

Covert Speech Arrest Induced by rTMS over Both Motor and Nonmotor Left Hemisphere Frontal Sites

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Abstract

■ Blocking the capacity to speak aloud (overt speech arrest, SA) may be induced by repetitive transcranial magnetic stimulation (rTMS). The possibility, however, of blocking internal speech (covert SA) has not been explored. To investigate this issue, we conducted two rTMS experiments. In the first experiment, we stimulated two left frontal lobe sites. The first was a motor site (left posterior site) and the second was a nonmotor site located in correspondence to the posterior part of the inferior frontal gyrus (IFG) (left anterior site). The corresponding right hemisphere nonmotor SA site was stimulated as a control. In the second experiment, we focused on the right hemisphere and stimulated a right hemisphere motor site (right posterior site), and, as control sites, a right hemisphere nonmotor site corresponding to the IFG (right anterior site) and a left hemisphere anteromedial site (left control). For both experiments, participants per-

formed a syllable counting task both covertly and overtly for each stimulation site. Longer latencies in this task imply the occurrence of an overt and/or covert SA.

All participants showed significantly longer latencies when stimulation was either over the left posterior or the left anterior site, as compared with the right hemisphere site (Experiment 1). This result was observed for the overt and covert speech task alike. During stimulation of the posterior right hemisphere site, a dissociation for overt and covert speech was observed. An overt SA was observed but there was no evidence for a covert SA (Experiment 2). Taken together, the results show that rTMS can induce a covert SA when applied to areas over the brain that are pertinent to language. Furthermore, both the left posterior/motor site and the left anterior/IFG site appear to be essential to language elaboration even when motor output is not required. ■

INTRODUCTION

Several laboratories have now documented overt speech arrests (SAs), as evoked by repetitive transcranial magnetic stimulation (rTMS) (Stewart, Walsh, Frith, & Rothwell, 2001; Epstein, 1998; Pascual-Leone, Gates, & Dhuna, 1991). This phenomenon is most commonly described as a slowing and distortion of speech, an inability to get words out, and an inability to formulate words. It generally occurs for the time period of the stimulation (commonly a few seconds) and, subsequently, speech is immediately recovered.

There has been some discussion about whether the SA evoked by rTMS is related to an interference with language processing or is, in fact, due to motor interference determined by cortical stimulation of orofacial muscles. In a review by Epstein (1998), the need to distinguish between different types of SAs was discussed. It was noted that, at the time, the most common form of SA was a motor one induced by interfering with motor areas involved with muscular control of speech. Supporting this interpretation was the observation that SA

could also be obtained with right hemisphere stimulation. However, on the basis of data obtained from stimulating the left and right hemisphere in epileptic patients for language dominant hemisphere assessment, Pascual-Leone et al. (1991) concluded that TMS-induced SAs may result from a disruption of language processing, and not only derive from motor interference.

Since then, Stewart et al. (2001) reported two different types of overt SAs induced by rTMS over two different left hemisphere sites. The first type, called “motor” SA, was determined by stimulation of a “posterior” site located in the motor area of the frontal lobe, and was associated with EMG activity evoked in lower facial muscles, through activation of the cortico-bulbar pathway. The second one, called a “nonmotor” SA, was caused by stimulation of an “anterior” site located in the posterior part of the inferior frontal gyrus (IFG) and was not associated with EMG activity in orofacial muscles. The “nonmotor” SA was thought to result from stimulation of Broca’s area. The two SA sites were further distinguished by their differing abilities to produce an SA following stimulation of the right hemisphere: The site corresponding to the left hemisphere posterior site produced an SA, whereas the site corresponding to

the left hemisphere anterior site did not produce an SA. Finally, participants reported different sensations during each kind of SA. For the motor SA, they reported an inability to control their facial muscles. By contrast, for the nonmotor SA, they reported a deficit described as an inability to “get the word out.” These findings are consistent with classical cortical electrical stimulation studies where also two classes of SAs, behaviorally similar with those described with rTMS, were found after stimulation of anterior and posterior frontal sites of the left hemisphere (Ojemann, Fried, & Lettich, 1989; Penfield & Rasmussen, 1949). Thus, although it is generally agreed that it is difficult to obtain a pure non-motoric SA with rTMS (Epstein, 1998), there is evidence that this type of SA does exist. In addition, the finding that stimulation of the anterior site produces an SA exclusively in the left hemisphere further indicates that the anterior site is related to language processing rather than to the control of speech emission.

Is it possible to produce a covert (internal) SA with rTMS as with overt (aloud) speech? Will stimulation of the anterior and/or posterior left hemisphere sites produce a covert SA as it does for overt speech?

There are important theoretical reasons for exploring the role of both a nonmotor and a motor site in covert language production. As far as the anterior site is concerned, several brain imaging studies have found Broca’s area active during covert speech (Bookheimer, 2002; Lurito, Lowe, Sartorius, & Mathews, 2000). If Broca’s area is essential for the organization of language production, regardless of whether or not the language is overtly communicated (via the mouth or the hands), then one may expect that rTMS of Broca’s area will interfere with covert speech as with overt speech.

The issue of a covert motor SA is more complicated. Covert speech is a component of language that, in theory, does not involve the motor system. There is no motor output during covert speech. Thus, one may expect that stimulation of a motor site will not influence covert speech. However, what exactly is covert speech? Is covert speech imagery of overt speech? If so, then it is possible that stimulation to motor areas, which are known to be active during motor imagery (Dechent, Merboldt, & Frahm, 2004; Fadiga et al., 1999; Parsons, Gabrieli, Phelps, & Gazzaniga, 1998), will also interrupt covert speech. In any regard, a covert SA during stimulation of motor areas would reveal that covert speech involves processing in motor areas and the disruption of this processing directly interferes with it.

