Mechanical Flutter Stimulation Induces a Lasting Response in the Sensorimotor Cortex as Revealed with BOLD fMRI

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Abstract: It has been recently shown that 20 min of mechanical flutter stimulation induces lasting motor cortical excitability changes, as assessed by transcranial magnetic stimulation in relaxed hand muscles. The present functional magnetic resonance imaging (fMRI) study aims to examine if such neuromodulatory changes are reflected in the BOLD signal during a motor test. Therefore, two groups were recruited: one group receiving whole-hand flutter stimulation with a frequency of 25 Hz (FSTIM group, $n = 22$) and a second group receiving no stimulation (NOSTIM group, $n = 22$). As motor test finger-to-thumb tapping was performed to activate a wide sensorimotor network during the fMRI measurements. Three fMRI measurements were obtained with this test: before stimulation (PRE), after stimulation (POST1), and 1 h after stimulation (POST2). Three regions of interest (ROIs) were defined: primary motor area (M1), primary somatosensory area (S1), and supplementary motor area. In the absence of baseline differences between both groups, the FSTIM group showed increased movement-related brain activations compared with the NOSTIM group, both at POST1 and POST2. ROI analysis revealed increased blood-oxygenation-level-dependent (BOLD) responses within contralateral S1 (+20%) and M1 (+25%) at POST1, which lasted until POST2. These poststimulatory effects within S1 and M1 obviously reflect neuroplastic changes associated with augmented cortical excitability. These findings are of high clinical relevance, for example, to improve the treatment of stroke patients. *Hum Brain Mapp* 34:2767–2774, 2013. © 2012 Wiley Periodicals, Inc.

Key words: somatosensory stimulation; sensorimotor cortex; neuromodulation; cortical plasticity; finger tapping paradigm; fMRI

INTRODUCTION

The human brain receives massive input from cutaneous mechanoreceptors informing about touch, pressure, and vibration [Mountcastle, 1984]. Their distribution and functional properties have been estimated using microneurography technique [Vallbo and Hagbarth, 1968]. The glabrous skin of the hand is innervated by about 17,000 mechanoreceptive afferents, which have been classified into fast adapting (Type I units with superficial nerve endings) and slow adapting (Type II units with nerve endings

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in deeper skin layers) receptors [Vallbo and Johansson, 1984]. In addition to cutaneous receptors, somatosensory input further comes from the proprioceptors in hand and finger muscles [Wiesendanger and Miles, 1982].

Earlier psychophysical studies demonstrated that mechanical stimulation in the frequency range between 20 and 40 Hz yields localized flutter sensations [Talbot et al., 1968], therefore the term “flutter stimulation.” Using microstimulation of single mechanoreceptive afferents, it was found that both Type I and Type II receptors produce time-locked and frequency-following electroencephalographic (EEG) responses in the vicinity of primary sensory cortex (S1) [Kelly et al., 1997] and accordingly hemodynamic responses were also found with fMRI [Trulsson et al., 2001]. Studies applying pulsed mechanical stimulation to the hand and fingers showed an amplitude maximum in the EEG response at a pulse frequency of 26 Hz [Snyder, 1992], 21 Hz [Tobimatsu et al., 1999], and 27 Hz [Müller et al., 2001]. This maximal response at around 25 Hz was interpreted as a resonance phenomenon within the somatosensory system, according to such phenomena observed from the visual (at around 10 Hz) and from the auditory cortex (at around 40 Hz). Using optical intrinsic signal imaging, it was further demonstrated that increasing the amplitude of a 25-Hz flutter stimulus lead to a proportional increase in absorbance within the forelimb representational region of S1 [Simons et al., 2005]. All these findings provide evidence that mechanical flutter stimuli should be very effective for entraining the activity of neurons in S1, but also in adjacent motor areas [Romo et al., 2002].

The goal of this study was to test if prolonged mechanical stimulation in the flutter frequency range induces lasting neuromodulatory effects within the sensorimotor brain areas. Using transcranial magnetic stimulation (TMS), lasting excitability effects in the motor cortex have been already demonstrated following application of peripheral electrical stimulation [Golaszewski et al., 2010; Kaelin-Lang et al., 2002], tendon vibration [Forner-Cordero et al., 2008], and mechanical flutter stimulation [Christova et al., 2011]. It has been suggested that temporal changes in the balance between glutamatergic excitatory and γ -aminobutyric acid (GABA) inhibitory cortical synaptic activity are responsible for this plasticity-promoting effect [Kaelin-Lang et al., 2002]. For this reason, somatosensory stimulation has been proposed as a novel tool to improve brain and motor functions in stroke patients [Conforto et al., 2007; Wu et al., 2006].

