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Effect of an 8-week practice of externally triggered speech on basal ganglia activity of stuttering and fluent speakers

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ABSTRACT

The neural mechanisms underlying stuttering are not well understood. It is known that stuttering appears when persons who stutter speak in a self-paced manner, but speech fluency is temporarily increased when they speak in unison with external trigger such as a metronome. This phenomenon is very similar to the behavioral improvement by external pacing in patients with Parkinson's disease. Recent imaging studies have also suggested that the basal ganglia are involved in the etiology of stuttering. In addition, previous studies have shown that the basal ganglia are involved in self-paced movement. Then, the present study focused on the basal ganglia and explored whether long-term speech-practice using external triggers can induce modification of the basal ganglia activity of stuttering speakers. Our study of functional magnetic resonance imaging revealed that stuttering speakers possessed significantly lower activity in the basal ganglia than fluent speakers before practice, especially when their speech was self-paced. After an 8-week speech practice of externally triggered speech using a metronome, the significant difference in activity between the two groups disappeared. The cerebellar vermis of stuttering speakers showed significantly decreased activity during the self-paced speech in the second compared to the first experiment. The speech fluency and naturalness of the stuttering speakers were also improved. These results suggest that stuttering is associated with defective motor control during self-paced speech, and that the basal ganglia and the cerebellum are involved in an improvement of speech fluency of stuttering by the use of external trigger.

Introduction

One of the most important observations regarding stuttering is that it does not appear under certain conditions. For example, speech fluency is temporarily improved when persons who stutter speak in unison with the sound of a metronome or with other speakers, and also when using masking or transformed auditory feedback (Andrews et al., 1982). The frequency of stuttering also critically varies in a context-dependent manner; stuttering does not appear when the stuttering person talks to him- or herself, small children, inanimate objects, or pets (Bloodstein and Ratner, 2007; DSM-5, 2013). Stuttering severity also shows long-term fluctuations, which may be influenced by personal circumstances. Since persons who stutter can speak fluently under certain conditions, this presumably suggests that stuttering speakers do not have an inherent disability of the articulatory organs that produce speech. Rather, they may employ inadequate procedures when producing speech in the brain, or have a disorder in the neural systems that modify speech production in the brain. This means that a simple concept such as motor area dysfunction, is not enough to explain the phenomenon of stuttering. The key neural substrates underlying malfunction presumably reside not only in the regions directly responsible for speech production, but also in other areas anatomically or functionally connected with the speech production areas. Recent studies have implicated the basal ganglia as one of these potential areas (Beal et al., 2013; Chang and Zhu, 2013).

The behavioral characteristics associated with basal ganglia impairment have been well illustrated in patients with Parkinson's disease (e.g., Donaldson et al., 2012). Because stuttering exhibits similar clinical characteristics to Parkinson's disease, the two disorders have been compared (Alm, 2004). The observations regarding behavior that is common to the two disorders are as follows: 1) most stuttering appears at the first segment of a movement, that is, at the beginning of the first sound or syllable of a word, while patients with Parkinson's disease also experience difficulty initiating movement (Alm, 2004); 2) speech fluency in stuttering speakers is improved by external pacing using a metronome (Bloodstein and Ratner, 2007), while patients with

Abbreviations: Self, self-paced speech condition; Ext, externally triggered speech condition; Lis, listening condition.

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Parkinson's disease also show improvement of upper and lower limb movement with external pacing (Howe et al., 2003; Jahanshahi et al., 1995; Lewis et al., 2007; Lim et al., 2005). Considering the fact that dysfunction of the basal ganglia causes Parkinson's disease, these comparable effects suggest that stuttering is also related to dysfunction of the basal ganglia, as one of the neural mechanisms characterizing speech dysfluency.

A number of previous studies support basal ganglia deficits as a potential etiology for stuttering. For example, both aggravation and disappearance of stuttering due to deep brain stimulation (DBS) of the basal ganglia–thalamocortical motor circuit have been reported (Bhatnagar and Buckingham, 2010; Burghaus et al., 2006; Nebel et al., 2009; Walker et al., 2009). Stuttering was induced when DBS of the subthalamic nucleus was performed, but disappeared after this stimulation was stopped in some types of patients with Parkinson's disease (Toft and Dietrichs, 2011; Tsuboi et al., 2014). The degree of speech dysfluency can also be changed by adjustments in thalamic stimulation (Allert et al., 2010). Tani and Sakai (2010) reported neurogenic stuttering following brain injury exclusively in the basal ganglia in five speakers with no history of developmental stuttering (Tani and Sakai, 2010). Speech dysfluency is also frequently observed in patients with Parkinson's disease (Donaldson et al., 2012).

