Supplemental Methods

During each trail, a pair of video clips was presented on a 24-inch CRT display located 10-inches in front of the participant. The task was simply to determine if both clips showed the same or different oral movements, by pressing a green or red button, respectively, with the left hand. On half the trials TMS was applied to BA while on the other trials (randomly interleaved) a sham TMS pulse was applied. Both sham and TMS trials consisted of four NeoPulse Neotonus® Model 3600 TMS pulses, applied 167, 267, 367 and 467ms after the onset of the second video. Nineteen subjects (mean age=24.68 [S.D.=4.46] males=12) participated in the experiment. Of these, 9 participants (mean age 23.61 [S.D.=4.93] males=5) also received an MRI scan to help determine the location of the TMS, which lead to the exclusion of one participant (see below). Participants wore a stereotaxic cap during TMS and subsequent MRI. All subjects were right handed, had normal or corrected to normal vision, and had no history of neurological or psychiatric illness. They were paid for their participation and were recruited from the University of South Carolina and the Medical University of South Carolina community. All subjects completed a TMS safety-screening questionnaire (Keel, Smith, & Wassermann, 2001) and signed a written informed consent approved by our Institutional Review board.

TMS Calibration

The first step in this experiment established each participant's motor hand area and resting state motor threshold (the minimum stimulation level that caused a visible hand contraction). Next, the location of BA was determined using a 10 Hz train of stimulation at 110% motor threshold applied for 5 seconds with a rest of 10s between stimulation. The experimenter placed the TMS wand where BA would be expected in the average human. This was estimated to be 30 mm ventral and 30 mm anterior to the motor hand area. The participant was then asked to produce speech. The topic of speech varied widely between subjects with the constraints that they were not allowed to say the same thing twice, sing, or say anything too automatic. The location of the TMS wand was then adjusted until the rTMS pulse train was able to significantly alter speech. A concerted effort was made to differentiate motor face area speech arrest from BA speech arrest. The procedure was complete when TMS stimulation was able to reliably alter speech in each of three consecutive trains of stimulation. Following completion, the location was marked with neon orange fingernail polish applied to the stereotaxic cap with a thin metal dowel that was inserted through the hole in center of the solid TMS coil used in localization. Significantly altered speech was most often characterized as

slurring and sluggish speech production, and ranged from barely perceivable sluggishness (but where the participant introspectively reported that speech was more difficult to produce) to the complete disruption of the ability to speak.

Following BA localization, two electrodes were placed in the location that was determined by localization. In 15 of the 19 subjects, the electrodes had to be placed slightly anterior to the TMS site due to the subjects' hairline. The TENS system was initially set at a level that was below the normal perceptual threshold of each subject. A sham coil was positioned posterior and slightly lateral to the active coil (Figure 1S). The participants then engaged in a forced choice task (TMS vs Sham coil firing with electrode stimulation) whereby the subject was asked to rate which of two consecutive stimulations was more painful. The Sham stimulation consisted of electrical stimulation paired with sham coil activation identical to the active coil (but not placed directly on the scalp). The sequence (TMS or sham stimulation) was presented randomly and each participant's subjective rating was used in order to adjust the intensity of the sham stimulation to make it more similar to the TMS sensation (using a psychophysical staircase algorithm). After the direction of modification of the intensity of electrode stimulation changed three times, sham calibration was completed and that value was used in the subsequent experimentation. After calibration, every subject reported that they were unable to tell the difference between the two forms of auditory and tactile/nociceptive stimulation (Arana et al., 2008; Borckardt et al., 2008).

Visual stimuli consisted of videos of the face, below the nose, of one speaker making oral speech or non-speech movement. The motor speech movements included 10 productions of nonsense syllables: /ba/, /bu/, /fa/, /ha/, /la/, /mu/, /na/, /pou/, /shei/, and /sha/. The non speech movements were carefully selected to not be recognizable as any possible syllables devoid of emotionally saliency and consisted of: unilateral tongue lateralization, bilateral tongue lateralization, tongue protrusion, pursed lip protrusion, raising the upper lip (and showing the upper teeth), biting the lower lip, lip contraction showing upper and lower teeth, unilateral lip contraction, complete mouth opening, and tongue thrust in left cheek. The speech stimuli used here have previously been shown to activate BA (Fridriksson et al, 2008). All stimuli in our study were displayed at 30 frames per second.

Experimental procedure

The main experiment commenced immediately after the TENS titration. Subjects were allowed to practice the task using two randomly selected stimuli from the pool of stimuli later used in the experiment. After sufficient practice, consisting of no less than three trials or

however many trials it took for the participant to get three consecutive correct responses, experimentation began. During the experiment, participants were shown stimuli for 2000ms with a 567ms pause between the two stimuli. Each video started and ended with the face in a relaxed and neutral position, with facial movement occurring around 267-333ms after the video onset. The stimuli were either the same two stimuli or not. Speech and non-speech oral movements were never shown together in a stimulus pair. Participants were simply instructed to respond as to whether or not the second stimulus was the same as the first. Starting 167ms into the second stimulus, participants received 4 TMS pulses every 100ms at 110% of their motor threshold. Each participant completed 120 trials, with trial order selected randomly without replacement. Therefore, each of the four conditions (speech with TMS, speech with sham, non-speech with TMS, non-speech with sham) was presented 30 times. Accuracy and reaction times, from the onset of the second stimulus, were recorded for all conditions. 2x2 repeated measures ANOVAs were performed in order to determine the effect of BA TMS on reaction times and accuracy while participants were actively involved in discriminating speech or non-speech stimuli.

