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Controlled retrieval and selection of action-relevant knowledge mediated by partially overlapping regions in left ventrolateral prefrontal cortex

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ABSTRACT

Information from long-term memory is used to identify appropriate responses to cues in the environment. Left ventrolateral prefrontal cortex (VLPFC) has been implicated in the effortful retrieval of semantic representations, as well as in the goal-directed selection between such representations. It has also been suggested that left posterior middle temporal gyrus (pMTG) stores the rules which VLPFC accesses to guide behavior. In the present event-related fMRI study, we examined the contributions of left VLPFC and pMTG in the controlled retrieval and selection of action-relevant knowledge associated with road signs. Controlled retrieval demands were manipulated by varying how recently the sign meaning was learned, and selection demands were manipulated by varying the number of competing meanings associated with a sign.
Activation in anterior VLPFC was consistent with controlled retrieval, activation in posterior VLPFC was consistent with selection, and activation in mid-VLPFC was sensitive to both manipulations. Left pMTG, while active, was not sensitive to these manipulations. These findings highlight the role of left VLPFC in accessing and maintaining goal-relevant information for the control of action.

Introduction

When deciding on a course of action, we often rely on previously learned rules, or prescribed guides for behavior (Merriam-Webster Dictionary, 1974). In recent years, neuroscientists have begun to explore the neural underpinnings of rule-guided behavior (Bunge and Wallis, 2008; Murray et al., 2000; Passingham et al., 2000). Neurophysiological and human neuroimaging studies have revealed that lateral prefrontal cortex (PFC) plays an important role in the learning and subsequent retrieval of rules from long-term memory. In particular, ventrolateral PFC (VLPFC; Brodmann's area [BA] 44, 45, 47) has been strongly implicated in rule representation (Bunge, 2004; Bunge et al., 2005; Bussey et al., 2001; Murray et al., 2000; Passingham et al., 2000). Indeed, in non-human primates, lesions to VLPFC or disruption of the connections between VLPFC and ipsilateral inferotemporal cortex result in performance impairments in rule learning and utilization (Bussey et al., 2002; Murray et al., 2000). Further, neuroimaging data show that left – and to a lesser extent right – VLPFC is active during rule retrieval, maintenance, and implementation, in a manner that is sensitive to rule complexity (e.g., Bunge et al., 2003; Crone et al., 2006; Donohue et al., 2008).

In humans, it is well-known that left VLPFC plays a critical role in language production and comprehension (Gabrieli et al., 1998). Thus, it is tempting to conclude that rules engage left VLPFC only because we tend to represent rules verbally. However, VLPFC is critical for rule representation even in non-human primates, who are largely devoid of linguistic capacity. VLPFC has strong associations with temporal cortex, and is therefore well-placed to assist in the retrieval of information stored therein (Petrides, 1996).

The literature on long-term memory in humans indicates that left VLPFC is involved in semantic encoding and retrieval (Badre and Wagner, 2002; Demb et al., 1995; Gabrieli et al., 1998; Poldrack et al., 1999; Wagner et al., 2001). One idea regarding left VLPFC function, known as the controlled retrieval hypothesis, argues that this region is important for guiding access to goal-relevant semantic knowledge (Goldberg et al., 2007; Wagner et al., 1997, 2001). An alternate idea, known as the selection hypothesis, contends that the role of left VLPFC is to select goal-relevant information from competing representations (Kan et al., 2006; Kan and Thompson-Schill, 2004; Persson et al., 2004; Thompson-Schill et al., 1997, 1999). Though in some cases manipulations of controlled retrieval can be bound to changes in selection (for discussion, Thompson-Schill et al., 2005), it is possible to manipulate controlled retrieval and selection demands separately, as selection is thought to operate post-retrieval (for review, Badre and Wagner, 2002).

Data from Badre et al., using a paradigm with materials modified from Wagner et al. (2001), used factor analysis to examine whether controlled retrieval and selection can be reduced to one putative

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cognitive process. Analysis of their behavioral and fMRI data supported a distinction between controlled retrieval and selection, with the former moderated by left anterior VLPFC (aVLPFC; BA 47/11), and the latter by mid-VLPFC (BA 44/45) and, to a lesser extent, posterior VLPFC (pVLPFC; BA 44/6) (Badre et al., 2005). Many of the aforementioned studies involved variants of a task in which participants must select a response from among a set of words. Here, we sought to test whether prior findings regarding the role of these left VLPFC subregions in controlled retrieval and selection would extend to a very different paradigm involving non-verbal stimuli and no overt response requirements.

Thus far, the majority of neuroscientific studies on rule representation have involved stimuli that have been arbitrarily associated with a task rule in the laboratory, immediately prior to testing. To examine how experience modulates rule-related activation in left VLPFC and temporal cortex for non-verbal stimuli, our group previously conducted a functional magnetic resonance imaging (fMRI) study in which participants retrieved the meanings to road signs that they had known for years ('Old'), learned immediately prior to testing ('New'), or never learned ('Untrained') (Donohue et al., 2005). We found that a large swath of left VLPFC (BA 44, 45, 47) activation was strongly and indiscriminately engaged across these three conditions. In contrast to left VLPFC, right VLPFC (BA 47/11) was sensitive to retrieval demands (New>Old), consistent with our prior work (Bunge et al., 2004). Finally, left posterior middle temporal gyrus (pMTG; BA 21) was exclusively active when participants were retrieving a sign meaning they learned prior to test (Old, New>Untrained), consistent with a role in representing rule knowledge.

