A single case report of a patient with stuttering who improved after open label TMS

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INTRODUCTION

Developmental stuttering is a speech disorder that occurs in spontaneous communication situations. It is characterized by repetitions, prolongations, or blocks during normal speech. Onset of stuttering is typically between 2 and 5 years of age. Stuttering has a prevalence of around 5% in early childhood, but many children recover spontaneously; thus, the prevalence across the general population is closer to 1% [1]. Adults who stutter (AWS) develop secondary behaviors, such as body and facial tics, and physiological (increased adrenaline and heart rate) and psychological (anxiety and depression) symptoms, associated with this phenomenon. These severely compromise AWS's quality of life.

The etiology and mechanisms underlying stuttering still remain unknown, and limited effective treatments are available for those affected. Speech-relevant cortical and subcortical neural systems appear to be malfunctioning in developmental stuttering, both in speech tasks and in non-speech tasks [2].

Transcranial direct current stimulation has shown a favorable effect on fluency in AWS [3]. To date, to the best of our knowledge, no previous published studies have investigated the effects of repetitive transcranial magnetic stimulation (rTMS) in patients with developmental stuttering. Previous reports [4,5] indicate that the most critical region for neuromodulation in stuttering is the left putamen (not accessible by TMS), left inferior frontal gyrus (tested in [3]) and supplementary motor area (SMA).

CONCLUSIONS

Stuttering has been describing as a motor and timing disorder [9]. Characterizing the functional differences and strength of connectivity of component areas might help elucidate possible mechanisms of speech disfluencies manifested as stuttering.

A previous report [10] suggested that dysfunctional activation of the SMA may contribute to insufficient activation of motor structures of the left hemisphere, followed by an exaggerated reaction of the temporal/motor structures of the right hemisphere, which then interfere with speech production.

As the pre-SMA/SMA support movement initiation and timing, this case study might supports that hypothesis, raising the possibility that SMA stimulation may be an approach for neuromodulating the impaired subcortical–cortical pathways that interfere with correct motor speech initiation.

To our knowledge, no previous study has used rTMS successfully as a therapy for stuttering. This case illustrated that rTMS over the SMA could be a promising way of research in more subjects, along with sham stimulation, both as therapy and to explore pathophysiological principals of stuttering

METHODS

We assessed the effect of rTMS at the SMA in a 30-year-old, right-handed man with developmental stuttering, as stuttering severity is related to increased structural connectivity of the motor response-inhibition network (composed of the supramarginal gyrus, preSMA, subthalamic nucleus, and putamen) [6]. The study adhered to the principles of the Helsinki Declaration for medical research involving human participants (World Medical Association, 2013) and oral informed patient consent was obtained, formally documented, and witnessed.

To evaluate stuttering severity, two 3-minute speech videorecorder samples were collected during spontaneous conversation before treatment and after every 5 treatment sessions. Each conversation sample involved new neutral topics. For each pair of samples, the percentage of disfluent syllables (%DS), defined as those containing repetition, prolongation, repeated phrases, or phrase revision, or blocks prior to a speech sound (core stuttering characteristics) were measured.

In addition, SSI-4, a standardized and norm-referenced index of disfluency [7], was used to characterize stuttering severity. Inter-rater reliability was measured by comparing our speech sample assessments with those of an independent, registered Speech and Language Therapist (A.G.).

Excitatory 10 Hz rTMS was delivered to the bilateral SMA (Figure 1A) on 15 consecutive working days. TMS was applied through an air-cooled 70-mm figure-of-eight coil, using a Rapid2 Stimulator (Magstim, Whitland, UK). The targeted area was identified through Brain Voyager neuronavigation software (Zebris CMS20S, Warwickshire, UK) on brain images obtained by MRI (Intera 1.5 T; Philips, Best, The Netherlands). Sixty trains of 10 Hz rTMS at 120% of resting motor threshold were delivered for 5 s, with 25-s inter-train intervals. Overall, a total of 3000 pulses were applied per session. The guidelines for safe use of rTMS were followed [8]. No adverse events were recorded. See figure 1 for experimental set-up

Figure 1. Experimental set-up. During the inter-train interval, the subject read aloud, following a 120-bpm metronome, to induce as much fluency as possible.

