**Differences in the effect of transcranial direct current stimulation of the pre-supplementary
motor area on imitation inhibition according to autism spectrum traits**

Short title: Trait differences in imitation inhibition

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Abstract

Objectives

Adequate inhibition of automatic imitative tendencies is crucial in our daily lives. There have been inconsistent reports regarding the neural mechanism of imitation inhibition. Previous studies have suggested that it involves the theory of mind and multiple-demand networks. However, individual differences in the neural mechanism of imitation inhibition have been rarely considered, which could have attributed to the inconsistent reports. Behavioral experiments have suggested variations in the mechanism underlying imitation inhibition according to autism spectrum traits. Therefore, this transcranial direct current stimulation study aimed to examine whether the involvement of stimulated brain regions in imitation inhibition differed according to autism spectrum traits, which could imply differences in the stimulation effects.

Methods

This study enrolled 27 adults (21 men, mean age: 21.44 ± 1.23 years). We applied transcranial direct current stimulation to the pre-supplementary motor area, which is a node of the multiple-demand network, and analyzed the stimulation effects according to autism spectrum traits measured using the Autism-Spectrum Quotient.

Results

Transcranial direct current stimulation of the pre- supplementary motor area did not alter imitation

inhibition. However, on incongruent trials requiring imitation inhibition, a significant negative correlation between the Autism-Spectrum Quotient score and reaction time under the anodal condition was observed. This indicated that the effect of anodal transcranial direct current stimulation of the pre- supplementary motor area on imitation inhibition differed according to autism spectrum traits.

Conclusions

Our findings suggest that brain regions involved in imitation inhibition vary according to autism spectrum traits.

Keywords: Transcranial direct current stimulation; Imitation inhibition; Autism spectrum traits

Introduction

Humans have an involuntary tendency to imitate other people's actions. Although this is crucially involved in social interaction, it is not always appropriate. Many situations require inhibition of this tendency to prioritize some actions. Previous studies have suggested the existence of such an inhibitory mechanism of automatic imitation [1]. Studies have used the cognitive psychology paradigm or imitation-inhibition tasks to measure the ability to inhibit automatic imitation [2].

Two brain networks have been proposed to be centrally involved in imitation inhibition. One is the theory of mind (ToM) network, which mainly comprises the medial prefrontal cortex and right temporoparietal junction [3]. Here, it is suggested that control over automatic imitation requires inhibition of the representation of others' actions and enforcement of one's intended actions. Accordingly, imitation-inhibition tasks have been applied to assess social cognition processes, including self-other distinction [1]. The other proposed brain network is the multiple-demand (MD) network, which extends to the dorsolateral and dorsomedial frontoparietal cortex; moreover, it is involved in executive functions, including inhibition, working memory, and attention [4]. The MD network theory suggests that similar to the inhibition of pre-potent tendencies, a domain-general network inhibits the automatic imitative tendency [5]. There have been inconsistent reports regarding the neural mechanism underlying control of this tendency [6].

Recent studies have investigated individual differences in the ability to inhibit automatic

imitation according to personality or sex [7,8]. Spengler et al. [9] reported that individuals with autism spectrum disorder (ASD) have poor imitation inhibition compared with the control group; however, more recent large-scale studies have not observed an influence of autistic-like traits on imitation inhibition [7,8]. Further, several studies have reported differences in the effect of experimental manipulation between ASD and control groups [10,11]. This suggested variations in the mechanism underlying control over automatic imitation during imitation-inhibition tasks according to autism spectrum traits. For example, Cook and Bird [11] showed that, unlike healthy participants, patients with ASD lacked poor imitation inhibition in prosocial contexts compared with antisocial contexts. Therefore, even if autism spectrum traits have a weak effect on task performance, there might be trait-based differences in the neural mechanisms activated during the task.