To explore these questions, we ran two experiments. In both of them, to test for both covert and overt SAs, we asked participants to count the number of syllables in words presented on a computer monitor. The syllable counting task has been used in previous brain imaging studies on covert language and has been found to significantly activate left hemisphere frontal regions (Poldrack et al., 1999; Price, Moore, Humphreys, & Wise,

1997). Words were chosen such that the task could not be completed visually and thus, in order to count the syllables, participants needed to produce the words. In half of the blocks, they were asked to complete the task overtly (aloud), whereas in the other half they completed it covertly (silently). Participants responded manually, with the hand ipsilateral to the site of stimulation in order to ensure that stimulation did not interfere with motor planning of the response, and reaction times were recorded. Longer reaction times indicate the occurrence of an SA.

In the first experiment, we stimulated the left anterior (nonmotor SA) site, the left posterior (motor SA) site, and the corresponding right anterior (control) site while participants performed the task covertly or overtly. To foreshadow the results, we found that stimulation over both left hemisphere sites produced both an overt and a covert SA. Motivated by these results, in Experiment 2 we focused on the right hemisphere. Can we observe an SA (covert or overt) in the right hemisphere? To explore this, in Experiment 2 we stimulated the right posterior site (motor representation of the *mentalis* muscle), the right hemisphere site symmetrical to the left hemisphere anterior site (right hemisphere control), and, as a further control, a left hemisphere anteromedial site (left hemisphere control) during performance of the same task as in Experiment 1.

EXPERIMENT 1

In the first experiment, we aimed to find evidence for a covert SA when stimulating the left hemisphere motor and nonmotor areas. Furthermore, we sought to replicate the results by Stewart et al. (2001) for distinguishing between two kinds of overt SAs, a motor SA as evoked through stimulation of a posterior frontal area and a nonmotor SA as evoked through stimulation of a more anterior left frontal area. Thus, we conducted rTMS over the left posterior site, the left anterior site, and the corresponding right hemisphere anterior site as a control. Participants were asked to determine the number of syllables (3, 4, or 5) in words presented on a computer monitor and to respond by pressing one of three buttons on a response box with the hand ipsilateral to the site of stimulation. Participants performed the task covertly in half of the blocks and overtly in the second half.

Results and Discussion

All participants reported a syllable counting strategy that involved production of the word, which took place within the time window of rTMS. Furthermore, they reported performing the task by either internally or overtly producing the word in order to count the number of syllables. Further evidence for this word production strategy was observed by the time it took to report how many syllables there were in different

words. Three syllable words were found to have the shortest response latencies, followed by four- and then five-syllable words (1671, 1946, and 2025 msec, respectively). This difference was present irrespectively of the number of letters in the word. As expected, overt speech trials had significantly longer latencies than covert speech trials [means: 1960 and 1747 msec, respectively; $F(1,5) = 8.61, p = .033$]. None of the included participants reported rTMS as more than mildly painful on a 4-point subjective pain rating scale. Excessive pain from stimulation was considered an exclusion criterion (see Methods). On average, motor threshold (MT) was 51% of maximum stimulator output and SA was found at 115% of MT.

The position of the stimulated sites is depicted in Figure 1A. The anterior site was 3.0 ± 0.7 cm rostral to the posterior site. This distance is somewhat smaller than the one reported by Stewart et al. (2001). Direct comparisons with the anatomical data provided by these authors cannot be possibly done because they provide no measures standardized by head size. Nevertheless, we can infer that the stimulated sites had two distinct functional identities from several lines of evidence. The stimulation of the anterior site did not evoke motor-evoked potentials (MEPs) from the *mentalis* or the *mylohyoid* muscles (see below). Although it is not possible to make any claim about the precise location of the stimulus, probabilistic maps of the scalp according to the international 10–20 system show that the anterior sites all fall within a surface that is likely to overlay the IFG, whereas posterior sites are located around the central sulcus (Okamoto et al., 2004).

Overt Speech Task

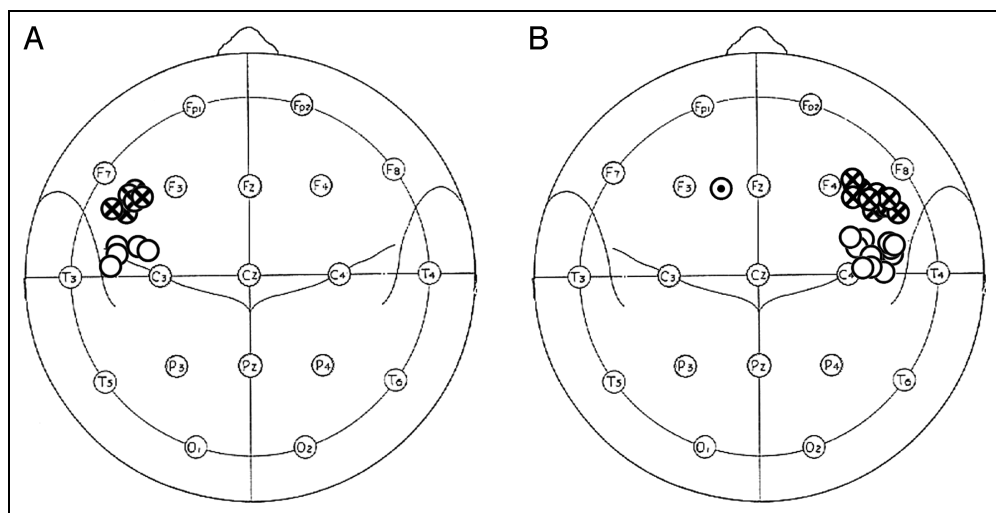
Overt speech disturbance was evoked in all participants during stimulation of both the anterior and posterior sites of the left hemisphere. In both cases, this was

