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(Article begins on next page)

All Talk and No Action: A Transcranial Magnetic Stimulation Study of Motor Cortex Activation during Action Word Production

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Abstract

■ A number of researchers have proposed that the premotor and motor areas are critical for the representation of words that refer to actions, but not objects. Recent evidence against this hypothesis indicates that the left premotor cortex is more sensitive to grammatical differences than to conceptual differences between words. However, it may still be the case that other anterior motor regions are engaged in processing a word's sensorimotor features. In the present study, we used single- and paired-pulse transcranial magnetic stimulation to

test the hypothesis that left primary motor cortex is activated during the retrieval of words (nouns and verbs) associated with specific actions. We found that activation in the motor cortex increased for action words compared with non-action words, but was not sensitive to the grammatical category of the word being produced. These results complement previous findings and support the notion that producing a word activates some brain regions relevant to the sensorimotor properties associated with that word regardless of its grammatical category. ■

INTRODUCTION

Among the basic desiderata of a theory of the neurobiology of language is an understanding of how individual words are represented in the brain. Intuitively, the neural specification of a word must include at least a sequence of speech sounds—the linguistic sign—and the concept with which it is associated (Bally & Sechehaye, 1922). In fact, research with both normal speakers and brain-damaged subjects has shown that lexical representations have a rich internal structure, with components that code for knowledge about a word's semantic category, grammatical features, and syllabic organization (see, e.g., Caramazza, 1997; Dell, 1986).

The cortical network activated by a particular word may also comprise regions encoding information that is not purely linguistic or conceptual in nature. A number of researchers, inspired by associationist theories of learning (Hebb, 1949), have proposed that a word's neural substrate includes circuits that represent sensorimotor properties linked to the concept it signifies. Thus, the retrieval of words associated with motor schemata, like *throwing*, is thought to rely in part on areas of the

brain involved in motor planning, such as the left frontoparietal cortex; an ensemble of neurons linking this area to “core” language areas encodes the word–action contingency. Likewise, networks representing object names are thought to have components in sensory (primarily visual) association areas in the left hemisphere (Pulvermüller, Lutzenberger, & Preissl, 1999).

Is There Evidence for the Sensorimotor Account?

Experimental support for this view is thought to come from neuropsychological (Bak, O'Donovan, Xuereb, Boniface, & Hodges, 2001; Daniele, Giustolisi, Silveri, Colosimo, & Gainotti, 1994; Damasio & Tranel, 1993), neuroimaging (Martin, Wiggs, Ungerleider, & Haxby, 1996; Warburton et al., 1996; Perani et al., 1999), and electrophysiological (Pulvermüller, Harle, & Hummel, 2000, 2001) studies that have documented functional and anatomical dissociations in the processing of nouns and verbs. In general, these studies have shown that verbs are subserved by left anterior (frontal and frontoparietal) cortical regions, while nouns are subserved by more posterior (temporal) regions, a pattern that is at least theoretically consistent with the sensorimotor model. The key assumption here is that nouns prototypically refer to concrete objects with many sensory features, and that verbs prototypically refer to actions.

However, it is unclear whether these observed dissociations actually reveal the differential impairment or

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activation of sensory and motor features. Most neuropsychological and neuroimaging studies that purport to address this issue have not explicitly distinguished between nouns and verbs on the one hand, and actions and objects on the other. For example, Bak et al. (2001) reported that patients with motor neuron disease (associated with pathological changes in the motor and premotor cortex, as well as Brodmann's areas 44 and 45) presented with particular difficulties in action verb production, acknowledging that this pattern could be interpreted either as a grammatical or a conceptual deficit. This confound has rendered it difficult to determine whether the brain areas isolated in these studies represent systems involved in encoding grammatical knowledge or knowledge about various aspects of word meaning (Caramazza & Shapiro, in press; Shapiro & Caramazza, 2003a).

While it is possible that some studies support the sensorimotor account, in at least a few cases, it has been shown that noun/verb dissociations involving putative sensorimotor regions, such as left prefrontal/premotor cortex, arise because of problems in accessing grammatical knowledge associated with the two word classes. Such dissociations persist even when subjects are asked to produce pseudowords, with no obvious sensorimotor associations, as nouns or verbs (Shapiro, Shelton, & Caramazza, 2000; Shapiro, Pascual-Leone, Mottaghy, Gangitano, & Caramazza, 2001; Shapiro & Caramazza, 2003b). This suggests that grammatical knowledge about nouns and verbs may reside in neural circuits adjacent to or interleaved with sensorimotor association areas (Caramazza, 1994).

