Neuroscience and Biobehavioral Reviews 47 (2014) 22–35

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Direct and crossed effects of somatosensory stimulation on neuronal excitability and motor performance in humans

M.P. Veldman[a], N.A. Maffiuletti[b], M. Hallett[c], I. Zijdewind[d], T. Hortobágyi[a,e,*]

[a] Center for Human Movement Sciences, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
[b] Neuromuscular Research Laboratory, Schulthess Clinic, Zurich, CH, Switzerland
[c] Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA
[d] Department of Neuroscience, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
[e] Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, UK

ARTICLE INFO

Article history:
Received 23 April 2014
Received in revised form 7 July 2014
Accepted 14 July 2014
Available online 23 July 2014

Keywords:
Afferent stimulation
Motor cortex
Primary sensorimotor cortex
Motor practice
Cross-education

ABSTRACT

This analytic review reports how prolonged periods of somatosensory electric stimulation (SES) with repetitive transcutaneous nerve stimulation can have 'direct' and 'crossed' effects on brain activation, corticospinal excitability, and motor performance. A review of 26 studies involving 315 healthy and 78 stroke and dystonia patients showed that the direct effects of SES increased corticospinal excitability up to 40% (effect size: 0.2 to 6.1) and motor performance up to 14% (effect size: 0.3 to 3.1) but these two features did not correlate. SES did not affect measures of intracortical excitability. Most likely, a long-term potentiation-like mechanism in the excitatory glutamatergic connections between the primary sensory and motor cortices mediates the direct effects of SES on corticospinal excitability and motor performance. We propose two models for the untested hypothesis that adding SES to unilateral motor practice could magnify the magnitude of inter-limb transfer. If tenable, the hypothesis would expand the evolving repertoire of sensory augmentation of cross-education using mirrors and add SES as an alternative to conventional rehabilitation strategies such as constraint-induced movement therapy.

Contents

Abbreviations: ICF, intracortical facilitation; IHI, interhemispheric inhibition; MEP, motor evoked potential; M1, primary motor cortex; PAS, paires associative stimulation; SES, somatosensory electrical stimulation; SICI, short interval intracortical inhibition; S1, primary sensory cortex; S2, secondary sensory cortex; TMS, transcranial magnetic brain stimulation.

* Corresponding author at: Center for Human Movement Sciences, University Medical Center Groningen, A. Deusinglaan 1, 9700 AD Groningen, The Netherlands. Tel.: +31 50 361 2645.
E-mail address: t.hortobagyi@umcg.nl (T. Hortobágyi).

http://dx.doi.org/10.1016/j.neubiorev.2014.07.013
0149-7634/

1. Introduction

Sensory inputs are necessary for the successful execution and acquisition of skillful voluntary movements. Stimuli from the environment activate skin, pain, temperature, pressure, tendon, and muscle receptors that provide feedback for, for example, finger movements while typing, monitoring the position of the arm in space during reaching, and fine tuning facial expressions (Bastian, 1887; Farrer et al., 2003; Gentilucci et al., 1997; Rabin and Gordon, 2004; Yao et al., 2002). Sensory inputs are also required for learning motor skills (Hemami and Dariush, 2012; Rosenkranz and Rothwell, 2012; Salinas and Abbott, 1995; Wolpaw and Tennissen, 2001). In contrast, patients with dysfunctional peripheral sensory receptors execute voluntary movements inaccurately or in severe cases are unable to grasp a pen, write, and fasten shirt buttons with one hand (Rothwell et al., 1982; Sanes et al., 1984; Sesto et al., 2003). Primates with ablated somatosensory cortex have great difficulty in learning to catch a falling food pellet (Pavlides et al., 1993) and somatosensory deficits caused by an ischemic stroke interfere with the recovery of voluntary movements (Nudo et al., 2000; Reding and Potes, 1988; Xerri et al., 2004).