MRI

In order to anatomically ascertain stimulation location, 9 participants underwent MRI scanning following the TMS procedure. They were scanned with their stereotaxic cap oriented to their scalp landmarks and a vitamin E capsule was placed on the location used for TMS stimulation. All MRI data were collected using a Siemens Trio 3T with a twelve channel head coil. The specifics of the T1-weighted MRI sequence were as follows: TI of 900ms, a TR of 2250ms between TFE shots and a 9 degree flip angle, TE= 4.52ms, 160-slices with an isotropic 1mm resolution and a 256x256 matrix. All images were linearly normalized to the MNI152 template using SPM5 (Welcome Department of Imaging Neuroscience, University College London). MNI cortex coordinates were extrapolated from the scalp location of the vitamin E capsule. One subject showed stimulation location in motor face area (MNI coordinates (-88,-16,32), and this subject was excluded from analysis. The other 8 participants were observed to have an average fiducial location of MNI = -81.14 (sd=5.4), 20 (sd=10.13), 13.14(sd=19.73) this corresponds to a cortical stimulation site of (MNI= -64, 16, 11) (see Figure 2S).

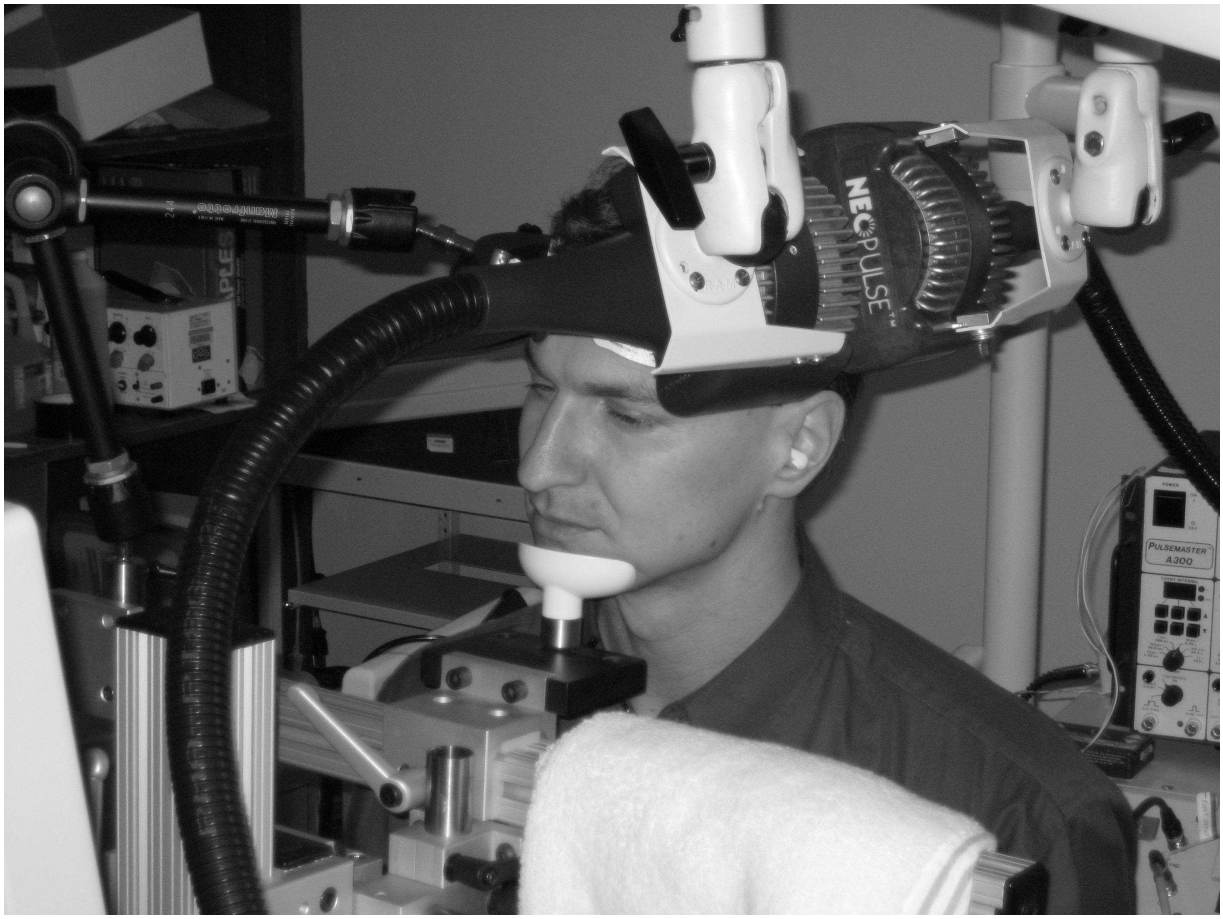

Figure 1S

Experimental setup. Two TMS wands are positioned over the head, with the anterior wand directly touching the scalp, generating the TMS pulse, while the posterior wand is used during sham trials – generating the same sound as the TMS trials, but without disrupting the brain. The white