学位論文の要旨

論 文 題 目 (和文) 一致タイミング課題の時間的適応学習における小脳の役割
(英文) The role of the cerebellum during temporal adaptive learning in a coincident timing task

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論文の要旨

Chapter 1: General Introduction

Time and space are fundamental factors in our daily lives, or sports scenes. To show sports skills, spatio-temporal control and perception is essential. For example, fastball sports like baseball, table tennis, and tennis demand us to be able to treat hand tools, such as a bat or a racket, as freely as their own body, and precise spatio-temporal control under severe time constraints to hit high-speed or braking ball. How does our brain process these external information and enable us to move smoothly?

The cerebellum has been shown to play an important role in error-based learning, e.g., it contributed to spatial adaptive learning in a visuomotor reaching task (Schlerf et al. 2012; Spampinato et al. 2017). In these studies, changes in cerebellar–M1 connectivity have been detected after motor learning in humans using paired-pulse TMS. In these studies, the cerebellum was stimulated by delivering a conditioning stimulus (CS) to a location 3 cm lateral to the inion, on the line joining the inion and the external auditory meatus (Ugawa et al. 1995; Pinto and Chen 2001). Stimulating this site leads to the activation of Purkinje cells (PCs), probably in the cerebellar lobules V, VII and VIII (Hardwick et al. 2014; Spampinato and Celnik 2020). Compared with MEPs elicited by the delivery of a TS alone, those seen after the delivery of a CS to the cerebellum followed by the delivery of a TS to the contralateral M1 were suppressed. This suppression, i.e., cerebellar brain inhibition (CBI), has been suggested to reflect the activation of cerebellar PCs (Celnik 2015; Fernandez et al. 2018). The CBI technique is useful for assessing how cerebellar–M1 connectivity is affected by spatial adaptive learning (Schlerf et al. 2012), and the changes in CBI found following visuomotor adaptation were found to occur in a somatotopic-specific manner (Spampinato et al. 2017).

In general, timing is functionally classified into four dimensions, i.e., explicit vs. implicit, and motor vs. perception (Coull and Nobre 2008). The interception tasks used in previous studies (Bares et al. 2007, 2010, 2011; Markova et al. 2020) and the Coincident timing task (CoIT task) used in this thesis are considered to be implicit motor timing tasks. Previous studies showed that the CoIT task has been useful to explore the function of cerebellum, involving patients with cerebellar damage or baseball players (Bares et al. 2007, 2010, 2011; Marcova et al. 2020). They also indicated that this task required for better performance both the accurate perception of target information (Merchant et al. 2003) and a precise predictive motor response (Caljouw et al. 2004). These cognitive and motor responses are important for movement skills seen in everyday lives or sports, such as catching, riding a motorbike, shooting, or playing fastball sports (Causer et al. 2011; Davoodi et al. 2012; Iacoboni 2001). However, so far, no studies have investigated the physiological mechanism of the cerebellum in temporal adaptive learning. In this thesis, I carried out two experiments using CoIT task, and transcranial magnetic stimulation (TMS) to evaluate the relationship the function of cerebellum and CoIT performance.

Chapter 2: Modulation of cerebellar brain inhibition during temporal adaptive learning in a coincident timing task

The aim of this chapter was to investigate the role of the cerebellum in temporal adaptive learning. We hypothesized that the cerebellum also plays an important role in temporal adaptive learning, as was reported for various other kinds of adaptation in previous studies (Donchin et al. 2012; Izawa et al. 2012; Morton and Bastian 2006; Prsa and Their 2011; Rabe et al. 2009; Schlerf et al. 2012; Schlerf et al. 2013; Spampinato et al. 2017). To examine this hypothesis, we used the paired-pulse TMS paradigm to assess the changes in cerebellar–M1 connectivity that occur before, during, and after temporal adaptive learning.

I programmed a CoIT task, i.e., a baseball-like hitting task involving a moving ball presented on a computer monitor. The subjects were required to change the timing of their responses based on imposed temporal perturbations. Using paired-pulse transcranial magnetic stimulation, we measured cerebellar brain inhibition (CBI) before, during, and after the temporal adaptive learning. Reductions in CBI only occurred during and after the temporal adaptive learning, regardless of the direction of the temporal perturbations. In addition, the changes in CBI were correlated with the magnitude of the adaptation. Here, we showed that the cerebellum is essential for learning about and controlling the timing of movements during temporal adaptation. Furthermore, changes in cerebellar-primary motor cortex connectivity occurred during temporal adaptation, as has been previously reported for spatial adaptation.

Chapter 3: Role of the cerebellum for adapting the change of target velocity in a coincident timing task

The tasks that rely on implicit motor timing have showed central role for the cerebellum (Bares et al. 2019). Interception task, considered to be similar to CoIT task used in this thesis, has been used in previous studies (Bares et al. 2007, 2010, 2011). They demonstrated that cerebellum may have internal models of predictive motor behavior. If the models exist in the cerebellum, training involving prediction of future state of the circumstances would improve the CoIT skill. Another study (Markova et al. 2020) showed baseball players showed significantly higher quantitative, not qualitative, performance than control subjects. They pointed out that the result of their experiment reflected the possibility that same cerebellar mechanism as non-athletes selectively refined due to athletes' rigorous training over years. Based on these findings, I modified CoIT task to investigate basic timing skill in more realistic conditions, i.e. the subjects, not trained, were required to adapt the changes of velocity of a moving target. Previous fMRI research indicated that the high activation in the cerebellum associated with increasing speed occurred (Filip et al. 2016). Using same paired-pulse TMS technique in chapter 2, I investigated whether the changes of the cerebellar-M1 connectivity with adaptive learning occurred under the condition above mentioned.

The reduction of cerebellar-M1 connectivity occurred despite no improvement of the CoIT performance. In addition, Similar changes were observed in a random condition. There were some differences from previous researches, but these results indicated that the cerebellum played an important role for integrating incoming visual information with timely adjusted motor output in conditions, similar to the actual sports scenes.

Chapter 4: General discussion and conclusion

Timing control, of course, doesn't only depend on the cerebellum. The cerebellum is a part of timing network (basal ganglia, supplementary motor area, and the right inferior frontal gyrus, etc.). However, many previous researches have indicated that the cerebellum has an essential role for timing control (Raghavan et al. 2016). In this research, it demonstrated that cerebellum plays an essential role for integrating visual information with timely motor output, and even in an experimental environment that is as close to actual sports scenes as possible, it is possible to investigate the neural mechanism of CoIT task using TMS paradigm. I hope this research will be an important basis for future researches.