The electrophysiological literature provides evidence for a distinction between neural systems underlying different kinds of knowledge about lexical items. A number of studies have provided evidence for topographically or functionally distinct electrocortical responses to concrete nouns and action verbs (Pulvermüller et al., 2000, 2001; Koenig & Lehmann, 1996), consistent with the sensorimotor account,¹ while other studies have suggested that grammatical context effects contribute to distinctions between nouns and verbs (Federmeier, Segal, Lombrozo, & Kutas, 2000). When grammatical and visual or motor properties of stimulus words have been manipulated parametrically, it has been shown that these factors are associated with different electrophysiological correlates (Kellenbach, Wijers, Hovius, Mulder, & Mulder, 2002).

In light of these results, it seems worth revisiting the question of whether lexical processing engages parts of the cortex that are functionally relevant to the sensory/motor properties of the word being produced. We used transcranial magnetic stimulation (TMS) to test the hypothesis that left primary motor cortex is maximally activated during the retrieval of words associated with specific actions, including verbs (e.g., *to throw*) as well as nouns referring to manipulable objects (e.g., *the key*).

By the same token, this region should be less activated during the retrieval of verbs referring to relations (*to belong*) or to psychological states (*to aspire*), or nouns that are nonmanipulable or not typically related to actions (*the cloud*).

A crucial advantage of TMS is that it allows for both measurement and modulation of neural activity in motor cortex. Applied in single pulses, TMS can be used to obtain direct measurements of corticospinal excitability, reflected in the size of motor-evoked potentials (MEPs) recorded from peripheral muscles. Yet changes in resting MEPs measured with single-pulse TMS are difficult to interpret and could be due to alterations at synapses within the spinal cord rather than in motor cortical areas (Di Lazzaro et al., 2001).

This limitation can be overcome with the use of paired-pulse TMS. In paired-pulse TMS, a conditioning stimulus (CS) below the threshold intensity needed to elicit an MEP is followed at short interstimulus intervals (ISIs) by a suprathreshold test stimulus (TS). At ISIs of 1–5 msec, the CS results in MEP inhibition, while longer ISIs of 7–20 msec produce MEP facilitation. This modulation of MEP size takes place at the cortical level and is thought to reflect the activation of separate populations of inhibitory and excitatory cortical interneurons without affecting spinal circuits (Kujirai et al., 1993). Therefore, paired-pulse TMS provides a reliable index of motor cortical activation.

RESULTS

We applied single- and paired-pulse TMS to the left motor cortex while subjects produced words in a simple transformation task. The MEPs elicited on trials with action verbs and action-related nouns were compared with those elicited during processing of nouns and verbs without specific motor associations. If action-related words elicit greater activation of motor cortex than non-action-related words, paired-pulse TMS applied on action-related trials should produce increased intracortical motor facilitation (at long ISIs), reduced intracortical inhibition (at short ISIs), or both. We would not necessarily expect to find differences on these trials using single-pulse TMS.

We found a significant main effect of TMS condition, $F(2,14) = 13.1$, $p < .001$, indicating that MEP amplitude was clearly modulated by the type of TMS used in a given trial. Paired-pulse TMS with an ISI of 1 msec significantly reduced MEP area compared with both single- ($p < .05$) and paired-pulse TMS with an ISI of 10 msec ($p < .001$). Conversely, paired-pulse TMS at the longer ISI increased MEP area compared with single-pulse stimulation ($p < .05$).

The main effect of grammatical category (noun or verb) was not significant, $F(1,7) = 2.7$, *ns*. This suggests that motor cortex activation did not vary with the grammatical class of the word to be produced. On the other

hand, we found a robust effect of sensorimotor type [action- or non-action-related, $F(1,7) = 5.9, p < .05$] that was independent of grammatical category [interaction: $F(1,7) = 0.05, ns$], demonstrating that action-related nouns and action verbs elicited greater activation in primary motor cortex than did non-action-related words (Table 1).