RESULTS

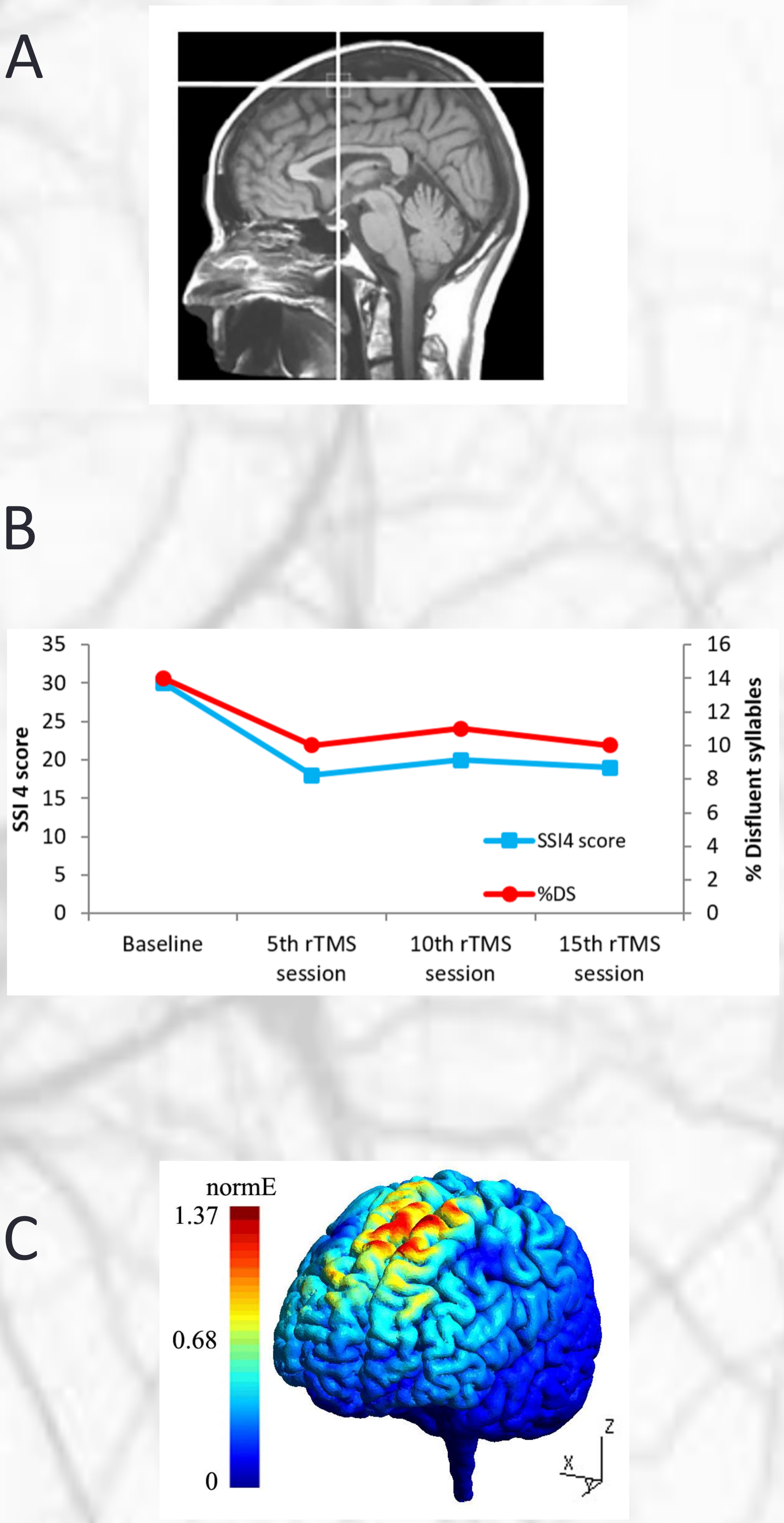

Figure 2. A Cortical supplementary motor area (SMA) coordinates targeted (MNI: x = 0, y = 6, z = 66). **B Changes in stuttering evaluation parameters across the number of rTMS sessions**. SSI-4 scores range from 0 to 46, with higher scores indicating greater severity. **C SimNIBS electric field mesh generation**, NormE (modulus) is given in V/m.

We found a significant decrease in %DS and SSI-4 score after 5 rTMS sessions; the fluency improvement was maintained during the subsequent 10 sessions (Figure 1B), and a final 36% decrease in SSI-4 score (from 30, moderate, to 19, mild) and a 28% decrease in %DS were obtained. The patient reported "fewer and less intense blocks than before treatment." A high intraclass correlation (ICC) was found for the inter-rater measurements (ICC = 0.91, $P < 0.001$), indicating a high level of reliability. No other significant changes were detected.

To visualize the induced electric field, a software simulation SimNIBS (www.simnibs.de) using an 8-type coil positioned on a realistic head model, with an 11.6 cm radius, in the same position as for the subject, was used. Three-dimensional distribution of the electric field modulus is shown in Figure 1C. The preSMA and SMA were the main regions in which the electric field was induced, although the premotor cortex and frontal areas also received stimulation.

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