observed as a slowing and distortion of speech both when the participant was asked to count from 1 to 10 as well as when they produced words overtly during the syllable counting task. Particular care was taken in measuring, when present, the onset latency of the motor responses, in the *mentalis* (M) muscle. This was done to assess whether activations had a cortical or peripheral origin. We discarded the results of participants displaying short latency responses in the M muscle at stimulation intensities lower than the SA threshold (see Methods) for both anterior and posterior spots. Stimulation of the left or right hemisphere anterior sites did not evoke M muscle activation. In addition, in three participants, we recorded the activity of the *mylohyoid* muscle using surface electrodes placed under the subject's chin. MEPs were observed in the *mylohyoid* muscle always in association with *mentalis* muscle responses.

In addition to the difference in whether or not MEPs were observed from the posterior versus anterior sites, qualitative differences in the SA were observed for each left hemisphere site. When stimulated over the posterior site, participants generally reported an inability to control mouth muscles. By contrast, when stimulated over the anterior site, participants generally reported an inability to “get the word out.” These findings are in accord with those by Stewart et al. (2001), and support the notion that the posterior site induces a motoric SA, while the anterior site induces a nonmotor SA. Finally, during stimulation of the right hemisphere site, which was localized as the symmetrical point of the left anterior site, no SA was observed nor were MEPs recorded from the *mentalis* (or *mylohyoid*) muscle.

rTMS over both the anterior and posterior sites in the left hemisphere induced significantly longer reaction time latencies as compared with stimulation over the right hemisphere site ($F = 11.23, p = .0074$ and $F = 5.81, p = .037$, respectively). The results are

Figure 1. Representation of the left and right hemisphere stimulation sites in relation to the international 10–20 system. (A) Left hemisphere sites for Experiment 1 (6 participants); (B) Right hemisphere sites (12 participants) and the left hemisphere control site (F1) in Experiment 2. Empty circles indicate the posterior site locations and crossed circles indicate the anterior site locations for each participant. The dotted circle indicates the F1 spot stimulated as a control in the left hemisphere in 6 of the 12 participants. Due to overlap among participants, not all points are visible.



shown in Figure 2. Note that, compared with the right hemisphere site, the two left frontal lobe sites showed similar reaction time patterns. Thus, both left hemisphere sites seem to be critical for the task, albeit, possibly, not for the same functional reasons. It might be that the stimulation of the anterior left hemisphere site caused reaction time increases due to interference with language processing, whereas the stimulation of the posterior left hemisphere site caused the reaction time increases due to a motor factor. The covert task tested this possibility.

Covert Speech Task

The reaction time latencies during the covert speech task are shown in Figure 2. Reaction times during the covert speech task were significantly faster than those during the overt speech task during stimulation of all sites. Most interestingly, as with overt speech, rTMS over both the anterior and posterior sites in the left hemisphere induced significantly longer latencies as compared with stimulation over the right hemisphere site ($F = 7.89, p = .019$ and $F = 6.29, p = .031$, respectively).

Thus, disruption of processing in the left anterior and posterior sites affected covert and overt speech similarly. Reaction times for the overt task and the covert task during stimulation of the different sites mirrored one another. These findings suggest that not only the left anterior site, most likely corresponding to Broca's area, but surprisingly, also the posterior site, a motor area, seems to be essential to speech, regardless of the presence of a motor output. However, before we speculate further on this point, we were interested in a follow-up question.

Right hemisphere motor sites contribute to the control of muscles involved in speech production. In contrast, they do not appear to be involved with the linguistic aspect of speech (Wildgruber, Ackermann, Klose, Kardatzki, & Grodd, 1996; Cadalbert, Landis, Regard, & Graves, 1994). Thus, if the right hemisphere motor areas are interfered with, the SA occurs because of an impairment in the speech output control (Stewart et al., 2001; Epstein, 1998). By contrast to overt speech disruption, covert speech disruption should not be, therefore, expected following right hemisphere stimulation. In Experiment 2, we explored this possibility.

EXPERIMENT 2

Participants performed the same task as in Experiment 1. The stimulated sites were the "anterior" and "posterior" sites, but of the right hemisphere. In addition, in 6 of the 12 participants, we also stimulated a left hemisphere control site, which corresponded to F1 of the 10–20 international EEG electrode placement system. We chose the F1 spot because it has been reported to correspond, with good probability, to the projection on the scalp of the middle portion of the superior frontal gyrus (Okamoto et al., 2004). Furthermore, in a recent meta-analysis, this area was not activated in neither silent nor aloud reading, and can thereby serve as a nonlinguistic control stimulation site in the left hemisphere (Turkeltaub, Eden, Jones, & Zeffiro, 2002).

As in Experiment 1, the posterior site corresponded to the site that evoked MEPs from the *mentalis* muscle. In half of the blocks, participants were asked to perform the syllable counting task overtly, while the other half were asked to perform the task covertly.

