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The Origin of Word-related Motor Activity

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Conceptual processing of verbs consistently recruits the left posterior middle temporal gyrus (lpMTG). The left precentral motor cortex also responds to verbs, with higher activity for action than nonaction verbs. The early timing of this effect has suggested that motor features of words' meaning are accessed directly, bypassing access to conceptual representations in lpMTG. An alternative hypothesis is that the retrieval of conceptual representations in lpMTG is necessary to drive more specific, motor-related representations in the precentral gyrus. To test these hypotheses, we first showed that repetitive transcranial magnetic stimulation (rTMS) applied to the verb-preferring lpMTG site selectively impoverished the semantic processing of verbs. In a second experiment, rTMS perturbation of lpMTG, relative to no stimulation (no-rTMS), eliminated the action–nonaction verb distinction in motor activity, as indexed by motor-evoked potentials induced in peripheral muscles with single-pulse TMS over the left primary motor cortex. rTMS pertubation of an occipital control site, relative to no-rTMS, did not affect the action–nonaction verb distinction in motor activity, but the verb contrast did not differ reliably from the lpMTG effect. The results show that lpMTG carries core semantic information necessary to drive the activation of specific (motor) features in the precentral gyrus.

Keywords: brain stimulation, concepts, embodied cognition, functional connectivity, nouns and verbs

Introduction

Conceptual processing of verbs has been consistently associated with activity in the left posterior middle temporal gyrus (lpMTG) (Kable et al. 2005; Bedny et al. 2008; Willms et al. 2011; Peelen et al. 2012; Romagno et al. 2012; Watson et al. 2013). In particular, while the specific content of representations in lpMTG remains elusive, its activity appears sensitive to semantic distinctions between words (e.g., Grossman et al. 2002; Rodriguez-Ferreiro et al. 2011), including those that capture the difference between the content of verbs and nouns (e.g., relational structures vs. entities; see Bedny et al. 2008; Bedny and Caramazza 2011; Peelen et al. 2012).

Activity for verbs has also been observed in the left precentral gyrus. The left precentral gyrus shows a specific response profile, with higher responses to verbs denoting motor actions than to verbs denoting abstract relations (see Pulvermüller 2005; Binder and Desai 2011). Furthermore, for verbs denoting motor actions, this cortical effect overlaps with activity associated with actual motor performance (Hauk et al. 2004; but see Postle et al. 2008). Larger responses to action versus nonaction verbs have also been shown using transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) and recording motor-evoked potentials (MEPs) from peripheral muscles that respond to the stimulated area (e.g., Oliveri et al. 2004; Papeo et al. 2009). MEPs are a measure of corticospinal excitability, reflecting the level of activity in the motor cortex.

On one current hypothesis, individuals recognize and understand actions thanks to a neural mechanism that maps "directly" the percept onto the corresponding representation for motor production (Rizzolatti and Craighero 2004). In the same spirit, it has been assumed that information from the visual/acoustic representation of words directly activates the motor system, where the motor components of words' meaning are represented (Pulvermüller 2005). In support of this view, it is argued that verb-related precentral activity is too early (~250 ms after word onset) to be mediated by semantic processes, which have been associated with a 400-ms latency activity-peak originating in the posterior temporal cortex (Pulvermüller 2005). Thus, access to a motoric representation of verbs would be independent of (or parallel to) semantic-related processes in the posterior temporal cortex. Aside from this inference, which is based on the timing of precentral cortex effects, no other evidence rules out the alternative hypothesis that verb-related motor effects are driven by the conceptual processing of verbs in the network that encompasses lpMTG. The current study was designed to investigate the relationship between lpMTG and precentral activity in verb processing, specifically in the time window during which these regions might interact.

Using fMRI-guided TMS, we addressed the following question: What happens to verb-related motor effects if we interfere with verb processing in the semantic regions of the temporal cortex? We reasoned that if precentral motor cortex is sufficient on its own to compute the distinction between action and nonaction meanings directly from visually presented words, its response profile to verbs should remain unchanged whether or not verb processing in the temporal cortex is allowed to proceed unhindered. Alternatively, on the hypothesis that the temporal cortex is necessary for computing verb meanings, perturbation of its activity should not only impoverish participants' semantic analysis of verbs but should also disrupt verb-related motor effects. We recruited participants who had previously taken part to fMRI studies, at our facility, where verb-related activity in lpMTG was individually (and functionally) localized. In Experiment 1, using fMRI-guided repetitive TMS (rTMS) as a perturbation technique, we examined the consequences of disruption of "verb-preferring" lpMTG activity on semantic processing of verbs. We found that rTMS applied over lpMTG disproportionately interfered with semantic processing of verbs relative to nouns. Showing that the target lpMTG site is causally involved in verb processing is a prerequisite for the design of Experiment 2 where we investigated how disruption of verb processing in lpMTG affects

