Published in final edited form as:

Exp Brain Res. 2012 June ; 219(3): 403–408. doi:10.1007/s00221-012-3102-z.

Reduced surround inhibition in musicians

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Abstract

To investigate whether surround inhibition (SI) in the motor system is altered in professional musicians, we performed a transcranial magnetic stimulation (TMS) study in 10 professional musicians and 15 age-matched healthy non-musicians. TMS was set to be triggered by self-initiated flexion of the index finger at different intervals ranging from 3 to 1000 ms. Average motor evoked potential (MEP) amplitudes obtained from self-triggered TMS were normalized to average MEPs of the control TMS at rest and expressed as a percentage. Normalized MEP amplitudes of the abductor digiti minimi (ADM) muscles were compared between the musicians and non-musicians with the primary analysis being the intervals between 3 and 80 ms (during the movement). A mixed-design ANOVA revealed a significant difference in normalized ADM MEPs during the index finger flexion between groups, with less SI in the musicians. This study demonstrated that the functional operation of SI is less strong in musicians than non-musicians, perhaps due to practice of movement synergies involving both muscles. Reduced SI, however, could lead susceptible musicians to be prone to develop task-specific dystonia.

Keywords

Transcranial magnetic stimulation; Surround inhibition; Motor evoked potential; Musician; Dystonia

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The authors report no conflict of interest.

Introduction

Surround inhibition (SI), suppression of excitability in an area surrounding an activated neural network, is a physiological mechanism that focuses neuronal activity in both sensory and motor systems. In the motor system, it aids the selective execution of desired movements (Mink 1996). Functional existence of SI can be demonstrated in the human motor system using transcranial magnetic stimulation (TMS) (Sohn and Hallett 2004b). Motor evoked potential (MEP) amplitude of a little finger muscle was significantly suppressed during voluntary flexion of the index finger, despite an increase in spinal excitability (Sohn and Hallett 2004b). Modulation of intracortical inhibition could assist the selection of desired movements (with reduced inhibition) as well as the prevention of unwanted movements (with increased inhibition) (Stinear and Byblow 2003; Zoghi et al. 2003). A disturbance in SI with impaired modulation of intracortical inhibition was demonstrated in patients with focal hand dystonia (Sohn and Hallett 2004a; Stinear and Byblow 2004; Beck et al. 2008).

Focal dystonias, particularly those involving the arms, are often task-specific that is, they occur exclusively or primarily when the patient performs a specific task. Tasks capable of inducing action dystonia almost always require either highly repetitive movements or extreme motor precision (Tolosa and Marti 1997). Professional musicians, with their years of practice involving repetition of precise and complicated movements, are prone to this condition, and about 1% of professional musicians may develop dystonia (Altenmüller and Jabusch 2009). Professional musicians, particularly those who began training early in life, have structural and functional differences in the motor regions in the brain associated with musical training (Schlaug et al. 1995; Schneider et al. 2002; Gaser and Schlaug 2003; Koeneke et al. 2004). Musicians have improved skill making individuated finger movements (Slobounov et al. 2002). In this study, we hypothesized that repetitive hand exercise such as musical instrument training for a long-period of time may increase SI along with the structural and functional changes in the human motor cortex (M1).

Methods

Subjects

Ten healthy, right-handed professional musicians (mean age: 23.3 years, range: 21–28 yrs; 9 women) and 15 right-handed non-musician volunteers of similar age (mean age: 23.0 yrs, range: 21–25 yrs; 4 women) participated in this study after giving their written informed consent. Handedness of each subject was assessed using the 10 items related to hand dominance of the 12-item version of the Edinburgh Handedness Inventory (Oldfield 1971). The musicians were either undergraduate or postgraduate students in the college of music who majored in piano playing. All musicians started their piano lessons from early childhood (7 yrs or younger), and since then, continued their practice of piano playing daily for at least 2 hours or longer. Cumulative life practice time ranged from 11680 to 37230 (mean, 20951) hours. Non-musicians were selected to have a major subject outside of music, no hobby for playing musical instruments, and no experience of piano lessons before formal elementary school education. This study was approved by the local ethics committee.

TMS

Surface electromyography (EMG) activity was recorded (bandpass, 10–2000 Hz) from the flexor digitorum superficialis (FDS) and the abductor digiti minimi (ADM) muscles of the right hand using a conventional amplifier (P511 High Performance AC Preamplifier, GRASS Instrument, West Warwick, USA). The signal was digitized at a frequency of 5 kHz and fed into a laboratory computer for further off-line analysis. A figure-of-eight shaped coil (each loop measuring 70 mm in diameter) connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK) was placed flat on the scalp over the M1 at the optimal site for eliciting maximal amplitude MEPs in the contralateral ADM. The individual resting motor threshold (RMT) was determined to the nearest 1% of the maximum stimulator output and was defined as the minimal stimulus intensity required to produce MEPs of $>50 \mu\text{V}$ in at least 5 of 10 consecutive trials.

