Cognitive Control, Semantic Memory, and Priming: Contributions from Prefrontal Cortex

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ABSTRACT Cognitive control refers to an ensemble of mechanisms that constrain our thoughts and responses in accordance with our goals. Functional brain imaging studies have provided important insights regarding the functional and neuroanatomical bases of cognitive control and have illustrated that cognitive control has an influence on and is influenced by long-term memory. This chapter provides an overview of elemental forms of cognitive control, their relation to working memory, and their dependence on prefrontal cortex (PFC). The interaction between cognitive control and memory is then considered within the context of retrieving goal-relevant knowledge from semantic memory, with a focus on understanding how PFC guides controlled retrieval. Finally, the nature of priming—a form of nondeclarative (or implicit) memory that is reflected as nonconscious effects of previous experience on future behavior—is described en route to illustrating how reductions in cognitive control demands can follow experience-based changes in nondeclarative memory.

Cognitive control refers to mechanisms that permit an individual to access and work with internal representations in a goal-directed manner. In so doing, cognitive control supports context-relevant stimulus processing, the retrieval and online maintenance of knowledge, and the transformation of representations to satisfy our goals. Prefrontal cortex (PFC) is a central component of the neural circuitry underlying cognitive control, including the control of memory; flexible behavior often depends on PFC mechanisms that support access to long-term knowledge. Accordingly, the specification of cognitive control processes, their dependence on PFC, and their interactions with long-term memory is of fundamental importance (Stuss and Benson, 1984; Goldman-Rakic, 1987; Schacter, 1987b; Shallice, 1988; Petrides, 1994; Shimamura, 1995; Fuster, 1997; Miller and Cohen, 2001; Wagner, 2002).

In this chapter, we consider neuroimaging evidence regarding PFC contributions to cognitive control, and the interactions between control mechanisms and memory. We first delineate the elemental processes that constitute working memory and cognitive control, and their organization within PFC. We then provide an in-depth discussion of one control mechanism to illustrate how cognitive control can interact with long-term memory. This discussion considers how cognitive control supports retrieval from declarative (or explicit) memory, as revealed through PFC contributions to the controlled retrieval of task-relevant semantic knowledge. We conclude by exploring the relation between this PFC control mechanism and priming, a nondeclarative (or implicit) form of memory, to illustrate how reductions in cognitive control demands can follow experience-based changes in long-term memory.

Working memory and cognitive control

Language comprehension, problem solving, goal satisfaction, and other high-level cognitive functions depend on working memory, which refers to our ability to maintain and manipulate active representations (Miller, Galanter, and Pribram, 1960; Fuster and Alexander, 1971; Goldman-Rakic, 1987). Working memory is a multifaceted rather than unitary faculty. A prominent model of human working memory proposes that this ability depends on at least three components: a buffer for the short-term maintenance of verbal information, a buffer for the maintenance of visuospatial information, and a “central executive” that gates and manipulates representations held in these buffers (Baddeley and Hitch, 1974; Baddeley, 1986). This influential perspective has proved to be an effective framework for examining the architecture of working memory, although, as
we will see, working memory can also be conceptualized as an integrated set of cognitive control processes.

**Verbal Working Memory** Verbal working memory constitutes the maintenance of speech-based (phonological) representations, as when we subvocally rehearse a phone number while preparing to dial it. Verbal working memory depends on a system termed the phonological loop, which consists of two components: a phonological store, which represents active phonological information, and an articulatory control process, which rehearses the contents of the store and reactivates long-term phonological knowledge (Baddeley and Hitch, 1974). Support for this architecture comes from behavioral and neuropsychological observations that the two components of the phonological loop are dissociable (Baddeley, 1986; Smith and Jonides, 1995).

Neuroimaging studies of verbal working memory consistently implicate frontal, parietal, and cerebellar regions that work together to support the phonological loop (Smith and Jonides, 1999; figure 51.1). Demands on the articulatory control process elicit activation in structures important for speech production, including left ventrolateral PFC (approximately Brodmann’s area [BA] 44; Broca’s area) and left premotor and supplementary motor cortices (BA 6) (Pauleau, Frith, and Frackowiak, 1993; Awh et al., 1996; Fiez et al., 1996). These frontal regions are thought to maintain active phonological representations stored in left or bilateral inferior parietal cortices (Awh et al., 1996; Jonides, Schumacher, et al., 1998; Bunge et al., 2001; but see Chein and Fiez, 2001). Cerebellar subregions may integrate inputs from ventrolateral PFC and parietal regions, providing a corrective signal that refines the rehearsal process (Desmond et al., 1997).