The latter effect of sensorimotor type was related to the TMS condition [interaction: $F(2,14) = 3.5; p = .05$]. Post hoc comparisons revealed that processing of action-related words induced a greater facilitation of MEPs at the ISI of 10 msec as compared with non-action-related words ($p < .01$). This effect was present in seven out of eight subjects for both noun and verb stimuli. No significant differences between the two sensorimotor classes were observed following single-pulse TMS or paired TMS with 1-msec ISI (Figure 1). This finding suggests that the increased cortical activity observed during the production of action-related words might specifically reflect the increased facilitation of motor cortical interneurons.

DISCUSSION

Our results demonstrate that the excitability of the hand area of the motor cortex is modulated by spoken words with sensorimotor associations, even when the task in

Table 1. Lexical Stimuli Used in the Experiment

| <i>Action Verbs</i> | <i>Action Nouns</i> | <i>Non-action Verbs</i> | <i>Non-action Nouns</i> |
|---------------------|---------------------|-------------------------|-------------------------|
| To bite | The axe | To adore | The cage |
| To climb | The ball | To aspire | The carpet |
| To dig | The cup | To belong | The cloud |
| To fold | The fork | To crave | The column |
| To kick | The gun | To deem | The diamond |
| To pour | The key | To detest | The dome |
| To sculpt | The keyboard | To hate | The hill |
| To swim | The ladder | To ignore | The kidney |
| To throw | The pencil | To loathe | The pearl |
| To weave | The racket | To mourn | The planet |
| To fondle | The razor | To prefer | The rainbow |
| To polish | The shovel | To regret | The star |
| To pummel | The spear | To wish | The tomb |
| To ride | The sword | To yearn | The town |
| To rub | The napkin | To retain | The triangle |
| To strangle | The pen | To revere | The attic |
| To tweak | The rake | To owe | The cone |
| To wipe | The rifle | To admire | The cube |

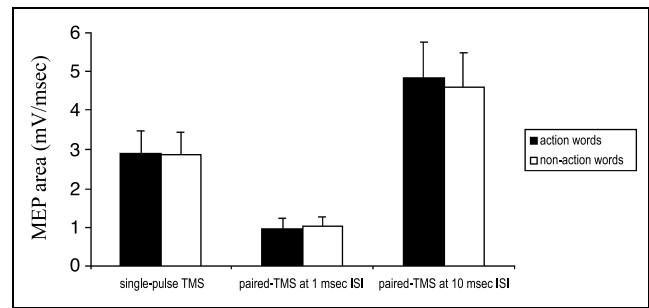


Figure 1. Mean MEP area (mV/msec) as a function of the three TMS conditions (single-pulse TMS, paired-pulse TMS at 1-msec ISI, and paired-pulse TMS at 10-msec ISI) for the two sensorimotor classes (action- vs. non-action-related words). The only significant difference between action and non-action words emerged during paired-pulse TMS at 10-msec ISI.

which the words are produced does not require subjects to access this type of knowledge. Specifically, we found that processing of action-related words (both nouns and verbs) induces greater activation of the left motor cortex² than does processing of words that are not associated with actions. At the same time, motor cortex activation does not vary as a function of the grammatical category of the word being produced.³

A few previous studies with TMS have shown increased activation in motor cortical areas not directly engaged in speech production in tasks that involved reading aloud (Meister et al., 2003; Seyal et al., 1999; Tokimura, Oliviero, Asakura, & Rothwell, 1996). This finding has been interpreted in various ways; for example, Tokimura et al. (1996) conjectured that it was the result of a nonspecific spreading of cortical activation from areas involved in language production to motor areas controlling peripheral muscles, whereas Meister et al. (2003) argued for a specific functional connection between language areas and the hand area of the motor cortex. Our results suggest that this observation might be attributable at least in part to activation elicited during the processing of action-related words.

More generally, these findings shed light on the neural correlates of word knowledge, showing that the retrieval of words associated with motor schemata activates motor processing areas. In line with this view, a few studies using positron emission tomography have shown activation of left premotor areas (primarily in the left posterior frontal cortex) during silent naming of tools (Grafton, Fadiga, Arbib, & Rizzolatti, 1997; Martin et al., 1996). However, these studies did not distinguish frontal areas involved in tool naming from those involved in naming other objects.