Using a LabVIEW program (National Instrument, Austin, TX, USA) and a Schmitt discriminator, TMS was set to be triggered by EMG activity of FDS (self-triggered TMS) similar to previous studies (Sohn and Hallett 2004a; Sohn and Hallett 2004b). The sensitivity of the Schmitt discriminator was set at a level sufficient to correctly detect the onset of EMG activity, but not to produce triggering at rest (usually 100–150 μV peak-to-peak EMG amplitude). ‘Go’ signals were given at random intervals between 5 and 9 s. Subjects were asked to flex their index finger briefly after the ‘go’ signal with a self-paced delay (subjects were instructed not to react immediately). Before the experiment, subjects practiced making a brief (duration around 100 ms) and selective movement while monitoring their own EMG activity. Seven sessions of self-triggered TMS were performed in a random order at variable intervals (3, 15, 40, 80, 200, 500, and 1000 ms) between EMG onset and TMS triggering. Two control sessions without self-triggering (still with the ‘go’ signal) were administered before and after self-triggered sessions. MEP size was determined by averaging the peak-to-peak amplitudes over 18 trials for each session at a stimulus intensity of 140% individual RMT in both self-triggered and control sessions. Average MEP amplitudes obtained from self-triggered TMS were normalized to average MEPs of the control TMS and expressed as a percentage.

Control experiment

Input-output curves of ADM MEPs with stimulation intensities of 0.9, 1.0, 1.1, 1.2 and 1.3 $\text{ST}_{1\text{mV}}$ (the minimal stimulation intensity required to produce MEPs of $>1\text{mV}$ in at least 5 of 10 consecutive trials) were measured at rest in 5 right-handed musicians (mean age: 23.6 years, range: 21 – 25 years; 2 men) and 5 right-handed non-musicians (mean age: 24.4 years, range: 24 – 25 years; all men). The selection criteria for musicians and non-musicians were identical to the primary experiment. The musicians and non-musicians participated in the control experiment were different from those in the primary experiment. TMS stimuli were delivered randomly between 5 and 7 seconds, with 12 stimuli at each stimulation intensity beginning with the lowest intensity, i.e., 0.9 $\text{ST}_{1\text{mV}}$. The stimulation intensities were chosen based on Rosenkranz et al’s observation (Rosenkranz et al. 2007), in which the slope of input-output curves was different between musicians and non-musicians in the range of these stimulation intensities.

Statistical analysis

Data are expressed as mean $\pm$ SEM. Demographic and physiological data were compared between two groups by using an unpaired t-test, and gender distributions were compared between two groups by using a χ^2 test. Resting MEPs in the two groups were compared before and after self-triggered sessions by using mixed-design ANOVA with two factors such as 'group' and 'time (before and after)'. Normalized MEP for the self-triggered sessions at the different intervals were compared between musician and non-musician groups, by using mixed-design ANOVA. In order to compare SI between the two groups, normalized MEPs at intervals only during index finger flexion (3, 15, 40 and 80 ms) were included in the primary analysis, because SI has been shown to be present only during this period (Sohn and Hallett 2004b; Sohn and Hallett 2004a). Input-output curves measured in the control experiment were compared between two groups, using mixed-design ANOVA. As allowed by the ANOVA, ADM MEPs at each stimulation intensity were compared between two groups, using unpaired t-test with Bonferroni correction for multiple comparisons. The assumption for use of parametric tests was verified by Kolmogorov-Smirnov test. We employed a mixed-design ANOVA with unstructured covariance pattern if the data were non-spherical as verified by Mauchly's test of sphericity. $P < 0.05$ was regarded as significant.

Results

Demographic and physiological data for the primary experiment are shown in Table 1. All subjects participated in this study were right-handed as assessed by Edinburgh Handedness Scale, but mean laterality quotients were significantly higher in non-musicians than musicians. Mean RMT was comparable between musicians and non-musicians. Control MEPs before and after self-triggered sessions were comparable between the two groups, analyzed by mixed-design ANOVA with 'group' and 'time' as factors (d.f.=1, $F=0.12$, $p=0.728$ for 'group'; d.f.=1, $F=0.27$, $p=0.612$ for 'time'; d.f.=1, $F=0.02$, $p=0.889$ for their interaction). Both musicians and non-musicians performed index finger flexion selectively and briefly. Off-line analysis of the EMG recordings (time window; up to 200 ms after movement onset) revealed that the average duration of the FDS was comparable statistically between musicians and non-musicians. Root mean square EMG activities of the FDS (measured from the EMG traces recorded at 200, 500 and 1000 ms intervals) were also comparable between the two groups. The ADM was usually quiet or slightly active with a small amount of EMG during index finger flexion. Root mean square EMG activities of ADM were also statistically comparable between musicians and non-musicians.