![Figure 51.1](image)

**Figure 51.1** Neural correlates and component processes of phonological working memory. (A) Left ventrolateral prefrontal cortex (VLPFC) and posterior parietal cortex demonstrate greater activation during the encoding and maintenance of visually presented words. (Data from D. Badre and A. D. Wagner, 2004. Selection and conflict monitoring in prefrontal cortex: Assessing the specificity of cognitive control. *Neuron* 41:473–487. Used with permission.) (B) Component processes supporting phonological working memory and their neural substrates. Visually presented information is translated into phonological representations, which are actively represented (stored) in posterior parietal cortex. These representations passively decay over the course of seconds in the absence of subvocal rehearsal, which is mediated by left VLPFC (Broca’s area). Recurrent loops between left VLPFC and posterior parietal cortex allow information to be actively maintained for a prolonged period. (Adapted with permission from E. E. Smith and J. Jonides, 1998. Neuroimaging analyses of human working memory. *Proc. Natl. Acad. Sci. U.S.A.* 95:12061–12068. Copyright 1998, National Academy of Sciences, U.S.A.)
The contributions of specific PFC subregions to verbal working memory partially depend on the amount of information that must be maintained. Whereas control processes mediated by left ventrolateral PFC appear sufficient to maintain low working memory loads, when the amount of information to be maintained begins to approach an individual's working memory capacity limit, activation also emerges in bilateral dorsolateral PFC (BA 9/46) (Rypma et al., 1999). Dorsolateral PFC activation may reflect a shift to reliance on additional cognitive control processes, such as those supporting the "chunking" of information (but see Veltman, Rombouts, and Dolan, 2003). This interpretation is consistent with the idea that central executive mechanisms are engaged when working memory maintenance demands approach or exceed capacity limits (Baddeley and Hitch, 1974), and further suggests that, in humans, dorsolateral PFC supports nonmaintenance cognitive control processes, a hypothesis to which we will return.

**Spatial and Object Working Memory** Visuospatial working memory allows us to maintain visual representations of objects and knowledge of the position of objects in space. As with verbal working memory, this ability depends on PFC–posterior neocortical interactions (Chafee and Goldman-Rakic, 2000; Miller and Cohen, 2001). However, whereas verbal working memory is associated with left PFC, visuospatial working memory in humans is differentially associated with right-lateralized or bilateral PFC (D'Esposito et al., 1998; Smith and Jonides, 1999; Prabhakaran et al., 2000). Visuospatial working memory also engages occipitotemporal and parietal cortices that support object and spatial representations; PFC is thought to control the maintenance of spatial and object codes through reciprocal interactions with these posterior representations. One hypothesis regarding rehearsal in spatial working memory is that spatial information is maintained through shifts of spatial selective attention to location-specific representations (Awh and Jonides, 1998).

In contrast to the traditional two-store model of working memory, according to which object and spatial representations are maintained by a single buffer, termed the visuospatial sketchpad (Baddeley, 1986), recent evidence suggests that object and spatial working memory may be separable (e.g., Farah, 1988; Baddeley, 1994; Carlesimo et al., 2001). Behaviorally, spatial distraction impairs spatial working memory more than visual working memory, whereas visuo-object distraction has the reverse effect (e.g., Tresch, Sinnamon, and Scannram, 1993). At the neural level, single-cell recordings in infrabulbar primates indicate that some PFC neurons maintain spatial representations, others maintain object representations, and yet others maintain an integration of spatial and object information (Rao, Rainer, and Miller, 1997; Rainer, Asaad, and Miller, 1998). Thus, segregation and interaction characterize working memory for space and objects.

Object working memory and spatial working memory are not strictly topographically segregated in PFC. In infrahuman primates, object, spatial, and integrative neurons are present in ventrolateral and dorsolateral PFC (Rainer, Asaad, and Miller, 1998; figure 51.2), with there being a moderate bias for a greater proportion of object working memory neurons in ventrolateral PFC and spatial working memory neurons in dorsolateral PFC (Wilson, O'Scalaidhe, and Goldman-Rakic, 1993). In humans, many neuroimaging studies have failed to observe a marked segregation between spatial and object working memory within PFC, with both forms of maintenance often eliciting activation in ventrolateral and dorsolateral PFC (e.g., McCarthy et al., 1996; D'Esposito et al., 1998; Nystrom et al., 2000). By contrast, other studies suggest that spatial working memory and object working memory are at least partially separable, with a subregion of the superior frontal sulcus being differentially associated with spatial working memory (Courtney et al., 1998; Haxby et al., 2000; Sala, Rama, and Courtney, 2003; see also Alain et al., 2001).

Although the degree of topographic segregation between spatial and object working memory in PFC remains uncertain, the collective data indicate that a comprehensive model of human working memory requires separable systems for object, spatial, and phonological information, and an understanding of how these different types of information are integrated. Neuropsychological, behavioral, and neuroimaging data also suggest that a fourth system may subserve working memory for semantic knowledge (e.g., Martin, Shelton, and Yaffe, 1994; Demb et al., 1995; Shivde and Anderson, 2001).

