Originally published:

Stewart, L., Walsh, V., Frith, U. and Rothwell, J.C. (2001) 'TMS Produces Two Dissociable Types of Speech Disruption' *NeuroImage*, 13, 472-478

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TMS Produces Two Dissociable Types of Speech Disruption

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Abstract

We aimed to use repetitive transcranial magnetic stimulation (rTMS) to disrupt speech with the specific objective of dissociating speech disruption according to whether or not it was associated with activation of the mentalis muscle. Repetitive transcranial magnetic stimulation (rTMS) was applied over two sites of the right and left hemisphere while subjects counted aloud and recited the days of the week, months of the year, and nursery rhymes. Analysis of EMG data and videotaped recordings showed that rTMS applied over a posterior site, lateral to the motor hand area of both the right and the left hemisphere resulted in speech disruption that was accompanied by activation of the mentalis muscle, while rTMS applied over an anterior site on the left but not the right hemisphere resulted in speech disruption that was dissociated from activation of the mentalis muscle. The findings provide a basis for the use of subthreshold stimulation over the extrarolandic speech disruption site in order to probe the functional properties of this area and to test psychological theories of linguistic function.

Introduction

Speech arrest is perhaps the most powerful example of TMS in its "virtual lesion" mode and several groups have achieved it by stimulating over left frontal areas. However, with the exception of Epstein et al. (1996b), the stimulation parameters required are much greater than those commonly used in TMS experiments, e.g., rates of between 8–50 Hz, durations between 1 and 10 s and intensities between 80 and 100% of maximum stimulator output. Even with these parameters, speech arrest is difficult to obtain, e.g., Michelucci et al. (1994) and Jennum et al. (1994) found it in only 7/14 and 14/21 subjects, respectively. Of the groups who have successfully achieved speech arrest with TMS, there is debate regarding the locus of the effect. Epstein et al. (1996), for example, argue that, despite the lateralization of the speech arrest effect to the left hemisphere, the sites at which the effect can be achieved overlap with sites at which TMS can produce contraction of the orbicularis oris muscle of the face and hence attribute the speech arrest to an effect on the muscles innervating the jaw and mouth. Pascual-Leone et al. (1991), on the other hand, based on a study with epileptic subjects, suggest the effect is mediated by interference with language processing, per se. These two apparently contradictory interpretations need not be mututally exclusive; indeed, using direct electrical stimulation, Penfield (1950) noted that two classes of speech arrest could be achieved in the same subject. One type of speech arrest, associated with muscular activity around the mouth and jaw, could be elicited by stimulation of rolandic cortex of the right and left hemisphere, while the other type of speech arrest did not seem to be accompanied by facial muscular activity and could be attained by stimulation at a more anterior site on the left hemisphere alone. The present study investigates whether such a dissociation can also be shown using TMS in normal,

nonepileptic subjects. This finding would shed light on the apparent contradiction between the findings of Epstein et al. and those of Pascual-Leone et al. Further, any area over which magnetic stimulation could produce speech arrest in the absence of any activation of facial musculature would be an interesting region to target with subthreshold stimulation combined with paradigms which could test psychological theories regarding this region's role in language processing. Last, a TMS-induced speech arrest, which could be objectively defined as nonmotor in origin and confined to one hemisphere, might have the potential to reveal language dominance in individual subjects. This technique could therefore be considered as a useful adjunct to the intracarotid amobarbital test which is currently used for this purpose in patients undergoing neurosurgery.

Method

Subjects

Subjects were 11 adults (8 male, 3 female), between the ages of 21 and 48 years. Two of the authors of this paper were subjects and all had previously taken part in at least one TMS experiment. All subjects were right-handed, according to a handedness questionnaire (Elias et al., 1999). Subjects reported absence of epilepsy or any other neurological condition in themselves and other family members. Ethical committee approval was granted for all procedures.

