学位（博士）論文　要旨

Excitability Change in Ipsilateral Primary Motor Cortex During a Fine-Motor Manipulation Task

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手指の複雑動作課題遂行時における同側一次運動野の興奮性変化について

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論文の要旨

Chapter 1: Introduction

Recently, interesting evidence has been proposed for human motor control. The primary motor cortex (M1) is known to mainly convey signals to the contralateral limbs, and excitability of the contralateral hemisphere, especially M1, which projects signals to the spinal motoneurons, was shown to be modulated during voluntary activity. However, performing a unilateral voluntary movement was shown to change activation of not only the contralateral M1, but also of the ipsilateral M1. An interesting suggestion is that this phenomenon is evident when the performed task is complex and difficult. Additionally, modulating ipsilateral M1 excitability was suggested to involve the corpus callosum, which connects two hemispheres at the midline; however, this theory has not yet been examined in detail especially during a complex task. In the present study, a fine-motor manipulation task (FM) task was conducted as a sensorimotor task to investigate the neural mechanism underlying activation of the ipsilateral M1, especially with regard to transcallosal inputs via the corpus callosum, during the performance of a complex task. In Introduction, a focused region, i.e., M1, and changes in ipsilateral M1 excitability during unilateral hand motor tasks have been briefly outlined. Because an FM task as a sensorimotor task was carried out in the present study, factors related to the task have been also discussed. Transcranial magnetic stimulation (TMS), which was used in the present study, and the neural circuits that can be tested with TMS have also been described.

Chapter 2: Increased excitability and reduced intracortical inhibition in ipsilateral primary motor cortex during a fine-motor manipulation task

<u>Objective:</u> Previously, I reported the effect of performing the FM task as a sensorimotor task on ipsilateral M1 excitability relative to the effect of a pseudo-FM (pFM) task (Morishita et al. 2010). In this study, increased ipsilateral M1 excitability was observed during the FM task with the non-dominant left hand. However, the mechanism of increasing ipsilateral M1 excitability during the performance of the FM task was unclear. It was hypothesized that changes in ipsilateral M1 excitability during the performance of a sensorimotor task could be explained by the modulation of intracortical circuits; therefore, changes in short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF) in the ipsilateral M1 were investigated during the FM task.

Methods: Ten right-handed subjects participated in the experiment. All subjects performed the FM task, which involved the repetitive picking up, transporting, and release of glass balls from one box to another as accurately and quickly as possible for 2 to 3 min using wooden chopsticks. In addition, the subjects also performed the pFM task as a control task. TMS was applied to evoke motor evoked potentials (MEP) from the contralateral resting first dorsal interosseous (FDI) muscle. The task-performing hand was either the dominant right hand or the non-dominant left hand. Changes in SICI and ICF in the ipsilateral M1 to the task-performing hand during the FM and pFM tasks were examined using the paired-TMS paradigm involving a subthreshold conditioning stimulus (CS) followed by a suprathreshold test stimulus (TS)at different interstimulus intervals (ISI).

Results and Discussion: Increased MEP was observed in the resting contralateral FDI during the FM task, and this effect was evident when the task-performing hand was the non-dominant left hand. Additionally, decreased SICI in the ipsilateral M1 was detected during the FM task with the non-dominant left hand. The asymmetry of changes in ipsilateral M1 excitability and SICI in the ipsilateral M1 were assumed to be due to asymmetric interhemispheric effects.

Chapter 3: Changes in interhemispheric inhibition from active to resting primary motor cortex during a fine-motor manipulation task

Objective: It has been hypothesized that the enhanced ipsilateral M1 excitability produced during the FM task was mediated by transcallosal inputs from the active to the resting M1. However, the effects of performing such a sensorimotor task on interhemispheric neural mechanisms have not been examined in detail. In order to explore this hypothesis, I examined changes in interhemispheric inhibition (IHI) from the active to the resting M1 during the FM task and compared them with those produced during a simple voluntary contraction task.

