings. HP matching to SCI participants according to gender, age (±1 year) and handedness were recruited as controls.

All participants provided informed written consent according to the statements of the Declaration of Helsinki. This study was performed under approval of the Lyon Civil Hospices ethics committee (CPP 2009-051-B), and was part of the Hospital Program for Clinical Research n° 2010-541/142, prospective registered under the trial number ACTRN12612001 030864.

Experimental design

SCI participants were hospitalized across the duration of experiments, and underwent daily standard medical care including physiotherapy (*e.g.*, passive limb mobilization, muscle strengthening above the lesion level, *etc*.) and occupational therapy.

We conducted repeated pre-test assessments over a 5-week period to define the baseline level (Fig. 1). Pre-tests were separated from each other by a minimum period of 1 week. Then, individual MI sessions were embedded to the classical course of physiotherapy (three sessions of 45 min per week). MI sessions were delivered in a quiet room at the hospital. SCI participants were seated on their wheelchair, in front of a table and performed imagined prehensile actions with