Speech Tasks

Subjects were asked to count briskly upwards from 1 to 10 and to recite the days of the week, months of the year, and nursery rhymes such as "Little Jack Horner" while stimulation was applied. All speech tasks were overlearned so as to place emphasis on automatic speech production. The particular speech tasks used were chosen in order to be consistent with the existing literature on TMS and speech disruption (Pascual-Leone et al., 1991; Epstein et al., 1996).

Stimulation

The stimulator used was a Magstim TM model 200 (Super-Rapid Magstim, Whitland, Dyfed) connected to a figure of eight coil with external wing diameters of 50 mm and a peak magnetic field of approximately 2T. The double coil windings carry two currents in opposite directions such that, where the two loops meet, there is a localized summation of current, and stimulation is more focal compared to coils with a single winding (Ueno et al., 1988). The coils are connected such that the initial phase of the stimulating current in the junction region flows toward the coil handle.

Mapping Speech Disruption

Motor threshold was first determined in order to equate starting intensity in the subsequent speech disruption mapping across all subjects. Since all the subjects who took part in the study had previously taken part in a study of motor and phosphene thresholds (Stewart et al., 2000), we used a visual assessment of each subject's motor threshold. Subjects sat with their right hand resting on the arm-rest of the chair. Single pulse TMS was delivered over a point 2 cm anterior and 2 cm lateral to the vertex and was moved around this point in steps of 1 cm until a muscle twitch was observed in the forefinger. When this occurred, the coil orientation was altered and the stimulus intensity reduced to find the lowest intensity at which an observable twitch could be elicited. Typically this threshold was found to be 40% higher than the same subjects threshold, as measured by EMG, in the previous

study. In order to dissociate speech effects which were associated with contraction of the facial musculature from those which were not, we measured surface EMG responses from the mentalis muscle using bipolar electrodes places 2 cm apart (Meyer et al., 1994). Responses were amplified by Digitimer D150 amplifiers (Digitimer, Welwyn Garden City, Herts) at a gain of 35000, filtered with a time constant of 3 ms and a high-pass filter set at 3 kHz.

The coil was positioned over an area slightly anterior and lateral to the site at which motor threshold was determined since pilot studies had shown that stimulation around this area was most likely to result in speech disruption. Stimulation was applied at a rate of 10 Hz for a duration of 1 s and at 120% of the visually assessed motor threshold while the subject performed one of the speech tasks outlined above. If speech disruption was not produced after four trials, intensity was increased in steps of 5% to a maximum of 140% of the visually assessed motor threshold. Consecutive trains were always given at least 30 s apart. These parameters are within published safety guidelines (Wassermann, 1998). If speech disruption could not be produced with these stimulation parameters, the coil was moved 1–2 cm to an adjacent site and the procedure was repeated. In this way, a systematic search for speech disruption sites was performed. Once speech disruption associated with an EMG response from the mentalis muscle had been demonstrated, the coil was moved approximately 5 cm anterior and 2 cm lateral to the previous site and the above procedure was repeated (see Fig. 1 for the relative location of stimulation sites in each subject). Again, a systematic search for effects on speech was performed by shifting the position of the coil and altering the stimulation intensity.

In order to gain an idea of the brain regions corresponding to the scalp locations at which speech arrest could be produced, an anatomical MRI scan was performed on two subjects. The two scalp locations over which TMS produced speech disruption were marked using gelatine capsules which showed up as dense white blobs on the MRI images. Figure 2 shows that the areas maximally targeted by TMS were the precentral gyrus and the middle frontal gyrus (Talairach and Tournoux, 1988). From here on, these sites will be, respectively, referred to as the posterior and anterior speech disruption sites.

Results

Of the 11 subjects tested, 3 subjects withdrew because they found the stimulation too uncomfortable, due to unavoidable activation of the facial nerves. Stimulation over two spatially nonoverlapping sites (average anterior–posterior distance 5 5.5 cm) produced two classes of speech disruption which could be segregated on the basis of presence or absence of EMG activity from the mentalis muscle (see Fig. 3). Videotaped recordings from the remaining eight subjects, comprising a total of 305 applications of TMS, were analyzed and classified into seven different categories (See Table 1).