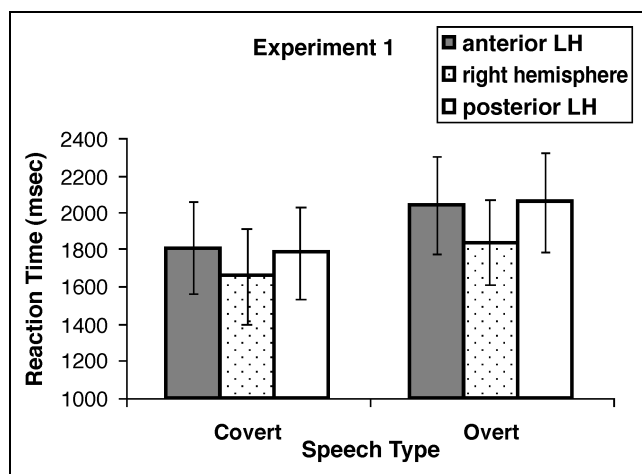


Figure 2. Experiment 1: Stimulation over the left hemisphere anterior site and the left hemisphere posterior site significantly induce longer response latencies for both the overt and covert language tasks as compared with stimulation over the right hemisphere control site. For overt speech trials, an observable slowing and distortion of speech was found following stimulation of both anterior and posterior left hemisphere sites.

Results and Discussion

As in Experiment 1, all participants reported a syllable counting strategy that involved production of the word, which took place within the period of rTMS. Latency measurements for the three-, four-, and five-syllable words also indicated word production, as longer syllable words were found to have longer response latencies (1407, 1686, and 1800 msec, respectively). This difference was observed irrespective of the number of letters in the word. None of the participants reported rTMS as being more than mildly painful. On average, resting MT of the right OP muscle was found at 55% of maximum stimulator output and SA was found on average at 110% of the MT. The stimulation locations are depicted in Figure 1B. The anterior site was on average 3.5 ± 0.9 cm anterior to the posterior site and evoked no cortical MEPs from the *mentalis* or *mylohyoid* muscles.

Stimulation over the posterior motor site evoked an overt SA. This was observed both when the participant was asked to count from 1 to 10 as well as when they produced words overtly during the syllable counting

task. This was similar to the SA evoked by stimulation over the corresponding *left* hemisphere posterior site. That is, participants showed a slowing and disturbance of speech and described the disturbance as an inability to control their mouth and/or tongue muscles. MEPs with latency between 10 and 14 msec were also recorded from the *mentalis* muscle, further indicating that motoric disturbance of the mouth/tongue muscles during stimulation of this site. Furthermore, in half of the participants, *mylohyoid* muscle activity was also recorded with results similar to those in Experiment 1.

Stimulation over the anterior site and the left hemisphere control site did not evoke an overt SA. No MEPs were evoked from the *mentalis* or from *mylohyoid* muscles. Our results are consistent with those of Stewart et al. (2001), who also found a right hemisphere SA with stimulation over the right hemisphere posterior site but not over the right hemisphere anterior site.

Figure 3 shows the reaction time latency during stimulation over the posterior and anterior right hemisphere sites, and the left hemisphere control site. As in Experiment 1, overt speech trials were significantly longer than covert speech trials [means: 1771 and 1490 msec, respectively, $F(1,11) = 11.17, p = .0066$]. No other significant effects or interactions were found. However, for the overt task, there was a trend for longer reaction times during stimulation of the right hemisphere posterior site as compared with the two control sites. By contrast, for the covert task, there was a trend for shorter reaction times for the same comparison. Thus, while there was a trend consistent with the occurrence of an overt SA as well as a behaviorally visible

overt SA during stimulation of the posterior site, the increase in reaction times did not reach significance, as presumably the participants were still able to complete the task covertly. Finally, the left hemisphere control site did not differ significantly from the right hemisphere anterior site, indicating that the latter serves as an adequate right hemisphere control for sites whose stimulation invokes SAs.

The fact that we see only an overt SA with stimulation of the posterior site is illuminating. As one may expect, rTMS of the motor representation of the orofacial muscles disrupts the production of speech. However, consistent with previous research, the right hemisphere motor representations do not appear to be essential to language elaboration (Wildgruber et al., 1996; Cadalbert et al., 1994). Thus, although stimulation of the right hemisphere posterior site disturbed overt speech, it did not disturb covert speech. In fact, covert production of the word remained unimpaired (Figure 3). Therefore, although the posterior left hemisphere site appears to be essential for speech production both overtly and covertly, rTMS over the corresponding right hemisphere site only affects overt speech, seemingly at a purely muscular level.

GENERAL DISCUSSION

Our data indicate that overt and covert SAs, as induced by rTMS, follow similar patterns in the left hemisphere. Both the anterior/Broca's site and the posterior/motor site of the left hemisphere are involved in covert speech as they are in overt speech. In contrast, the right hemisphere posterior/motor site elicits an overt SA, but it does not interfere with covert speech. SA in this case appears to be due exclusively to a motor interference with speech production related to the activation of the orofacial muscles.

There is now a large body of data, particularly from brain imaging research, which indicates that the posterior part of the IFG is active during both silent and overt language tasks (Bookheimer, 2002). This has been observed for a multitude of covert language tasks including sentence comprehension, semantic processing, and reading (Palmer et al., 2001; Gabrieli, Poldrack, & Desmond, 1998; Wildgruber et al., 1996).

