Alteration of sensorimotor integration in musician’s cramp: impaired focusing of proprioception

Karin Rosenkranz\textsuperscript{a,1}, Eckart Altenmüller\textsuperscript{b}, Sabine Siggelkow\textsuperscript{a}, Reinhard Dengler\textsuperscript{a,\ast}

\textsuperscript{a}Department of Neurology, Medical School Hannover, 30623 Hannover, Germany
\textsuperscript{b}Institute of Music Physiology and Performing Arts Medicine, Academy of Music and Drama, Hannover, Germany

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Abstract

Objective: The influence of muscle vibration (MV) as a strong proprioceptive input on motorcortical excitability was studied in 5 patients with musician’s cramp, 5 musician controls and 5 non-musician controls.

Methods: The relaxed flexor carpi radialis (FCR), involved in the dystonic movement in all patients, was vibrated using low frequency (80 Hz) and low amplitude (0.5 mm). Transcranial magnetic stimulation (TMS; intensity, 120\% of motor threshold) was applied without MV, 3 and 9 s after the onset of MV. Motor-evoked potentials (MEPs) in the FCR and in the antagonistic extensor carpi radialis (ECR) were recorded.

Results: With MV, musician and non-musician controls showed a facilitation of MEPs in the FCR and a decrease of MEPs in the ECR. In musician’s cramp, both phenomena were significantly less pronounced.

Conclusions: The reduced facilitation of MEPs in musician’s cramp indicates a reduced MV-induced activation of motorcortical areas representing the FCR. The less pronounced inhibition by MV reflects a reduced inhibitory control of the antagonistic ECR. As there were no differences between musician and non-musician controls, the observed changes in musician’s cramp refer to this special form of focal dystonia. An impairment of focused motorcortical activation by proprioceptive input from a muscle involved in the dystonic movement is suggested. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Musician’s cramp; Muscle vibration; Transcranial magnetic stimulation; Motor-evoked potentials; Sensorimotor integration

1. Introduction

Musician’s cramp is regarded as a task-specific focal dystonia associated with extensively rehearsed complex movements, such as playing a musical instrument at a professional level. It occurs in a relatively stereotypical manner, often involving involuntary cramping of single fingers (Lederman, 1988; Jankovic and Shale, 1989; Hallett, 1998). The pathophysiology is not well understood. Clinical evidence for the importance of the somatosensory input is provided by the observation that sensory tricks, such as playing with a latex glove, can improve the dystonic symptoms (Hallett, 1995; Berardelli et al., 1998). Experimental evidence for an essential role of the somatosensory system in the pathophysiology of dystonia is also growing. Stereotypical repetitive movements can induce enlargement and overlapping of sensory receptive fields, and consequently, cause an impairment of complex movements (Byl et al., 1996). Recent magnetoencephalographic studies in musicians suffering from focal hand dystonia revealed that there is a smaller distance or fusion between the representations of single digits in the somatosensory cortex (Elbert et al., 1998).

The symptoms of musician’s cramp are often only apparent in the context of instrumental playing (Altenmüller, 1998). This task specificity might represent a disorder of certain motor subroutines (Kaji et al., 1995b), which require sensory feedback, especially from muscle spindles. Therefore, proprioception seems to play an important role in the pathophysiology (Grünewald et al., 1997; Kaji et al., 1995a). This view is supported by PET studies in dystonic patients showing reduced responses to vibration in the primary sensorimotor area and the supplementary motor area (Tempel and Perlmutter, 1993). Muscle vibration (MV) applied at low frequencies and amplitudes mainly excites muscle spindle primaries (Burke et al., 1976; Roll et al., 1989) and, in healthy subjects, induces a bilateral frontocentral negativity indicating cortical activation (Münte et al., 1996). The latency of this negativity is similar to that of illusionary motion perception, another cortical...
phenomenon caused by vibration (Elbert and Rockstroh, 1987; Matthews, 1982). During MV, the motor-evoked potentials (MEPs) are enhanced in the vibrated muscle in response to transcranial magnetic stimulation (TMS; Claus et al., 1988a,b). By comparing the facilitatory effect of long-lasting MV on MEPs in response to electrical and magnetic brain stimulation, the vibration-induced enhancement of MEPS has been shown to occur only in response to TMS, convincing evidence for a cortical facilitatory effect of MV applied with this duration (Kossev et al., 1999). In antagonistic muscles, MV causes reciprocal inhibition which is thought to occur mainly on the spinal level (Gillies et al., 1969; Baldissera et al., 1983; Day et al., 1984). Recent studies, however, have shown an inhibition of antagonistic muscles by muscle afferents, also on the cortical level (Bertolasi et al., 1998).