TMS applied over a posterior site, lateral to the motor hand area, of the left hemisphere produced speech disruption associated with activity in the mentalis muscle in all eight subjects (see Fig. 3a). Subjects often described feeling as though they had lost control of their facial muscles. The most common subtype of speech disruption for the right and left rolandic sires was a distortion in the quality of speech, which did not render it incomprehensible (n 5 11), but instances of incomprehensible

distortion (n 5 3), interruption (n 5 6), slowing (n 5 3), and cessation (n 5 2) were also seen.

Stimulation over an anterior site (between 4 and 7 cm anterior to the site described above) of the left hemisphere alone, produced speech disruption that was not associated with any activity in the mentalis muscle in six of the eight subjects (see Fig. 3b). Subjects often described a feeling of being unable to "get the word out." Distortion in speech quality was again the most common effect (n 5 4), but instances of interruption (n 5 3), slowing (n 5 1), cessation (n 5 2), and stutter (n 5 2) were also seen. Dense sampling with TMS over the analogous site of the right hemisphere produced only one instance of distortion and one of cessation in two separate subjects, one of whom subsequently reported that a relative had successfully attempted to change his handedness from right to left when he was 4 years old. Significantly, this subject also scored lowest for right-handedness (65%, compared to the other subjects who scored between 73% and 96%). The degree of discomfort felt (due to unavoidable stimulation of the facial nerves) was judged to be the same for stimulation over both extrarolandic sites (left and right hemispheres).

Discussion

Three aspects of the present study enable us to say that these effects represent the TMS equivalent of those found by Penfield and Rasmussen; namely, that speech disruption can be motoric or nonmotoric, depending on where stimulation is applied. First, the EMG recordings provide an objective electrophysiological measure of the motor activity produced by stimulation. As in Penfield and Rasmussen's study, TMS applied over the most posterior of the two sites was associated with activation of the facial muscles while TMS applied over the anterior site of the left hemisphere was not. Second, the speech disruption associated with stimulation over the anterior site was lateralized to the left hemisphere while anterior stimulation site over either hemisphere was found to produce speech disruption, further supporting the dissociation of the effect into motor and nonmotor components. A third indicator that the two classes of speech disruption are separable comes from subjects' descriptions of the experience. Although there were no clear associations between the site of stimulation and subtype of speech disturbance, all subjects, without exception, described the two classes of effect (motor and nonmotor) as "feeling different." For instance, in the case of the speech disruption resulting from stimulation over the posterior site, subjects frequently reported that they felt as though they had lost control of their facial muscles while the most common description attached to stimulation over the anterior site was a feeling of being unable to "get the word out." Interestingly, they also found that while it was impossible to fight through the motor class of speech disruption, the nonmotor disruptions could, to some extent, be resisted. This is reminiscent of patients with left frontal damage in whom speech production can sometimes be facilitated when extra effort is expended (Geschwind, 1971).

It is worth noting that speech disruption with stimulation over the anterior site of the left hemisphere did not disrupt speech in two of the eight subjects we tested (Table 1). There are likely to be at least two reasons for this. First, since stimulation over this region inadvertently affected the facial nerves, the upper limit of stimulation intensity was often lower than 140% of visually assessed motor threshold and hence may not have been high enough to produce speech disruption. Second, individual variation in the anatomy of subjects' sulci and gyri may have precluded stimulation from reaching the cortical area at which interference can result in speech disruption. These findings

are consistent with those of Michelucci et al. and Jennum et al., who attained speech disruption in 7/14 and 14/21 subjects, respectively.