The finding that left VLPFC was not modulated by controlled retrieval demands (Donohue et al., 2005) was unexpected, given the prior studies indicating that this region plays a key role in representing task rules (see Bunge, 2004). We tentatively concluded that this region was indiscriminately engaged as participants attempted to interpret the signs presented to them in this open-ended task. The lack of an effect of New>Old may have been accounted for by the fact that participants were explicitly told the meanings of the New signs, but not the Old signs, prior to testing; this aspect of the task design may have served to reduce the differences in controlled retrieval demands between the conditions.

In an attempt to further probe the role of left VLPFC in rule-guided behavior, the present study manipulated both controlled retrieval and selection demands in a task adapted from our prior study (Donohue et al., 2005). Participants encountered four conditions: 'Old' meanings were domestic road signs with their corresponding meaning; 'New' meanings were never-before learned foreign road signs in which participants were taught the appropriate meaning; 'Re-Old' meanings were the original meanings to a different set of domestic road signs, and 'Re-New' meanings were new, arbitrary second meanings associated with the signs presented in the Re-Old condition. Participants were explicitly given the meanings of all signs during the study phase.

At test, during fMRI data acquisition, a red or green border cued participants to retrieve either a new or old sign meaning. For the signs with two meanings, this cue was needed to determine which meaning to focus on; for the familiar or newly learned signs with only one meaning, this cue was largely redundant, but was included to maximize comparability between conditions.

This design allowed us to manipulate controlled retrieval and selection demands separately, and to test the role of left and right VLPFC in retrieval and selection with respect to non-verbal stimuli. Specifically, we sought to test whether anterior VLPFC (BA 47) is primarily driven by controlled retrieval demands, and the more posterior extent of VLPFC (BA 44/45) by selection demands.

Although our primary goal was to characterize the activation profile of VLPFC in this task, we also sought to examine the activation profile in left pMTG (BA 21). We predicted that left pMTG would be insensitive to New>Old signs (Donohue et al., 2005), but that this region might be more active during the viewing of signs with two meanings, given prior evidence that this region is more active when more information is retrieved (Badre et al., 2005).

Methods

Participants

Seventeen healthy, right-handed volunteers were recruited from the University of California, Davis, and greater Sacramento area, and all were financially compensated for their participation. The success of the selection manipulation hinged on participants' ability to remember both meanings associated with a given sign. In light of this consideration, four of the participants were excluded on the basis of poor memory for sign meanings (<70% correct on any of the four road sign conditions as measured in a post-scan test). As such, thirteen participants (6 male; 18–30 years old, $M = 23.1$) were included in the study.

Given that the task required knowledge of the meanings of road signs, we recruited participants who possessed valid U.S. Driver's Licenses, and had been driving for a minimum of one year (range of driving experience: 1.5–14.3 years, $M = 6.9$). Because of the large range of driving experience in the group, we examined whether driving experience correlated with overall performance on the task. This analysis revealed a non-significant negative correlation, $r = -0.17$, $p = .59$, indicating that amount of driving experience did not affect task performance. Although 12 of the 13 participants included in the study had traveled outside the United States, only three had ever driven while abroad; as such, we expected that these participants would be largely unfamiliar with the meanings of foreign road signs introduced in the experiment. Informed consent was obtained from all participants, and study procedures were approved by the Institutional Review Board at UC Davis.

Stimuli

A total of 90 images of road signs from the United States (i.e. 'domestic') and 45 images of foreign road signs were included in the study. The foreign road signs originated from a number of countries, and were selected on the basis that they did not closely resemble any common U.S. signs. Where possible, signs that did not contain any text were selected for the experiment; for signs containing text, the wording was blurred so that participants would be unable to read them. The blurring was done in such a way as to simulate the way in which text on a sign might appear from a distance (Donohue et al., 2005).

The task included four conditions: Old, New, Re-Old, and Re-New (Fig. 1). Old stimuli consisted of 45 randomly selected domestic road signs whose correct meanings were provided during the study session. New stimuli consisted of 45 foreign signs whose correct meanings were provided during the study session. The labels 'Old' and 'New' refer to the fact that the participants were likely to have known the meaning of the U.S. signs but not the foreign signs prior to testing. Relearned stimuli consisted of 45 additional randomly selected domestic road signs, which had two different meanings during the study phase: the correct meaning (Re-Old), and a new meaning (Re-New). The new meanings were randomly assigned from a bank of 45 foreign road signs not already included in the study. The assignment of domestic signs to Old or Relearned conditions was counterbalanced across participants, such that each individual received one of four possible study lists.

Training session

In a pre-scan training session, participants were provided with a crib sheet including images of all the signs they needed to learn, domestic and foreign, along with their corresponding meaning(s). They participated in three interactive computerized training blocks in