patch visible above the eyebrow is one of the TENs leads, which is triggered on sham trials to elicit a muscle contraction and sensation that mimics the effect of the TMS trials. A chin rest and forehead rest help stabilized the head to ensure that the TMS wands remained in the same position.

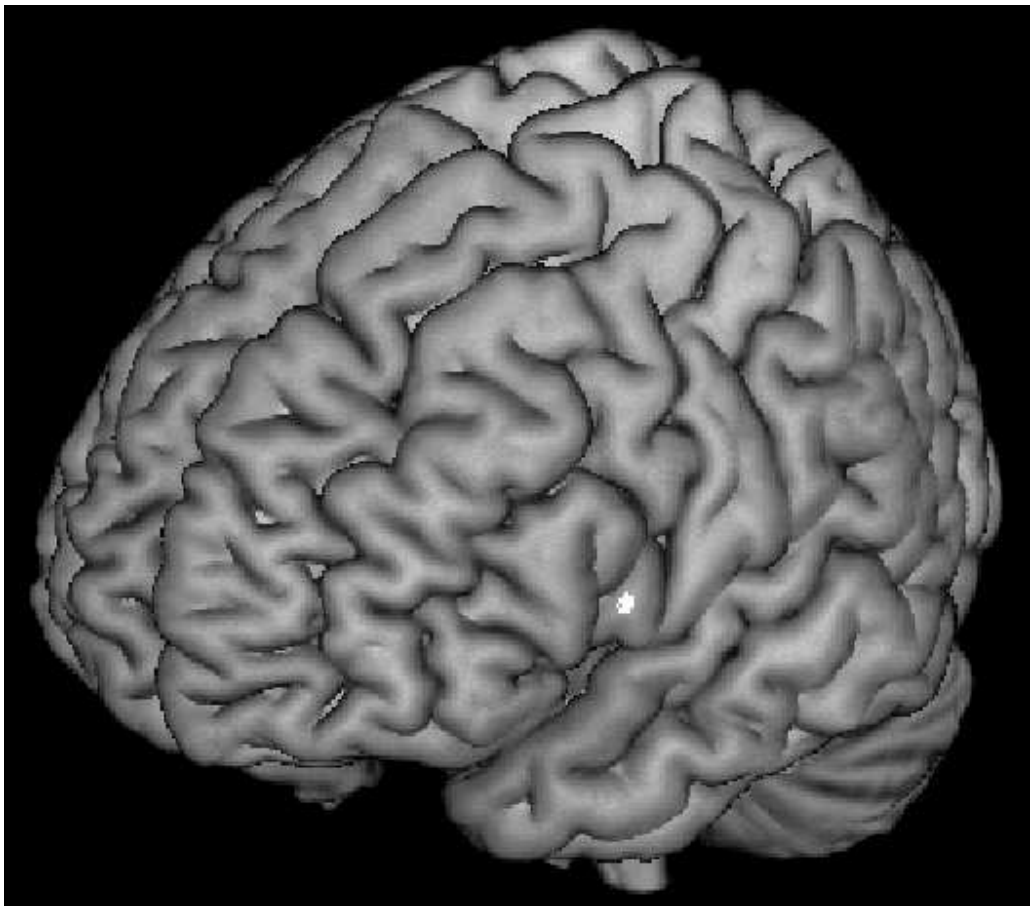

Figure 2S

Location of TMS stimulation (MNI= -64, 16, 11) based on the eight participants where an MRI demonstrated anterior wand placement. Each individual wore a stereotaxic head cap during TMS and during the subsequent MRI scan. During the MRI scan, a fiducial marker was placed at the site of stimulation. Each individual's scans were than normalized to standard space, and mean location plotted in stereotaxic space.

References

Arana, A.B., et al. Focal electrical stimulation as a sham control for repetitive transcranial magnetic stimulation: Does it truly mimic the cutaneous sensation and pain of active prefrontal repetitive transcranial magnetic stimulation. Brain Stimulation 1, 44-51 (2008).

Borckardt, J.J., et al. Development and evaluation of a portable sham transcranial magnetic stimulation system. Brain Stimulation 1, 52-59 (2008).

Fridriksson J, Moss J, Davis B, Baylis GC, Bonilha L, Rorden C. (2008) Motor speech perception modulates the cortical language areas. Neuroimage. EPub PMID: 18396063

Keel, J.C., Smith, M.J. & Wassermann, E.M. A safety screening questionnaire for transcranial magnetic stimulation. Clin Neurophysiol 112, 720 (2001).