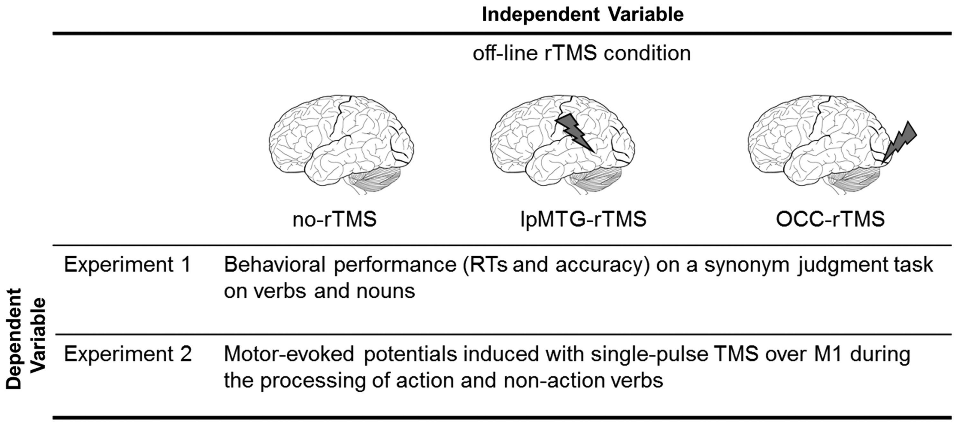

Figure 1. Design of Experiments 1 and 2. In Experiment 1, participants' performance in a semantic judgment task on verbs and nouns was measured in the no-rTMS condition, and after (i.e., in the refractory period of) rTMS delivery over lpMTG (experimental condition) and over OCC (control condition). In Experiment 2, motor activity (i.e., MEPs amplitude) for action and nonaction verbs was measured in the no-rTMS condition, and after (i.e., in the refractory period of) rTMS delivery over lpMTG (experimental condition) and over OCC (control condition).

verb-related motor activity. In this experiment, we applied rTMS over lpMTG and then measured motor activity (i.e., MEPs) by using single-pulse TMS over the left M1. We found that rTMS perturbation of lpMTG eliminated the distinction in motor activity that is typically associated with action versus nonaction verbs. Figure 1 shows a schematic of the experimental design of the study.

Experiment 1

Materials and Methods

Participants

Experiment 1 involved 14 right-handed (Oldfield 1971) native-Italian speakers (9 females, age range 19–35 years). All but 2 participants took part in previous fMRI research, at the Center for Mind/Brain Sciences (UNITN, Italy), where the individual verb-preferring site in lpMTG was individually defined by a localizer contrast between verbs versus nouns. In particular, for 8 participants, the verb-localizer task consisted of a simple memory task on verbs and nouns (50% related to concrete action-events and 50% related to states), matched for frequency and length (number of letters), and rated for imageability, age of acquisition and familiarity, included as regressors in the contrast analysis (for further details, see Peelen et al. 2012). For 4 participants, the verb-localizer task consisted of silent reading of verbs and nouns (50% with concrete meaning and 50% with abstract meaning), matched for frequency and length (number of letters) (see Papeo et al. 2012). Despite differences in task-demand and materials, both fMRI localizers yielded consistent verb-related effect in lpMTG. The peak Talairach coordinates of the participants in the fMRI study by Peelen et al. (2012) and by Papeo et al. (2012) are illustrated in Figure 2 (Peelen et al.: −57, −44, 4; Papeo et al.: −55, −43, 6). The remaining 2 participants had structural, but not functional MRI data available. For them, the target lpMTG site for stimulation was defined according to the group-average Talairach coordinates from Peelen et al. (2012). All 14 participants had normal or corrected-to-normal vision, and were clear of counter indications to TMS (Rossi et al. 2009). Before

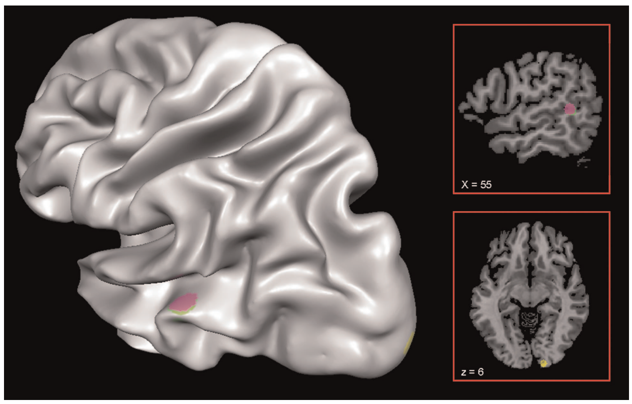

Figure 2. lpMTG and OCC sites for rTMS. Cortical targets of rTMS in the left posterior middle temporal cortex (lpMTG, overlapping pink and green dots) and in the left occipital control site (yellow dot). The green and the pink dots correspond to the group-average coordinates of lpMTG identified in Peelen et al. (2012) and in Papeo et al. (2012), respectively.

starting the experiment, participants gave informed consent. The study was approved by the ethics review board of the University of Trento.