The purpose of this study was to investigate the processing of proprioception by comparing the effects of MV on motor cortical excitability in patients with musician’s cramp and in healthy musicians, as well as non-musician controls.

2. Materials and methods

2.1. Subjects

Five patients with musician’s cramp, 5 healthy musicians and 5 non-musician controls were studied. Dystonic symptoms were localized on the dominant side in 3 patients (two right-handed, one left-handed) and on the non-dominant side in two patients (for further details see Table 1). Two right-handers (cases 1 and 3) also had writer’s cramp. One patient (case 4) reported an uncertain positive family history, with first degree relatives possibly affected by writer’s cramp. In the remaining patients, the family history was negative. No patient had other dystonic symptoms or evidence of secondary dystonia. Patients had no drug treatment at the time of the study.

The 5 healthy musicians were age-matched, and also skill-matched with the musician’s cramp patients concerning their ‘total-practice-life-time’. As a second control group, 5 healthy age-matched controls were studied, who had never played any musical instrument.

Patients and subjects gave written informed consent to the study, which was approved by the ethics committee of the Medical School Hannover.

2.2. Experimental design

Subjects were comfortably seated in a chair with one arm gently fixed in slight abduction from the trunk and flexion in the elbow. Trains of MV of 10 s duration, with random intertrial intervals of 4–7 s, were applied to the relaxed flexor carpi radialis muscle (FCR) using an electromagnetic mechanical stimulator (Ling Dynamics System Ltd., UK) with a disk surface of 2 cm in diameter. Low intensity MV (frequency, 80 Hz; amplitude, 0.5 mm) was employed to avoid generation of the tonic vibration reflex (Lance et al., 1966; Hagbarth and Eklund, 1968; Marsden et al., 1969).

The FCR on the symptomatic side was vibrated in the patients. In the controls, MV was applied to the right FCR in 8 subjects, and to the left in two. TMS (MagStim 200; MagStim Company Ltd., UK) was carried out using a circular stimulating coil with an outer diameter of 9 cm. The coil was centered over the scalp in a suitable position to obtain MEPS in the vibrated FCR and in the antagonistic extensor carpi radialis (ECR). A counterclockwise current flow in the coil (viewed from above) was chosen for stimulation of the left hemisphere and a clockwise flow for the right hemisphere. The intensity of the magnetic stimuli was 120% of the motor threshold, which was defined as the minimal intensity, to the nearest 1%, of stimulator output eliciting 3 responses of at least 50 μV peak-to-peak amplitude in 5 stimuli.

MEPS were simultaneously recorded from the vibrated FCR and the antagonistic ECR using conventional surface EMG techniques. The selectivity of these recordings was tested by voluntary muscle contraction of each muscle separately before starting the experiment. The absence of voluntary or reflex EMG activity was controlled by continuous on-line monitoring, as well as off-line analysis of each trial. EMG signals were amplified (band pass, 10 Hz–5 kHz) and digitized (sampling rate, 10 kHz). Epochs of 300 ms duration (100 ms prior to the stimulus and 200 ms after) were stored on disk. Five TMS trials were performed without MV. Then, MV was started and TMS was applied, either at 3 or 9 s after the onset of MV, in a random sequence until 5 responses were obtained for each time.

