Clinical Neurophysiology 128 (2017) 1015–1025

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

High frequency somatosensory stimulation increases sensori-motor inhibition and leads to perceptual improvement in healthy subjects

Lorenzo Rocchi [a,b,*,1], Roberto Erro [a,c,1], Elena Antelmi [a,d], Alfredo Berardelli [b,e], Michele Tinazzi [c], Rocco Liguori [d,f], Kailash Bhatia [a], John Rothwell [a]

[a] Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, WC1N 3BG London, United Kingdom
[b] Department of Neurology and Psychiatry, University of Rome "Sapienza", Viale dell'Universita' 30, 00185 Rome, Italy
[c] Department of Neuroscience, Biomedicine and Movement Science, University of Verona, Piazzale L.A. Scuro 10, 37134 Verona, Italy
[d] Department of Biomedical and Neuromotor Sciences, Alma Mater Studiorum, University of Bologna, 40123 Bologna, Italy
[e] IRCCS Neuromed Institute, Via Atinense, 18, 86077 Pozzilli, Italy
[f] IRCSS Institute of Neurological Sciences, Via Altura 3, 40139 Bologna, Italy

ARTICLE INFO

Article history:
Accepted 27 March 2017
Available online 8 April 2017

Keywords:
Tactile stimulation
Evoked potentials
High frequency oscillations
Transcranial magnetic stimulation
Cortical inhibition
Temporal discrimination

HIGHLIGHTS

- Repetitive tactile stimulation improves somatosensory spatial and temporal perception.
- The same intervention also modifies cortical sensorimotor interactions.
- These changes are likely due to an increased effectiveness of cortical inhibition.

ABSTRACT

Objective: High frequency repetitive somatosensory stimulation (HF-RSS), which is a patterned electric stimulation applied to the skin through surface electrodes, improves two-point discrimination, somatosensory temporal discrimination threshold (STDT) and motor performance in humans. However, the mechanisms which underlie these changes are still unknown. In particular, we hypothesize that refinement of inhibition might be responsible for the improvement in spatial and temporal perception.
Methods: Fifteen healthy subjects underwent 45 min of HF-RSS. Before and after the intervention several measures of inhibition in the primary somatosensory area (S1), such as paired-pulse somatosensory evoked potentials (pp-SEP), high-frequency oscillations (HFO), and STDT were tested, as well as tactile spatial acuity and short intracortical inhibition (SICI).
Results: HF-RSS increased inhibition in S1 tested by pp-SEP and HFO; these changes were correlated with improvement in STDT. HF-RSS also enhanced bumps detection, while there was no change in grating orientation test. Finally there was an increase in SICI, suggesting widespread changes in cortical sensorimotor interactions.
Conclusions: These findings suggest that HF-RSS can improve spatial and temporal tactile abilities by increasing the effectiveness of inhibitory interactions in the somatosensory system. Moreover, HF-RSS induces changes in cortical sensorimotor interaction.
Significance: HF-RSS is a repetitive electric stimulation technique able to modify the effectiveness of inhibitory circuitry in the somatosensory system and primary motor cortex.

1. Introduction

Godde and coworkers (Godde et al., 2000) were the first to demonstrate in healthy volunteers that high frequency repetitive somatosensory stimulation (HF-RSS) improves two point discrimination in the stimulated area. Since previous animal experiments

Abbreviations: ADM, abductor digiti minimi; APB, abductor pollicis brevis; FDI, first dorsal interosseous; HFO, high-frequency oscillations; HF-RSS, high-frequency tactile stimulation; ICF, intracortical facilitation; MEP, motor evoked potential; SEP, somatosensory evoked potentials; SICI, short intracortical inhibition; STDT, somatosensory temporal discrimination threshold; TSD, tactile spatial discrimination; TT, tactile threshold.

* Corresponding author at: Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, WC1N 3BG London, United Kingdom.

E-mail address: l.rocchi@ucl.ac.uk (L. Rocchi).

[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.clinph.2017.03.046
1388-2457/

(Godde et al., 1996) showed that HF-RSS enlarges cutaneous receptive fields in rat somatosensory cortex, it might have been expected that HF-RSS in humans would reduce spatial discrimination. However, the latter does not strictly relate to the size of individual neuron receptive field, but instead reflects the information present in the discharge of a large number of neurons (Godde et al., 1996, 2000; Dinse et al., 2006). More neurons activated in response to stimulation of an area of skin with overlapping but distinct receptive fields would code spatial representation with higher precision than single neurons.