A much larger literature has implicated the left prefrontal cortex in processing action verbs relative to concrete nouns. The evidence on this score comes from studies with positron emission tomography (Warburton et al., 1996; Wise et al., 1991), event-related potential (Pulvermüller et al., 1999, 2000, 2001), and a number of

reports of brain-damaged subjects (Hillis, Tuffiash, & Caramazza, 2002; Hillis, Wityk, Barker, & Caramazza, 2003; Bak et al., 2001; Daniele et al., 1994; Damasio & Tranel, 1993; McCarthy & Warrington, 1985; Miceli, Silveri, Villa, & Caramazza, 1984; Luria & Tsvetkova, 1967). As mentioned in the Introduction, it is unclear whether these differences emerged because the nouns and verbs used in the various studies differed in meaning and/or sensorimotor associations or because they differed in grammatical role.

It has previously been shown that repetitive TMS applied to the left prefrontal cortex selectively disrupts morphological processing of real verbs and pseudowords used as verbs compared with nouns and pseudowords used as nouns (Shapiro et al., 2001). These data suggest that the left prefrontal region is involved in representing grammatical rather than sensorimotor knowledge about verbs, although it is possible that grammatical knowledge comes to be localized in this area because of the strong association between verbs and action words during development (Caramazza, 1994).

By contrast, the left motor cortex seems to be recruited in processing words related to actions regardless of whether those words are nouns or verbs. The results of this study and the earlier study by Shapiro et al. (2001) are complementary, demonstrating that different aspects of knowledge about words (such as grammatical category and conceptual/semantic features) are associated with neural systems that appear to be functionally and topographically distinct. It follows that these systems may be impaired or spared differentially following brain damage, potentially leading to a diverse array of deficits in language production.

What Kinds of Representations in Motor Cortex Are Associated with Action Word Production?

What is particularly striking about the results of the present study is that subjects were not in any way instructed to consider the meanings of the words they were producing. In fact, the task was designed to minimize activation of this kind of knowledge. Why, then, are hand motor regions excited selectively when words related to actions are produced?

One possibility is that motor schemata associated with a given word are embedded within its cortical representation, and are activated automatically whenever that word is retrieved (Pulvermüller et al., 1999). Motor schemata would thus constitute an integral part of semantic knowledge of the word. This hypothesis might lead us to predict that the effects induced by TMS during action word production should be lateralized to the left hemisphere (but see Neininger & Pulvermüller, 2003, for evidence that right hemisphere damage may lead to difficulties in action word production).

On the other hand, it is possible that word production sometimes leads to the corollary generation of mental

images related to the concept being retrieved. It might then be the case that the increased amplitude of the motor response is related to these (epiphenomenal) “motor images,” rather than to the semantics of the word as such. In other words, the motor cortex activation that we observed might not strictly be necessary for action word production (for a related argument about the relation between sensorimotor representations and object concepts, see Mahon & Caramazza, in press). On a straightforward reading, this hypothesis predicts bilateral effects of TMS, although a bias toward increased facilitation of the left motor cortex might be explained by the fact that dextral subjects are by definition more likely to use their right hands to perform actions associated with words used in the task.

In either case, our results support the notion that word retrieval activates a distributed network of cortical regions with components at various levels of meaning, sound structure, and grammatical function. At least some of these components are common to words of different grammatical classes and appear to be involved in encoding contingencies between words and actions.

METHODS

Subjects

Eight native speakers of English (5 women and 3 men), aged 20–26 years (mean = 22.3), participated in the experiment. All were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971), and all but one were naive to TMS before taking part in this study. None of the participants had any history of neurological or psychiatric illness. Written informed consent was obtained from all subjects prior to their participation.

Lexical stimuli

The lexical stimuli used in this experiment consisted of 72 words divided equally among action verbs, action-related nouns, non-action verbs, and non-action-related nouns (Table 2).

In selecting verb stimuli, we took advantage of a solid linguistic tradition that provides effective criteria for distinguishing action verbs from so-called state verbs, including psychological verbs (Smith, 1997; Bache, 1995; Bertinetto, 1986; Dowty, 1979; Kenny, 1979; Taylor, 1977; Verkuyl, 1993; Vendler, 1957). The selection of nouns was somewhat more arbitrary. The action-related nouns used in this experiment are all names of objects that are associated with specific motor programs, are discrete and separable from the surrounding environment, and are easy to manipulate and firm to the touch (e.g., *key*, *razor*). Non-action-related nouns name objects that are difficult or impossible to grasp or manipulate or objects that are graspable but not typically involved in voluntary human actions (e.g., *cloud*, *kidney*). This classification partially mirrors Gardner’s