Methods: Ten right-handed subjects participated in the experiment. All subjects performed the FM task and an isometric abduction (IA) task as a control task. I examined changes in IHI from the active to the resting M1 during the FM and IA tasks, using the paired-TMS paradigm. The paired-TMS paradigm can be used to study IHI, which is mediated through the corpus callosum. IHI can be measured by applying a CS to one hemisphere, which inhibits the size of the MEP evoked by the application of a TS to the opposite hemisphere at ISI of between 6 and 50ms. The TS was applied to the left M1, and the CS was applied to the right M1. The task-performing hand was the non-dominant left hand.

Results and discussion: Increased IHI from the active to the resting M1 was observed during the FM task. Results of chapter 3 suggest that the increased IHI observed during the FM task could be the neural mechanism responsible for reducing SICI in the ipsilateral M1; i.e., disinhibition, during the FM task. As a result, decreased SICI in the ipsilateral M1 (results of chapter 2) leads to increased ipsilateral M1 excitability during the FM task. Results of chapter 3 also support the assertion that the projections from the transcallosal and the corticospinal pathways are distinct.

Chapter 4: Asymmetry of interhemispheric inhibition from active to resting primary motor cortex induced by a fine-motor manipulation task of either dominant or non-dominant hand

Objective: Increased MEP was observed in the resting contralateral FDI during the FM task, and this effect was evident when the task-performing hand was the non-dominant left hand (results of chapter 2). It has been hypothesized that this asymmetry in the effects of the sensorimotor task on ipsilateral M1 excitability was due to asymmetric interhemispheric effects. Therefore, I examined the changes in IHI from the active to the resting M1 during the FM task with the dominant hand or the non-dominant hand.

Methods: Eleven right-handed subjects participated in the experiment. All subjects performed the FM task and the IA task. I examined changes in IHI from the active to the resting M1 during the FM and IA tasks, using the paired-TMS paradigm. The task-performing hand was either the dominant right hand or the non-dominant left hand. The TS was applied to the ipsilateral M1 to the task-performing hand, and the CS was applied to the contralateral M1 to the task-performing hand.

Results and discussion: Increased MEP was observed in the resting right FDI during the FM task with the non-dominant left hand, and asymmetric IHI from the active to the resting M1 was only observed during the FM task. Results of chapter 4 also suggest that the increased IHI observed during the FM task could be the neural mechanism responsible for reducing SICI in the ipsilateral M1; i.e., disinhibition of the ipsilateral M1 during the FM task.

Chapter 5: Temporal suppression of ipsilateral primary motor cortex excitability induced by a fine-motor manipulation task

Objective: It was hypothesized that strong effects of performing the FM task (results of chapters2, 3, and 4) may last or change the neural circuits, and this could be a factor for changes in ipsilateral M1 excitability after performing the FM task. To explore this hypothesis, the FM task was conducted and the excitability of both M1s, SICI, and IHI from the contralateral M1 (innervating side) to the ipsilateral M1 (non-innervating side) were measured before and after performing the FM task.

Methods: Twenty right-handed subjects participated in the experiment. The FM task was carried out and the excitability of both M1s, SICI, and IHI were measured before and after performing the FM task. The subjects were instructed to perform the FM task for 6 sets (total 18 min with 7 min rest).

Results and discussion: Decreased MEP amplitude and decreased SICI were recorded in the right FDI after performing the FM task with the non-dominant left hand. No significant change in the MEP amplitude was recorded in the left FDI after performing the FM task. The mechanism of decreased ipsilateral M1 excitability after performing the FM task remains uncertain. However, one possible explanation that could account for decreased ipsilateral M1 excitability is a homeostatic mechanism.

Chapter 6: General discussion and conclusions

Our advanced dexterity is not only the result of the function of M1; other motor-related regions must also play crucial roles in human motor control. However, as suggested by a number of previous studies, the important role of M1 in human motor control cannot be doubted. In the present study, the first neurophysiological evidence of the mechanism underlying ipsilateral activation with regard to transcallosal inputs was proven during a sensorimotor task. The important finding of the present study is increased IHI from the active to the resting M1 during the FM task as a sensorimotor task, and increased IHI from the active M1 must play crucial roles in increasing ipsilateral M1 excitability.