Although it is possible that the activation of the IFG during covert language tasks is a mere epiphenomenon due to its strong connections with Wernicke's area and the parietal areas connected with it (Aboitiz & Garcia, 1997), evidence suggests that this cannot be the only reason for IFG activation in verbal tasks. IFG activation during covert tasks appears to play a fundamental role in various aspects of language processing. In her review, Bookheimer (2002) indicates that the IFG may consist of at least three different modular regions related to phonology, semantics, and syntax. These regions would therefore be necessary for covert language processing,

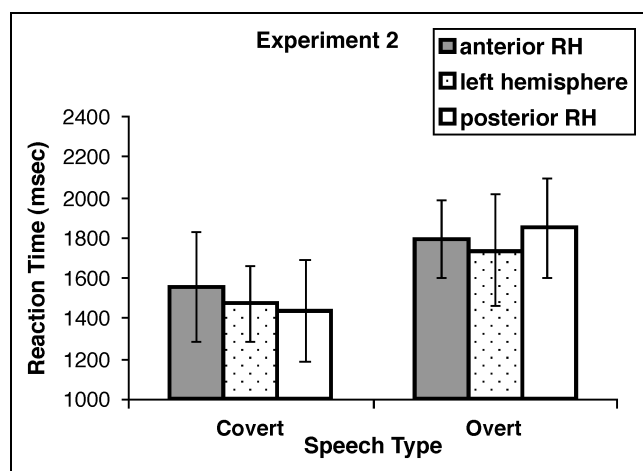


Figure 3. Experiment 2: Data from the six subjects who underwent stimulation of all three stimulation sites (right anterior, right posterior, left hemisphere control) are shown. There was a trend for longer latencies for the overt speech task during stimulation over the right hemisphere posterior site as compared with stimulation over the two control sites. By contrast, this trend was not observed for the covert speech task. For overt speech trials, an observable slowing and distortion of speech was found following stimulation of the posterior right hemisphere site.

as they would be for overt language processing. Furthermore, Poldrack et al. (1999), in an fMRI study in which they contrasted a semantic task (abstract/concrete decision) with a phonetic task (syllable counting, as in our task), found results suggesting that phonological processing is automatically engaged during performance of the semantic task, despite finding segregated regions for phonology and semantics in the IFG.

Our data are in accord with these theoretical positions. Broca's area does not seem to be activated simply because of its anatomical connections with the posterior speech areas, but it appears to play a critical role in covert language processing. However, it should be noted that a remote possibility remains that distant effects of local rTMS (that is to say on the posterior speech areas), as shown for different anatomical regions (Strafella, Paus, Fraraccio, & Dagher, 2003), could account for the results observed. Although this possibility cannot be excluded, it remains very unlikely.

Although it may be easy to understand why a language area in the IFG may process covert language, it is not as simple to understand why motor areas are also essentially involved. Why is covert speech affected by stimulation of the cortical representation of mouth and/or tongue muscles? To answer this, we must ask another question—what exactly is covert speech? Is covert speech truly language devoid of motor output and therefore does not require the motor system? Or is covert speech essentially motor (and auditory) imagery of overt speech and therefore intrinsically tied to the motor system?

Data from previous studies support the view that internal speech is strictly linked to the motor system. Electromyography (EMG) recordings from the tongue and lip muscles during silent speech showed that the tongue (but not the lip) muscles were active when participants visually processed the letter "T," but not while they visually processed the letters "P" or "C." Instead, the lip (but not the tongue) muscles were found to be active during visual processing of the letter "P" but not of the letter "T" (McGuigan & Dollins, 1989). This dissociation indicates that the muscles are activated in covert speech in the same manner as they would be in overt speech, albeit minimally. Furthermore, there is brain imaging evidence for substantial activation even of the motor cortex (precentral gyrus) during covert speech (Wildgruber et al., 1996).

The finding that covert speech may lead to muscle activations is reminiscent of observations of similar muscle activations during motor imagery (Jeannerod, 2001). An increase in the excitability of spinal reflexes has been reported during mental imagery of body actions, with activation specific to the muscle involved in the imagined actions (Bonnet, Decety, Jeannerod, & Requin, 1997). Further evidence comes from studies utilizing TMS and electrical stimulation of the motor cortex. An increase in the excitability of the primary

motor cortex was observed both during mental imagery of specific actions (Facchini, Muellbacher, Bhattaglia, Boroojerdi, & Hallett, 2002; Fadiga et al., 1999; Abbruzzese, Trompetto, & Schieppati, 1996) and during mental focus on one of the subject's hands (Haaland & Flaherty, 1984). There are further fMRI data indicating that the premotor areas (Rizzolatti, Fogassi, & Gallese, 2002) and occasionally the primary motor areas are active during motor imagery (Dechent et al., 2004; Porro et al., 1996; Rueckert et al., 1994). Thus, there exists a body of work indicating that mental imagery may involve the motor cortex and that inhibition of execution may occur further downstream from the cortex. Note, however, that the strict anatomical link between the primary motor cortex and the premotor areas, massively activated during motor imagery, does not allow one to conclude that the primary motor cortex play a real role in motor imagery.

Our finding that disruption of the motor areas induces a covert SA is strong evidence in support of the notion that the motor system, and namely, the ventral premotor areas caudal to Broca's area, is involved in covert speech together with the posterior IFG cortex. These data converge with those from motor imagery research to strongly suggest that covert speech may be a form of motor imagery of overt speech. Thus, disruption of motor imagery performance may disrupt covert speech performance. The fact that we do not find a covert SA when we stimulate the right hemisphere motor areas indicates that the motor areas of the left hemisphere evolutionarily acquired specific language-related properties besides simply controlling orofacial muscles, whose control over is also present in the right hemisphere.

Clearly, covert speech would involve not only motor imagery, but also auditory imagery. There is recent evidence for neurons in a monkey premotor area (F5) which are sensitive to visual, motor, and auditory components of the same action (Keysers et al., 2003; Kohler et al., 2002). In the human brain, this area is thought to be homologous to Brodmann's area 44, a component of Broca's area (Geyer, Matelli, Luppino, & Zilles, 2000; Petrides & Pandya, 1994; Von Bonin & Bailey, 1947), and with its multimodal processing of actions (in this case speech), it may serve as a good candidate for processing imagery involved in covert speech. Recent TMS evidence indicating a left hemisphere specialization for this multimodal system in humans further supports this claim (Aziz-Zadeh, Iacoboni, Zaidel, Wilson, & Mazziotta, 2004).

