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Note

The role of the prefrontal cortex in sentence comprehension: An rTMS study

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ABSTRACT

Using repetitive transcranial magnetic stimulation (rTMS), we investigated the role of the left and right dorsolateral prefrontal cortex (DLPFC) in sentence comprehension. Subjects were required to judge which of the two pictures correctly matched the meaning of active and passive semantically reversible sentences (subject–verb–object); the incorrect picture did not match the sentence in term of lexical items (semantic task) or agent–patient structure (syntactic task). The subjects performed the task while a series of magnetic stimuli were applied to the left or right DLPFC. When rTMS was applied to the left DLPFC, the subjects' performance was delayed only for the semantic task, while rTMS applied to the right DLPFC slowed the processing of syntactic information. The results of this experiment provide direct evidence of a double dissociation between the rTMS effects and the type of task, which may reflect a differential hemispheric involvement of working memory resources during sentence comprehension.

1. Introduction

The deceptively simple act of understanding the meaning of a common sentence requires a number of cognitive processes. Minimally, these include the analysis of its phonological and syntactic structure, as well as of the meaning of the composing lexical items. Sentence comprehension requires processing a sequence of words, and analyzing their syntactic and thematic organization in order to create a correct representation of the entire sentence. This elaboration needs to maintain in an activated state both single word meaning and the syntactic relations between words (Just and Carpenter, 1992). While current models of language comprehension make different predictions on the proposed time course of syntactic and semantic integration, there is general agreement about the fact that these processes require the temporary storage and manipulation of multiple classes of information (Friederici and Kotz, 2003). Both storage and manipulation are thought

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to depend upon working memory (WM) resources. Behavioural experiments indicate that the comprehension of syntactically complex sentences is a demanding process, often entailing a high memory load (Turkstra and Holland, 1998; Stromswold et al., 1996; Stowe et al., 1998).

The neural mechanisms involved in sentence comprehension have been investigated by means of lesion studies and of functional neuroimaging. Lesion studies have emphasised the role of damage to perisylvian areas of the left hemisphere in sentence comprehension disorders (Caplan et al., 1996). Nevertheless it has been difficult to ascribe specific functions to discrete regions within this network. The left ventral prefrontal cortex, in particular Broca's area, has traditionally been considered to play a central role in syntactic processing (see Grodzinsky, 2000, 2006, for a comprehensive discussion). Imaging studies have provided further evidence for a central role of Broca's area in syntactic processing (Dapretto and Bookheimer, 1999; Heim et al., 2003; Moro et al., 2001; Caplan et al., 1998, 1999, 2000). During online sentence comprehension, Broca's area is important not only for syntactic integration, but also for WM mechanisms relevant for language processing (Fiebach et al., 2005). The two factors of syntactic complexity and sentence length have been often confounded in the imaging literature. Some investigations have supported the view that the inferior frontal gyrus activation is specific for syntactic processing, while the engagement of the dorsolateral prefrontal cortex (DLPFC) may reflect the WM load (Caplan et al., 2002; Hashimoto and Sakai, 2002; Walsh and Rushworth, 1999; Martin et al., 2004). A recent fMRI study, which analyzed the areas involved in a sentence judgment task, has underlined the recruitment of the dorsal portion of left frontal cortex. Specifically, this area is involved during the processing of syntactic violations associated to a large WM load (Cooke et al., 2006).

It must also be underlined that language comprehension does not involve only the left hemisphere. Less extensive activations have also been observed in right prefrontal cortex during sentence comprehension (Wartenburger et al., 2004; Moro et al., 2001; Just et al., 1996). This finding may suggest a quantitative change of the activation of prefrontal cortex due to a more demanding task (Just et al., 1996) or an engagement of other processing operations, such as visual WM resources, in order to solve a more complex task (Rapp and McCloskey, 1997).

Transcranial magnetic stimulation (TMS), a technique that can be used to map the flow of information across different brain regions during the execution of a cognitive task (Walsh and Rushworth, 1999), is another tool which can be applied to the investigation of the neural mechanisms responsible for sentence comprehension. Only one study has investigated the effects of TMS on syntactic processing (Sakai et al., 2002). In that study, a double pulse TMS was delivered to the left inferior frontal gyrus or the left middle frontal gyrus, using three possible timings (0, 150, 350 msec after target onset) during a syntactic or semantic decision task. The main finding was that during syntactic decisions there was a shortening of reaction times, but only when TMS was applied to the left inferior frontal gyrus 150 msec after target onset. There is limited additional TMS evidence for a functional role of the prefrontal cortex in language processing. A recent study highlighted a functional dissociation in left inferior frontal cortex (LIFC), with rTMS on posterior LIFC slowing homophone judgments, while anterior LIFC slowed synonym judgments (Gough et al., 2005). An involvement of left prefrontal cortex in lexical–semantic processing was demonstrated using rTMS (Cappa et al., 2002; Devlin et al., 2003).

More extensive evidence is available that repetitive TMS (rTMS) applied to the prefrontal cortex can interfere with WM tasks. With a few exceptions (Hautzel et al., 2002), most studies support a relationship between, respectively, verbal and visual stimuli, and left and right prefrontal cortex (Manoach et al., 2004; Wendt and Risberg, 2001; Johnson et al., 2003). The activation of BA 46 observed during WM task is lateralized, with a left activation for verbal stimuli and a right activation for visual stimuli (Leung et al., 2002; Rowe and Passingham, 2001; Van der Linden et al., 1999; Stern et al., 2000).

A further functional distinction can be found between the dorsal and the ventral prefrontal cortex within each hemisphere (Sala et al., 2003). There is some evidence that the left ventral prefrontal cortex is more relevant for verbal WM, whereas right dorsal prefrontal cortex is more important for the spatial WM (Walter et al., 2003). Recent TMS studies showed that verbal WM is dependent on normal functioning of the middle frontal gyrus bilaterally, suggesting that right and left-sided areas might be involved in parallel processing of different features of stimuli (Mottaghy et al., 2002a, 2003). Moreover the same authors, in a different experiment, showed that the stimulation of the DLPFC impairs performance in spatial as well as non-spatial tasks. At the same time stimulation of the dorsomedial prefrontal cortex affects only spatial tasks while stimulation of the ventral portion affects only non-spatial task (Mottaghy et al., 2002b). A recent review of TMS studies of WM highlighted the involvement of prefrontal cortex both in maintaining the transient patterns of neural activity in other areas that maintain information available online, and in executive processes (Mottaghy, 2006).

The aim of this experiment was to evaluate the relative contributions of the left and right DLPFC to sentence comprehension, by comparing the effects of rTMS applied to these two regions. The experiment involved the presentation of a sentence and two pictures (see Fig. 1). Subjects were required to judge which of the two pictures correctly matched the meaning of a semantically reversible sentence (subject–verb–object) in the active or passive form. In the syntactic condition, one picture matched the true meaning of the sentence, while in the ''distracter'' picture, the subject and the object of the action were reversed. In the semantic condition, the distracter did not correspond to the meaning of the sentence because the subject, object or action did not correspond to the presented lexical items. rTMS was delivered over left or right DLPFC, at a frequency of 10 Hz for a period of 900 msec, starting 100 msec after the onset of the display. The paradigm was chosen with the idea to minimise the involvement of the retention component of WM, since the information is always present to the subject, and to require the manipulation of the linguistic and pictorial information in order to allow the correct resolution of the matching task. On the basis of lesion and imaging data, we predicted a greater interference with left-sided stimulation, in particular on the syntactic task. This could be attributed to a distant effect in the ventrolateral cortex, responsible for syntactic processing, or to a direct effect on the manipulation component of WM.