In the primary analysis concerning only the stimulus intervals during index finger flexion (i.e., 3, 15, 40, and 80 ms), the mixed-design ANOVA indicated a significant effect of 'group' (d.f.=1, $F=5.18$, $p=0.032$) and a tendency of a effect of 'interval' (d.f.=3, $F=2.62$, $p=0.075$), but no interaction (Fig. 1). The group effect was due to inhibition of the MEPs only in the control group, and the interval effect was due to smaller MEPs early in the interval. In musicians, cumulative amount of life practice time did not correlate to the average ADM MEPs during index finger flexion. However, an post-hoc exploration revealed that this amount correlated positively and significantly to the average ADM MEPs at

intervals of 3 and 15 ms ($r=0.64$, $p=0.046$; Fig. 2; these intervals were chosen because SI was shown to operate maximally during early phase of index finger flexion previously). Laterality quotients were not correlated with the average SI during index finger flexion in either group, although they were significantly higher in non-musicians than musicians. Because there was a significant difference in gender distribution between the two groups, a mixed-design ANOVA was performed to investigate the influence of the gender on SI in non-musicians, and revealed a significant effect of 'interval' (d.f.=3, $F=3.61$, $p=0.043$), but no effect of 'gender' and their interaction.

The control experiment demonstrated that musicians showed a steeper input-output curve than non-musicians (Fig. 3). Mixed-design ANOVA using 'group' (musician, non-musician) and 'intensity' (0.9, 1.0, 1.1, 1.2, and 1.3 ST_{1mV}) as factors revealed a significant effect of 'intensity' (d.f.=4, $F=54.85$, $p<0.0001$) and their interaction (d.f.=4, $F=4.21$, $p=0.008$), but no effect of 'group' (d.f.=1, $F=3.45$, $p=0.101$). Individual comparison of MEPs at each stimulation intensity with a correction for multiple comparisons revealed a significant difference at 1.3 ST_{1mV} ($p=0.003$), but failed to show statistically significant differences at other intensities.

Discussion

The present results demonstrated that during index finger flexion, MEPs of the ADM were different between musicians and non-musicians. Considering the results of previous studies showing enhanced spinal excitability of the surrounding muscles (assessed by F-wave or H-reflex measurements) during finger movements (Sohn and Hallett 2004a; Sohn and Hallett 2004b; Beck et al. 2008), the unchanged MEPs until 80 ms in both musicians and non-musicians likely indicates that there is some supraspinal inhibition, i.e., SI, is exerted on the ADM during index finger flexion and counterbalances the influence of spinal excitation on that muscle. The results appear to indicate, contrary to our hypothesis, that SI exerted on the ADM operates less well in musicians than in non-musicians. EMG recordings revealed comparable EMG activity in the ADM between musicians and non-musicians; excluding a difference in co-contraction of the ADM during index finger movement that might also explain the difference in SI. SI is modulated according to the force applied from the active muscle (Beck et al. 2009). Comparable FDS EMG activities during index finger flexion may indicate comparable force applied between the two groups. Because spinal excitability was not assessed in this study, the potential contribution of differences in spinal excitability to the current result cannot be excluded. Our participants showed a significant difference in gender distribution between musicians and non-musicians, which might have biased the present results. However, lack of difference in SI between male and female non-musicians participating in this study may minimize this possibility.

In the additional experiment, musicians showed a steeper input-output curve than non-musicians, as has been previously demonstrated by Rosenkranz et al. (Rosenkranz et al. 2007). Although the mechanism of this change in musicians is unclear, the steeper slope of musicians means that any change in inhibition/facilitation would lead to a greater change in MEP than in non-musicians. Given that, for a similar amount of inhibition, there might be more MEP changes in musicians, but in fact the MEP moved in the opposite direction. Thus,

the input-output curve difference does not explain the present results. The stimulation intensities employed in input-output curves in this study may not represent conventional measures of corticomotor excitability, which usually include sub-RMT intensities. However, the main reason of input-output curve measurements in this study is to compare our participants to those in Rosenkranz et al.'s study (Rosenkranz et al. 2007), and to evaluate the slope in the region of stimulation rather than to measure corticomotor excitability itself.