Stimuli

The lists of stimuli used in the current TMS study are available as Supplementary Materials. These stimuli, consisting of word-pairs were selected as follows. We created 460 pairs of: 1) synonymous verbs with concrete meaning (i.e., hand-action verbs); 2) synonymous verbs with abstract meaning (i.e., cognitive or psychological-state verbs); 3) nonsynonymous verbs with concrete (hand action) meaning; 4) nonsynonymous verbs with abstract meaning; and 480 pairs of: 5) synonymous nouns with concrete meaning (i.e., physical entities perceivable through the senses); 6) synonymous nouns with abstract meaning (i.e., nouns that refer to things that are not material objects); 7) nonsynonymous nouns with concrete meaning; 8) nonsynonymous nouns with abstract meaning. We considered "synonyms" 2 words that can be interchanged in "many" contexts, without affecting the truth value of the statement (Miller 1999). For each pair, this relation was quantified by having 10 native Italian speakers rate the semantic distance between the 2 items on a 5-points Likert-scale (1 = different meanings; 5 = synonyms). In addition, with 10 new native Italian speakers, we collected the average reaction times to make synonym judgments (button press). RTs served as a measure of task difficulty that also reflects the contribution of word familiarity and frequency (Connine et al. 1990). For Experiments 1 and 2, we selected word pairs with ≥80% agreement on synonym/nonsynonym judgment; synonym pairs had a semantic distance of <2.5 points, and nonsynonym pairs had a semantic distance of >3.5 points. Decision times and word length were matched across all experimental conditions (*t*-tests, all *P*'s > 0.05).

Two lists of stimuli were created for Experiment 1 (List 1 and 2), each including 20 pairs of each of the 8 conditions listed above (i.e., 80 verb pairs, 80 noun pairs). Each pair appeared once in only one list, while each word could appear for a maximum of 3 times, each time paired with a different item. Verbs were in first-person singular form of the present tense (*io scrivo, I write*), and nouns were all singular forms, preceded by the appropriate article (*la gabbia, the cage*).

Procedures of Experiment 1

Experiment 1 aimed at assessing the effect of lpMTG perturbation on the semantic analysis of verbs. To test this effect, participants performed a synonym-judgment task on verbs (and nouns) after rTMS delivery over lpMTG. In addition, they performed the same task in 2 control conditions: A condition with no-rTMS and a control-site condition with rTMS over a left occipital site (OCC). OCC was selected under the assumption that it plays no critical role in our experimental task. The inclusion of an rTMS control site allows us to establish that a difference in lpMTG-rTMS is not due to nonspecific effects of stimulation on a left posterior site. The inclusion of the no-stimulation condition instead serves to compare the effect of rTMS to a target site with a no-rTMS condition. This comparison is crucial because comparing directly the effects of rTMS at 2 different sites (here, lpMTG and OCC) raises the concern that the same rTMS parameters could have different (often unpredictable) effects on different brain regions, due to different stimulation characteristics of different cortical locations, which are mostly unknown or impossible to quantify (see Sack and Linden 2003).

In each condition (lpMTG-rTMS, OCC-rTMS, and no-rTMS), the task included 2 blocks: One with verb pairs and one with noun pairs. For each pair, participants had to decide whether the 2 items were synonyms (50% participants began with the verb block). Each trial lasted 3.5 s, including fixation (500 ms) and the presentation of the 2 words above and below the center of the screen (2 s). Stimulus presentation was chosen to be sufficiently long to perform the task, as indicated by the above norming study. A 1-s blank separated consecutive trials. Stimuli appeared on a computer screen (using E-prime, Psychology Software Tools) in front of the participant, who provided "yes" or "no" responses by key press. The whole task lasted 9.36 min.

The order of the 3 conditions (lpMTG-rTMS, OCC-rTMS, and no-rTMS) was counterbalanced across participants with the following constraints: The 2 rTMS-conditions were always administered on different days, and the no-rTMS condition was administered either on the first or the second day, together with either rTMS condition, and always before it. If List 1 was presented in the no-rTMS condition, List 2 was presented in the 2 rTMS conditions (the opposite was true in 50% of the cases); thus, participants never saw the same list twice on the same day.

Individual T_1-weigthed structural MRI images, available for all participants, were used to guide the TMS coil positioning over lpMTG and over the OCC control site. In the lpMTG-rTMS condition, participants received low-frequency (1 Hz) rTMS for 20 min, leading to a refractory period that extends up to ~20 min beyond the stimulation (Rossi et al. 2009). Participants performed the synonym-judgment task during this period (offline protocol). Using the Brainsight system 2 (Rogue Research, Montreal, Canada), the individual lpMTG site was identified on the T_1-weigthed structural MRI image of the participant. Throughout the stimulation, the participant's head position was tracked with an infra-red device (Polaris, Northern Digital, Ontario, Canada), and co-registered with the MRI image with frameless stereotaxy using the Brainsight system. This co-registration system determined the scalp position corresponding to the target site. Stimulation was delivered with an intensity corresponding to 65% of the maximum stimulator output, through a 70-mm figure-of-eight coil connected to a Magstim Rapid2 stimulator (Whitland, UK). The coil, tangential to the scalp surface, was supported by an articulated arm and maintained in position with the experimenter's assistance. The same TMS procedures and parameters were applied to locate and stimulate the control site (OCC). This control site was defined according to the group-average Talairach coordinates (−8, −85, −4) corresponding to a left primary visual cortex location identified in 7 participants from a study on visual motion processing (Lingnau et al. 2009). These coordinates were converted to the *x*, *y*, and *z* coordinates of the native space of each participant and adjusted using the calcarine fissure as individual anatomical landmark.