The inconsistency in reports regarding the neural basis of imitation inhibition could be attributed to individual differences. For example, when performing the imitation-inhibition task, some individuals may use more general processes (the MD network) while others may use more social processes (the ToM network). This could lead to differences in findings regarding the neural basis of imitation inhibition based on the participants enrolled in each study. Accordingly, intervention methods, such as transcranial direct current stimulation (tDCS) could be applied to examine individual differences in the neural mechanism of imitation inhibition. The effect of non-invasive brain stimulation is dependent on not only the brain stimulation type but also the original cortical excitability

of the stimulated region during a task [12]. Therefore, individual differences in the neural mechanism can lead to differences in the stimulation effect even with the application of the same stimulation type to the same brain region.

The present study focused on the MD, rather than ToM, network since recent imaging studies, including a meta-analysis, have emphasized the involvement of the MD network in imitation inhibition [13,14]. The pre-supplementary motor area (pre-SMA), which is a node of the MD network [4,6], has been reported to be involved in the imitation inhibition task [15,16], as well as in the initiation of movement, alteration of movement plans, and response inhibition [17]. Moreover, numerous studies have shown that anodal stimulation of the pre-SMA enhances the performance of cognitive tasks, including response inhibition [18]. This tDCS study aimed to investigate individual differences in the involvement of the MD network in imitation inhibition according to autism spectrum traits. We hypothesized that the presence of trait-based individual differences in the neural mechanism of imitation inhibition would lead to differences in the effect of tDCS of the pre-SMA (positive, negative, or no effect) on the performance of the imitation inhibition task.

Methods

Participants

This study enrolled 27 adults (6 females and 21 males, mean age: 21.44 ± 1.23 years). All participants were right-handed according to the Edinburgh Handedness Inventory. Moreover, they were healthy and lacked a history of developmental or neurological disorders. Each participant underwent all three stimulation conditions (anodal, cathodal, and sham stimulation) on different days in a counterbalanced randomized order. The participants provided written informed consent after reading a tDCS information sheet and confirmed having no contraindications to tDCS. This study was approved by the Ethics Committee of the Faculty of Education at Hokkaido University (approval number: 19-23). The procedures followed the principles of the Declaration of Helsinki (1964).

Procedures

On the first day, each participant completed the Japanese version of the Autism-Spectrum Quotient (AQ) questionnaire to assess autism spectrum traits [19]. After receiving tDCS, the participants performed the imitation inhibition task. After the task, they were asked to indicate how uncomfortable were they with tDCS on a scale of 1–5 (1 = not at all, 5 = very much).

tDCS

We applied tDCS to the pre-SMA through a pair of saline-soaked surface sponge electrodes (5×5 cm), which were connected to a neuroStym tESr (Neuro Device, Płowiecka). The stimulation site was

identified according to the electroencephalogram 10/20 system. The target and reference electrodes were placed at Fz (pre-SMA) and the left cheek, respectively. For the anodal condition, the anodal and cathodal electrodes were placed at Fz and the left cheek, respectively, with this placement order being reversed for the cathodal condition. For the sham condition, both patterns of electrode placement were equally used. For the anodal and cathodal conditions, stimulation began with a 15-s ramp-up to 2mA, followed by 2-mA stimulation for 15 min and ending with a 15-s ramp-down period. For the sham condition, only the same ramping procedure was applied with the electrodes attached being attached for the same total duration to mimic the experience of real stimulation. Impedance was maintained under 20 k Ω . During the stimulation, the participants were required to sit quietly with their eyes closed and to think of nothing specific. After stimulation, they completed the imitation-inhibition task within 15 min. Given previous reports that the neuromodulatory effect of 13 minutes of tDCS is robust for 90 post-stimulation minutes [20], the study procedures were completed within the critical window of the tDCS effects.

