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The role of the left frontal lobe in action naming: rTMS evidence

[Articles]

Cappa, S. F. MD; Sandrini, M. PsyD; Rossini, P. M. MD; Sosta, K. PsyD; Miniussi, C. PsyD, PhD

From IRCCS S. Giovanni di Dio (Drs. Sandrini, Rossini, Sosta, and Miniussi), Brescia; Centro di Neuroscienze Cognitive (Dr. Cappa), Università Vita–Salute S. Raffaele, Milano; and Neurologia (Dr. Rossini), Università Campus Biomedico, Roma, Italy.
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Address correspondence and reprint requests to Dr. Stefano F. Cappa, Centro di Neuroscienze Cognitive, Università Vita-Salute S. Raffaele, DIBIT Via Olgettina 58, 20132 Milano, Italy; e-mail: cappa.stefano@hsr.it

Outline

Graphics

Abstract—

Background: Neuropsychological and neuroimaging studies suggest that whereas the left temporal neocortex plays a crucial role in all tasks involving lexical–semantic processing, some regions of the left prefrontal convexity are selectively recruited during verb processing.

Objective: To determine if there are different neural correlates for noun and verb processing in the human brain.

Methods: Repetitive transcranial magnetic stimulation (rTMS), 20 Hz at 90% of the motor threshold, was applied to left or right prefrontal brain during object- and action-naming tasks in nine healthy subjects.

Results: A shortening of naming latency for actions was observed only after stimulation of left prefrontal cortex.

Conclusion: The involvement of the left dorsolateral frontal cortex in action naming was demonstrated using rTMS.

Several reports [1] have established the existence of patients with selective, or relatively selective, disorders in naming and comprehension of nouns and verbs. Most of the patients with selective disorders of noun processing had posterior lesions, in particular involving the left temporal lobe; verb impairment, conversely, was associated with damage extending or limited to the left prefrontal cortex. [2] A recent large-scale lesion study has confirmed the association between action-naming impairment and lesions involving the left premotor/prefrontal areas. In addition, the authors observed disproportionate action-naming defects in association with damage to the left mesial occipital cortex and to the paraventricular white matter underneath the supramarginal and posterior temporal regions. [3] Noun– verb dissociations have been observed also in patients with degenerative conditions. [4,5] In a previous study, we reported that whereas patients with probable AD were more impaired in action naming than in object naming, the discrepancy was much larger in patients with a clinical diagnosis of frontotemporal dementia. [6] Taken together, these neuropsychological findings indicate a link between left frontal cortex and action naming. Functional neuroimaging has also been used to investigate the neural correlates of noun and verb processing in the normal brain. Many imaging studies of the “ verb generation” task, in which subjects produce a verb in response to a target noun, have shown extensive activations of the left prefrontal cortex. [7,8] In a version of the “ verb generate” task, a selective activation of the left frontoparietal cortex, the middle temporal gyrus, and the cerebellum has been reported during action naming. [9] Finally, a PET study using lexical decision has shown the presence of “ verb-specific” areas in the left hemisphere (Broca’ s, left middle temporal gyrus). [10] Evoked potential studies [11-13] have given similar results.

Transcranial magnetic stimulation (TMS) is an excellent tool for the direct investigation of the functional participation of a brain area in a cognitive process, [14,15] as it does not depend on the measurement of the metabolic or hemodynamic response to cognitive challenge, but it can directly interact with the functioning of the neural circuitry responsible for a task. Repetitive TMS (rTMS) can modulate cortical excitability, improving or impairing cognitive performance in normal subjects. The aim of this rTMS study was to determine whether the left dorsolateral prefrontal cortex (DLPFC) has a specific role of in action naming. To do this, we performed a naming experiment in which high-frequency rTMS was applied to either the right or the left DLPFC and compared with a sham stimulation condition.

Subjects and methods.

Subjects.

Nine healthy volunteers (three men and six women), aged 25 to 32 years (mean age 29 years), gave their written informed consent prior to the experiment. The local Human Ethics Committee approved the protocol. The subjects had no history of implanted metal objects, seizures, or other neurologic diseases. All were right-handed (mean score on the Edinburgh Handedness Inventory = 91.2) and had normal or corrected-to-normal vision. All were native Italian speakers.

Experimental conditions.