Table 2. Mean (SD) MEP Area (mV/msec) in the Various Experimental Conditions

| <i>TMS Condition</i> | <i>Lexical Stimuli</i> | | | |
|---------------------------|------------------------|-------------------------|---------------------|-------------------------|
| | <i>Action Nouns</i> | <i>Non-action Nouns</i> | <i>Action Verbs</i> | <i>Non-action Verbs</i> |
| Single-pulse TMS | 2.50 (2.50) | 2.48 (2.34) | 3.29 (2.15) | 3.24 (2.21) |
| Paired TMS at 1-msec ISI | 0.93 (1.10) | 0.93 (1.05) | 1.01 (1.02) | 1.09 (1.03) |
| Paired TMS at 10-msec ISI | 4.68 (3.78) | 4.45 (3.66) | 5.00 (3.91) | 4.76 (3.66) |

(1973) distinction between operative and figurative items.

It is possible that some subjects associated specific actions with some of the nouns (or verbs) that we took not to be action related. If this were true, however, it would tend to minimize any measurable differences between the action- and non-action-related groups. In other words, it would work in favor of the null hypothesis, and against the alternative hypothesis that the two types of words are processed by distinct neural mechanisms.

Stimulus words were matched across sets for written length, number of syllables, frequency, and mean response latency (action verbs: 467 ± 67 msec; action nouns: 464 ± 70 msec; non-action verbs: 463 ± 75 msec; non-action nouns: 468 ± 75 msec). The latter measure was obtained in a pilot reading task performed by 10 native English speakers, none of whom took part in the TMS study reported below.

Transcranial Magnetic Stimulation

TMS was applied using two MagStim 200 magnetic stimulators, connected to a figure-of-eight coil (70 mm in diameter) through a BiStim module (MagStim, Whitland, UK). For each subject, we first identified the optimal scalp location for induction of MEPs in the right first dorsal interosseus muscle. The target site was marked on a tightly fitting Lycra cap worn by the subject, and the coil was maintained in that position for the duration of the experiment.

The coil was positioned tangentially to the scalp, pointing anteriorly, 45° from the midsagittal axis. This orientation was chosen based on the finding that the lowest motor threshold is achieved when the induced electric current in the brain is flowing approximately perpendicular to the line of the central sulcus (Brasil-Neto et al., 1992).

Single-pulse TMS was then applied at decreasing intensities to determine the subjects' motor threshold (Rossini et al., 1994), which was defined as the minimum TMS intensity necessary to induce MEPs of greater than 50 mV peak-to-peak amplitude in more than 4 of 8 successive trials. An intertrial interval of at least 7 sec was chosen to avoid carry-over effects of consecutive stimuli. Stimulation began at suprathreshold intensity

and then decreased in steps of 2% of the stimulator output. Threshold was determined under complete muscle relaxation, which was monitored on an electromyogram for 50 msec prior to the application of TMS. The mean motor threshold for the eight subjects was $44.5 \pm 5.6\%$ of the maximum stimulator output.

Task

The task performed by subjects in the experiment was similar to the task described by Shapiro et al. (2001) and was conducted on a Macintosh computer (Apple Computers, Cupertino, CA) using Psyscope and a button box. At the beginning of each trial, subjects fixated on a crosshair at the center of the computer screen for 300 msec. The fixation crosshair was followed by a stimulus word, which was either a noun (e.g., "the key") or a verb (e.g., "to throw"). After 250 msec, the word was replaced by a symbolic cue indicating the morphological form in which the word was to be produced aloud. If the stimulus word was a noun, the cue consisted of one or three triangles indicating that the target should be produced in either the singular or plural form. If the stimulus was a verb, circle cues (○ or ○○○) instructed a subject to produce the target in the third-person singular or plural form. We used this task in part because it does not require subjects to attend to word meaning; in fact, a previous study has shown that processing of real words and pseudowords in this task is affected similarly by application of repetitive TMS to the prefrontal cortex (Shapiro et al., 2001).

Application of TMS was triggered through the button box 500 msec after the onset of each stimulus word (250 msec after the appearance of the symbolic cue). This time interval corresponds roughly to the mean vocal response latency in our pilot experiment and is also consistent with a previous electrophysiological study (Pulvermüller et al., 1999) that recorded event-related potentials in response to a lexical decision task approximately 500–800 msec after stimulus onset.

