

# Cross-modal plasticity of the motor cortex while listening to a rehearsed musical piece

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## Abstract

Learning a musical piece requires the development of a strong linkage between sensory and motor representations. Audition plays a central role and a tight cortical auditory–motor corepresentation is a characteristic feature of music processing. Recent works have indicated the establishment of a functional connection between auditory and motor cortices during the learning of a novel piece, although no causal relation has yet been demonstrated. Here transcranial magnetic stimulation of the cortical motor representation involved in musical performance was used to test excitability changes in piano players during auditory presentation of a rehearsed and a non-rehearsed piece. Results showed an increased motor excitability for the rehearsed but not for the non-rehearsed piece. Moreover, we observed an increase of excitability over time as intracortical facilitation was already present after 30 min of training whereas cortico-spinal facilitation increased after a longer training period (5 days).

## Introduction

Auditory–motor integration can be differentiated into two perspectives. The first involves the modulation of auditory representations by motor output. A learned motor behaviour triggers top-down auditory expectations that facilitate and refine auditory processing. The second involves the modulation of motor representations by auditory stimuli. Familiar sounds can facilitate and refine motor responses that have previously been associated with those sounds (Watkins *et al.*, 2003). Playing music is a particular case of an extremely complex process of integration between the auditory system (Pantev *et al.*, 2001), proprioceptive feedback and motor control.

Naive subjects show an auditory–sensorimotor electroencephalographic coactivity in the contralateral motor cortex, and in right fronto-temporal regions, after only 20 min of right-hand piano play that consolidates after 5 weeks of training, both during silently executed movements and passive listening (Bangert & Altenmüller, 2003). The training-induced activity in one of the two systems (either motor by silencing the instrument or auditory by passive listening) causes a preparatory activation in the other (Bangert *et al.*, 2001). For instance, a right hemispheric auditory cortex activation was found during silent tapping of a violin concerto (Lotze *et al.*, 2003a). The association between these maps is bidirectional and can also be observed with auditory stimuli. In expert pianists, activity of the primary motor cortex was observed during passive listening to music (Haueisen & Knösche, 2001). Such an association between cortical maps may result from a basic associative learning mechanism, in which both functional units are repeatedly temporally coactive (Hebb, 1949).

Although these studies demonstrated a linkage between auditory and motor cortices, little information has been provided about the underlying neurophysiological mechanisms. Therefore, we planned an experiment to extend previous results. For this purpose, transcranial magnetic stimulation offers the unique opportunity to display relations between areas with both high spatial and temporal definition as well as some insight into the underlying neurophysiological mechanisms.

The experimental procedure aimed to investigate the primary motor cortex activity in amateur musicians, while listening to a musical piece, before and after rehearsal. Furthermore, we tried to address more precisely the issue of the time-course of these putative adaptations. For this purpose, we evaluated changes in motor cortex excitability for the muscle involved in motor rehearsal. Excitability was measured with a single and a paired-pulse technique after both a short and a long training period.

## Materials and methods

Subjects ( $n = 15$ ; 11 females and 4 males; age  $\pm$  SD  $27.66 \pm 8.54$  years) were measured in two separate sessions with a  $5.40 \pm 1.41$ -day gap. Right-handed (assessed with the Edinburgh Inventory; Oldfield, 1971) amateur piano players with more than 8 years of instrumental practice were selected. Musical experience was measured from the start of piano lessons (mean  $\pm$  SD,  $7.26 \pm 2.15$  years), lifetime practice ( $17.60 \pm 8.95$  years; with average time without practice of  $3.60 \pm 4.48$  years) and actual training time per week ( $5.20 \pm 7.25$  h). All subjects gave their informed consent for the procedures, which were approved by the Ethics Board of the Medical Faculty of the University of Tübingen.