**Cognitive Control** The central executive, as originally proposed, is a limited-capacity attentional system that coordinates working memory maintenance buffers and manipulates their contents (Baddeley, 1986). The executive also is thought to mediate selective attention and the inhibition of task-irrelevant representations. Although it was once conceptualized as a monolithic component of working memory, there is little behavioral evidence for a single executive processor (e.g., Towse and Houston-Price, 2001). Rather, executive functions, which may include both working memory manipulation and maintenance processes, likely emerge from a set of elemental cognitive control mechanisms.

Cognitive control refers to processes that constrain our thoughts and responses in accordance with our goals. Putative control functions include dual-task coordination and task switching (task management); retrieval of goal-relevant information from long-term memory (controlled retrieval); selection of appropriate responses (response selection) and
Inhibition of inappropriate responses (response inhibition); resolution of distraction from competing representations (interference resolution); transformation, reordering, or updating of information maintained in working memory (manipulation); and evaluation of whether information in working memory meets the criteria associated with one's goal (monitoring).

**Biased competition theory** According to the biased competition framework (Desimone and Duncan, 1995), a similar neural mechanism may underlie each of the control functions just hypothesized (Miller and Cohen, 2001). Biased competition theory asserts that, in the absence of cognitive control, the representation most strongly activated by response cues in an automatic, bottom-up fashion will serve as the basis for behavior, irrespective of whether the representation is task relevant. However, cognitive control, in the form of top-down excitatory signals deriving from PFC, can bias information processing in favor of weaker but task-relevant representations, enhancing these representations and indirectly suppressing task-irrelevant competitors through lateral inhibitory interconnections between representations (Cohen,
Dunbar, and McClelland, 1990). This top-down bias signal is argued to constitute the fundamental basis of cognitive control, enabling the selection of appropriate goal representations, the retrieval of target knowledge from working memory and long-term memory (LTM), and the execution of context-appropriate responses (see also Shinamura, 1995).

Intimately related to the biased competition framework is the hypothesis that the anterior cingulate cortex (ACC) and PFC play distinct roles in cognitive control (Cohen, Braver, and O’Reilly, 1996; MacDonald et al., 2000; figure 51.3). From this perspective, the rostral zone of ACC serves to detect the presence of conflict (i.e., the simultaneous activation of multiple competing representations) and signals PFC to resolve the conflict by up-regulating control (i.e., increasing the top-down biasing of task-appropriate representations). Computational models and some neuroimaging data suggest that ACC may selectively detect conflict between competing responses (Botvinick et al., 2001; Milham et al., 2001; van Veen et al., 2001). However, other evidence points to a more general function, with ACC detecting conflict at multiple processing stages (see van Veen and Carter, 2002; Badre and Wagner, 2004).

Dissociable mechanisms in dorsolateral and ventrolateral PFC A complementary perspective on cognitive control is the hypothesis that “maintenance” and “manipulation” constitute interacting but dissociable control mechanisms that differentially depend on distinct PFC subregions. From this perspective, the rehearsal processes that support maintenance in verbal, object, and spatial working memory are themselves forms of cognitive control. Accordingly, ventrolateral PFC regions are argued to control the retrieval of task-relevant representations and their active maintenance. By contrast, dorsolateral PFC functions monitor the contents of working memory and/or manipulate active representations in the service of completing the current goal (Petrides, 1994; Owen, Evans, and Petrides, 1996; D’Esposito et al., 1996; but see Raye et al., 2002; Veltman, Rombouts, and Dolan, 2003).

Neuroimaging data provide empirical support for the differential roles of ventrolateral and dorsolateral PFC subregions in cognitive control. As already discussed, neuroimaging studies indicate that dorsolateral PFC is recruited at higher verbal working memory loads, suggesting that it is not involved in maintenance per se but instead may play a role in reorganizing or manipulating representations to facilitate maintenance (Rypma et al., 1999). Dorsolateral regions are also differentially engaged when we reorder (D’Esposito, Postle, Ballard, et al., 1999; Postle, Berger, and D’Esposito, 1999; Wagner, Maril, Bjork, et al., 2001) or update (Salmon et al., 1996; Garavan et al., 2000) representations in working memory (figure 51.4). Thus, dorsolateral PFC mechanisms may operate on and transform the contents of working memory.