The above described effects have been mainly revealed with TMS in relaxed muscles and until now such stimulation-induced effects have been investigated only in a few fMRI studies with motor tests. Motor tests, such as finger tapping, activate a wide sensorimotor network [Moriyama et al., 1998], allowing the assessment of stimulation-induced activations beyond the motor cortex. Poststimulatory activations within S1 as well as within primary motor (M1), premotor, and supplementary motor areas (SMA) have been documented following prolonged electrical

Figure 1.

Experimental procedure for FSTIM and NOSTIM group.

stimulation [Golaszewski et al., 2004; Wu et al., 2005]. However, lasting cortical activations following chronic mechanical stimulation have not yet been reported.

For this study, unilateral finger-to-thumb tapping was used to test if whole-hand flutter stimulation with a frequency of 25 Hz evokes lasting neuromodulatory changes within the sensorimotor network. We hypothesize that following 20-min stimulation, the movement-related BOLD response remains increased compared with the prestimulation response. To test this hypothesis, two independent study groups were recruited: the FSTIM group receiving mechanical flutter stimulation and the NOSTIM group performing the same experimental procedure but receiving no stimulation. In addition to the baseline fMRI measurements (PRE), two poststimulation measurements were performed: immediately after stimulation (POST1) and 1 h after stimulation (POST2).

MATERIALS AND METHODS

Subjects and Experimental Design

A total of 44 healthy right-handed volunteers [according to the Laterality Quotient from Edinburgh Handedness Inventory, Oldfield, 1971] without any record of cardiovascular and neurological disease participated in the study. Subjects were informed and instructed about the experimental procedure and filled out an informed consent approved by the local ethics committee. The subjects were randomly assigned to the FSTIM group ($n = 22$, 11♂ and 11♀, mean age 29.21 ± 11.12 years) receiving flutter stimulation at the right hand and to the NOSTIM group ($n = 22$, 11♂ and 11♀, mean age 28.50 ± 12.65 years) receiving no stimulation.

For both groups, the experimental protocol consisted of four sessions: a baseline fMRI measurement (PRE), a 20-min intervention receiving either stimulation or no stimulation, a poststimulation fMRI measurement immediately after the intervention (POST1), and a second poststimulation fMRI measurement 1 h after the intervention (POST2), see schema in Figure 1. For intervention, the scanner table was moved out of the magnet bore but subjects remained lying on the table. In the pause between the two poststimulation measurements (POST1 and POST2), subjects also remained lying on the table. As fMRI activation paradigm, both groups performed unilateral finger-to-thumb tapping with the right hand. The whole experiment had a total duration of about 100 min.

Mechanical Flutter Stimulation

For flutter stimulation, a commercial moving coil vibrator (Type V 400 Series, Ling Dynamical Systems, England) was used, which was mounted tiltable on a base plate. To further increase the payload capacity of the moving coil, an additional external suspension (Type AUX 400) was fitted to the vibrator. This electrodynamic device can be operated inside the fMRI room, behind the 20 mT line [Gallasch et al., 2006]. To transmit the mechanical stimulation to the subject's hand, a curved hand pad connected by a stiff carbon tube (length 1.3 m) was constructed. For comfortable stimulation, the tilt angle and the position of the vibrator were adjusted individually, so the right-hand palm and the fingers rested on the pad. The stimulation amplitude was adjusted to ± 2 mm (peak amplitude) at a constant frequency of 25 Hz (sinusoidal waveform) by using a waveform generator (Type AFG 33120A, HP, USA) and a power amplifier (Type PA100E, Ling Dynamical Systems, England). Subjects of the NOSTIM group also placed the right hand on the pad with the power amplifier being switched off. During stimulation exposure, subjects were instructed to distract attention from the vibrating stimulus.