Subjects were comfortably seated on a reclining chair. Motor evoked potentials (MEPs) were recorded from surface electrodes

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overlying the left extensor carpi radialis (ECR) muscle. Fatigue and transcranial magnetic stimulation discomfort imposed a forced reduction of the length of the study by limiting the investigation to one hemisphere. We decided to test the right hemisphere and train with the left hand only. After amplification and band-pass filtering (5–1000 Hz; Neuroscan, Herndon, USA), the electromyographic signal was digitized at 5 kHz. Electromyographic epochs were cut from 250 to 50 ms prior to the magnetic pulse in order to measure the basal muscle activity and to discard spurious MEPs. Focal transcranial magnetic stimulation was delivered to the optimal scalp position for activation of the left ECR using a figure-of-eight coil connected to two Magstim 200 magnetic stimulators through a BiStim module (Magstim, Whitland, Dyfed, UK). The coil was positioned to induce a current perpendicular to the line of the right central sulcus and marked to ensure identical coil placement throughout the experiment (Werhahn *et al.*, 1994). The resting motor threshold (rMT), measured at the beginning of each session prior to other recordings, was defined as the minimum stimulus intensity that produced MEPs of > 50  $\mu$ V in at least three of five consecutive trials (Rossini *et al.*, 1994). Measures included a cortico-spinal excitability recruitment curve (RC) and intracortical facilitation (ICF). For the RC measurement, MEPs of three intensity steps (140, 150 and 160% of the rMT) were obtained in 10 trials per step, randomized across subjects. MEP amplitudes were measured peak-to-peak for each trial and later averaged off-line. All of the 15 subjects participated in this part of the study.

A paired conditioning–test stimulus technique (Kujirai *et al.*, 1993; Ziemann *et al.*, 1996) was used to study ICF. The test (second) stimulus intensity was adjusted to elicit an MEP of about 500–1000  $\mu$ V in peak-to-peak amplitude. The conditioning (first) stimulus was set to 80% of the rMT of the ECR muscle. Inter-stimulus intervals of 8 and 12 ms and a test stimulus alone were presented in a randomized order and applied 10 times each. Ten of the 15 subjects (eight females; age  $31.40 \pm 12.30$  years) participated in this part of the study.

Subjects were presented with three conditions: baseline, experimental and control. ICF and RC measures were taken during each condition. The baseline served as a reference point to establish the amount of excitability increase during the experimental and control conditions. The experimental condition consisted of passively listening to the left-hand part of a piano piece (J.S. Bach, Prelude no. 20 in A minor from the Wohltemperiertes Klavier, Second Book, Bach Werke Verzeichnis 889a). The control condition consisted of passively listening to a flute piece (J.S. Bach, Allemande for flute solo in A minor, Bach Werke Verzeichnis 1013) selected because the music is structurally very similar to the piano piece (sounds generated by MIDI Synthesizer, QuickTime; Apple Inc.). Both the piano and flute piece were unknown to the subjects, and require a fine and separate control of finger movements, both involving a continuous activation of the left ECR muscle. Subjects were asked to concentrate on the piece, while relaxing. Each presentation block was followed by a visual analogue scale questionnaire to rate their ability to concentrate on melody, rhythm and tempo, as well as the strength of the feeling of 'being driven' by the piece presented. We also asked how much the transcranial magnetic stimulation pulses disrupted their ability to concentrate. During Session 1 (~2 h), baseline, experimental and control blocks were recorded. The first part of the experiment was followed by 30 min of practice of the left-hand score of the experimental piece, using a professional keyboard (SL-990; Studio-logic). The performance was recorded at the end of this practice period (SX 1.0.51; Cubase). A 30-min interval was then used to lower the cortical activity enhanced by the intense motor training to a normal level (Classen *et al.*, 1998). Subsequently, one experimental and one

control block were again recorded. Subjects agreed to train the left hand part of the piano-piece at home. They received a personal diary and the left-hand musical score of the experimental piece, and were asked to report the amount of time spent practicing (average  $90.66 \pm 67.62$  min) until the second session of measurements (Session 2). The second session was, on average,  $5.4 \pm 1.45$  days after the first. During Session 2 (~1 h), new baseline, experimental and control blocks as well as a new performance were recorded. Experimental and control conditions were always presented in a randomized manner.