Covert speech is canonically considered to be analogous with Baddeley's (2003) "phonological loop" for working memory. The need for participants to covertly repeat a briefly presented word in our task would indeed involve the phonological component of working memory. Thus, another angle from which to consider the present findings is in relation to verbal working memory. An fMRI study on the phonological loop found Broca's area (BA 44) to be crucial for subvocal rehearsal

(Paulesu, Frith, & Frackowiak, 1993), as did an rTMS study investigating the role of the pars opercularis on phonological working memory (Nixon, Lazarova, Hodi-nott-Hill, Gough, & Passingham, 2004). Activations were furthermore found in areas commonly attributed to motor speech planning and execution (Paulesu et al., 1993). The convergence of data from previous studies together with data from the current study strongly suggests that Broca's area and motor areas are essential for phonological memory.

METHODS

Participants

Six healthy volunteers (3 women, 3 men, aged 19–23) participated in Experiment 1, and 12 healthy volunteers (8 women, 4 men, aged 19–30) participated in Experiment 2. All participants were native Italian speakers and strongly right-handed according to a modified Oldfield Handedness Questionnaire (Oldfield, 1971). The participants were screened for neurological, psychiatric, and other medical problems, and contraindications to TMS (Wassermann, 1998), and they all signed consent forms approved by the Ethics Committee of the Medical Faculty of the University of Parma. An additional group of seven participants were recruited but not included in the analysis due to: (a) experiencing too much pain and/or displaying short latency responses in the *mentalis* muscle (<8 msec), compatible with direct facial nerve stimulation (5 participants); (b) inability to complete the cognitive task with substantial accuracy (1 subject); or (c) technological recording errors (1 subject).

Transcranial Magnetic Stimulation

In Experiment 1, our aim was to stimulate the left anterior (nonmotor SA) site, the left posterior (motor SA) site, and the corresponding right anterior (control) site. In Experiment 2, our aim was to stimulate the right posterior site (motor representation of the *mentalis* muscle), the right hemisphere site symmetrical to the left hemisphere anterior site (right hemisphere control), and, as a further control, a left hemisphere anteromedial site (left hemisphere control).

Participants were preliminarily tested to localize the optimal stimulation sites (hot spots) on the scalp over the left (or right, for Experiment 2) hemisphere of the *opponens pollicis* (OP) and *mentalis* (M) muscles and their respective MT. In both experiments, recordings were made from muscles on the contralateral side to the stimulated site. Participants were also preliminarily tested to localize the spot and optimal intensity of the nonmotor (anterior) SA, as described below. The right hemisphere anterior site was determined as the site symmetric to the left hemisphere anterior site in the right hemisphere, based on measurements from the

vertex. Finally, the left hemisphere control site in Experiment 2 corresponded to F1 of the 10–20 international EEG electrode placement system.

Recordings from muscles were made with surface Ag/AgCl electrodes and a velcro ground electrode placed on the right (or left) arm. We used a Magstim Rapid stimulator (the Magstim Company, Whitland, UK), powered by two booster modules and connected to a figure-of-eight coil, 7 cm in diameter.

Single biphasic TMS pulses were delivered on the scalp over the left (or right) hemisphere, moving on a grid of approximately 1 by 1 cm in order to find the hot spot for eliciting MEPs in the OP muscle (i.e., the spot where the MEPs with larger amplitude were evoked with the minimum stimulation intensity). The coil handle formed a 45° angle with the midline, pointing laterally and caudally. MEPs were collected with hand muscles at rest (amplification: ×1000; sampling rate of 4000 Hz/channel, band pass: 5–5000 Hz). Participants were provided with visual feedback of EMG activity. The resting MT was defined as the minimal intensity that induced MEPs greater than 50µV peak-to-peak amplitude in 5 out of 10 trials. This site was used as an anatomical marker for locating further sites of interest and its MT was used as a reference for adjusting stimulation to subsequent sites.

From the OP muscle hotspot, the coil was moved laterally to find the optimal scalp site for evoking MEPs in the M muscle contralateral to the stimulated side at latencies compatible with a cortical origin of the MEP. Motor responses in the lower facial muscles are generally considered to originate from activation of the cortico-bulbar tract when their onset latency is comprised between 10 and 14 msec (Facchini et al. 2002; Meyer et al., 1994; Cocito et al., 1993; Cruccu et al., 1990; Benecke et al., 1988). We discarded participants who displayed muscle responses at short latencies (<8 msec) at stimulation intensities below threshold for excitation of the face-associated motor cortex. Such motor responses likely represent volume-conducted compounded motor action potentials (c-MAPs) from direct activation of the facial nerve ipsilateral to the stimulated side. In all participants, a slight voluntary preactivation of the muscle was required to induce stable MEPs. The resting MT for this spot was also assessed as with the OP muscle hot spot and all subsequent stimulation was conducted above this MT.

On the M muscle hot spot, we subsequently looked for the optimal stimulation intensity capable of evoking a motor SA, with short trains of 10 magnetic pulses at a frequency of 5 Hz. This was done by having participants count aloud from 1 to 10 during stimulation and looking for an SA.

Subsequently, we moved anteriorly from the motor SA spot by 1 cm steps and looked for the optimal point and intensity of stimulation capable of evoking a nonmotor SA, under constant monitoring of the EMG activity

recorded from the M muscle. Once more, participants were asked to count from 1 to 10 during stimulation while observing for an SA. Stimulation intensity was increased until an SA was evoked or until the subject reported pain from the stimulation. In three participants from each experiment, we also recorded from the *mylohyoid* muscle, with surface Ag/AgCl electrodes placed under the subject's chin. This was performed in consideration that a motor SA might be evoked not only by activation of the M muscle, but also of muscles associated with the tongue. Thus, the *mylohyoid* muscle was used as a further measure that stimulation of the anterior site was not due to activation of either mouth or tongue muscles, but was in fact non-motoric in origin.