Motor Task

To reduce cortical and subcortical activation from attentional cues, self-paced finger tapping was used as motor task. This task consisted of consecutive forward and backward finger-to-thumb tapping (between the second and the fifth finger) performed with the right dominant hand. Before the experiments, subjects were trained to gain a stable tapping performance: first, the tapping sequence (duration 26 s) was paced acoustically by means of a metronome (frequency 2.0 Hz) and then self-paced tapping was practiced until reaching sufficient accuracy. The start and stop commands for the tapping sequences were given via an auditory cue. During scanning, the subject's behavior was controlled by the observer. The total number of finger taps per each run was counted to assure constant tapping rate throughout the experiment and between groups. After the experiment, subjects of the FSTIM group were interviewed if their tapping performance was influenced or impaired following flutter stimulation. For all subjects, this was not the case.

Scanning Procedure

The experiment was performed on a clinical scanner (Siemens Magnetom Trio Tim syngo MR B15) equipped with an EPI-capable gradient system and a Siemens-issued 32-channel head coil. For fMRI, we used T_2^* -weighted single-shot echo-planar sequences (TR = 2,570 ms; FA = 78°; TE = 30 ms; matrix = 64×64 ; 40 slices; 3 mm slice thickness; and 0.75 mm slice gap).

Whole-brain scans with 40 slices were taken parallel to the bicommissural plane. In every run, a series of 75 sequential volume images was acquired. Additionally, high-

resolution anatomical images were acquired for all subjects during the second run. Therefore, a 3D magnetization-prepared, rapid-acquisition gradient echo was used with the following parameters: TR = 2,300 ms; TE = 2.91 ms; 160 slices; slice thickness = 1.20 mm; in-plane resolution = $1.0 \text{ mm} \times 1.0 \text{ mm}$; and FA = 9°.

During each run, 10 scans of rest (A) alternated with 10 scans of finger tapping (B) were repeated three times according to the scheme: A B A B A B A. Throughout the runs, subjects were instructed to lie relaxed with their hands upon the abdomen, not to rise the hand during tapping, and to keep their eyes closed during the recordings.

Data Analysis and Statistics

Data preprocessing and statistical analysis were performed with SPM8 software (The Wellcome Department of Cognitive Neurology, London; <http://www.fil.ion.ucl.ac.uk/spm/>). The first five functional images of each subject were discarded from the analysis to ensure signal stabilization. Functional data were realigned and unwarped and then normalized to the mean image, which was warped to match the echo planar imaging (EPI) template, provided by SPM8. Spatial smoothing was performed with 8 mm full width half maximum (FWHM) Gaussian kernel. For the first-level single-subject general linear model analysis, a rectangle function of the block onsets with the block duration for each condition (activity/rest) was convolved with a canonical form of the hemodynamic response function. A high-pass filter (128 s cutoff) and a correction AR(1) error model for serial correlations were used. The contrast images of the two groups of subjects were entered into a second-level analysis. One and two sample *t*-tests were used to assess within- and between-group random effects. Resultant statistical maps were thresholded at $P < 0.005$, uncorrected, reporting only clusters that were significant at $P < 0.05$, corrected.

Three regions of interest (ROIs) were selected: primary motor cortex (M1), primary somatosensory cortex (S1), and SMA. The ROIs were first defined based on the Jülich probabilistic atlas of Brodmann's areas (BAs) from the SPM Anatomy Toolbox [Eickhoff et al., 2005] as follows: for M1: BA4a and BA4p [Geyer et al., 1996], for S1: BA1, BA2, and BA3 [Geyer et al., 2000; Grefkes et al., 2001], and for SMA: BA6 [Geyer, 2003]. Then, the anatomical ROIs were intersected with the activated clusters, defined from the fMRI analysis (activity/rest, $T = 15$). These activated clusters within the sensorimotor (precentral/postcentral gyrus) area of the hand knob [Sarfeld et al., 2012] and within the SMA (superior frontal gyrus) were intersected with the corresponding anatomical ROIs.

For analysis of variance (ANOVA), the signal change was measured within each ROI and presented as contrast between activity/rest. The differences in the contrast response between both groups at baseline (PRE) were examined separately for each ROI (M1, S1, and SMA) using independent two sample *t*-test. The effect of vibration on the

signal intensity change was assessed with two factorial ANOVA separately for each ROI with within-subject factor time (PRE, POST1, and POST2) and between-subject factor group (FSTIM and NOSTIM). When significant interaction effect was found, further one-way ANOVAs for each group with factor time (PRE, POST1, and POST2) were carried out, followed by post hoc tests.