We used a repeated-measure design to allow a double within-subjects control, one granted by the parallel measurement during listening to a control piece, and the other by measuring before and after the training. This control is necessary to reduce possible effects due to the use of different pieces, instruments, pattern of movements and level of expertise. If the control and the experimental piece do not differ statistically before training, we can exclude the aforementioned source of errors as a principal factor.

Transcranial magnetic stimulation measures (rMT, RC and ICF) were compared using three ANOVAs. rMTs were evaluated with factor DAY (Session 1/Session 2) and RCs with factors CONDITION (EXP/CONTROL), TIME (PRE/POST/Session 2) and INTENSITY (140%/150%/160%). ICF was tested with factors CONDITION (BASE/EXP/CONTROL), TIME (PRE/POST/Session 2) and INTERVAL (8 ms/12 ms). All ANOVAs were followed by post-hoc *t*-tests corrected for multiple comparisons (Duncan's correction). All statistical tests were performed with the software STATISTICA 6 (StatSoft Inc., Tulsa, OK, USA).

Blinded performance evaluations (Sessions 1 and 2) were conducted by a professional musician (E.A.) for the following items: (i) number of pitch errors, (ii) number of rhythmic errors and (iii) expression using a visual analogue scale (0–10). A paired *t*-test analysis was applied to explore differences between the two sessions and subjective visual analogue scale ratings.

## Results

The rMT did not differ [ $t = 0.55$ , not significant (ns)] between the two separate sessions of testing (Session 1,  $39.4 \pm 5.04\%$ ; Session 2,  $40.3 \pm 4.54\%$ ). Electromyography of the target muscle during baseline (average 0.017  $\mu$ V) and listening to the rehearsed (average 0.023  $\mu$ V) and non-rehearsed (average 0.003  $\mu$ V) piece was also not different ( $F_{2,28} = 1.51$ , ns). These results indicate that MEP differences between conditions and sessions are not due to differences in resting muscle tension (electromyographic) or a different baseline cortical excitability (rMT).

The ANOVA for RC revealed a significant main effect for the CONDITION ( $F_{1,14} = 5.15$ ,  $P < 0.05$ ), TIME ( $F_{2,28} = 3.38$ ,  $P < 0.05$ ) and CONDITION–TIME interaction ( $F_{2,28} = 5.73$ ,  $P < 0.01$ ). Post-hoc *t*-tests showed that the RC amplitudes while listening to the piano after the long training period were higher than for the other condition and measurement time ( $P < 0.05$ ; Fig. 1). The ANOVA for ICF showed significant main effects for CONDITION ( $F_{2,18} = 11.84$ ,  $P < 0.001$ ) and a CONDITION–TIME interaction ( $F_{4,36} = 2.71$ ,  $P < 0.05$ ). In this case, listening to the piano resulted in a larger increase of facilitation than the other condition ( $P < 0.05$ ) after both the short and long training periods (Fig. 2). The baseline measure of RC (140%,  $t_{14} = 1.23$ , ns; 150%,  $t_{14} = 1.10$ , ns; 160%,  $t_{14} = 1.42$ , ns) and ICF (8 ms,  $t_9 = 1.35$ , ns; 12 ms,  $t_9 = 0.84$ , ns) showed no difference between the two sessions of recording. The pre-training measure of RC ( $t_{14} = 0.29$ , ns) and ICF ( $t_9 = 0.19$ , ns) showed no difference between the experimental and control conditions.

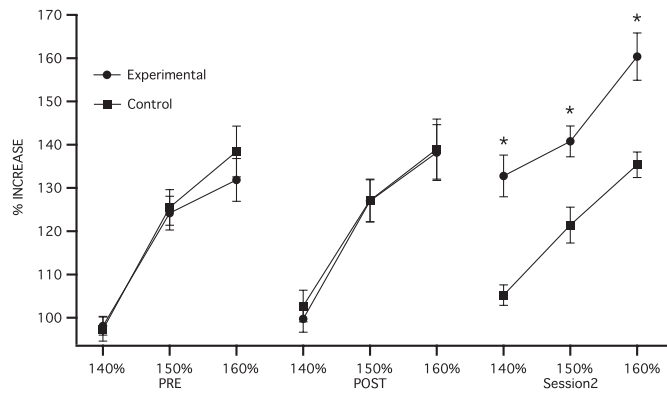


FIG. 1. Recruitment curve (RC) results. The RC motor evoked potential (MEP) amplitude increased with respect to the subjects' own baseline. Error bars indicate SEM across subjects. Listening to the rehearsed piece resulted in a larger increase of MEP during the Session 2 measurement ( $*P < 0.05$ , post-hoc  $t$ -tests).

