Left Prefrontal Cortex Contributes to Motor Imagery: A Pilot Study

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Abstract Transcranial magnetic stimulation (TMS) over the motor cortex during motor imagery results in increased amplitudes of motor evoked potentials (MEPs) in muscles specific to the imagined movement. Functional MRI studies demonstrate that motor imagery involves a widespread neural network including prefrontal and parietal areas. The purpose of this pilot TMS study was to explore whether the left prefrontal cortex (PFC) is an active part of the motor imagery network. MEPs were recorded in 5 healthy subjects in tibialis anterior (TA) muscles during the imagined right ankle dorsiflexion while the neural processes in the left PFC were disturbed by a single TMS pulse 300ms prior to the leg area stimulation with TMS. Motor imagery alone significantly increased MEP amplitudes in the target TA muscle compared to rest (440% on average, p=0.004). The left PFC stimulation prior to test stimulus significantly reduced the facilitation of MEPs during motor imagery (326%, p=0.031) but left PFC stimulation had no effect when delivered during rest (103%). This suggests a functional link between the left PFC and sensorimotor cortex actively involved in motor imagery. Appropriately timed TMS over the left PFC most likely disturbed the kinesthetic working memory required for maintaining motor imagery.

Keywords Prefrontal Cortex, Motor Cortex, Transcranial Magnetic Stimulation, Kinesthetic Working Memory, Motion Imagery, Ankle Dorsiflexion

1. Introduction Imagining motor actions, i.e. performing covert movements, is known to modulate corticospinal excitability [3, 4, 12]. Various neuroimaging studies utilizing PET or functional MRI support the idea that mental simulation of movements involves congruent brain areas that are active during action execution and during observation of actions performed by others [1, 2, 11, 16]. The motor evoked potentials (MEPs) evoked by a single pulse transcranial magnetic stimulation (TMS) are higher in amplitude in the target muscle when subjects imagine muscle contractions compared to rest and this effect is specific to the muscles involved in the imagined movement [3, 4, 12]. Moreover, there is reportedly a positive correlation between the MEP amplitude increase and the individual imagery ability [10, 17]. Besides a transient enhancement in the excitability of the involved corticospinal motor pathway, motor imagery also causes a reduction in the intracortical inhibition within the primary motor cortex (M1) [14]. These excitability changes have not been ascribed to the global arousal in the brain and spinal cord but instead to the subliminal and focused changes in very specific areas involved in cognitive processes, such as short-term maintenance of kinesthetic information during motor imagery. This kinesthetic working memory involves a widespread neural network and activates also the ventrodorsal stream of the left hemisphere as shown e.g. by Fiehler et al. 2008 [5]. The network includes the dorsolateral prefrontal cortex (PFC) and it may play a role in maintaining motor imagery as the representations of a given motor act are internally rehearsed during imagery tasks. Considerable evidence indicates that the PFC-mediated cognitive control of behavior covers a wide range of specific cortical operations [6, 8, 9]. In the present study, we explore short-term kinesthetic memory function in the PFC. Memory functions are represented by distributed, interactive, and overlapping networks of neurons in the association cortex. According to Fuster [7], the frontal association cortex contains executive cognits, including also parasensory and premotor cortex cognits representing simple percepts or motor acts. In addition, posterior and frontal networks are associated by long reciprocal cortico-cortical connections forming a basis for the network [7]. The dorsolateral PFC is presumably a part of the explicit working memory network involved in establishing a novel association between visual cues and motor commands. Trained visuomotor skills appear to increase specifically the left hemisphere activity [8] and left M1 dominance for motor imagery was also suggested in healthy subjects [15]. This shift to the left hemisphere has been observed regardless of the side of the practiced motor activity suggesting the left hemispheric dominance in storage...
of visuomotor skills[8].

The PFC regions that connect the primary somatosensory cortex (S1) were recently used as the targets for TMS in a working memory study[13]. The results showed that the prefrontal topdown suppression via the middle frontal gyrus-S1 link plays a role in the maintenance of tactile working memory. Although it is apparent that aroused attention and kinesthetic working memory contribute to motor imagery, it is unclear if the left PFC has any role in imagery. To explore this, we utilized in this pilot study the TMS for selective and transient functional silencing of the left dorsolateral PFC during motor imagery and assessed its effect on the responses to M1 stimulation.

Based on the timing presented by Savolainen et al.[13], we used a 300ms delay between the left PFC and M1 stimulation. Our hypothesis was that the involved kinesthetic working memory processes maintaining imagery within the left PFC will be disturbed by the TMS and will therefore result in lesser facilitation of M1 during motor imagery.