In addition to its role in active maintenance, ventrolateral PFC supports the control of thought and action in ways that are just beginning to be understood. Subregions of ventrolateral PFC are implicated in the controlled retrieval and selection of task-relevant long-term knowledge (Petrides, 1994; Thompson-Schill et al., 1997; Badre and Wagner, 2002), a point to which we return in the next section. Other subregions of left ventrolateral PFC appear to resolve interference in verbal working memory (Jonides, Smith,
Frontopolar control processes  Extant data also implicate frontopolar cortex (FPC) as central to cognitive control. However, perhaps owing to a paucity of comparative data, FPC remains poorly understood at the functional level, even though neuroimaging studies consistently observe FPC activation during episodic retrieval, complex working memory, and higher-level cognitive tasks (Fletcher and Henson, 2001; Ramnani and Owen, 2004). Findings from the task management literature suggest that FPC is active when subjects must maintain a primary task goal or task-relevant information while simultaneously attending to a secondary goal or task (Koechlin et al., 1999; Brauer and Bongiolatti, 2002; Badre and Wagner, 2004). An emerging literature on analogical reasoning further suggests that FPC is important for integrating disparate representations or relations (Christoff et al., 2001; Kroger et al., 2002). Given these findings, FPC involvement in episodic retrieval may reflect processes that integrate retrieved information with response criteria or context information held in working memory, thus permitting decisions about whether the retrieved information satisfies the mnemonic goal (e.g., Rugg and Wilding, 2000).

As suggested by this formulation of frontopolar function, one intriguing development over the past decade has been the emerging conceptualization of cognitive control as an ensemble of processes that intimately interact with mnemonic and cognitive systems. Accordingly, efforts to delineate cognitive control may benefit from approaches that examine the role of control processes in a variety of memory domains. With this in mind, we now turn to consider evidence regarding the interaction between cognitive control and LTM, with an in-depth discussion of a particular form of control (controlled retrieval). In the next section, we delineate how controlled retrieval serves to activate declarative knowledge structures through a top-down biasing of semantic memory. The chapter concludes with a consideration of how nondeclarative memory influences controlled retrieval demands.

Cognitive control and semantic memory

Recovering context-relevant meaning about the world allows us to flexibly use long-term knowledge to generate goal-consistent responses. Let us say that we need to pound a nail and the only objects available are standard office supplies, such as a stapler, computer, and the like. Although information strongly associated with each concept (e.g., that staplers are used to bind documents) is of little assistance in this context, we are capable of accessing other weakly associated, but context-relevant, knowledge about the objects. Thus, we recall that staplers are heavy and fairly w - objects, whereas computers tend to be fragile. Such knowledge may ultimately support the inference that the stapler is a suitable substitute for a hammer. Importantly, our ability to retrieve this information requires processes that guide
access to, or control the retrieval of, relevant knowledge when strongly associated semantic information is insufficient to meet task demands.

This example illustrates how some situations require control processes that guide retrieval from semantic memory, which is a declarative (or explicit) form of LTM that represents our general knowledge about the world, including facts, concepts, and vocabulary (Tulving, 1972). In this section, we consider when and how cognitive control mediates semantic retrieval. We begin by briefly introducing basic concepts regarding the organization of semantic knowledge, and then consider how semantic information can be retrieved through automatic or controlled processes. The consequences of left PFC lesions for semantic retrieval are subsequently discussed as a foundation for understanding neuroimaging data regarding the role of PFC in controlled semantic retrieval.

**Structure of Semantic Knowledge** Our aim is to consider the contributions of PFC to cognitive control and to specify how control processes interact with LTM; as such, a full discussion of the structure of semantic knowledge is beyond the scope of this chapter (see Smith and Medin, 1981; Martin and Chao, 2001). However, a few characteristics of semantic memory are relevant for understanding the processes that retrieve semantic knowledge. First, semantic information is stored in a distributed, associative network that links conceptual representations and components of representations. Second, the associations between representations vary in strength, depending on the frequency of their prior co-occurrence, their overlap in features, and their categorical relations. Finally, multiple representations can compete for processing and retrieval through mutually inhibitory interactions.

At the neural level, semantic knowledge is distributed throughout posterior neocortex, including lateral and ventral regions of the temporal lobes (for review, see Martin and Chao, 2001). Patients suffering from the temporal variant of semantic dementia demonstrate a marked loss of semantic knowledge due to degeneration of temporal cortices, and more focal temporal lesions can result in category-specific dementia—the loss of knowledge associated with certain taxonomic categories. These latter deficits suggest that different semantic primitives correlate more strongly with certain categories, with their representation being differentially dependent on particular posterior cortical regions (Farah and McClelland, 1991; Martin and Chao, 2001; Thompson-Schill, 2003; but see Caramazza and Shelton, 1998). In line with this interpretation, neuroimaging studies demonstrate a systematic relation between activation in temporal cortical subregions and the processing of specific semantic categories or features (Martin and Chao, 2001). For example, subregions within inferotemporal cortex are differentially active during the processing of living versus non-living concepts (figure 51.5), perhaps revealing markers of stored primitives related to visual versus functional semantics (e.g., Martin et al., 1996; Chao, Haxby, and Martin, 1999; Thompson-Schill et al., 1999; but see Pilgrim et al., 2002). Other putative primitives, such as knowledge about color versus action, result in functional dissociations in lateral temporal cortex (e.g., Martin et al., 1995; see also Kourtzi and Kanwisher, 2000; Kellenbach, Brett, and Patterson, 2003). Collectively, these data indicate that semantic knowledge is stored in a distributed (Haxby et al., 2001) but systematic manner in posterior neocortex.