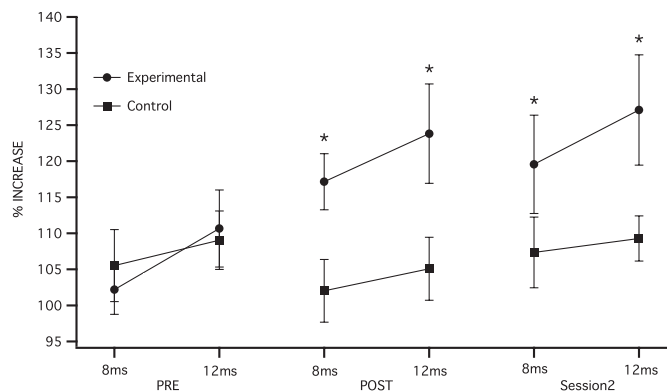


FIG. 2. Intracortical facilitation (ICF) results. The ICF mean amplitude increased with respect to the test stimulus. Error bars indicate SEM across subjects. Listening to the rehearsed piece resulted in a significant increase of ICF after training periods (both the short and long) ( $*P < 0.05$ , post-hoc  $t$ -tests).

The subjects' performance revealed a significant improvement between the two sessions. Pitch ( $t_{14} = 1.82$ ,  $P < 0.05$ ) and rhythmic errors ( $t_{14} = 2.76$ ,  $P < 0.01$ ) decreased significantly, and expression ( $t_{14} = 3.03$ ,  $P < 0.01$ ) was rated as improved. Moreover, subjects reported a larger feeling of 'being driven' by music while listening to the trained piece after practicing (short training,  $t_{14} = 2.55$ ,  $P < 0.05$ ; long training,  $t_{14} = 2.71$ ,  $P < 0.05$ ) compared with the experimental piece before training (see Table 1). The feeling of 'being driven' did

TABLE 1. Visual analogue scale (VAS) rating of feeling of 'being driven' by music

	VAS rating, session 1		VAS rating, session 2
	Pre-training	Post-training	
Experimental piece	2.97 ± 0.50	4.73 ± 0.76*	5.08 ± 0.66*
Control piece	2.42 ± 0.61	2.49 ± 0.74	2.00 ± 0.46

The feeling of 'being driven' by music, as reported using a VAS ranging from 0 to 10. Data are presented as mean ± SEM. Subjects gave significantly higher ratings for the experimental piece but only after training (short and long).  $*P < 0.05$ , compared with control conditions (paired  $t$ -test).

not differ between the control and experimental conditions ( $t_{14} = 1.73$ , ns) before training but did differ after training (short training,  $t_{14} = 3.24$ ,  $P < 0.01$ ; long training,  $t_{14} = 5.73$ ,  $P < 0.01$ ). The ability of the subjects to concentrate on the task did not differ between sessions ( $t_{14} = 1.60$ , ns).

## Discussion

Mastering a musical instrument requires considerable training for years in order to perform extremely precise movements, with regard to their timing and spatial characteristics. Musicians provide an exceptional opportunity to study how intense motor training can shape sensory and motor primary cortex representation (Pascual-Leone *et al.*, 1995; Pantev *et al.*, 2001; Münte *et al.*, 2002) as well as multimodal integration (Schon & Besson, 2005). Less is known about the cardinal feature during musical skill acquisition, i.e. the auditory motor information integration.

