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Brain Research

Review

Descending motor pathways and cortical physiology after spinal cord injury assessed by transcranial magnetic stimulation: a systematic review

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ARTICLE INFO

Article history:
Accepted 15 September 2014
Available online 22 September 2014

Keywords:
Spinal cord injury
Motor evoked potentials
Transcranial magnetic stimulation
Repetitive transcranial magnetic stimulation
Central motor conduction
Intracortical inhibition
Therapeutic applications

ABSTRACT

We performed here a systematic review of the studies using transcranial magnetic stimulation (TMS) as a research and clinical tool in patients with spinal cord injury (SCI). Motor evoked potentials (MEPs) elicited by TMS represent a highly accurate diagnostic test that can supplement clinical examination and neuroimaging findings in the assessment of SCI functional level. MEPs allows to monitor the changes in motor function and evaluate the effects of the different therapeutic approaches. Moreover, TMS represents a useful non-invasive approach for studying cortical physiology, and may be helpful in elucidating the pathophysiological mechanisms of brain reorganization after SCI. Measures of motor cortex reactivity, e.g., the short interval intracortical inhibition and the cortical silent period, seem to point to an increased cortical excitability.

However, the results of TMS studies are sometimes contradictory or divergent, and should be replicated in a larger sample of subjects. Understanding the functional changes at brain level and defining their effects on clinical outcome is of crucial importance for development of evidence-based rehabilitation therapy. TMS techniques may help in identifying neurophysiological biomarkers that can reliably assess the extent of neural damage, elucidate the mechanisms of neural repair, predict clinical outcome, and identify therapeutic targets. Some researchers have begun to therapeutically use repetitive TMS (rTMS) in patients with SCI. Initial studies revealed that rTMS can induce acute and short

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http://dx.doi.org/10.1016/j.brainres.2014.09.036
0006-8993/

duration beneficial effects especially on spasticity and neuropathic pain, but the evidence is to date still very preliminary and well-designed clinical trials are warranted.

This article is part of a Special Issue entitled SI: Spinal cord injury.

Contents

1. Introduction

The motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) represent a highly accurate diagnostic test with a very high sensitivity value in spinal cord disorders (Di Lazzaro et al., 1999). In most patients affected by traumatic spinal cord injury (SCI) the involvement of spinal cord is clinically evident, and the MEP contribution to the diagnosis is therefore mainly confirmatory. However, in these patients MEP studies may be useful in localizing levels of functional defects, or in detecting a subclinical involvement of central motor pathways, and the neurophysiological evaluation may also provide a useful adjunct to clinical impairment scales and functional correlate to radiological abnormalities.

Topographical map reorganization of primary motor cortex (M1) and premotor cortices after SCI has been reported in several experimental and human studies (for a review, see Nardone et al., 2013; Moxon et al., 2014). TMS also represents a useful non-invasive approach for studying cortical physiology (Hallett, 2000). Several studies have been performed to neurophysiologically characterize the functional reorganization that occurs after SCI.

Furthermore, preliminary studies revealed that repetitive TMS (rTMS) can induce beneficial effects on sensorimotor functions, as well as in the treatment of spasticity and neuropathic pain. Future well-controlled studies with appropriate methodology in larger patient cohorts are warranted in order to replicate and extend the initial findings.

The present review first focuses on studies that assessed the value of MEPs in defining the extent and severity of damage to corticospinal tract. We also performed a systematic review of the most important TMS reports that have assessed changes in cortical excitability and plasticity in humans after SCI. Finally, we briefly reviewed and critically appraised the preliminary studies that have therapeutically used rTMS in SCI patients. To the best of our knowledge, this is the first comprehensive review that covers all these aspects of TMS/rTMS in subjects with SCI.

2. Principal findings

2.1. *Motor conduction studies*

Subjects with incomplete cervical or thoracic SCI were more likely to demonstrate volitional and TMS-evoked contractions in distal lower limb muscles controlling their foot and ankle compared to proximal lower limb muscles (Calancie et al., 1999). When TMS did evoke responses in muscles innervated at levels caudal to the spinal cord lesion, MEP latencies of muscles in the lower limbs muscles were delayed equally for persons with cervical or thoracic SCI, thus suggesting normal central motor conduction in motor axons caudal to the