Imitation-inhibition task

The imitation-inhibition task used in this experiment was based on the tasks designed by Brass et al. [2] and Hogeveen et al. [21]. The participants were required to lift either their right index finger or middle finger in response to the number cue 1 or 2, respectively. Moreover, as a task-irrelevant

stimulus, a left hand from a third-person perspective was displayed orthogonally to the orientation of the participant's hand to allow isolation of imitation from spatial compatibility. The task comprised three trials (Fig. 1). In the baseline trials, the stimuli hand was at rest throughout the trial. In the congruent and incongruent trials, the stimuli hand lifted the same and different fingers, respectively, with respect to those required to respond to the cue. Therefore, incongruent trials required the participants to inhibit their automatic imitative tendency. Baseline trials were used to confirm the effect of tDCS of the pre-SMA on the simple response speed. After 24 practice trials, the participants completed 32 trials of each trial type, which were split into two blocks of 48 trials. The task was created and implemented using MATLAB R2019a (MathWorks, U.S.A), with Leap Motion (Leap Motion, U.S.A) being used to record. Only trials in which the number cue was "1" were analyzed due to the measurement accuracy of the apparatus.

We excluded data from three participants with mean reaction time (RT) scores in the extremes as determined by $1.5 \times$ interquartile range rule (Tukey's test) [22]. The RT and accuracy rate obtained from the remaining participants were analyzed using analysis of variance, with stimulation condition (anode, cathode, and sham) and compatibility (compatible and incompatible) as the within-subject factors. Additionally, to assess for differences in the tDCS effects (positive, negative, or no effect) on the ability to inhibit automatic imitation according to the autism spectrum traits, we analyzed

the correlation between the AQ score and RT on incongruent trials under each stimulation condition.

Statistical significance was set at $p < 0.05$.

Results

There was a significant main effect of compatibility on the accuracy rate [$F(1,23) = 7.13$, $p = 0.01$, $\eta^2 = 0.23$], indicating that participants made more errors in the incongruent trials than in the congruent trials (Fig. 2 A). No other significant main effect or interaction was observed (both $p > 0.05$). Moreover, compatibility showed a main effect on RT ($F(1,23) = 33.17$, $p < 0.01$, $\eta^2 = 0.59$), indicating that responses in the congruent trials were executed faster than those in the incongruent trials (Fig. 2 B). However, no other significant main effect or interaction was seen (both $p > 0.05$).

The AQ score showed a significant negative correlation with RT in the incongruent trials under the anodal condition ($r = -0.49$, $n = 24$, $p = 0.01$; Fig. 2 C) but not the other conditions (both $p > 0.05$). However, the AQ score was not significantly correlated with the RT in the congruent and baseline trials under the anodal condition (both $p > 0.05$). This suggested that the tDCS effect was peculiar to incongruent trials under the anodal condition.

The difference in the discomfort with tDCS among the stimulation conditions was not

significant ($p = 0.08$), which was similarly observed after post hoc multiple comparisons with Bonferroni correction (all $p > 0.05$). Regarding the influence of practice, the number of practice times (first, second, and third time of the three times) showed no significant effect on the accuracy rate and RT (all $p > 0.05$). In this analysis, the stimulation conditions (anode, cathode, and sham) were collapsed. Finally, tDCS had no significant effect on the simple response speed in the baseline trials ($p = 0.99$).

Discussion

This study had three main findings. First, tDCS of the pre-SMA did not generally alter imitation inhibition, which is inconsistent with the findings of previous reports indicating the involvement of pre-SMA in imitation inhibition [15,16]. This suggests that the pre-SMA is not crucially involved in the inhibition of automatic imitative tendency in all people. Second, there was a non-significant relationship between the autism spectrum traits and imitation inhibition in the sham condition, which is consistent with the findings of recent reports [7,8] showing no effect of autism spectrum traits on the performance of the imitation-inhibition task. Third, there was a significant negative correlation between the autism spectrum traits and RT on incongruent trials under the anodal condition. This suggested that anodal tDCS of the pre-SMA had different effects (positive, negative, or no effect) on

imitation inhibition according to the autism spectrum traits. Moreover, this result is consistent with that of previous reports of differences in the effect of the experimental manipulation between patients with ASD and healthy controls [10,11]. In our study, there was no significant effect of tDCS on the simple response speed in baseline trials. Further, discomfort with tDCS and the number of practice days did not influence task performance.