The experiment included three blocks, counterbalanced between subjects as to order of presentation (stimulation with rTMS to the right and left DLPFC and sham stimulation). For each block, 20 pictures (10 representing objects and 10 actions) were presented in a pseudo-random order on the monitor for 500 ms at two intertrial intervals (7,000 and 8,000 ms). A fixation point preceded images for 1,000 ms, and subjects were instructed to name the picture as quickly as possible (figure 1). A total of 60 pictures were used. The objects belonged to different semantic categories (both natural and artifacts); the actions involved largely, but not exclusively, tool utilization. Nouns and verbs were matched for lexical frequency on the basis of a lexicon of written Italian [16] (mean frequency: objects 69.5, actions 78.01; difference NS). It must be underscored that the responses could always be unambiguously assigned to the noun– verb category. Verbs in Italian are characterized by the final suffix; for example, telephone as an object name (telefono) is different from the corresponding action name (telefonare). The visual stimuli were the same, which we have employed in patient studies showing noun– verb differences, [6,17] and were presented using Superlab software (Cedrus Corp., CA) running on a personal computer with a 17-inch monitor. Subjects were sitting comfortably in a reclining chair at the distance of 85 cm from the screen. The recording session lasted approximately 20 minutes.

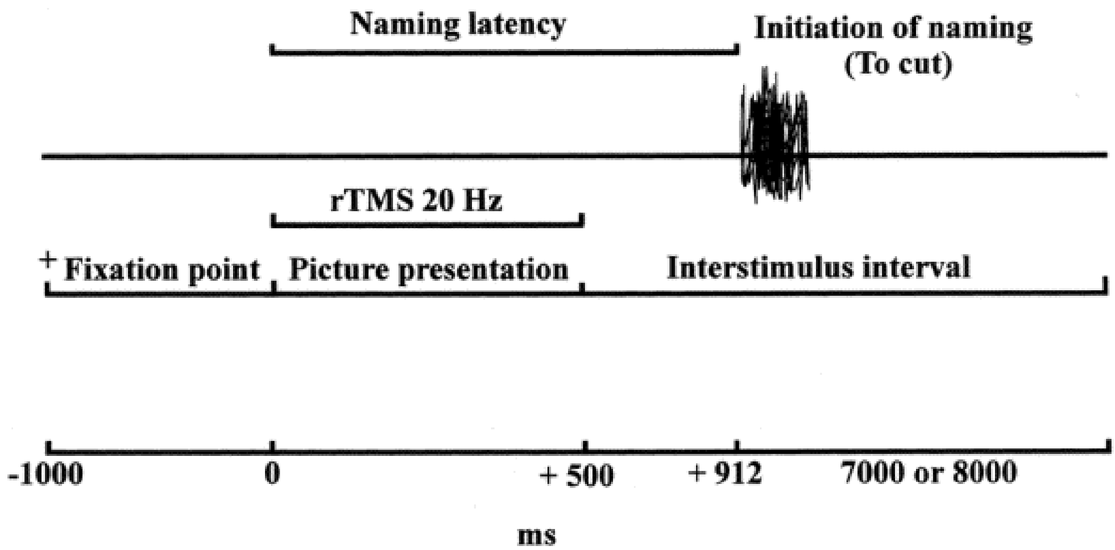

Figure 1. Time course of the experimental condition with respect to visual stimulation and repetitive transcranial magnetic stimulation (rTMS). A fixation point preceded images for 1,000 ms, and subjects were instructed to name the picture as quickly as possible. The picture was present on the monitor for 500 ms. Trains of rTMS (500 ms, 20 Hz, 10% subthreshold) were delivered simultaneously with the picture presentation. A representative sample of verbal reaction time for an action is reported. Verbal responses were recorded with a microphone and transformed into speech wave envelopes that allowed the exact determination of naming latency.

Recording and stimulating procedures.