Recently, a few studies have explored the existence and time course of such a functional connection between auditory and motor primary cortices. Haeuissen & Knösche (2001) demonstrated primary motor cortex activation during passive listening to music in expert musicians and two functional magnetic resonance imaging studies showed the shared substrates of both listening and producing a melody with functional magnetic resonance imaging (Lotze *et al.*, 2003a; Bangert *et al.*, 2005). Another study showed an increase in auditory–sensorimotor synchrony due to the learning of a novel auditory–motor mapping (Bangert & Altenmüller, 2003). Results presented here support the idea that the concurrent presence of a movement and its auditory feedback, as is the case for rehearsal of a musical piece, leads to a functional link between the auditory representation and the primary motor cortex.

Consistent with other studies on training-induced plasticity (Classen *et al.*, 1998; Lotze *et al.*, 2003b), we observed no change in rMT, a measure related to resting membrane potential properties of cortical and spinal motor neurones (Ziemann *et al.*, 1996), between the two sessions. We found increased motor excitability of the ECR primary motor cortex representation, as evaluated by increasing single-pulse stimulations, after the long training period. However, an increase of the ICF after both the short and long training period was observed. This differential sensitivity of motor excitability and ICF underlines the idea that they target two different functional mechanisms. The single-pulse technique has been related to the functional evaluation of the cortico-spinal pathway (Devanne *et al.*, 1997; Chen *et al.*, 1998) and the size of the RC MEPs reflects more globally the corticospinal input–output balance involved in long-term learning (Ziemann *et al.*, 2001). However, the paired-pulse technique reflects the synaptic excitability of inhibitory and excitatory neural circuits at the level of the motor cortex that, in turn, control the excitability of the cortico-motor neurones (Kujirai *et al.*, 1993; Ziemann *et al.*, 1996). According to recent pharmacological studies, the GABA<sub>A</sub> receptor agonist and *N*-methyl-D-aspartate receptor antagonist result in a decrease of paired-pulse facilitation (Ziemann *et al.*, 1996, 1998; Di Lazzaro *et al.*, 2000). In parallel with this, a motor learning study showed that the *N*-methyl-D-aspartate receptor activation and GABAergic inhibition are involved in plasticity processes operating during the acquisition of a new motor skill (Donchin *et al.*, 2002). The early increase of the ICF could be seen as a plasticity process triggered by the passive listening to the trained piece. This may be interpreted best as an early shift in the balance of the synaptic efficacy of the horizontal motor cortical circuits towards less inhibition and more facilitation (Kujirai *et al.*, 1993; Ziemann *et al.*, 1996, 2001).

Nevertheless, some possible sources of confounding errors could not be fully controlled with the parameters in this study and no final conclusion can yet be drawn. It could be questioned whether the effect is due to the longer exposure to the experimental piece with respect to the control. If that is the case, passive listening could be a crucial factor in establishing an effective audio-motor coupling. In our opinion, this is not likely as listening to music is ubiquitous and done for hours each day by music students as well as non-musicians who are not capable of playing any instrument. In our view, an actual movement has to be performed and associated with a sound for an auditory-motor mapping to be learnt. Furthermore, our experiment does not take all of the structural differences present between the two musical pieces into account. The aim of our study was to explore whether motor facilitation was measurable during passive listening and after training, and to see whether the single and double pulse were effective for such a purpose. As a conservative approach, two quite different pieces were chosen. In fact, the extent to which the effects reported are triggered by specific structural variables in the pieces and how the system generalizes to novel material is the future key question to be addressed. Gender and hemispheric differences are other interesting and crucial issues in need of future research, keeping in mind that relevant processing in more experienced musicians shifts from the right to the left hemisphere and that we only investigated the right motor cortex.

Our data demonstrate that even a 30-min training period produces an increased ICF that, with longer training, develops into corticospinal facilitation, both absent before training. This result might lead to speculation that the subject is supposedly re-enacting his motor experience through this anticipatory mechanism, while passively listening. This view is supported by the behavioural data showing an increased subjective feeling of 'being driven' by music specific for the trained piece, and only after training. We can further speculate that simple listening to a piece vs. rehearsal and listening to the same piece would lead to two qualitatively different states of consciousness, characterized by the different amount of motor activity involved.

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## Abbreviations

ECR, extensor carpi radialis; ICF, intracortical facilitation; MEP, motor evoked potential; ns, not significant; RC, recruitment curve; rMT, resting motor threshold.

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