The dependent variables of Experiment 1 were reaction times (RTs) and accuracy expressed as *d* prime (d'), a bias-corrected measure of sensitivity in discriminating between 2 categories (in this case, synonymous from nonsynonymous pairs; MacMillan and Creelman 1991). RTs and d' were subjected to 3 × 2 repeated-measures ANOVAs with factors TMS condition (no-stimulation, lpMTG, and OCC) and Word-Class (verbs and nouns). For the RTs analysis, we considered only trials in which the response was correct (93.45% of trials) and within 1.5 SD from the individual condition mean, leading to the exclusion of 11% of trials with correct response. The d' analysis considered yes-responses to synonym pairs as "hits" and yes-responses to nonsynonym pairs as "false alarms." In these and in the following analyses within-subject standard errors of the mean were calculated with Cousineau's (2005) modification of Loftus and Masson's method (Loftus and Masson 1994). As the present experiment was designed to test the specific hypothesis that the perturbation of the functionally identified verb-preferring site in lpMTG would disproportionately impoverish the semantic analysis of verbs, the subset of pair-wise comparisons between critical conditions specifically addressing this hypothesis were implemented as planned contrasts of the Least Squares Means with a significance level of 5% (Keppel and Wickens 2004).

Experiment 2

Materials and Methods

Participants

Experiment 2 involved 12 participants from Experiment 1 and 3 new volunteers, for a total of 15 right-handed (Oldfield 1971) native-Italian speakers (10 females, age range 19–35 years). Only one of them did not take part in either fMRI session including the verb functional localizer task. In the remaining 14 participants, verb-related lpMTG activity was identified with the localizer task included in Peelen et al. ($N = 10$) or in Papeo et al. ($N = 4$) (see Experiment 1: Materials and Methods: participants). For the participant with no fMRI data available, group-average Talairach coordinates from Peelen et al.'s (2012) study were used to target the lpMTG site for stimulation. All had normal or corrected-to-normal vision, and were clear of counter indications to TMS (Rossi et al. 2009). Before starting the experiment, participants gave informed consent. The study was approved by the ethics review board of the University of Trento.

Stimuli

Stimuli for Experiment 2 were verb pairs of: 1) synonymous verbs with concrete meaning (i.e., hand-action verbs); 2) synonymous verbs with abstract meaning (i.e., cognitive or psychological-state verbs); 3) nonsynonymous verbs with concrete (hand action) meaning; 4) nonsynonymous verbs with abstract meaning. With the very same procedure and criteria for stimulus selection as in Experiment 1, 2 lists of stimuli were created, each including 25 pairs of each of the 4 conditions, for a total of 100 items, in each list.

Procedures of Experiment 2

In Experiment 2, we aimed at investigating whether, and how, perturbation of lpMTG activity through rTMS affected the pattern of motor activity associated with verb processing. Therefore, the dependent variable in Experiment 2 was the motor activity recorded in the form of MEPs induced with single-pulse TMS over left M1, during the processing of action and nonaction verbs. This measure was obtained in 3 conditions: 1) no-rTMS; 2) after a session of rTMS over lpMTG; and 3) after rTMS over a control site (OCC).

In each condition, participants saw 1 block of synonym and nonsynonym pairs of either hand action or nonaction verbs. Each trial included a fixation period (500 ms), a verb pair (2 s), and a blank period (3.5 s), for a total of 6 s. Participants sat in front of the screen, keeping their right hand still and relaxed on a pillow over their lap. They were instructed to think of whether the 2 verbs where synonymous, while single-pulse TMS was applied over the hand representation of the left M1, randomly at 250 ms (50% trials) or 500 ms after the stimulus onset. The optimal scalp position for inducing MEPs in the participant's right-hand muscles was indicated by visible twitches and was marked on a cap worn by the participant. TMS was delivered through a 70-mm figure-of-eight coil tangential to the scalp surface. Intensity was adjusted at 120% of the individual resting motor threshold, defined as the minimum intensity to evoke MEPs with $\geq 50\ \mu V$ peak-to peak amplitude in the relaxed muscles, in at least 3 of 5 consecutive pulses (Rossini et al. 1994). Group-mean motor threshold was $56 \pm 8.5\%$ of the maximum stimulator output. MEPs were recorded by gold surface electrodes placed over the first dorsal interosseous and abductor minimi digiti muscles (active electrodes), the metacarpophalangeal joint of index finger (reference electrode), and the ventral surface of the right wrist (ground electrode). The electromyographic signal (EMG) was recorded with a 5-kHz sampling rate, amplified, filtered (band pass, 10–500 Hz), and transferred to a second computer for online monitoring and offline analysis (LabChart software, ADInstruments). The block lasted 10 min and began with 6 trials where TMS pulses were delivered but no stimulus was shown.

The procedure for offline rTMS and the arrangement of the 3 conditions (no-rTMS, after rTMS over lpMTG, and after rTMS over OCC) were identical to Experiment 1. Stimulus presentation and synchronization with TMS and with the system for recording MEPs were controlled through the software "ASF" (Schwarzbach 2011), based on MATLAB Psychtoolbox.