Complementary data indicate that long-term semantic knowledge is not stored in PFC, although PFC mechanisms appear to affect our ability to work with semantic information. For example, multidimensional scaling reveals that the structure of semantic memory is similar in patients with PFC damage and in healthy control subjects (see figure 51.5), although such patients sometimes demonstrate difficulties in retrieving stored knowledge (Sylvester and Shimamura, 2002). These latter deficits beg the question, when and how does cognitive control interact with semantic memory to support knowledge retrieval?

**Multiple Routes to Memory** Semantic retrieval constitutes the recovery of conceptual representations, and accordingly depends on processes that activate stored knowledge, essentially bringing long-term information into working memory. Behavioral evidence indicates that the retrieval of task-relevant semantic knowledge can occur in a relatively automatic (or bottom-up) fashion or in a more controlled (or top-down) manner, with these two retrieval routes representing the ends of a continuum (for review, see Neeley, 1991).

*Automatic retrieval* occurs when the association between a retrieval cue and relevant knowledge is sufficiently strong that presentation of the cue serves to automatically activate, or make accessible, the target knowledge (figure 51.6). Automatic retrieval is thought to derive from an associative mechanism whereby bottom-up activation of the cue's representation serves to activate other, strongly associated representations. Automatic retrieval (1) occurs rapidly, (2) is obligatory, and (3) is context independent, resulting in recovery of strongly associated knowledge regardless of whether the knowledge is task relevant.

By contrast, *controlled retrieval* mechanisms are recruited when automatically retrieved knowledge is insufficient to meet task demands or when an individual comes to expect that the strategic retrieval of certain conceptual representations will aid performance. Controlled retrieval is thought to depend on a top-down bias mechanism whereby task or context representations facilitate activation of weakly associated, task-relevant knowledge (see figure 51.6).
Relative to automatic retrieval, controlled retrieval (1) is slower and more effortful, (2) can bias retrieval of task-relevant information even in the presence of more strongly associated but task-irrelevant information, and (3) can either directly or indirectly inhibit the retrieval of prepotent, task-irrelevant information.

**Semantic Retrieval and Prefrontal Cortex** Left ventrolateral PFC lesions result in impairments on semantic tasks that require some form of cognitive control during semantic or lexical retrieval (e.g., Swick and Knight, 1996; Thompson-Schill et al., 1998; Metzler, 2001). For instance, although patients with Broca’s aphasia, a language disorder that follows left PFC damage, show intact semantic priming effects that are due to automatic retrieval processes (Blumstein, Milberg, and Shrier, 1982; Hagoort, 1997), they fail to show normal levels of semantic priming when the cue–target associative strength is weak or ambiguous (Milberg, Blumstein, and Dworetzky, 1987; Metzler, 2001) or when the context requires strategic assessment of the utility of primes in cuing upcoming targets (Milberg et al., 1995). Left PFC lesions also result in difficulty retrieving a weak associate of a cue when faced with competition from other associated knowledge (Thompson-Schill et al., 1998). Thus, deficits occur in situations in which healthy individuals likely use cognitive control to effectively access relevant semantic knowledge. Consistent with this interpretation, even temporary disruption of anterior left ventrolateral PFC with transcranial magnetic stimulation results in a performance deficit when controlled access to semantic knowledge is required, but not when stimuli are processed in a nonsemantic manner (Devlin, Matthews, and Rushworth, 2003).

Neuroimaging studies provide complementary high spatial resolution evidence that more precisely maps semantic processing functions to ventrolateral PFC. Extensive
imaging data indicate that anterior left ventrolateral PFC (BA 47/45), which falls rostral and inferior to the left PFC region associated with phonological working memory, is engaged when access to semantic knowledge is required (Buckner, Raichle, and Petersen, 1995; Fiez, 1997; Poldrack et al., 1999; Wagner, 1999). For example, greater left PFC activation is observed during the retrieval of semantic knowledge associated with a word than during word reading (e.g., Petersen et al., 1988), and when making semantic relative to nonsemantic decisions about stimuli (e.g., Kapur et al., 1994; Gabrieli et al., 1996). This is the case even when task difficulty is greater during nonsemantic processing, indicating that left PFC activation is modulated by semantic retrieval demands rather than by demands on global attentional resources (Demb et al., 1995). Thus, extant data implicate anterior left ventrolateral PFC in some form of cognitive control that facilitates access to task-relevant semantic knowledge.