2.3. Analysis of data

Data processing was performed off-line. The MEP parameters measured were total-voltage-time-integral (area) and latency. For each condition (without MV, 3 and 9 s after

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Duration of disease (years)</th>
<th>Handedness</th>
<th>Affected side</th>
<th>Clinical symptoms</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>7</td>
<td>Right</td>
<td>Right</td>
<td>Flexion of fingers 3 and 4 when playing guitar and writing</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>2</td>
<td>Right</td>
<td>Left</td>
<td>Flexion of finger 4 when playing clarinet</td>
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<td>3</td>
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<td>5</td>
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<td>Right</td>
<td>Flexion of fingers 3–5 when playing guitar and writing</td>
</tr>
<tr>
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<td>5</td>
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<td>Left</td>
<td>Flexion of finger 4 when playing clarinet and saxophone</td>
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<tr>
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<td>10</td>
<td>Right</td>
<td>Left</td>
<td>Flexion of finger 4 when playing viola</td>
</tr>
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</table>
onset of MV), 5 trials were obtained for each subject and pooled to calculate the mean values. The mean values with MV were normalized separately for each subject to the mean value of MEPs obtained without MV, which was set at 100%. These normalized values were pooled for each group. Within each group, the MEP values of each condition were compared using the paired t test.

The subject age, motor threshold, and normalized mean values of MEPs after 3 and 9 s MV were compared between the groups using the unpaired t test. Additionally, the non-normalized parameter of MEP (raw data) without MV was compared between groups using the unpaired t test. The effects of subject type (patient/control) and MV on the MEPs were analyzed using repeated measures analysis of variance (ANOVA), with subject type as the between group factor, MV in 3 conditions (without, after 3 and 9 s of MV) as the within group factor (repeated measures) and MEP parameters as dependent variables. Differences were considered significant when P, 0.05.

### 3. Results

The MEPs (mean ± SD) obtained without MV (baseline condition) and the normalized mean values of MEPs after 3 and 9 s of MV are listed in Table 2. In all groups, the motor threshold at rest and the MEP parameters of FCR and ECR without MV (baseline condition) were not significantly different.

### 3.1. Effect of MV on MEPs in the vibrated FCR

Continuous EMG monitoring showed that, with the MV parameters used, neither patients nor controls produced reflex activity, such as the tonic vibration reflex, in the vibrated FCR.

Comparing the two control groups, musicians and non-musicians, there were no significant differences between the MEP values of the FCR during MV. With MV, musician and non-musician controls revealed a significant increase of MEP areas in the FCR to a mean of 249% (±165%) after 3 s and 328% (±314 %) after 9 s (P, 0.05). In contrast, this MV-induced increase in the FCR was clearly less pronounced in musician’s cramp patients, showing 119% (±18%) after 3 s and 133% (±21%) after 9 s (n.s. after 3 s; P, 0.03 after 9 s; Figs. 1 and 2). The facilitatory effect of MV on MEP areas in the FCR was significantly smaller in patients than in musician and non-musician controls (ANOVA, P < 0.04; Figs. 1 and 2).

The MV-induced shortening of MEP latencies in the FCR was not significantly different between patients, musician controls and non-musician controls.

### 3.2. Effect of MV on MEPs in the functional antagonist ECR

As in the FCR, the MEP values in the ECR during MV were not significantly different between the musician and non-musician controls.

The MEP areas in the ECR were decreased with MV in musician and non-musician controls to a mean of 69 (±15%)
and 65% (±21%) after 3 and 9 s (P < 0.001), respectively. The decrease of the MEP areas in the patients showing 91 (±18%) and 87% (±26%) after 3 and 9 s, respectively was clearly less pronounced and without significant difference compared with the baseline condition (Figs. 1 and 2).

The MV-induced decrease of MEP areas in the ECR was significantly smaller in the patients than in the musician and non-musician controls (ANOVA, P < 0.01; Figs. 1 and 2). With MV, the MEP latencies of the ECR showed no significant differences between patients and musician and non-musician controls.

4. Discussion

The main findings of this study using TMS in patients with musician’s cramp are, compared with controls, a reduction of the MV-induced MEP facilitation in the vibrated FCR and of the simultaneous inhibition of MEPs in the antagonistic ECR.

Both control groups, the healthy musicians and the non-musicians, showed similar MEP changes during MV, providing convincing evidence that these alterations refer to musician’s cramp as a special form of focal action-induced dystonia. Since MEP sizes in the FCR without MV were fairly similar between patients and controls, the differences in MEP facilitation with MV point to alterations in the central processing of the proprioceptive input.