Statistical analysis was carried over the MEP peak-to-peak amplitude values (mV) averaged across the 2 muscles, within 1.5 SD from the individual mean of the block (88% of the total MEPs). The present experiment was designed to test the specific hypothesis that the perturbation of the verb-preferring lpMTG would affect the processing of verbs in the precentral motor cortex. The subset of critical comparisons assessing this hypothesis was implemented as planned contrasts of the Least Squares Means with a significance level of 5% (Keppel and Wickens 2004).

Results

Experiment 1

No significant effect was found in the RTs analysis (all P's > 0.05). The d' analysis revealed that participants' performance was worse on verb than on noun trials only in the lpMTG stimulation condition (Fig. 3). Specifically, a 3 (TMS Condition) × 2 (Word-Class) ANOVA revealed significant main effects of TMS Condition ($F_{2,26} = 3.186$, $P = 0.05$) and Word Class ($F_{1,13} = 5.03$, $P = 0.04$), and a significant interaction between the 2 factors ($F_{2,26} = 3.54$, $P = 0.04$). Planned contrasts showed that performance on noun pairs did not differ across TMS conditions (all Ps > 0.1). Instead, semantic sensitivity was significantly reduced for verb pairs after lpMTG stimulation, relative to both no-rTMS ($P < 0.05$) and OCC stimulation

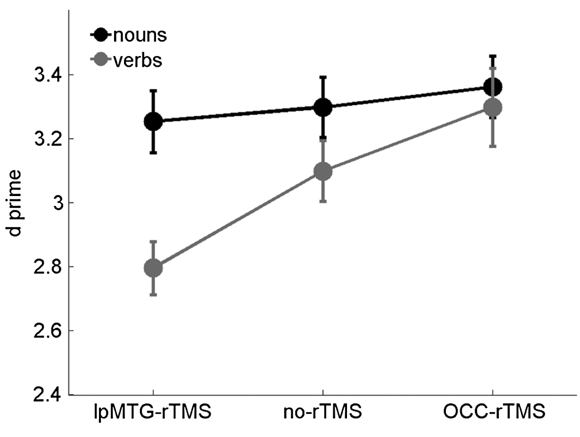

Figure 3. Behavioral results of Experiment 1. Performance (expressed as d') in the synonym-judgment task on nouns and verbs in the no-rTMS condition and in rTMS to lpMTG and to OCC. Error bars represent within-subject standard error of the mean.

($P < 0.01$). Performance on verbs in the no-rTMS and OCC stimulation conditions did not differ ($P > 0.1$). In both these conditions, participants performed equally well with verb and noun pairs; while lpMTG stimulation yielded a significant difference in performance with the 2 word classes ($P < 0.001$).

With a 3 (TMS Condition) × 2 (Verb Category) ANOVA, we further assessed whether the effect of lpMTG-rTMS on verb processing was different for concrete (action related) versus abstract verbs. The effect of verb category was significant ($F_{1,13} = 66.358$, $P < 0.001$), showing that participants were on average more accurate with concrete than abstract verb pairs. The effect of TMS Condition was also significant ($F_{2,26} = 6.36$, $P < 0.01$): Performance was poorer after lpMTG stimulation than in the no-rTMS ($P = 0.03$) and after OCC stimulation ($P < 0.01$). Critically, the factor TMS Condition did not interact with Verb Category ($F_{2,26} = 0.23$, $P = 0.7$), indicating that lpMTG perturbation affected the processing of action and nonaction verbs equally. Comparable effect of lpMTG–TMS on concrete (action related) and abstract verbs implies that the differential involvement of lpMTG in verb versus noun processing cannot be accounted by possible differences in concreteness–imageability between the 2 word classes.

The results of the d' analysis are supported by the analysis carried over raw accuracy data. A 3 (TMS condition) × 2 (Synonym and Nonsynonym trials) × 2 (Word-Class: nouns and verbs) repeated-measures ANOVA on the proportion of correct responses revealed significant effects of TMS condition ($F_{2,26} = 3.99$, $P = 0.03$), Synonym–Nonsynonym trials ($F_{2,26} = 8.16$, $P = 0.01$), and a trend for TMS condition by Word-Class interaction ($F_{2,\ 26} = 3.05$, $P = 0.06$). Pair-wise comparisons for this interaction showed that performance on noun pairs did not differ across TMS conditions (Ps > 0.1); while accuracy was significantly reduced for verb pairs after lpMTG stimulation, relative to both no-rTMS ($P = 0.02$) and OCC stimulation ($P < 0.01$). Verb processing in no-rTMS and OCC stimulation conditions did not differ ($P > 0.1$). A 3 (TMS condition) × 2 (Verb Category) ANOVA was performed on the raw accuracy data, to assess whether verb semantics (concrete versus abstract) interacted with the effect of TMS over lpMTG. In line with the results of the d' analysis, we found significant main effects of TMS condition ($F_{2,26} = 5.89$, $P < 0.01$) and Verb Category ($F_{2,26} = 13.32$, $P < 0.01$), but no interaction between the 2 ($F_{1,13} = 0.69$, $P = 0.5$). In sum, the analysis of raw accuracy data confirmed the pattern observed in the d' analysis, which, in addition to the sensitivity of performance, also accounts for putative response bias (a general tendency to respond "yes" or "no") in a yes-or-no or forced-choice task (e.g., Stanislaw and Todorov 1999).