RESULTS

The first-level analysis revealed significant movement-related activations induced by the finger tapping paradigm for all subjects (peak T values = 13.33). Therefore, data from all 44 subjects (22 FSTIM and 22 NOSTIM) were included into the second-level analysis. Across all fMRI measurements, the motor task activated a wide sensorimotor network: left precentral area (M1), left and right postcentral areas (S1), left SMA, and left and right cerebellum for both groups. The most pronounced brain activations occurred within the contralateral M1, S1, and SMA.

Movement-Related Brain Activations Before Conditioning by Flutter Stimulation

At baseline, before intervention (PRE), the number of activated voxels within the contralateral precentral (M1) and postcentral gyrus (S1) as well as within the superior frontal area (SMA) was comparable for both groups (Table I). In addition, in the ROI analysis, no baseline between-groups differences were revealed for M1 ($P = 0.09$), S1 ($P = 0.97$), and SMA ($P = 0.42$).

Movement-Related Brain Activations After Conditioning by Flutter Stimulation

The random effects analysis revealed significant difference in brain activation between the FSTIM group and the

TABLE I. Cluster voxels at baseline for the FSTIM group and for the NOSTIM group

	FSTIM	NOSTIM
Precentral L		
MNI (x, y, z)	-39 -19 61	-36 -19 64
Cluster voxels	711	743
Postcentral L		
MNI (x, y, z)	-42 -28 58	-42 -16 58
Cluster voxels	783	824
SMA L		
MNI (x, y, z)	-3 -4 55	-3 -4 55
Cluster voxels	407	440

Clusters are reported if they surpassed a threshold $P < 0.005$, uncorrected, with P value of <0.05 , corrected on cluster level. MNI (x, y, z) coordinates corresponding to the brain standard of the Montreal Neurological Institute.

Figure 2.

Random effects between-groups analysis. FSTIM group versus NOSTIM group, immediately after stimulation in POST1 (left plot) and 1 h poststimulation in POST2 (right plot). Significant changes in activation pattern within the left precentral/postcentral gyrus ($P = 0.005$, uncorrected and $P < 0.05$, corrected on cluster level).

NOSTIM group during both poststimulation measurements (POST1 and POST2), see Figure 2. Immediately after flutter stimulation (POST1), an increased BOLD response within the left sensorimotor area (precentral, postcentral, and BA3, 4, and 6) was found in comparison to the NOSTIM group ($T = 5.07$), cluster peak (MNI, $x = -33$ mm, $y = -22$ mm, and $z = 61$ mm). Furthermore, in the second poststimulation measurement, this contrast difference was still present (precentral, postcentral, and BA1, 3, 4, and 6), cluster peak (MNI, $x = -30$ mm, $y = -28$ mm, and $z = 52$ mm). However, the effect was weaker ($T = 3.80$).

Poststimulation effects were also shown with the ROI analysis, which was carried out separately for M1, S1, and SMA. The results are presented in Figure 3. For M1, the three factorial ANOVA revealed significant interaction effect of time $\times$ group ($F_{(2,84)} = 4.52$; $P = 0.01$), main effect of group ($F_{(1,42)} = 8.12$, $P = 0.006$), and main effect of time ($F_{(2,84)} = 3.42$, $P = 0.03$). Furthermore, main effect of time was revealed only for the FSTIM group where post hoc analysis showed significant change in the contrast response between PRE and POST1 ($P = 0.00$) and between PRE and POST2 ($P = 0.04$). For S1, significant interaction effect of time $\times$ group ($F_{(2,84)} = 4.09$, $P = 0.02$) was found. Again, significant effect of time was found only for the FSTIM group where significant BOLD response contrast was observed between PRE and POST1 ($P = 0.02$) and between PRE and POST2 ($P = 0.04$). For SMA, ANOVA revealed slight but insignificant increase in signal intensity in both poststimulation measurements.

Figure 3.

Signal intensity contrast (activity/rest) for FSTIM and NOSTIM group, for each ROI (M1, S1, and SMA) at baseline (PRE), immediately after stimulation (POST1), and 1 h after stimulation (POST2).

DISCUSSION

The purpose of this fMRI study was to enhance our understanding of the neuromodulatory effects induced by mechanical flutter stimulation. The results show significant focal brain activations within the primary motor and somatosensory areas, outlasting the stimulation period for 1 h. With respect to recent findings on corticomotoneuronal excitability [Christova et al., 2011], these results support the evidence that the movement-related BOLD response reflects neuroplastic changes.