The results reported here for stimulation over the anterior site correspond well with those reported by Pascual-Leone et al. (1991), who found that stimulation over an area of the left but not the right frontal lobe produced speech arrest in six epileptic subjects. The present study builds on Pascual–Leone's findings to show that speech arrest attained by stimulation over a left anterior site can produce a class of speech arrest, which can be objectively defined as nonmotor via EMG and, furthermore, is also seen in normal, nonepileptic subjects. Epstein et al.'s finding, that the site at which speech arrest could be obtained overlapped with the site at which activity in the orbicularis oris muscle was elicited, corresponds to our results with TMS applied over the posterior site. However, Epstein et al.'s speech arrest was lateralized to the left hemisphere, whereas the speech disruption produced in our study was bilateral. An explanation for these contradictory results may lie in the different nature of the coils used in the two experiments. Epstein et al. use a solid core coil which has never been systematically compared to the air core-type of coil normally used (and used in the present study). The magnetic field it induces has a different shape and Epstein et al. have consistently reported speech arrest at lower intensities and rates than groups using air core coils (1996a and b), both of which suggest that the air core coil and the solid core coil may differ in terms of the populations of axons stimulated and sensitivity to factors such as direction of current flow or axonal orientation.

In our study, the MRI scan, performed in two subjects suggests that the anterior site at which TMS was applied corresponds to the middle frontal gyrus. Figure 1 shows the relative location of stimulation sites on the scalp in all subjects. The variance of the scalp sites at which speech could be disrupted is 2 cm in the anteroposterior direction and 3 cm in the lateral direction, suggesting that TMS was most likely targeting the middle or inferior frontal gyrus in all subjects. Over the past decade, electrical stimulation mapping studies have shown that speech production can be disrupted by targeting many different extrarolandic areas. Evidence from lesion studies (Rostomily et al. (1991), electrical stimulation mapping (Penfield and Roberts, 1959), and PET imaging (Ingvar, 1983) has shown that, in addition to posterior inferior frontal cortex, the supplementary motor cortex and superior frontal cortex are also involved in speech production. Outside of the frontal lobe, inferior parietal cortex, and superior temporal gyrus have additionally been suggested to have "essential roles" in speech production (Ojemann and Mateer, 1979; Ojemann, 1983). A plausible scenario would seem to be that that speech production is subserved by several "essential" areas in addition to which there may exist neuronal circuits, which are widely dispersed (even to the nondominant hemisphere; Creutzfeld, 1989a). Electrical stimulation mapping studies have also highlighted huge variance in cortical language organization between subjects. One study in which 90 subjects underwent stimulation mapping in frontal and temporoparietal cortex during object naming showed that 15% of subjects were not impaired by stimulation over frontal perisylvian areas while 17% of subjects were only impaired by stimulation over this area and not over temporoparietal cortex. The inferior frontal gyrus could be stimulated in more than 20% of subjects without any disruption to naming (Ojemann et al., 1989).

What the present study has shown is that, in 6 of 8 subjects we tested, TMS applied over two spatially distinct areas could produce two qualitatively different classes of speech disruption; one associated with activation of facial muscles and one dissociated from it. This latter, nonmotoric class of speech arrest is interesting for at least two reasons. First, the ability of TMS to produce a nonmotoric class of speech

disruption suggests the possibility that stimulation that is subthreshold speech disruption may be delivered over such an area while subjects perform reaction-time based cognitive tasks in order to further probe the functional characteristics of this area and, in particular, to test psychological models of linguistic function (Mottaghy et al., 1999; Wasserman et al., 1999). Second, the ability of TMS to produce a nonmotor class of speech disruption suggests that TMS may have potential benefits in a clinical setting. TMS could, for instance, be used as an adjunct to the intracarotid amobarbital test (IAT) as a means of assessing hemispheric dominance for language processing. A study by Jennum et al. (1994) specifically compared the speech disruption induced by TMS with the effects of the IAT test on language in 21 epileptic patients and concluded that the results from the two techniques were highly concordant. The circular nature of the coil used in that study and the fact that no objective physiological measure was taken as an index of facial muscle activity, lead the authors to claim that "the contralateral facial and the laryngeal muscle contractions causing dysphagia were difficult to differentiate from aphasia." Hence a further study in which an explicit attempt is made to dissociate a motor from a nonmotor class of speech arrest should provide a clearer estimate of the degree to which TMS could contribute in such a clinical setting.