The coil was positioned on the hot spot for the M muscle with the handle directed horizontally, pointing posteriorly. This seemed to be the preferential coil position for evoking MEPs from the M muscle without facial nerve activation (Dubach, Guggisberg, Rosler, Hess, & Mathis, 2004) in most subjects. For stimulation of the nonmotor spot, the coil position was horizontal, with the handle pointing anteriorly, because this was, in most participants, the position that minimized discomfort from rTMS. For the left hemisphere control site in Experiment 2, the coil handle was directed posteriorly.

Experimental Setting

Participants were sitting comfortably in a dimly lit room, in front of a computer screen. Visual stimuli were presented in blocks of 25 words. Participants were first given two practice sessions, one where they performed the task covertly and the second overtly. At the beginning of the experimental sessions, baseline blocks were run, again once while the participant performed the task overtly and once covertly. This was followed by experimental blocks of the same length during which rTMS was applied to different points on the scalp. In Experiment 1, there were a total of six counterbalanced blocks of 25 visual stimuli, in each of which one of three different scalp sites was stimulated and one of two different tasks (overt or covert speech) was completed. This accounted for the following conditions: (1) left anterior site—covert speech; (2) left posterior site—covert speech; (3) right anterior site—covert speech; (4) left anterior site—overt speech; (5) left posterior site—overt speech; (6) right anterior site—overt speech. In Experiment 2, there were a total of four (or six) counterbalanced stimulation blocks: (1) right anterior site—covert speech; (2) right posterior site—covert speech; (3) right anterior site—overt speech; (4) right posterior site—overt speech [in 6/12 participants also: (5) left control site—overt speech; (6) left control site—covert speech].

rTMS during the visual stimulus presentation consisted of a train of 12 pulses at 5 Hz, at the same

intensity for all stimulation sites. The intensity was equal to the minimum intensity needed to obtain an SA in the preliminary testing. The train was delivered starting 200 msec prior to stimulus presentation.

Task

Equal numbers of three-, four-, and five-syllable words were pseudorandomly presented (stimulus duration = 500 msec) on a computer screen. Words were chosen in order to avoid a possible visual recognition of the number of syllables; the number of syllables could not be directly inferred from the number of letters in the word. Furthermore, only nouns and adjectives were used as stimuli. Verbs and emotional words were avoided (see Appendix). A fixation point preceded each trial as a ready signal. Participants were required to determine the number of syllables for each word, and to manually respond as quickly and as accurately as possible by pressing one of three keys on a response box. Responses were made with the hand ipsilateral to the stimulated side in order to minimize any effects stimulation may have on manual responses. Baseline measures without TMS stimulation revealed that reaction times are not significantly different for the left versus the right hand in this task and thus the effects observed are not related to response hand laterality (on average, the right hand was about 100 msec slower than the left hand, although this difference was not significant).

In half of the blocks the participant was required to perform the syllable counting task covertly and in the other half they were asked to perform it speaking aloud. The participant was furthermore not permitted to use finger movements of either hand as a counting aid. At the end of testing, a questionnaire was given to the participants asking them the type of strategy they used to complete the task, the amount of pain felt at each location site, and their SA experience at each site.

Data Analysis

As participants performed highly accurately (95% accuracy on average), reaction time latencies for correct trials were used as the dependent variable. In the design used in this study, every experimental trial was accompanied by TMS stimulation. Given discomfort and arousal levels of stimulating anterior frontal sites, comparisons are best made between two different TMS sites with similar discomfort and arousal levels rather than to a non-TMS condition. Therefore, the reported effects are taken from a comparison between two different stimulation sites and absolute latency measures were used rather than percentage changes from a non-TMS baseline.

Mean reaction times for each syllable group (3, 4, 5) during each stimulation site and speech type were calculated for each subject. A three-way analysis of

variance (ANOVA) [speech type (covert, overt), stimulation site (Experiment 1: anterior left, posterior left, anterior right; Experiment 2: anterior right, posterior right, or anterior right, posterior right, left hemisphere control), number of syllables (3, 4, 5)] was conducted. For Experiment 2, two ANOVAs were conducted, the first including the anterior right and posterior right sites in 12 participants, and the second including the anterior right, posterior right, and left hemisphere control site in 6 subjects. To test our specific predictions (e.g., longer latencies during stimulation of the left anterior site as compared with the right anterior site), mean comparisons were performed.

APPENDIX

3 Syllables

BABBUCCIA	FRAMMENTO	QUINQUENNIO
BANCHIERE	GHIOTTONE	RACCHETTA
BARCHETTA	GHIRLANDA	RANOCCHIO
BICCHIERE	GIACCHETTA	RICCHEZZA
CAPOCCHIE	GIANCHETTI	RINTOCCHI
CAVICCHIO	GINOCCHIO	SCACCHIERA
CENTINAIA	GIUBBOTTO	SCHELETRO
CESPUGLIO	GIUSTIZIA	SCHERZETTO
CHIACCHIERE	GROSSEZZA	SCHIAMAZZO
CHIAREZZA	GUANCIALE	SCHIODATO
CHIOCCIOLA	IMBROGLIO	SCREANZATO
CIAMBELLA	LUNGHEZZA	SCRICCIOLO
CINQUANTA	MACCHIATA	SCROCCONE
CIUFFETTI	MANDRIANO	SECCHIELLO
COCCHIERE	MARMAGLIA	SELVAGGIO
COLLOQUIO	MERCANZIE	SGUATTERO
COMMERCIO	MESSAGGIO	SINGHIOZZI
COMPAGNIA	MOTTEGGIO	SLOVACCHIA
COMPENDIO	PARROCCHIA	SMARGIASSO
COMPRESSE	PASSAGGIO	SMERIGLIO
CONGIUNTO	PERVINCHE	SOGGHIGNO
CONSIGLIO	PIATTELLO	SOGGIORNO
COSCIENZA	PIAZZISTA	SPAGHETTI
CRISTIANO	PIUMAGGIO	SPALLIERA
DESCRITTO	PREGHIERA	SPAREGGIO
FINOCCHIO	PRINCIPIO	SPECCHIERA
FORCHETTA	QUARTIERE	SPERGIURO
FORMAGGIO	QUATTROCCHI	SPRANGHETTA