Activations Within the Sensorimotor Network

The relationship between a stimulus and the corresponding BOLD response is determined by the peripheral

afferent discharge, the corresponding firing of the target brain neurons, and the elicited neuronal activation [Logothetis et al., 2001]. Concerning fMRI responses during somatosensory stimulation (online effects), studies on humans showed clusters of activations bilaterally within the secondary somatosensory cortex (S2) and contralaterally within S1 [Disbrow et al., 2000], but also within M1 [Francis et al., 2000] and SMA [Golaszewski et al., 2002]. Single-cell recordings in cats [Ferrington and Rowe, 1980] and in primates [Zhang et al., 2001] demonstrated that neurons in S1 were more responsive to lower frequencies of vibration, whereas those in S2 were more responsive to higher frequencies. However, imaging studies on humans have not yet demonstrated such a differential representation.

Increased poststimulation fMRI responses were reported after electrical stimulation. In the study of Golaszewski et al. [2004], the finger tapping paradigm was applied showing an increased BOLD response within S1 and M1 following 30 min of whole-hand stimulation with a mesh glove. In the study of Wu et al. [2005], 2-h stimulation was applied to the median nerve at the wrist and as activation paradigm visually paced thumb movements were performed. After stimulation, increased activations up to 1 h were found in M1, S1, and dorsal premotor cortex. In both these studies, but also in this study, activations within S2 were not reported, suggesting that the region around S2 is rather involved in stimulus perception generation than in processing the afferent input [Radovanovic et al., 2002].

In this study, clusters of activations were obtained within the left precentral and postcentral gyrus in the vicinity of the hand area. Furthermore, the ROI analysis—based on anatomical data—confirmed that both the specific sensory and motor regions showed a higher responsiveness to finger tapping than other coactivated areas within the sensorimotor network. Compared with the NOSTIM group, these movement-related BOLD activations remained increased 1 h poststimulation, indicating synaptic processes related to neuroplasticity.

In comparison to the results reported by Golaszewski et al. [2004], this study displays shorter lasting poststimulation effects localized within smaller brain regions. Beside differences in the induction method (electrical versus mechanical), differences in the motor task may account for these effects. In the study of Golaszewski et al., finger tapping was performed with the nondominant hand, and further speed and accuracy of tapping was less thoroughly trained before scanning. Thus, it seems likely that learning occurred during task repetition in the scanner. During learning (dominant hand), activations including premotor cortex and SMA have been demonstrated, whereas with practice these activations decreased [Park et al., 2010]. Furthermore, during learning with the nondominant hand, a stable increase of cerebral blood flow (CBF) was found specifically within the ipsilateral SMA in addition to several other brain areas [Grafton et al., 2002]. For these

reasons, it is conceivable that significant activation of the ipsilateral SMA appeared in the study of Golaszewski et al. and that the fading of the stimulation-induced effect could have been delayed through the learning-induced effect.

Somatosensory-Evoked Neuroplastic Effects

The outlasting effect as found by the increased movement-related BOLD response indicates some cortical remodeling as a consequence of changed synaptic efficacy. Current evidence suggests various plasticity-promoting mechanisms in the sensorimotor cortex, such as rapid modulation of GABA concentration and induction of long-term potentiation (LTP). Modulation of GABA concentration with cortical map reorganization was described first in rats following peripheral nerve transection [Jacobs and Donoghue, 1991], but later also in humans during motor learning [Floyer-Lea and Matthews, 2005] and somatosensory stimulation [Kaelin-Lang et al., 2002]. During such interventions, GABA concentration reduces, resulting into a regional disinhibition of cortical neurons associated with an enlarged cortical representation. LTP-like plasticity further depends on *N*-methyl-D-aspartate receptor activation followed by a cascade of synaptic processes [Shaw et al., 1994] including synaptogenesis [Kleim et al., 2004]. Both plasticity-promoting mechanisms seem to be entangled as, for example, a reduction in GABA inhibition is thought to facilitate LTP-like plasticity [Benali et al., 2008].

An important question is how these synaptic mechanisms are reflected in the poststimulation increased BOLD signal, as fMRI only provides an indirect measure of neural activity by measuring task-related changes in cerebral hemodynamics. Concerning the first mechanism, it was shown with MR spectroscopy that synaptic inhibition as measured with baseline GABA concentration is inversely correlated with the BOLD signal change in human visual cortex [Donahue et al., 2010; Muthukumaraswamy et al., 2009] and in rat somatosensory cortex [Chen et al., 2005]. For our study, it can be interpreted that a reduction of GABA concentration should then generate an increased BOLD signal, which is in line with our results. On the other hand, less is known about how LTP-like plasticity is reflected in the BOLD signal. However, it can be assumed that the recruitment of additional functional synapses (Hebbian plasticity) rather should generate an increased task-related hemodynamic response.