Cognitive Control and Recovering Meaning The precise nature of this left ventrolateral PFC control process and its role in semantic retrieval remain controversial (e.g., Thompson-Schill et al., 1997; Gabrieli, Poldrack, and Desmond, 1998; Badre and Wagner, 2002; Gold and Buckner, 2002). From one perspective, left ventrolateral PFC supports controlled semantic retrieval, wherein PFC represents the conceptual context and biases retrieval of context-relevant information when that information is not recovered through automatic retrieval processes. By contrast, a selection hypothesis posits that left ventrolateral PFC does not support semantic retrieval (Thompson-Schill et al., 1997). Rather, retrieval is argued to emerge entirely within posterior neocortex, where knowledge associated with a given cue is retrieved upon cue presentation through bottom-up processes. Once representations are retrieved, left PFC selects those that are task relevant from among competing, irrelevant representations.

A critical prediction of the controlled retrieval hypothesis, but not the selection account, is that increased left PFC activity should occur when the associative strength between a retrieval cue and target knowledge is weak relative to when it is strong, and that this should be the case even when using a semantic processing task that requires minimal selection. A recent fMRI study (Wagner, Paré-Blagoev, et al., 2001) tested this prediction, varying controlled retrieval demands by (1) manipulating the preexperimental associative strength between the cue and the correct target and (2) further manipulating retrieval demands by varying the number of targets to be considered (figure 51.7) (cf. Thompson-Schill et al., 1997). fMRI results revealed that, even when selection demands are held constant and to a minimum, activation in anterior left ventrolateral PFC increases with the number of targets to be considered, and, critically, is greater when the cue–target associative strength is weak rather than
strong. Conceptually similar effects of associative strength on left PFC activation are also seen when subjects make categorical decisions about less prototypical exemplars (e.g., bird-astirch) than about more prototypical exemplars (e.g., bird-robin) (Roskies et al., 2001), and when subjects make analogical reasoning decisions about weakly associated relative to strongly associated word pairs. Such findings indicate that left ventrolateral PFC is engaged when target semantic knowledge must be retrieved in a controlled manner.

It should be emphasized that controlled retrieval and selection demands are likely to be highly correlated, suggesting a possible reconciliation of the two perspectives (Badre and Wagner, 2002). Specifically, controlled retrieval is necessary when task-relevant information does not come to mind through automatic, bottom-up processes. This can occur either because task-relevant information is weakly associated with a presented retrieval cue, resulting in insufficient bottom-up activation, or because more strongly associated information competes with recovery of the target knowledge, resulting in high selection demands. In both cases, a top-down bias signal may be required to effectively retrieve the relevant representation (see figure 5.1.6). Accordingly, controlled retrieval demands typically increase as selection demands increase, but also increase because of other factors that make automatic access to relevant information insufficient or ineffective, such as weak cue–target associative connections.

Cognitive control and priming: On the road to automaticity

The evidence discussed in the preceding section indicates that a controlled retrieval process interacts with declarative memory to support knowledge recovery, thus guiding flexible, goal-directed behavior. Because controlled retrieval is one end of a processing continuum, it is important to understand how knowledge recovery shifts from depending on more controlled to more automatic retrieval mechanisms. As we discuss in this final section, neuroimaging studies of repetition priming indicate that reductions in controlled retrieval demands follow experience-based modifications of semantic memory.

Repetition priming is a nondeclarative (or implicit) form of LTM that is expressed as an experience-based change in behavior, is not necessarily accompanied by conscious recollection, and is preserved following medial temporal lobe damage (Schacter, 1987a; Squire, 1992; Gabrieli, 1998). At the behavioral level, priming refers to instances in which an earlier encounter with a stimulus alters later responding to that same stimulus or to a related stimulus. Behavioral changes include an increased speed of responding, increased response accuracy, or biased responding.

Although there are multiple forms of priming, most instances fall into one of two broad categories, perceptual and conceptual (Roediger and McDermott, 1999). Perceptual priming refers to an enhanced ability to identify a stimulus due to previous exposure to the stimulus, whereas conceptual priming refers to facilitated processing of the meaning of a stimulus or enhanced access to a concept due to prior processing of the stimulus’s meaning or retrieval of the concept. In this section, we discuss perceptual and conceptual priming, and describe neuroimaging correlates of these forms of nondeclarative memory. We then focus on the relation between conceptual priming and controlled retrieval, emphasizing how priming-related changes in PFC activation mark a shift from controlled to automatic retrieval.

Perceptual Priming  Perceptual priming is often revealed as either an increased likelihood of completing a perceptual fragment, such as a word stem (e.g., sta____), with a previously encountered stimulus (e.g., stamp), or a faster and more accurate identification of degraded stimuli as a result of prior
exposure to those stimuli. Perceptual priming is sensitive to the degree of perceptual overlap between the initial and repeated encounter with a stimulus. For example, this form of priming is modality-specific, being greater when the initial and repeated encounters occur in the same modality as opposed to different modalities (Jacoby and Dallas, 1981). By contrast, perceptual priming is comparable irrespective of whether attention at study is focused on the meaning of the stimulus or on its structural form (Jacoby and Dallas, 1981).