Analogous tests of the effect of TMS conditions separately for concrete and abstract noun pairs revealed no significant effect or interaction (for d' and raw accuracy data, all P's > 0.1). Mean d', raw accuracy values and RTs (and the within-subjects standard errors of the mean) in the 3 TMS conditions for the synonym judgments on abstract and concrete verbs and on abstract and concrete nouns are reported in Tables 1 and 2, respectively.

Experiment 2

As mentioned above, early timing of motor facilitation, characterized by relatively higher activity for action than for nonaction verbs, is crucial information to relate this effect to lexical-semantic processing (Pulvermüller 2005). With a 2 (Stimulation Time: 250 and 500 ms) × 2 (Verb Category: action and nonaction) repeated-measures ANOVA carried out for the MEP values obtained in the no-rTMS condition, we found greater MEP amplitude at 250 ms than at 500 ms after stimulus onset (main effect of stimulation time: $F_{1,14} = 8.46$, $P = 0.01$). The main effect of verb category ($F_{1,14} = 3.38$, $P = 0.09$) and the interaction of verb category by stimulation time ($F_{1,14} = 3.50$, $P = 0.08$) did not approach significance. Planned contrasts revealed that at 250 ms MEPs were greater for action (mean: 0.81 ± 0.03) than for nonaction verbs (mean: 0.73 ± 0.03; $P = 0.01$), but this effect disappeared at the later stimulation point (mean action verbs: 0.68 ± 0.02, mean nonaction verbs: 0.66 ± 0.02; $P < 1$). This analysis thus established that the "target" effect investigated in the analyses that follow is the motor facilitation that has been shown to initiate in early stages of word processing (within 250 ms) and has been interpreted as a signature of semantically relevant processing (Pulvermüller 2005).

Table 1

Experiment 1: Mean d', raw accuracy (expressed as proportion of correct responses) and RTs for the synonym-judgment task on abstract and concrete verbs in the no-rTMS, lpMTG, and OCC stimulation conditions. Within-subjects standard errors of the means are reported in brackets for each condition

	no-rTMS		lpMTG		OCC	
	Abstract	Concrete	Abstract	Concrete	Abstract	Concrete
d'	2.72 (0.07)	3.31 (0.09)	2.43 (0.07)	3.12 (0.12)	2.90 (0.07)	3.50 (0.11)
Raw accuracy	0.92 (0.007)	0.95 (0.01)	0.90 (0.007)	0.94 (0.01)	0.94 (0.006)	0.97 (0.01)
RTs	1062.97 (8.39)	1045.74 (10.14)	1055.40 (16.78)	1036.48 (18.69)	1025.31 (16.89)	996.45 (18.67)

Table 2

Experiment 2: Mean d', raw accuracy (expressed as proportion of correct responses) and RTs for the synonym judgment task on abstract and concrete nouns in the no-rTMS, lpMTG, and OCC stimulation conditions. Within-subjects standard errors of the means are reported in brackets for each condition

	no-rTMS		MTG		OCC	
	Abstract	Concrete	Abstract	Concrete	Abstract	Concrete
d'	2.99 (0.11)	3.06 (0.09)	2.99 (0.07)	2.82 (0.10)	3.13 (0.07)	2.94 (0.07)
Raw accuracy	0.94 (0.01)	0.94 (0.01)	0.93 (0.007)	0.92 (0.01)	0.95 (0.006)	0.93 (0.008)
RTs	1050.23 (15.12)	1023.76 (12.00)	1034.76 (19.01)	1008.16 (20.07)	1021.38 (22.46)	992.46 (24.89)

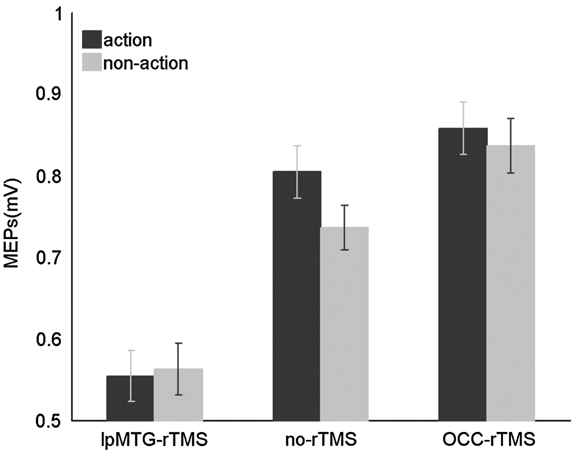

Figure 4. MEPs results of Experiment 2. Peak-to-peak MEP amplitude (mV) for action and nonaction verbs, in the no-rTMS condition and after offline lpMTG stimulation and offline OCC stimulation. Error bars represent within-subject standard error of the mean.

Then, with a 3 (TMS condition: no-rTMS, lpMTG-rTMS, and OCC-rTMS) × 2 (verb category: action and nonaction) repeated-measures ANOVA, we assessed the effect of rTMS on early motor responses to action and nonaction verbs. On average, MEPs were greater for action than nonaction verbs in the no-rTMS and OCC-rTMS conditions; this difference disappeared in the lpMTG-rTMS condition, where the overall MEP amplitude was also visibly reduced (see Fig. 4). In particular, the ANOVA yielded significant effects of verb category ($F_{1,14} = 5.65$, $P = 0.03$) and TMS condition ($F_{2,28} = 3.91$, $P = 0.03$) and a significant interaction between the 2 factors ($F_{2,28} = 3.58$, $P = 0.04$).