For interpretation of present results, we also refer to a previous TMS study where an identical stimulation protocol was examined [Christova et al., 2011]. In that study, the paired-pulse paradigm [Kujirai et al., 1993] was applied to assess intracortical inhibition (related to GABA) and intracortical facilitation independently. After 25-Hz flutter stimulation, we found a disinhibition in the contralateral motor cortex lasting for 1 h and a facilitation lasting at least for 2 h. These results support evidence that first a

rapid GABAergic response is generated, which fades out after formation of more stable functional synapses. Similar poststimulation effects on cortical excitability were also reported in other TMS studies, as described in the Introduction section.

It has to be pointed out here that TMS assessments are commonly performed over relaxed muscles, thus our previous study [Christova et al., 2011] reflects stimulation-induced plastic changes in resting networks. In this study, we observed task-related CBF changes, thus these results reflect plastic changes in activated networks. As noted above, there are some potential drawbacks of studying task-related CBF changes, such as dependence on the motor task, learning-induced effects, and handedness. Therefore, in addition to task-related fMRI, resting-state fMRI (R-fMRI) is suggested for future research. With R-fMRI, spontaneous slow (<0.1 Hz) fluctuations of the BOLD signal are observed, reflecting functional connectivity of resting networks [Biswal et al., 1995]. Here, in the last years, a vast body of knowledge has accumulated [Friston, 2011] and recently also motor learning- [Vahdat et al., 2011] and stimulation-induced neuroplastic effects [Polanía et al., 2011] have been described.

Concerning the frequency of stimulation, 25 Hz showed very effective to induce outlasting cortical changes. Because of the frequency-following properties, cortical neurons become strongly entrained [Kelly et al., 1997] and according to the BCM (Bienenstock, Cooper, Munro) rule [Bienenstock et al., 1982] spiking at such frequency rather evokes LTP than long-term depression [Pitcher et al., 2003]. Other studies have applied pulse stimuli with a carrier frequency of 100 Hz [Siedentopf et al., 2008] or 128 Hz [Snyder, 1992; Tobimatsu et al., 1999] to demonstrate stable online effects. However, for chronic stimulation, frequencies above 50 Hz are less suited because of the evocation of spinal reflexes [Bongiovanni and Hagbarth, 1990] and proprioceptive illusions [Goodwin et al., 1972]. In a previous fMRI study with pneumatic stimulation (index and middle fingers), it was further shown that pulsed stimulation with randomly changing frequencies is advantageous to evoke more stable online effects [Gallasch et al., 2010]. Further studies are necessary to evaluate which stimulus patterns are most effective to generate outlasting neuromodulatory effects and how these effects depend on stimulus duration.

For clinical practice, the finding that M1 remains activated 1 h following flutter stimulation is of potential relevance. For patients with motor deficits secondary to stroke, it has been shown that electrical afferent stimulation [Conforto et al., 2007; Wu et al., 2006] enhances the effectiveness of neurorehabilitation. Recently, also mechanical stimulation (muscle vibration above 60 Hz) was shown to improve motor recovery [Liepert and Binder, 2010; Marconi et al., 2011]. Compared with electrical nerve stimulation typically applied for 1 or 2 h to evoke lasting neuromodulatory effects, mechanical stimulation apparently requires shorter time to obtain similar effects. At

least, mechanical flutter stimulation should also be beneficial in robotic rehabilitation applications. By superposition of mechanical oscillations during a movement training [Christova et al., 2010], additional afferent input is provided such increasing motor cortical excitability with potential to influence motor performance in patients with brain lesions.

CONCLUSIONS

The present analysis demonstrates that 20 min of mechanical flutter stimulation induces robust poststimulatory activations within the sensorimotor cortex. With respect to previous TMS studies demonstrating functional plastic changes within M1, this research states that the movement-related hemodynamic response also reflects these effects. In summary, the study sheds more light on interpretation of such results from TMS and fMRI measurements and advances our understanding on the stimulation-evoked neuromodulatory effects in the sensorimotor network.

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