Perceptual priming is thought to reflect learning in perceptual representation systems (Tulving and Schacter, 1990). Perceptual representation systems encode and retain pre-semantic perceptual information (in the form of perceptual records) about encountered words and objects, and are thought to depend on modality-specific sensory cortices. Perceptual representation systems include a word form system that can be further differentiated into visual and auditory systems that represent seen and spoken words, respectively, and a structural representation system that represents the visual form of objects.

Neuroimaging studies of perceptual priming typically demonstrate decreased activation in modality-sensitive cortical regions that were engaged during initial stimulus processing (Schacter and Buckner, 1998; Wagner and Koutstaal, 2002; figure 51.8), although increases are sometimes observed on repetition of unfamiliar stimuli (Schacter et al., 1995; Henson, Shallice, and Dolan, 2000). Priming-related activation decreases persist across delays of multiple days, indicating that such experience-based reductions in activation depend on a form of LTM (van Tuerkouw, Ellmore, and Martin, 2000).

Neural priming effects in human sensory cortex resemble the phenomenon of repetition suppression in infrahuman primates, wherein repeated exposure to a stimulus leads to a reduction in the firing rate of neurons in higher-order

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**Figure 51.8** Repetition priming paradigm, neural priming effects, and a hypothesized neural “sharpening” mechanism. (A) On priming tasks, subjects initially study a set of stimuli; in this instance, making a semantic decision (size judgment) about visually presented objects. Subsequently, during the critical test, semantic decisions are made about previously studied (primed) and novel (unprimed) stimuli. (B) fMRI scanning during the critical test revealed priming-related activation reductions in fusiform cortex (circled) and left ventrolateral PFC (arrow); the former reflect neural correlates of perceptual priming and the latter reflect correlates of conceptual priming. (Data from W. Koutstaal, A. D. Wagner, M. Rotte, A. Maril, R. L. Buckner, and D. L. Schacter, 2001. Perceptual specificity in visual object priming: Functional magnetic resonance imaging evidence for a laterality difference in fusiform cortex. *Neuropsychologia* 39:184–199. Copyright 2001, with permission from Elsevier.) (C) Hypothesized experience-based changes in a neural network representing visual object features. Initially, neurons coding for relevant and irrelevant features respond during object processing, but each encounter serves to prune or sharpen the representation such that only neurons coding relevant features subsequently fire. Such a change may result in more efficient perception (i.e., behavioral priming) and an overall reduction in the mean firing rate of a population of neurons (i.e., repetition suppression or neural priming). (Reprinted from C. L. Wiggs and A. Martin, 1998. Properties and mechanisms of perceptual priming. *Curr. Opin. Neurobiol.* 8:227–233. Copyright 1998, with permission from Elsevier.)
visual regions (Desimone, 1996). Given this parallel, one hypothesis is that priming-related activation reductions in neuroimaging studies reflect a "sharpening" or "tuning" of perceptual representation systems (Wiggs and Martin, 1998). From this perceptive, multiple neurons are engaged during initial perception of a stimulus, with some coding less relevant features than others. In the course of this initial processing, the perceptual representation system is sharpened such that neurons that code unnecessary features of the stimulus are pruned, resulting in reduced responding by those neurons on reencounter with the stimulus (see figure 51.8). This sharpening of the representation may result in efficient stimulus reprocessing, thus giving rise to facilitated behavior. Although an intriguing possibility, priming-related activation reductions could also reflect a reduction in the duration of neural processing due to (1) experience-based strengthening of synaptic connections (see figure 51.6), thus resulting in more rapid network settling (Henson and Rugg, 2003), or (2) rapid stimulus-response learning and a shift to a response retrieval strategy of stimulus processing on reencounter (Dobbins et al., 2004).

Conceptual Priming Conceptual priming refers to the increased likelihood of generating a concept in response to a test cue due to previous processing of the concept during an unrelated study phase. For example, when participants are presented with a category cue (e.g., "fruit") and are asked to generate the first few exemplars that come to mind, the probability of spontaneously generating a given exemplar (e.g., "cherry") is higher if the exemplar had appeared on a prior study list. Conceptual priming is also revealed on semantic classification tasks, wherein prior processing of a stimulus's meaning results in faster classification of the stimulus along a particular semantic dimension.

In contrast to perceptual priming, conceptual priming is modality-independent. For example, cross-modality priming (auditory study, visual test) is comparable to within-modality priming (visual study, visual test) on semantic classification tasks (Vaidya et al., 1997). Moreover, whereas perceptual priming is insensitive to the level of semantic elaboration during initial processing, conceptual priming is greater when semantic features of a stimulus are attended during study than when perceptual features are attended. Finally, conceptual priming is intact following focal lesions to modality-specific sensory cortices, whereas such lesions impair perceptual priming (e.g., Gabrieli et al., 1995). By contrast, conceptual priming is impaired in patients with Alzheimer's disease, who suffer pathological changes in amodal association areas of frontal, temporal, and parietal cortex, as well as in the medial temporal lobe (Heindel et al., 1989). This pattern suggests that temporal association cortices that represent semantic knowledge, and perhaps frontal cortices that permit controlled access to this knowledge, may be important for conceptual priming (Swick and Knight, 1996).