A microphone recorded verbal responses. We digitized acoustic information with the program GoldWave v.4.24 (Shareware) at a 16-bit resolution and a sampling rate of 22 kHz. We measured the latency of the verbal responses on the screen using the speech wave envelopes and checked the semantic correctness of each verbal response off-line. Semantically incorrect responses as well as responses proceeded by verbal searching (“ tip-of-the-tongue” phenomenon) were marked and excluded from further statistical analysis. Verbal searching can be seen in pauses filled by interjections such as “ ehm” or by self-commenting phrases as well as by prolonged empty pauses. Such tip-of-the-tongue phenomena can have an impact on picture-naming latencies and may obscure specific facilitatory or inhibitory effects of TMS. Three different categories of exclusions were defined: 1) semantically incorrect responses, 2) responses with multiple onset due to verbal searching, and 3) no responses. RTMS was applied using a Magstim Super Rapid with a figure-of-eight (double 70-mm) coil with stimulation procedure identical to previous studies from this laboratory. [14] The subjects wore a Lycra cap on which the positions of all the electrodes from the International 10/20 EEG system were reproduced. Before rTMS was applied, individual resting excitability thresholds of stimulation were determined for both hemispheres, by measuring the intensity of TMS able to elicit reproducible motor twitches evoked by single TMS stimuli in the contralateral first dorsalis interosseous muscle, with a rate of occurrence of about 50% in a cascade of 10 stimuli. [18] The stimulating figure-of-eight coil rested tangential to the scalp surface over the primary motor cortex (i.e., positions C3 or C4 of the 10/20 EEG International System), with the handle directed posteriorly and angled at about 45° to the midline. Once individual threshold had been determined, the intensity of stimulation was reduced by 10%. Then, left and right DLPFC were stimulated by placing the anterior end of the junction of the two coil wings between F_3F_5 (left) and F_4F_6 (right). The coil position on the scalp was also determined in relation to the optimal location for first dorsalis interosseous muscle responses (approximately 5 cm anterior; head size and shape were taken into account). These points were estimated to be overlying the DLPFC in the two hemispheres, using a standard brain atlas. [19] Trains of rTMS (500 ms, 20 Hz) were delivered according to the experimental design simultaneously to picture presentation. The same intensity and timing of rTMS were used for sham stimulation: In this case, the coil was centered on C_z but was perpendicular to the scalp surface. By adopting this procedure, no magnetic stimulation reached the brain during the sham condition, while subjective feeling of coil– scalp contact and discharge noise were similar to the real simulation.

Results.

Correct verbal reaction time (VRT) only contributed to the analysis. VRT that fell below or above 2 SD from each individual’ s average VRT were eliminated. This procedure eliminated 3.1% of responses for actions and 0.4% for objects. Overall, subjects showed high levels of accuracy in task performance, and the error rate was 3.15% (object naming 0.74%, left: 2.2%, sham: 0%, right: 0%; action naming 5.55%, left: 8.8%, sham: 2.2%, right: 5.5%). No consistent differences were found between error rates and site of stimulation (left DLPFC, sham, right DLPFC). Differences on VRT were assessed by repeated-measures analysis of variance, using the Greenhouse– Geisser epsilon correction where appropriate. The tested factors were category (actions versus objects) and site of stimulation (left DLPFC versus sham versus right DLPFC). The main effect of category was significant ($F[1.00, 8.00] = 74.17$, $p < 0.05$), indicating that overall naming latency was shorter for objects than for actions. The main effect of site of stimulation ($F[1.98, 15.88] = 6.91$, $p < 0.05$) was also significant, with left site eliciting the fastest VRT. In addition, the interaction between category and site of stimulation ($F[1.96, 15.71] = 3.327$, $p < 0.05$) was significant.

Directed post hoc comparisons (*t*-tests) showed that only in action naming were VRT after left stimulation (850 ms) faster than VRT to both sham (911 ms) and right (970 ms) stimulation ($p < 0.05$). Inspection of individual VRT showed that all nine subjects had a significant task facilitation effect (namely, faster VRT) when stimulation was given over left DLPFC compared with sham or right DLPFC. We found no significant difference in latency when stimulation was given over right DLPFC compared with sham. Post hoc comparisons for object-naming conditions revealed no differences between stimulation sites ($p > 0.05$) (left 758 ms, sham 768 ms, right 779 ms) (see figure 2).