Four different TMS conditions were used in the experiment. Single-pulse TMS was applied in separate conditions at the intensity of the CS and TS. The two paired-pulse conditions consisted of a subthreshold CS followed by a suprathreshold TS after an ISI of either 1

or 10 msec. The shorter ISI of 1 msec is presumed, in accordance with the results of motor cortex paired-pulse TMS, to enhance intracortical inhibition, while the longer ISI of 10 msec is predicted to potentiate cortico-cortical facilitation (Kujirai et al., 1993). However, applied to other cortical regions the behavioral effects of such paired-pulse TMS might be different (Oliveri et al., 2000). CS intensity was set at 80% of each individual's resting motor threshold (mean = $41.1 \pm 6.4\%$ maximum output) while the TS intensity was set at 120% of motor threshold (mean = $48.5 \pm 12.5\%$).

MEPs induced by TMS were recorded from the right first dorsal interosseous muscle. Pairs of silver/silver chloride surface electrodes were placed over the muscle belly (active electrode) and over the associated joint or tendon of the muscle (reference electrode). A circular ground electrode with a diameter of 30 mm was placed on the dorsal surface of the right wrist. The MEPs were amplified and filtered using a Dantec Counterpoint electromyograph (Dantec, Skovlunde, Denmark) with a band pass of 20–2000 Hz. Signals were then digitized (digitization rate 5 kHz) through a CED 401 laboratory interface (Cambridge Electronic Design, Cambridge, UK) and fed to a personal computer for off-line analysis.

The full set of 72 words was presented twice in each of the four TMS conditions, such that every stimulus word appeared once with a singular cue and once with a plural cue in each condition. Stimulus words were blocked by grammatical category (nouns/verbs), but not by semantic type (action/non-action). The order of stimuli within a block was pseudorandom, with the constraints that no phonologically or semantically related words appeared consecutively, and no more than three consecutive trials involved words of the same semantic type or required the same morphological operation (producing the plural or singular form). Two practice trials were presented at the beginning of each block, but were not included in the final analysis.

The entire experiment thus consisted of 16 blocks with 38 trials per block. The order of the blocks was counterbalanced across subjects, with a 5-min rest period between the first and last eight blocks.

Data Analysis

We measured the area under the curve of the MEPs (mV/msec) for each trial (excluding those trials in which the subject responded incorrectly, self-corrected, or hesitated) and submitted averaged areas to a repeated measures analysis of variance (ANOVA), with grammatical category (nouns vs. verbs), semantic type (action vs. non-action), and TMS condition (single pulse at TS intensity vs. paired pulse at 1-msec ISI vs. paired pulse at 10-msec ISI) as within subjects factors. Because single-pulse stimulation at the intensity of the CS never induced MEPs, this condition was not included in the analysis. We made post hoc comparisons between single

factors using Duncan's test ($\alpha = .05$). Values outside the cut-off of 2.5 SDs above or below the mean of each block were excluded from the analysis. Discarded data constituted 6.7% of the total number of trials.

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Notes

1. However, as Federmeier et al. (2000) point out, the P200 response for verbs reported by Pulvermüller et al. (1999) was observed for non-action words as well as for action words.
2. Although we assume that the effects we observed were primarily due to stimulation of primary motor cortex, it is possible that TMS applied to this region induced a spread of cortical activation to more peripheral (premotor or prefrontal) areas; this might, in turn, have contributed to differences in processing action-related and non-action-related words. Even if this were true, we would still conclude that functionally distinct neural populations are activated by action- and non-action-related words. Moreover, the fact that we observed no grammatical differences in this study implies that these populations are different from (possibly adjacent) neural systems sensitive to the distinction between nouns and verbs (Shapiro et al., 2001).
3. Since nouns and verbs were administered in blocks, whereas action- and non-action-related words were randomized items, one could argue that the blocking procedure could lead to overall changes of excitability between nouns and verbs that might obscure real differences between these categories. Although this hypothesis cannot be excluded, our previous findings (Shapiro et al., 2001), showing a significant difference between the two grammatical classes using a similar blocking procedure, suggest that grammatical and semantic effects are related to the brain region rather than to the mode of stimulus presentation.

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