2. Participants and Methods

The study participants were five healthy adults who reported no neurological symptoms (4 males, 1 female, mean age 56±6 years). They signed informed consent and the study was approved by the local institutional review board for human research. Subjects were seated comfortably in a custom-made chair, kept their eyes open, and were asked to imagine smooth ankle dorsiflexion (DF) motion during the presentation of a visual cue (2 s on, 2 s off) displayed on the monitor about 1 m in front of them. They were asked to use presentation of a visual cue (2 s on, 2 s off) displayed on the monitor about 1 m in front of them. They were asked to use

The MEP amplitudes in the right TA muscle significantly increased to an average of 440% (p=0.004) during imagined DF movements compared to relaxation (Table 1, IMG-Cz). This remarkable facilitation was significantly diminished to 326% (p=0.031) when the TMS to left PFC was delivered 300ms prior to M1 stimulation (Table 1, IMG-F3+Cz). When analyzing the effect of imagery to rest, Cohen’s d was 1.74 indicating about 80% probability of increased amplitude whereas during PFC stimulation while performing imagery the effect size was less, 1.01. Therefore our hypothesis was confirmed, i.e., the left PFC stimulation decreased the facilitation of M1 during motor imagery. The effect sizes of these amplitude changes differ by 0.7, which could be considered at least moderate (effect size 0.8 is often considered large). In the control experiment, the PFC stimulation during relaxation left MEPs unchanged (103%), clearly indicating that there is no effect of the left hemisphere PFC on M1 in the absence of motor imagery. An example of the averaged individual waveforms from the main experiment is shown in Fig. 1A-C. The additional control experiments performed in the same subject illustrate no effect on MEPs when the combined left PFC and Cz stimulations were delivered during relaxation (D), delivered simultaneously during motor imagery (E), or delivered 300ms apart during 2s relaxation portion of the imagined task (F). The box and whiskers plot (Fig. 2) illustrates the group data for the three main experimental conditions.
Figure 1. MEPs (each waveform is an average of four trials) recorded in the right TA muscle illustrated with schematic drawing of the coil placements and visual cues presented on the monitor. A) Cz stimulation during relaxation (control condition, time scale 0ms = stimulus onset), B) Cz stimulation during motor imagery of the right ankle dorsiflexion, C) Cz stimulation during motor imagery preceded by F3 stimulation (300ms inter-stimulus interval, ISI), D) Cz stimulation during relaxation preceded by F3 stimulation (ISI=300ms), E) Cz and F3 stimulations delivered simultaneously (ISI=0ms) during motor imagery, and F) Cz stimulation during the relaxation portion of the imagery task preceded by F3 stimulation (ISI=300ms).

Figure 2. MEP amplitudes in the right TA muscle during motor imagery of the right ankle dorsiflexion evoked by TMS over Cz (IMG-Cz), combined F3 and Cz TMS 300ms apart during motor imagery (IMG-F3+Cz), and during relaxation (CTRL-F3+Cz) are expressed as a percent of MEPs evoked by TMS over Cz during relaxation (CTRL-Cz). The bar and whiskers plots indicate the respective minimum, 25th percentile, median, 75th percentile, and maximum values.
Table 1. The group mean MEP amplitudes (±SEM) of the right TA muscle evoked by TMS over the leg motor cortex (M1) at Cz location during relaxation (CTRL-Cz), during motor imagery of the right ankle dorsiflexion (IMG-Cz), during relaxation while the left PFC was stimulated 300ms prior to M1 (CTRL-F3+Cz), and during TA motor imagery while the left PFC was stimulated 300ms prior to M1 (IMG-F3+Cz). The percentage changes (means ±SE) were calculated in relation to the values during relaxation (CTRL-Cz). Note the facilitation of MEP’s during motor imagery that was significantly decreased when the left PFC stimulation was delivered during imagery but not during relaxation.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean (mV)</th>
<th>SEM (mV)</th>
<th>Mean (%CTRL-Cz)</th>
<th>SEM (%CTRL-Cz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTRL-Cz</td>
<td>0.242</td>
<td>0.089</td>
<td>100%</td>
<td>0%</td>
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<tr>
<td>IMG-Cz</td>
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<td>0.122</td>
<td>440%</td>
<td>158%</td>
</tr>
<tr>
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<td>0.225</td>
<td>0.099</td>
<td>103%</td>
<td>21%</td>
</tr>
<tr>
<td>IMG-F3+Cz</td>
<td>0.454</td>
<td>0.092</td>
<td>326%</td>
<td>128%</td>
</tr>
</tbody>
</table>

5. Conclusions

Our results suggest that there is a clear a functional link between the left dorsolateral PFC and sensorimotor cortex in healthy subjects which contributes to motor imagery. This justifies pursuing further studies with more precise neuronavigation in order to precisely map the involved PFC areas and their extent. Also further studies should explore whether this link is dysfunctional in pathological conditions (e.g., stroke) and which type of lesions limit the use of imagery for restoration of motor functions.

REFERENCES

observed, imagined, and imitated actions are dissociable and hierarchically organized. Neuroimage. 2012, 59:2798-807.