This result suggests that the significant difference in MEP amplitude (action verbs > nonaction verbs) observed in the no-rTMS condition is different in either or both rTMS conditions. To investigate further the source of the TMS condition by category interaction, we performed the following 3 separate 2 (TMS condition) × 2 (verb category) ANOVAs.

The ANOVA with factors 2 TMS conditions (lpMTG-rTMS and OCC-rTMS) and 2 verb categories revealed significantly greater MEP amplitude (main effect of the TMS site: $F_{1,14} = 6.5801$, $P = 0.02$), in the OCC condition for both action ($P = 0.02$) and nonaction verbs ($P = 0.02$). No significant interaction was found ($F_{1,14} = 1.09$, $P = 0.31$). This comparison on its own, however, does not clarify know which rTMS-condition significantly impacted motor activity, relative to the absence of stimulation over either site. To address this issue, each rTMS condition was compared against no-rTMS. The comparison between lpMTG stimulation and no-rTMS revealed significant effects of TMS condition ($F_{1,14} = 4.32$, $P = 0.05$), verb category ($F_{1,14} = 6.19$, $P = 0.02$), and their interaction ($F_{1,14} = 5.90$, $P = 0.02$). lpMTG stimulation led to an overall drop of MEP amplitude relative to no-rTMS, which was significant for action verbs ($P = 0.03$) but not for nonaction verbs ($P = 0.1$). In effect, the MEP difference between action and nonaction verbs was abolished, and qualitatively reversed (i.e., nonaction > action). The comparison between rTMS over OCC and no-rTMS yielded an effect of verb category only ($F_{1,14} = 5.68$, $P = 0.03$), with higher MEPs for action than nonaction verbs. The effect of TMS condition ($F_{1,14} = 0.52$, $P = 0.5$) and the interaction between the 2 factors ($F_{1,14} = 3.15$, $P = 0.1$) did not approach significance. Thus, although there was a qualitatively reduced difference between MEPs for action and nonaction verbs in the OCC stimulation condition (see Fig. 4), it was not significantly different relative to no-rTMS.

Discussion

The results reported here show that perturbation of lpMTG activity results in selective disruption of the semantic processing of verbs and in the abolition of the "action > nonaction verbs" motor effect, which has been reported in previous studies (e.g., Oliveri et al. 2004; Papeo et al. 2009; Willems et al. 2010) and replicated here.

More specifically, a special role of lpMTG in verb processing (and, by contrast, the lack of a critical role of OCC) is supported by the following constellation of converging observations: 1) lpMTG (but not OCC) was individually identified with fMRI, as a region showing consistent response to verb processing; 2) lpMTG-rTMS affected the participants' performance in verb processing, but OCC-rTMS did not; 3) the suppression of MEP amplitude after lpMTG-rTMS resulted in an action versus nonaction MEP effect, significantly different (and even qualitatively reversed) relative to no-rTMS; 4) the comparison between lpMTG-rTMS and OCC-rTMS showed that the strong suppression of MEP amplitude after lpMTG-TMS was not a general effect of stimulation at any part of the brain; 5) while a reduction of the action > nonaction difference was visible in the OCC-TMS condition, the difference in the magnitude of the effect was statistically comparable to the difference obtained in the absence of any TMS delivery (i.e., no-rTMS). Below, we discuss each of these observations in detail.

Experiment 1 showed that rTMS over lpMTG led to selective deterioration of participants' performance on verb-pairs, but not on noun-pairs, when judging whether 2 words were synonymous. This result, specific to lpMTG stimulation and not found with OCC stimulation, provides a direct demonstration that lpMTG is an essential node within the network for the semantic analysis of verbs.

Could this effect reflect unequal task difficulty—the verb task more difficult than the noun task—rather than a differential involvement of lpMTG in verb and noun processing? Task difficulty could interact with the effect of TMS, such that more difficult tasks would be more susceptible to TMS. Cognizant of this possibility, in the preliminary phases of the study (see Materials and Methods: Stimuli), the 2 task conditions were carefully matched for semantic distance between word pairs (which defined each trial/pair as synonymous or nonsynonymous) and RTs (which is also an indirect measure of familiarity and frequency). Perhaps most important, participants' performance in the no-rTMS condition of Experiment 1, where no significant effects in RTs or accuracy rates for the 2 word classes were observed, provides a clear confirmation that task difficulty for verb and noun judgments was comparable.

The observation that rTMS over plMTG disrupts disproportionately semantic processing of verbs is consistent with neuroimaging findings that have implicated this region in the semantic analysis of words (Binder and Desai 2011; Watson et al. 2013), including the semantic distinction between verbs and nouns (Bedny et al. 2008; Willms et al. 2011; Peelen et al. 2012). For instance, lpMTG could capture the distinction between nouns denoting entities (or arguments) and verbs denoting relational structures (or predicates). However, it is important to remark that the fact that information carried by lpMTG appears to be central to verbs' representations does not imply selective specialization for this word class. Certain categories of nouns could also recruit lpMTG information (e.g., tool nouns implying action or an acting subject; see Kable et al. 2005). Likewise, TMS results showing that lpMTG is recruited whether the verb is concrete (action related) or abstract (nonaction related) does not exclude the possibility of an internal organization of contents, or relative differences in the amplitude of the response, which might be detected with the more sensitive fMRI measurement (e.g., Grossman et al. 2002; Rodriguez-Ferreiro et al. 2011).