HF-RSS also improves somatosensory temporal discrimination threshold (STDT), which is regarded as the smallest time interval between two tactile stimuli for them to be detected as separate (Erro et al., 2016). However, the reason for this effect is unclear since it is difficult to explain how larger spatial receptive fields can influence temporal discrimination between stimuli. In a previous work using transcranial magnetic stimulation we argued that temporal threshold depends on the effectiveness of short duration inhibition in the somatosensory system, which is used to sharpen temporal processing following the arrival of the initial sensory input (Rocchi et al., 2016). The aim of the present experiments was to test whether HF-RSS might improve STDT by enhancing this inhibitory effect. If so, it would imply that HF-RSS has two consequences, both of which are spatially limited to the area of stimulation: increased size of spatial receptive fields and increased effectiveness of somatosensory inhibition. In fact it could be that both effects are complementary. Thus, increased spatial discrimination between stimuli would benefit both from larger receptive fields as well as increased effectiveness of inhibitory connections between adjacent fields. Similarly, increased temporal discrimination might benefit from engagement of larger numbers of neurons in temporal processing, along with an augmented efficacy of inhibitory connections between them. We therefore correlated changes produced by HF-RSS on spatial and temporal discrimination with our measures of somatosensory inhibition (recovery of P14 and N20-P25 waves with paired-pulse somatosensory evoked potentials and area of high frequency SEP oscillations) to test its relative contribution to temporal and spatial discrimination. We used STDT as our measure of temporal discrimination. For spatial discrimination we employed two different tests: the ‘‘bumps” test, which is a simple measure of tactile threshold, and the JVP test, which is a more complex measure of spatial discrimination that assesses the ability to detect the orientation of a tactile grating. Lastly, since HF-RSS has been further shown to improve motor performance (Kalisch et al., 2008; Smith et al., 2009; Kalisch et al., 2010), we also explored possible effects of HF-RSS on processing in the primary motor area (M1), using measures of short intracortical inhibition (SICI; a GABAa-ergic inhibition) and intracortical facilitation (ICF; a glutamatergic excitation).

2. Methods

2.1. Subjects

Fifteen right handed (Oldfield, 1971) subjects (11 male, 4 female, age 54.5) participated in the study. They had no history of any diseases related to the central or peripheral nervous system; they did not have metal or electronic implants and were not on medications acting on the nervous system. Subjects signed a written informed consent before the experimental session. The local institutional review board approved the experimental procedure, which was conducted according with the Declaration of Helsinki and common safety guidelines. and all experimental procedures were approved by the local ethical committee and conducted in accordance with the Declaration of Helsinki and according to international safety guidelines.

2.2. Somatosensory temporal discrimination threshold

STDT was tested administering paired electrical stimuli, with an initial interstimulus interval (ISI) of 0 ms (simultaneous pair) that was progressively increased in steps of 10 ms (Conte et al., 2012; Rocchi et al., 2013; Conte et al., 2014). This ascending method has been reported to yield results similar to common psychophysical assessment (Rocchi et al., 2016).

Stimulation was delivered separately to the third phalanx of the right and left thumb and index finger using surface electrodes separated by 0.5 cm (anode placed distally than the cathode). Current was applied by means of a constant current stimulator (Digitimer DS7A) in the form of square-wave pulses. The intensity for STDT testing was the lowest at which each subject could perceive a tactile stimulus in 10 out of 10 consecutive trials (Conte et al., 2012, 2014). This was obtained by stimulation of the left index finger starting from 2 mA and increasing the current in steps of 0.5 mA; on the other fingers, the current intensity was adjusted to match the perceived intensity on the left index finger. Before the actual testing subjects had to familiarize with the task, achieving a stable performance. During the procedure, they had to report if they perceived a single stimulus or two discrete stimuli. The first of three consecutive ISI at which subjects reported two stimuli was considered the STDT. Each session consisted of four separate blocks; we entered in the analysis the average of four STDT values (i.e. one for each block). To keep subjects' attention level constant during the test some ‘‘catch” trials, consisting of single stimuli, were delivered at random during the procedure.

2.3. Tactile tasks

Tactile spatial discrimination (TSD) was measured using a set of JVP domes (Van Boven and Johnson, 1994). Each dome is a circular, convex grating surface of 20 mm diameter, on top of a cylindrical handle 30 mm long. The set is made of eight domes with equidistant groove and bar widths ranging from 3.0 to 0.35 mm. Testing was performed according to previous recommendations. Subjects were required to judge the orientation of the grating (i.e., horizontal or vertical to the fingertip). The thinnest grating which was reliably detected 75% of the times provided an estimate of the spatial resolution, as previously suggested (Van Boven and Johnson, 1994). We avoided using two-point discrimination as a measure of TSD because its threshold often falls under the receptor spacing (Johansson and Vallbo, 1979, 1980, Johnson and Phillips, 1981). Thus, several investigators have questioned the validity of two-point discrimination as a measure of spatial acuity (Johnson and Phillips, 1981; Stevens and Patterson, 1995; Lundborg and Rosen, 2004; Tong et al., 2013), while grating orientation can be considered a more rigorous alternative (Craig and Johnson, 2000). Tactile threshold (TT) was tested using the Bumps device (Kennedy et al., 2011). It is a smooth surface divided into 12 squares, each containing 5 colored circles, only one of which one has a circular bump in the middle. Bumps are 550 μm in diameter but have different height. The device consists of two such plates (plates A and B), which are identical but for bumps heights: the latter are 2.5–8 μm and 8.5–14 μm, on plate A and B, respectively (e.g., bump heights on each plate increases in 0.5-μm increments). Participants were asked to locate the bump in each square (testing order: plate B always first). Two trials were performed for each plate and TT was defined as the lowest bump such that it and the following two higher bumps were successfully detected in either trial, as previously described (Kennedy et al., 2011). Both tests were done on the right and the left index finger.