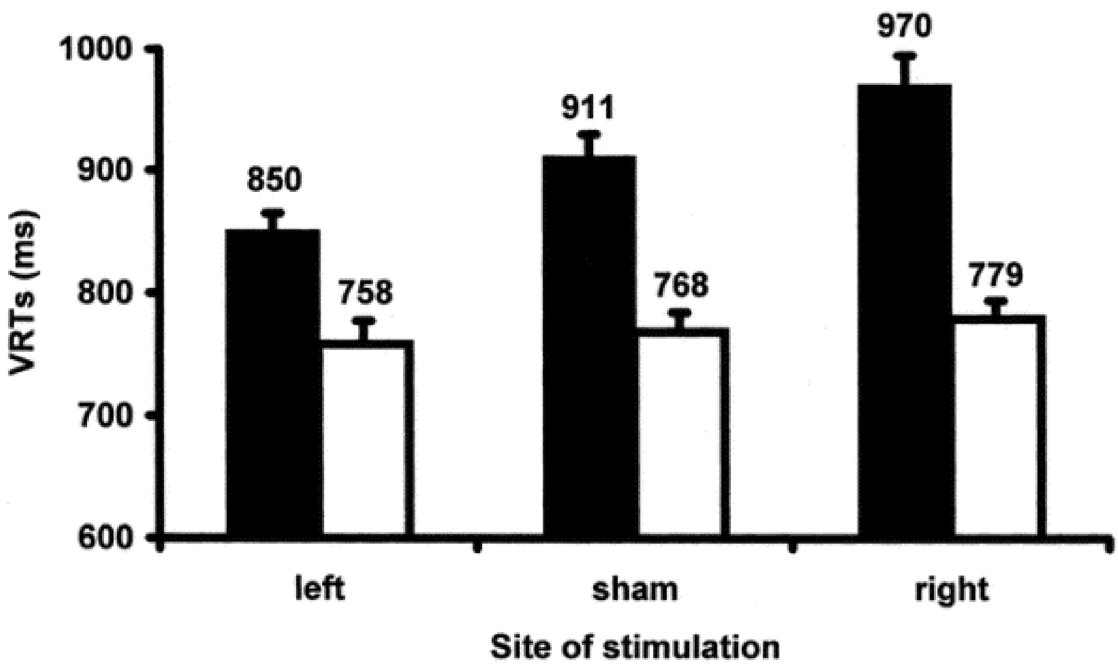

Figure 2. Hemispheric interaction of repetitive transcranial magnetic stimulation effects on action (filled columns) and object (open columns) naming. Verbal reaction times (VRT) for actions were consistently faster after left dorsolateral prefrontal cortex stimulation compared with the other two conditions. No significant differences were present for object naming. Errors bars indicate SEM.

Discussion.

The current findings provide direct evidence for a specific role of the left DLPFC in naming actions. The capacity to noninvasively excite or inhibit focal cortical areas with TMS has been demonstrated by several studies. In particular, it has been shown that the different parameters used in rTMS (frequency) affect the extent and type of neurophysiologic modifications. Fast rTMS (high frequency) results mainly in excitatory changes, whereas slow rTMS (low frequency) has a net inhibitory effect. [20,21] This has been demonstrated by the increase in motor evoked potential (MEP) amplitude and lowering of the MEP threshold, [22,23] by the paired-pulse technique, [22] and by cerebral perfusion imaging. [24] TMS has also been reported to facilitate many language-relate tasks, including oral word associations [25] and digit span, [26] in particular, reducing the latency in picture naming. [27-29] However, the basis for the facilitatory effects of rTMS on behavior remains essentially unknown. The possibility that the action-specific effect may be due to a " ceiling" performance in object naming appears to be unlikely, as all naming latencies were well within the average range for this kind of task (from 600 to 1,200 ms). [30]

It is worth noticing that stimulation applied to the right hemisphere resulted in an opposite, albeit not significant, effect for both actions and objects. This finding may indicate an interference with the naming process, which, however, shows more interindividual variability in comparison with the left hemispheric effect. A similar trend was presented by one group [28] but not another. [29]

A possible explanation for the current findings is that rTMS to the left prefrontal cortex affects the neural system dedicated to action observation and action representation. Recognition of actions of co-specifics is a genuine ability, which seems to be highly developed in humans and nonhuman primates. [31] In primates, " mirror" neurons in the left rostral part of the inferior area 6 (the so-called F_5) become active when the same action is actively performed by the monkey or when it is made by the experimenter and observed by the monkey. [32] A comparable activation was found in humans while observing motor actions (grasping of meaningful objects with the right hand). [33] The same area was part of a network of brain structures that became active during the observation of meaningful pantomimes in comparison with meaningless gestures. [34] These findings might be related to the representation of the semantics of action and are possibly the basis of the recognition of meaningful motor events. The observation/execution matching system (" mirror neurons") identified both in monkeys and in humans can thus be considered as a putative system specialized both for the encoding and for the production of actions.

This “ semantic” interpretation of the link between prefrontal cortex and action naming requires the additional assumption of a lateralization of the “ mirror” system to the left hemisphere in humans. It must be underlined that the retrieval of words denoting actions results in the production of items from the linguistic class of verbs. Verbs can be differentiated from nouns on the basis of multiple factors, which are not limited to semantics, but include morphologic, syntactic, and maybe even phonologic features. A recent TMS investigation 35 provides evidence for the possible role of morphosyntactic factors, independent of semantics. An increased latency was observed after left DLPFC stimulation, but not after sham stimulation, in the production of inflected forms of verbs and also of pseudo-verbs, in comparison with nouns and pseudo-nouns. These data suggest that extrasemantic factors are responsible for the noun– verb difference: The specificity of the effect remains unknown, as the right side was not stimulated. Further investigations are required to tease apart the contribution of multiple linguistic and conceptual factors to the possible anatomic specificity of verb processing.

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