SPROLOQUIO	STRASBURGO	TESCHIETTO
SQUILIBRIO	STRASCICHI	TRANSFUGA
STORNELLO	STRATTONI	VANTAGGIO
STRANIERO	STRETTEZZA	VENTAGLIO
STRAPAZZO	TEPPAGLIA	
STRAPIOMBO	TERRAGLIA	

4 Syllables

ACCOGLIENZA	DESCRIZIONE	OTTANTENNE
AMBIZIONE	DISCREZIONE	OTTIMISTA
AMMUCCHIATA	DISTINZIONE	PAGAMENTO
ARGENTINA	DOLCISSIMO	PELEGRINO
ASTERISCO	ESPANSIONE	PERSONALE
ASTEROIDE	FIGLIOLANZA	PERSUASIONE
AUTOCARRO	GABINETTO	PESTILENTE
AVVENTORE	GIAVELLOTTO	PIEDESTALLO
BABILONIA	GIOIELLIERE	PIROSCAFO
BELLISSIMO	GIORNALIERA	POLIGAMIA
BIBLIOTECHE	GIORNALIERO	POSIZIONE
BIMESTRALE	GIORNALISMO	POSSESSIONE
BOMBONIERA	GOBBETTINO	PRIMAVERA
BOTTEGAIO	GRANDISSIMA	PROVINCIALI
BOTTICELLA	IMPORTANTE	QUATTORDICI
BURATTINO	IMPRESARIO	RAMOSCELLO
BUSSOLOTTO	IMPROPERIO	REGRESSIONE
CACCIATORE	IMPRUDENZA	RESTRIZIONE
CANCELLIERE	INCOMBENZA	RETROMARCIA
CANZONACCIA	INDULGENZA	RIBELLIONE
CAPPELLETTI	LUCERTOLA	RITORNELLO
CATTIVERIA	LUCIGNOLO	SCIAGURATO
CHERUBINO	LUNGOLAGO	SCULACCIONE
CINQUECENTO	LUNGOMARE	SFACCHINATA
CIRCONCISO	MALCONTENTI	SITUAZIONE
CONCESSIONE	MAMMIFERO	SOPRABITO
CONCORRENTE	MANOMETRO	SPAVENTATO
CONCUSSIONE	MELAGRANA	TRAVESTITO
CONFUSIONE	MELANZANA	ULTRASUONO
CONOSCENZA	MENINGITE	VANDALISMO
CONTADINO	MOSCHICIDA	VENTISETTE
CONTRAZIONE	OGNISSANTI	VERTEBRALE
CORRISPOSTA	OLTRETOMBA	VETRINISTA
CROCEFISSO	OMBRELLONE	

ABBANDONATO	IMPUDICIZIA	MUCILLAGINE
ABITUDINE	IMPUNEMENTE	MUNIFICENZA
ABORIGENO	IMPUTAZIONE	MUSICOMANE
ACCAVALLATA	INAMIDATE	NAPOLETANO
ACCIDENTALE	INCANTESIMO	NUMERAZIONE
ADDIRITTURA	INCOLUMITA'	NUMISMATICA
AFFATICATO	INDOVINELLO	OPERATORE
AFFERMATIVO	INESTETISMO	OPERAZIONE
AGEVOLATO	INOPINATA	ORINATOIO
AGITAZIONE	INSENATURA	OSPEDALIERO
ALIMENTATO	INSERIMENTO	OSSIDAZIONE
ALLONTANATO	INTEGRATORE	OZONOSFERA
ALTERAZIONE	INTENDITORE	POLICLINICO
AMERICANO	INUMAZIONE	POLINESIANO
AMMIRAZIONE	INVALIDITA'	POLITICANTE
AMOREVOLE	IPERMERCATO	RADIOFONICO
ANTECEDENTE	IPTENUSA	RAPINATORE
ANTONOMASIA	IPPOPOTAMO	RECITAZIONE
ARCIVESCOVO	IRRIGAZIONE	REGOLAMENTO
BIOCHIMICA	IRRITAZIONE	REGOLARITA'
CICLOMOTORE	ISOLAMENTO	REGOLATEZZA
DENOMINAVI	ITINERARIO	REGOLATORE
DIMENTICATO	LACERAZIONE	REPUTAZIONE
ECONOMICA	LAVORATORE	RESPIRATORE
EDIFICATO	LEGISLATURA	RICATTATORE
EPIDEMICA	LOCOMOTORE	RINVIGORITO
ESAGERATO	LOGORAMENTO	RIPARAZIONE
ESORBITANTE	MATERASSINO	TELECOMANDO
FEDELISSIMO	MATERIALONE	UMANESIMO
GOVERNATORE	MENOMAZIONE	VENERABILE
GUARNIGIONE	MISERABILE	

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