Acknowledgements

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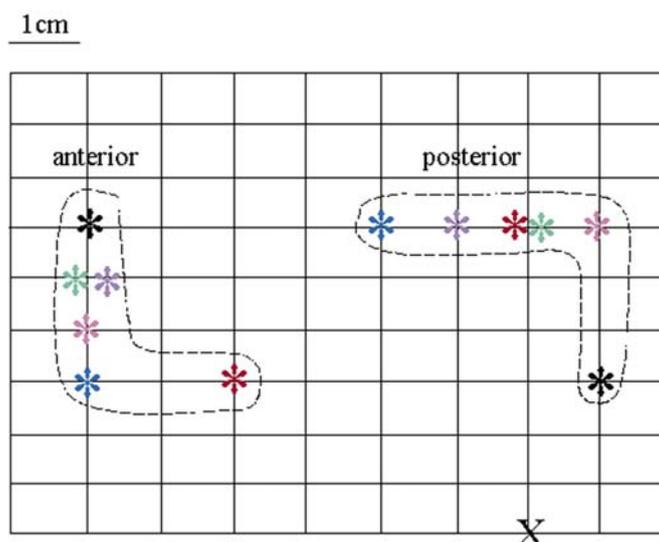
FIG. 1. The grid shows the location at which speech disruption was elicited in six subjects. The sites at which speech disruption was produced are represented by a differently colored asterisk for each subject. TMS applied over two nonoverlapping areas of the scalp (average anteroposterior distance between these points 5 5.5 cm) produced two dissociable classes of speech arrest; the posterior one associated with EMG activity recorded from the mentalis muscle and the anterior one dissociated from it. X represents a point located 5 cm above the tragus.
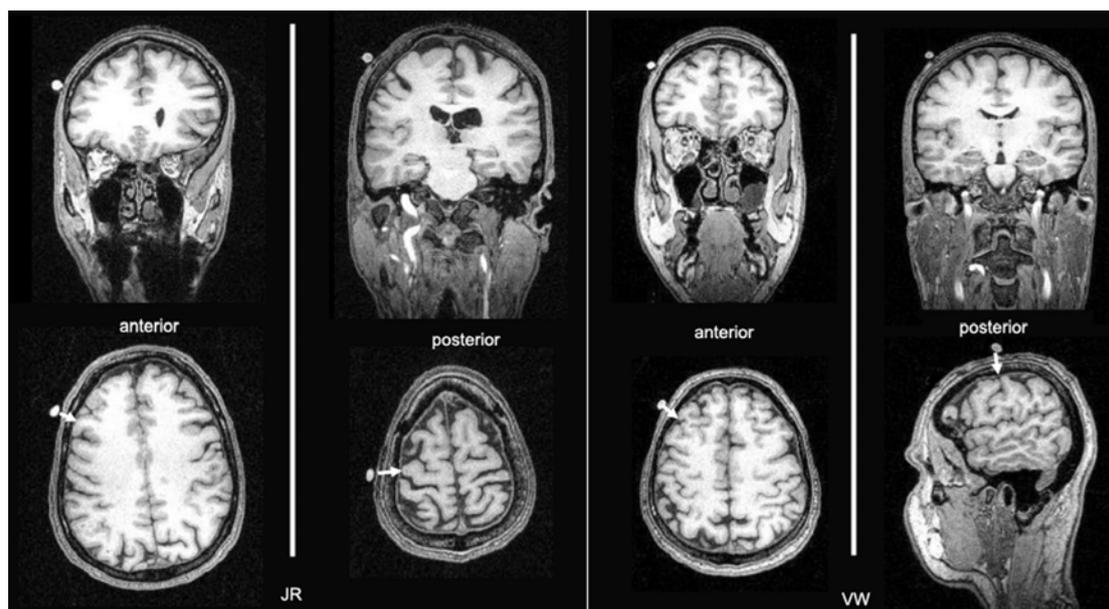
FIG. 2. Structural MRI of subjects J.R. and V.W. The upper images show coronal sections; lower images, horizontal sections (with the exception of the image furthest to the right which is shown in a saggital plane). The white arrows indicate the point at which stimulation was likely to be maximal when the coil was placed over the anterior and posterior site.
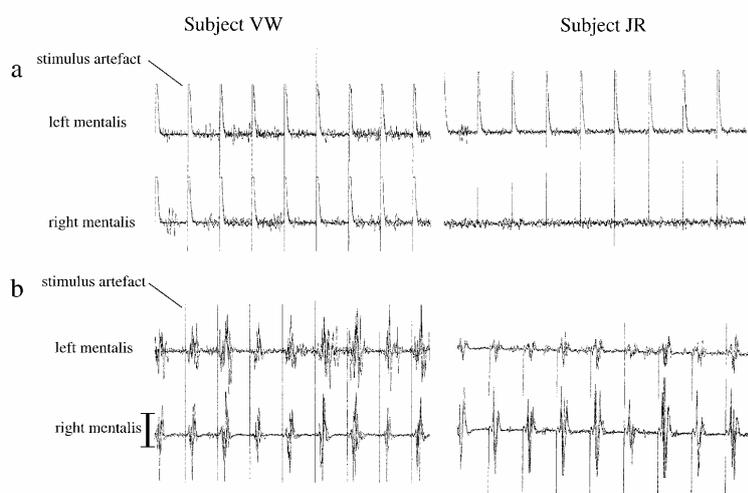