The empirical and clinical observations concerning the key role of sensory inputs in motor function gave rise the hypothesis that augmenting sensory inputs through somatosensory electrical stimulation (SES) could perhaps improve function and reduce weakness by enhancing the excitability of the neuronal path projecting to muscles and joints wherein the sensory receptors are stimulated (Conforto et al., 2002; Dobkin, 2003; Fraser et al., 2002; Hamdy et al., 1998; Johansson et al., 1993; Powell et al., 1999; Uy et al., 2003). However, the mechanism of how, if at all, SES increases motor function is incompletely understood. While transcranial magnetic brain stimulation (TMS) and imaging studies report consistent increases in the excitability of the primary motor (M1) and sensory (S1) cortices and other elements in the sensorimotor network (see below), such changes do not always improve motor function (cf. Sorinola et al., 2012) as many studies report actually reductions in motor excitability after SES (Chen et al., 1999; Delwaide and Olivier, 1990; Maertens de Noordhout et al., 1992; Tokimura et al., 2000; Zittel et al., 2007). In addition, the optimal SES parameters (duration, intensity, frequency) for modulating plasticity in M1 and S1 are unclear and there is also ambiguity if the parameters that increase neuronal excitability also improve motor function. Although the direct effects of SES are focal within, for example, the hand area, there is also evidence that SES can give rise to effects that cross to remote brain areas in particular to contralateral homologous structures (Bonato et al., 1996; Kossev et al., 2001; Manganotti et al., 1997; Swayne et al., 2006).

Targeting neurologists, physical therapists, and other rehabilitation experts, the present narrative review provides an integrative analysis of the direct and crossed effects of electrical SES on neuronal excitability and motor function. Here we consider a form of SES that could be used in a clinical setting to improve motor function and define it as painless, low frequency and prolonged ($\geq$20 min) transcutaneous electrical stimulation of a peripheral nerve or motor point at current intensities below, at, or just above motor threshold (Sorinola et al., 2012). The hypothesis is that such SES modality would increase corticospinal and motor cortical excitability, and brain activation, and also produce improvements in motor function in healthy individuals or in patients who suffer from a motor dysfunction. The hypothesis focuses on the motor brain due to minimal data on the effects of SES on spinal excitability in upper extremity muscles. First, we review the neuroanatomical paths that convey sensory signals to target motor areas in the brain. Second, we analyze the mechanisms of how SES increases corticospinal and M1 excitability and review how SES parameters affect corticospinal and M1 plasticity. Third, we examine the association between changes in corticospinal and M1 plasticity (cf. Chipchase et al., 2011b) and the ensuing changes in motor function. Finally, we present models for the direct and crossed effects of SES. Within the conceptual framework of cross-education (Carson, 2005; Farthing, 2009; Hortobágyi, 2005; Howatson et al., 2013; Munn et al., 2004; Ruddy and Carson, 2013; Zult et al., 2013), we propose the untested and provocative hypothesis that adding SES to unilateral motor practice could magnify the magnitude of inter-limb transfer. If tenable, the hypothesis would expand the evolving repertoire of sensory augmentation of cross-education (Howatson et al., 2013; Zult et al., 2013) and provide alternatives to conventional methods such as constraint-induced movement therapy (Taub et al., 1999) which are not suitable for patients with a unilateral orthopedic injuries (Magnus et al., 2010, 2013; Papandreou et al., 2009, 2013).

To reduce variation between studies in methods and subjects, the analysis includes studies that used prolonged SES in the form of electrical stimulation, functional electrical stimulation, peripheral nerve stimulation, electrical nerve stimulation, and paired associative stimulation (PAS) directly to a peripheral nerve or to the motor point of an upper extremity muscle. PAS, which we consider here as a form of SES, combines peripheral electrical nerve stimuli with magnetic pulses delivered to the motor cortex with specific interstimulus intervals and intensities (Carson and Kennedy, 2013). We included PAS with the understanding that it produces heterotopic plasticity presumably through associative long-term potentiation (Stefan et al., 2000). In contrast, other forms of SES, using electrical-only stimuli, produce homotopic plasticity (Table S1). Because of this important difference, we analyzed PAS as a separate form of PAS. We did not consider studies designed to probe the immediate (>1 s) effects of single cutaneomuscular stimuli on the motor brain (Chen et al., 1999; Classen et al., 2000; Delwaide and Olivier, 1990; Maertens de Noordhout et al., 1992; Manganotti et al., 1997; Tokimura et al., 2000; Zittel et al., 2007). We excluded electrical muscle stimulation that produces strong muscle contractions in the form of neuromuscular electrical stimulation (Hortobágyi and Maffiuletti, 2011), uses high frequency transcutaneous nerve stimulation to manage pain (Simpson et al., 2013), and studies targeting lower extremity muscles (Khaslavskaia et al., 2002; Knash et al., 2003; Leonard et al., 2013; Roy and Gorassini, 2008). We also excluded mechanical vibration from the analysis because of its unique nature as a sensory stimulus (Rothwell and Rosenkranz, 2005). Using such inclusion criteria, we found that the effects of SES on corticospinal excitability were tested in healthy participants only in the age range of 25.5–36.5 years without testing motor performance. In contrast, the studies that determined changes in motor performance used only patients and did not measure changes