Previous studies have shown a facilitation of MEPs in the vibrated muscle when the vibration begins 9–14 ms before the transcranial stimulus, which was thought to result from the summation of descending pyramidal and ascending monosynaptic Ia afferents at the motorneuronal pool (Claus et al., 1988b). In addition, with long-lasting vibration, a significant enhancement of MEPs, which begins 120 ms after the onset of vibration and lasts up to 5000 ms, is described (Claus et al., 1988a,b), suggesting an influence of Ia afferents on the output cells of the motor cortex itself (Claus et al., 1988a). A recent study compared the effects of long-lasting MV on the MEPs of the vibrated muscle in response to transcranial electrical stimulation (TES) and magnetic stimulation (Kossev et al., 1999), which allows to distinguish between cortical and spinal
facilitations because of the known different sites of action of both stimulation techniques in the motor cortex when applied at low intensities (Rothwell, 1991). The fact that MEPs are enhanced 3 s after the onset of MV only in response to TMS is convincing evidence for a cortical site of facilitation. Therefore, it appears that the weaker MEP facilitation observed in the patients reflects a reduced cortical activation by MV in musician’s cramp, at least those areas representing the vibrated muscle. PET studies in patients with writer’s cramp further support the assumption of an altered cortical activation in focal dystonia. The increase of cerebral blood flow usually observed in the contralateral primary sensorimotor area and supplementary motor area during vibrotactile stimulation is significantly reduced in patients (Tempel and Perlmutter, 1993). Writer’s cramp patients also show a reduced activation of the contralateral primary motor cortex, but an enhanced activation of the frontal association cortex while writing a stereotypical word repetitively (Ceballos-Baumann et al., 1997). In addition, movement-related cortical potentials in writer’s cramp reveal a reduction of the early part of the negative slope in the contralateral and midline central recordings, suggesting a deficiency of contralateral motor cortex activation just prior to the EMG-onset. A failure to achieve normal motor cortex activation is proposed, which may have a significant impact in the final stages of sensorimotor integration required for normal skillful movement. In task-specific focal dystonia, these alterations closer to each other (Bara-Jimenez et al., 1998). Recent magnetoencephalographic investigations in dystonic musicians confirm these results, revealing a fusion of the representation of single digits in the somatosensory cortex, which leads to the suggestion that use-dependent susceptibility to digital representation fusion in the cortex may be involved in the etiology of focal dystonia (Elbert et al., 1998). Due to this misguided cortical plasticity, the further processing and integration of somatosensory input originating from fused receptive fields may cause a disturbance in the target motor cortical areas, as well as in the subcortical circuits involved.

A displacement and distortion of corticomotor maps has been described in writer’s cramp, which is suggested to reflect slowly evolving reorganizational changes in the primary motor cortex in response to alterations in sensorimotor input (Byrnes et al., 1998).

The pathophysiological role of the basal ganglia in focal, task-specific dystonia is still under debate and not well understood. The above mentioned assumption of an essential cortical component in this disorder and the role of the basal ganglia are not necessarily contradictory. An important function of the basal ganglia appears to be the modulation of cortical activation by filtering and focusing the thalamocortical input. A conceptual model has suggested that the basal ganglia facilitate selected motor mechanisms and inhibit competing motor mechanisms by balancing facilitation and inhibiting their cortical output targets (Hallett, 1998; Mink and Thach, 1993; Mink, 1996). A disturbance of this selection process may contribute to a more diffuse activation of sensorimotor cortical areas, which results in a less focused activation of the target area, also including adjacent areas. Both observed phenomena, the reduced facilitation of MEPs in the vibrated muscle and the impaired MEP inhibition in the antagonist, may therefore be an expression of a failure of focusing the proprioceptive input, which leads to an impairment of differentiated movements associated with involuntary muscle activation, occurring as highly task-specific and action-induced, in this form of focal dystonia.

In conclusion, our data confirm the special role of the proprioceptive input in task-specific focal dystonia. In patients with musician’s cramp, MV is less effective in facilitating MEPs following TMS in the vibrated muscle and inhibiting those in its antagonist than in normal subjects.

We suggest that this alteration is caused by impaired central sensory processing, which leads to an impairment of focused motorcortical activation.
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