FIG. 3. Examples of the EMG recordings obtained during speech arrest when TMS applied over an anterior (a) and posterior (b) site of the left hemisphere in subjects V.W. and J.R. The scale bar indicates 50 mV.

Table 1.

Quantification of Types of Speech Disruption Observed with Stimulation over Anterior and Posterior Sites of the Left and Right Hemisphere (Categories Defined Below) in Eight Subjects.

	Interruption 1	Interruption 2	Distortion 1	Distortion 2	Slowing	Cessation	Stutter
I. rolandic	1	2	5	2	1	1	0
I. extrarolandic	1	2	4	1	1	2	2
R. rolandic	1	2	4	1	2	1	2
R. extrarolandic	0	0	1	0	0	1	0
Total	3	6	14	4	4	5	4
VW							
I. rolandic			X				
I. extrarolandic		X	X			X	X
R. rolandic			X				X
I. extrarolandic							
IR							
I. rolandic		X		X			
I. extrarolandic		X			X		
R. rolandic		X			X		X
R. extrarolandic							
EC							
I. rolandic			X		X		
I. extrarolandic			X	X			
R. rolandic			X		X		
R. extrarolandic			X				
DM							
I. rolandic	X	X					
I. extrarolandic	X					X	X
R. rolandic	X	X				X	
R. extrarolandic						X	
WR							
I. rolandic			X	X			
I. extrarolandic			X				
R. rolandic			X	X			
R. extrarolandic							
SC							
I. rolandic			X			X	
I. extrarolandic			X				
R. rolandic							
R. extrarolandic							

Note. Interruption 1, subject gets "stuck" on one part of speech and does not continue e.g., one, two, three, fff_. Interruption 2, subject leaves a noticeable gap between two words or two parts of a word e.g., one, two, three, f_our or: one, two three, four_five. Distortion 1, quality of speech is distorted but still comprehensible. Distortion 2, quality of speech is distorted and not comprehensible. Slowing, rhythm of speech is slowed. Cessation, subject stops mid word or mid sentence: e.g., one, two, three, f_ or: one, two, three, four_. Stutter, subject repeats part of the word but continues.