Recent neuroimaging studies have supported the involvement of the basal ganglia in stuttering. In addition to different patterns of activity in basal ganglia nuclei (Chang et al., 2009; Kell et al., 2009; Toyomura et al., 2011; Watkins et al., 2008), differences in the strength of connectivity within basal ganglia–thalamocortical circuits were found between stuttering and non-stuttering adults (Lu et al., 2009, 2010). Furthermore, Chang and Zhu (2013) demonstrated that children who stutter already exhibit decreased connectivity within basal ganglia circuits (Chang and Zhu, 2013), while Beal et al (2013) found that the gray matter volume in the putamen and inferior frontal gyrus was decreased in children who stutter relative to those who do not (Beal et al., 2013). These studies suggest that children who stutter already have both functional and morphological abnormalities of the basal ganglia, which may have a critical influence on the development of speech motor learning. Among other species, songbirds also display stuttering-like dysfluent singing after ablation of Area X, which is anatomically equivalent to the basal ganglia in humans (Kobayashi et al., 2001).

Human movement can be classified into two categories according to timing generation: self-paced (or self-initiated) and externally triggered movements. The common effect of a metronome on both stuttering and Parkinson's disease is one of the phenomena demonstrating that externally triggered movement functions properly. A number of previous studies have reported that the basal ganglia are involved in self-paced movement (Cunnington et al., 2002; Francois-Brosseau et al., 2009; Jahanshahi et al., 1995; Lewis et al., 2007; Taniwaki et al., 2006; Toyomura et al., 2012). The fact that stuttering is temporarily suppressed when an external trigger is presented, but occurs in self-paced speech, indicates that the differences between self-paced and externally-triggered speech may be important for understanding the neural mechanisms of stuttering. Toyomura et al (2011) investigated the neural activity of people who stutter when they spoke under metronome-timed, choral, and self-paced speech conditions, and showed that the activity of the basal ganglia of persons who stutter is significantly lower than that of non-stuttering controls under the self-paced speech condition, but equivalent to non-stuttering controls under the metronome-timed condition (Toyomura et al., 2011). These results indicate that an external speech trigger can temporarily compensate for the low basal ganglia activity that is observed in the self-paced speech of persons who stutter. The question then arises whether their activation could increase to the level of that in those who do not stutter after they practice for a prolonged period using the trigger. If so, externally triggered speech could potentially induce plasticity in neural networks, including the basal ganglia, which could impart a more permanent change.

In this study, we firstly examined differences in activation of the basal ganglia of stuttering and non-stuttering speakers under self-paced and externally triggered speech conditions before practice. We then required both groups of participants to practice speaking using an external trigger for eight weeks, and examined the effect of this practice on the neural activity in the basal ganglia of both groups, again for both the self-paced and externally-triggered conditions.

Material and methods

Participants

This study consisted of two functional magnetic resonance imaging (fMRI) experiments: one before the eight weeks of speech practice, and one after the practice period. Therefore, we recruited only participants who agreed to undertake continuous engagement for the eight weeks of practice between the two fMRI experiments. Participants included 20 male adults, 10 of these were adults who stutter (aged 20–31 years with a mean age of 25.4 years, $SD = 3.9$) and 10 were adults who do not stutter (aged 22–33 years with a mean age of 25.4 years, $SD = 3.7$). They were native Japanese speakers and were right handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The two participating groups were similar in age ($p = 1.00$). Other than stuttering in the experimental groups, none of the participants had a self-reported history of speech, language, or hearing problems. Among the participants, seven stuttering and two non-stuttering speakers had participated in an experiment that our group conducted previously (Toyomura et al., 2011). In addition, independent 10 naïve non-stuttering participants (6 men, 4 women, aged 21–24 years with a mean age of 22.2 years, $SD = 1.0$) were recruited as speech evaluators. They assessed speech naturalness (Ingham et al., 2009; Martin et al., 1984) based on video recordings after the experiments. This study was approved by the ethics committee of Tokyo Denki University.

fMRI experiments

Experiment 1

We conducted two MRI experiments, one before and one after speech practice. The MRI acquisition and analysis methods were partly based on the procedures we used previously (Toyomura et al., 2011). In the first experiment, participants wore an MR-compatible headset, and were restrained by two belts to avoid head movement caused by the experimental task. Cushions were inserted between the headset and head coil to further fix the participant's head. A sentence was presented on a screen that was viewed through a mirror incorporated into the head coil. A sparse image acquisition protocol (Hall et al., 1999) with a 7-s delay was used in this experiment. In this protocol, non-scanning periods (7-s in this study) are set between each two successive volumes. Participants were required to perform tasks during the non-scanning periods and to stop before the next scan, which can eliminate an effect of scanner noise in speech tasks and artifacts due to speech production in imaged data. Because the blood-oxygen-level-dependent (BOLD) responses are known to have a late peak after rising due to task, this method is expected to collect images in the period after the increases in BOLD signals. Participants were instructed to start reading aloud immediately after each sentence appeared on the screen, and stop reading immediately after the stimulus disappeared, even if they did not finish reading. To prevent the continuation of speech into the next scanning period, the sentence was presented only for the first 4.5 s of the 7-s period. The sentences used here were passages from simple essays that were plainly written. Prior to the experiment, the participants were required to thoroughly practice the three task conditions (outlined below) with the help of the experimenters.

Stuttering speakers are known to exhibit an increase in speech fluency when the auditory feedback of their own voices is altered

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