In a pattern that parallels that seen during comparisons of automatic versus controlled retrieval conditions, neuroimaging investigations of conceptual priming reveal that the anterior and posterior extents of left ventrolateral PFC show reduced activation during repeated (primed) relative to initial (unprimed) semantic processing of stimuli (e.g., Raichle et al., 1994; Gabrieli et al., 1996; Wagner et al., 1997; Schacter and Buckner, 1998). For example, activation is weaker when making semantic classification decisions about primed relative to unprimed objects or words (see figure 51.8), and this is the case even following study–test retention intervals of more than 24 hours (Wagner, Maril, and Schacter, 2000). Reductions in left ventrolateral PFC activation are observed in patients with global amnesia, suggesting that these changes reflect computational benefits deriving from the nondeclarative memory processes that support conceptual priming at the behavioral level (Buckner and Kontstal, 1998; Gabrieli, Poldrack, and Desmond, 1998). In addition to changes in PFC activation, conceptual priming is correlated with activation reductions in posterior cortical regions that may represent long-term conceptual knowledge, including ventral and lateral temporal cortices (e.g., Raichle et al., 1994; Blaxton et al., 1996). These outcomes indicate that conceptual priming stems from experience-based "tuning" of semantic memory, mirroring at the conceptual level the sort of processes hypothesized to underlie perceptual priming (cf. Dobbins et al., 2004).

The changes in semantic memory that support conceptual priming could emerge in a number of ways. For example, the tuning of semantic memory may constitute a sharpening of conceptual representations, perhaps through retrieval-induced suppression, whereby the initial retrieval of relevant stimulus features serves to suppress or inhibit less relevant features (Anderson, Bjork, and Bjork, 1994). Suppression of irrelevant features would reduce the degree to which these features compete for retrieval, thus facilitating the subsequent recovery of recently retrieved knowledge. In addition, modifications in semantic memory are likely to emerge at least partially from a strengthening of the connections or associations between a response cue and the initially retrieved relevant features associated with the cue/concept. This strengthening of cue–target associations facilitates subsequent retrieval of these target representations by increasing the effects of bottom-up inputs on knowledge recovery.

Controlled Retrieval and Conceptual Priming The consistent observation that reductions in left PFC activation accompany conceptual priming suggests that cognitive control demands can decline following experience-based changes in semantic memory (see figure 51.6). That is, PFC
priming effects may mark the beginnings of a transition from reliance on more controlled to more automatic retrieval mechanisms (Raichle et al., 1994; Demb et al., 1995; Fletcher, Shallice, and Dolan, 2000). From this perspective, controlled semantic retrieval tunes semantic memory, strengthening the representations of initially recovered knowledge and perhaps weakening those of competing knowledge. Critically, this increased accessibility of recently relevant knowledge reduces the computational demands on controlled retrieval when this knowledge must be retrieved in the future. Such reductions in controlled retrieval demands reflect both an increased automaticity of target knowledge retrieval due to strengthened cue–target associations (Raichle et al., 1994) and a reduction of competition from task-irrelevant representations (Thompson-Schill, D'Esposito, and Kan, 1999). Thus, these neural priming effects illustrate the point that interactions between cognitive control and LTM are bidirectional: cognitive control affects retrieval from LTM, with the resulting changes in LTM affecting subsequent demands on cognitive control.

Conclusions

Memory systems can produce outputs based on bottom-up mechanisms that unfold automatically in response to inputs, although in many situations these outputs are insufficient to support flexible cognition. In such instances, cognitive control processes must be recruited to retrieve, maintain, and manipulate relevant knowledge and to select against or resolve interference from competing representations. The past decade of cognitive neuroscience research has highlighted that an understanding of cognitive control processes requires consideration of their intimate relation with memory. Future investigations undoubtably will continue to delineate the elemental forms of control and their dependence on prefrontal cortex. In so doing, these efforts promise to provide important insights into the workings of memory, revealing how memory can be brought to bear in a controlled manner, to support flexible behavior.

NOTE

1. Other evidence indicates that functional distinctions exist within left PFC. One putative distinction is that between anterior and posterior left ventrolateral PFC, based on semantic and phonological processing demands (for discussion, see Bookheimer, 2002; Buckner et al., 1995; Fiez, 1997; Gabrieli et al., 1998; Gold and Buckner, 2002; Poldrack et al., 1999; Wagner, Koutstaal et al., 2000).

REFERENCES