Previous studies have reported differences in the tDCS effects according to the participants' personalities, which could be attributed to the level of original neural activation in the target region [12]. Similarly, the different effects of anodal tDCS in our study could be attributed to the level of original neural activation in the pre-SMA during the incongruent trials. Specifically, anodal tDCS could have different effects on imitation inhibition due to individual differences in the engagement of the pre-SMA during incongruent trials according to the autism spectrum traits. Therefore, our findings suggest differences in the involvement of brain regions in the imitation-inhibition task according to the traits. This implies that imaging studies on the neural mechanism of imitation inhibition would report different findings according to the participants' personalities. Consistent with this hypothesis, Nishimura et al. [23] demonstrated that the personal cognitive style affects mu wave desynchronization, which is an index of the mirror neuron system, during the imitation-inhibition task. Individual differences in the neural mechanism could explain the inconsistency in the findings regarding the neural mechanism underlying imitation inhibition.

In our study, cathodal tDCS, which decreases cortical excitability, did not affect the performance of the imitation-inhibition task. This is consistent with the findings of previous reports regarding the weak effect of cathodal tDCS on cognitive tasks [24]. Moreover, other studies on imitation and response inhibition have reported no significant effect of cathodal tDCS [18,25]. Contrastingly, anodal tDCS, which increases cortical excitability, has been shown to enhance the performance of cognitive tasks [18,21,22,25]. Therefore, anodal tDCS could enhance the ability of participants with higher autism spectrum traits to inhibit automatic imitation because pre-SMA, a node of the MD network, has a more crucial role for the participants to succeed incongruent trials. As a result, we found a significant negative correlation between the autism spectrum traits and RT on incongruent trials under the anodal condition. The notion that individuals with high traits tend to mainly use the MD, rather than ToM, network is consistent with the findings of previous reports of no effect of social manipulation on imitation-inhibition task performance in patients with ASD [10,11].

However, a conclusive interpretation cannot be reached since we cannot determine how anodal tDCS generated a significant negative correlation between the traits and RT in the incongruent trials. This correlation can be explained by the positive and negative effects of anodal tDCS on participants with high and low autism spectrum traits, respectively. Nonetheless, our findings demonstrate that the effect of anodal tDCS varies according to the traits. Moreover, there could be individual differences in the neural mechanism of imitation inhibition according to the traits. Future

studies, including imaging research, are warranted to elucidate the individual differences.

In conclusion, our findings suggest that although the pre-SMA is not crucially involved in inhibiting automatic imitative tendency, the engagement of the pre-SMA during imitation inhibition differs depending on the autism spectrum traits. This is suggestive of individual differences in the neural mechanism of imitation inhibition. Therefore, there is a need for further studies on individual differences in imitation inhibition at not only the recently examined behavioral level [7,8], but also the neural activity level.

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325 **Figure**

326 Fig. 1. Imitation-inhibition task. In the congruent and incongruent trials, the resting hand and a fixation
327 point were first displayed for 800–2400 ms, followed by lifting movement of the index or middle
328 finger for 64 ms. Subsequently, the fully lifted finger and number cue was displayed for 500 ms. In
329 the baseline trials, the resting hand and a fixation point were first displayed for 864–2464 ms, followed
330 by presentation of the cue for 500 ms.

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Fig. 2. (A) The mean accuracy rate and (B) mean reaction time (RT) in the congruent and incongruent trials under anodal, cathodal, and sham conditions. (C) Scatterplot and linear correlation between the Autism-Spectrum Quotient (AQ) score and RT in the incongruent trials under the anodal condition. Error bars represent the standard error of the mean; ** $p < 0.01$; n.s. not significant.