Results of Experiment 1 were prerequisite for investigating whether verb-related motor activity is independent of access to the verb-relevant conceptual information in lpMTG. In Experiment 2, we found that perturbation of lpMTG activity during verb processing led to a change in the general state of the motor cortex toward suppression of activity. Relative to the no-rTMS, the reduced level of activity, as indexed by smaller MEP amplitude, was statistically significant in the case of action verbs, resulting in the disruption of the early differential response to action versus nonaction verbs.

We did not find statistically different effects for action versus nonaction words for the rTMS conditions over lpMTG and OCC. Qualitatively, the difference action > nonaction persisted with OCC-rTMS while it was reversed with lpMTG-rTMS, but the lack of a significant interaction between rTMS site and verb category might suggest that the abolition of the action > nonaction effect was not specific to lpMTG-rTMS. While this circumstance leaves open a possibility that OCC-rTMS too had an impact on the verb-related motor activity, a conclusion along these lines would require showing that the result of rTMS in a specific region (here, OCC) is demonstrably different from the normal functioning of that same brain area (i.e., no-TMS). On the contrary, the comparison of the OCC-rTMS condition against no-rTMS revealed a significant effect of verb category (action > nonaction) that was statistically comparable for the 2 conditions (i.e., no interaction), undermining the idea that OCC has an effect on MEP amplitudes over and above the case of no TMS stimulation. This pattern of results contrasts with the comparison of lpMTG-TMS versus the no-rTMS where there was a clear difference in MEP amplitudes and an interaction between TMS condition and verb category. Crucially, the inclusion of OCC-TMS, which showed comparable MEP amplitudes to the no-rTMS condition, served the important function of excluding that the strong suppression of precentral activity after lpMTG-TMS was a general effect of stimulation to any part of the brain. The joint consideration of these contrasting patterns of effects of lpMTG-rTMS and OCC-TMS by comparison to the no-rTMS suggests a causal role of lpMTG for verb-related motor activity.

The overall pattern of results reported here demonstrates that functional connectivity between lpMTG and precentral motor cortex is established as early as 250 ms, during the semantic processing of verbs. Moreover, they show that verb-related motor responses are vitally dependent on the successful processing of verb representations in lpMTG (or in the network that lpMTG belongs to). On this view, perceptual recognition of a spoken or written verb activates its conceptual representation in the temporal cortex, which interacts with the precentral cortex whenever motor information is relevant for the task (i.e., when a verb with action content is being processed). This interaction would explain why the "action > nonaction verbs" motor effect is abolished when lpMTG is perturbed: Disruption of verb processing in lpMTG would result in a failure to deliver the relevant information for motor differentiation in precentral cortex. In brief, the semantic information for distinguishing, say, the verb "jumping" from the verb "wondering," is represented in lpMTG; the retrieval of this information drives the activation of related representations in other brain regions, such as the motor features of "jump" in precentral cortex.

It is important to note that none of our observations imply anatomical connectivity between lpMTG and the hand representation in the precentral gyrus and, by extension, lack of connectivity between the OCC and the precentral site. Moreover, we emphasize that the current study was not designed to investigate how TMS perturbation of motor cortex affects semantic processing. To address this issue, one could test whether the detrimental effect due to lpMTG perturbation would be worsened if the motor cortex were perturbed concurrently or, more simply, whether TMS over the motor cortex alone would affect semantic performance. Insight into this question can be gleaned from the available literature. Consistent with the present TMS investigation, damage to the left temporal lobes results in lexical-semantic deficits (e.g., Tranel et al. 1997; Campanella et al. 2009); while there is no neuropsychological report of semantic deficits that can be unambiguously attributed to precentral lesions (Mahon and Caramazza 2008; Papeo et al. 2011; Arévalo et al. 2012; Kemmerer et al. 2012; Papeo and Hochmann 2012). TMS methodology has been used in the attempt to assess the effect of precentral cortex disruption on semantic processing, but the results so far are uncertain, fluctuating between facilitation of performance (Willems et al. 2011), inhibition (Lo Gerfo et al. 2008), and lack of effect (Papeo et al. 2009; for a discussion, see Papeo et al. 2013).

In conclusion, we have shown that lpMTG activity is causally involved in verb semantics, and that activity in this area affects word-related processing in motor cortex. The action versus nonaction verb distinction in the motor cortex depends upon the outcome of—or is "cognitively mediated" by—processes taking place in lpMTG: The motor system does not represent on its own action verbs but serves to instantiate the semantic representations computed in the conceptual network that encompasses lpMTG. Thus, verb-related motor activity is not an isolated phenomenon in the brain, but it occurs within the well-known language-semantic network distributed over frontal and temporo-parietal cortices. Ultimately, these results contribute to integrate in a single neurocognitive model the multiple neural phenomena related to word processing.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

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