Plastic changes in the M1 can be induced by repetitive motor practice involving the digits (Classen et al. 1998) and acquisition of hand motor skills (Karni et al. 1995; Pascual-Leone et al. 1995). In professional musicians, playing a musical instrument for a long period of time, which requires complex skills, and intensive motor and sensory training, is expected to produce changes in the functional properties and connectivity of the neurons in the sensorimotor cortex. As expected, musicians' brains often show various structural and functional changes, which include increase in gray matter volume in the sensorimotor cortex (Gaser and Schlaug 2003), and enlarged cortical somatosensory representations of the fingers (Elbert et al. 1995). Long-term practice of complex finger movements in musicians may also induce enhanced functional coupling of different finger muscles, which could be linked to reduce SI between them. If the little finger (or the ADM) is heavily trained in pianists, long-term practice of the little finger simultaneously with the index finger might induce a facilitatory interconnection between these two fingers, and reduced inhibitory influence (i.e., SI). More reduction of SI in musicians with higher cumulative practice time than those with lower practice time shown in this study supports this assumption. Rosenkranz and colleagues (Rosenkranz et al. 2005) demonstrated that healthy musicians showed overlapped and fused sensorimotor interaction between the thumb and index finger muscles, compared to non-musicians. They concluded that this finding might indicate an increased functional connectivity, which could be advantageous for the performance of complex movements, and speculated that further progression of this basic pattern of reorganization might cause musician's cramp (Rosenkranz et al. 2005). Thus, reduced SI in musicians may not indicate functional disturbance, but represent strengthening of functional coupling between different finger muscles, which could help the performance of complex synergistic finger movements. However, if this change progresses further in susceptible musicians, then it could lead to complete loss of SI as shown in patients with focal hand dystonia.

Acknowledgments

This work was supported by the Brain Korea 21 Project for Medical Science, Yonsei University. Dr. Hallett is supported by the NINDS Intramural Program. We thank Hye S. Lee, MS, for her helpful assistance in statistical analysis.

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Fig. 1.

Normalized MEP amplitudes of ADM during self-triggered TMS. Normalized MEP amplitudes were significantly higher in musicians than non-musician controls during index finger flexion, analyzed by a mixed-design ANOVA. Error bars indicate standard error of the mean.

Fig. 2.

A scattergram showing the relationship between the cumulative life practice time and the average ADM MEPs at 3 and 15 ms intervals. The cumulative life practice time in musicians correlated positively and significantly to the average ADM MEPs ($r=0.64$, $p=0.046$).

Fig. 3.

Input-output curves of resting ADM MEPs. Musicians showed a steeper slope of input-output curve than non-musicians. An asterisk indicates a significant difference between musicians and non-musicians.

Table 1

Demographic and physiological data

Variables	Non-musicians (n=15)	Musicians (n=10)	p-values
Age (years)	23.0 ± 0.3	23.3 ± 0.9	0.704
Gender (M:F)	11 : 4	1 : 9	0.001
Laterality quotient (%)	96.4 ± 2.0	79.5 ± 7.0	0.014
RMT (% MSO)	52.6 ± 2.0	54.1 ± 4.2	0.723
MEP at 140% RMT (mV)			0.728*
before self-triggered sessions	1.04 ± 0.22	1.19 ± 0.25	0.612**
after self-triggered sessions	1.00 ± 0.22	1.15 ± 0.27	0.889***
FDS EMG duration during index finger flexion (ms)	127.9 ± 10.2	111.4 ± 8.6	0.263
FDS EMG activity during index finger flexion (RMS EMG activity, mV.ms)	4.60 ± 0.49	4.31 ± 0.58	0.710
ADM EMG activity during index finger flexion (RMS EMG activity, mV.ms)	1.40 ± 0.12	1.56 ± 0.10	0.342
Surround inhibition (self-triggered MEP / resting MEP, %)			
3 ms interval	85.2 ± 6.3	110.1 ± 6.5	
15 ms interval	95.3 ± 5.8	116.0 ± 7.8	
40 ms interval	103.3 ± 7.1	110.7 ± 8.0	
80 ms interval	108.8 ± 7.1	131.8 ± 15.2	
200 ms interval	145.8 ± 13.4	165.2 ± 27.7	
500 ms interval	123.0 ± 8.6	130.6 ± 29.0	
1000 ms interval	116.9 ± 7.9	133.9 ± 19.1	

RMT, resting motor threshold; MSO, maximal stimulator output; MEP, motor evoked potential; FDS, flexor digitorum superficialis; EMG, electromyography; RMS, root mean square; ADM, abductor digiti minimi;

*, **, *** p-values for 'group', 'time, and their interaction, respectively.