

Chapter 30

Forgetting and Retrieval

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Retrieval of episodic memories—conscious memories of past events—often provides critical information that can shape current thought and behavior. Although successful remembering is generally thought of as far more desirable than forgetting, it is likely that forgetting is also an important component of an adaptive memory system (M. C. Anderson, 2003; Bjork, 1989; Schacter, 1999). To fully understand the functioning of episodic memory, it is important to consider both the situations and mechanisms that lead to successful remembering as well as those that contribute to forgetting. Indeed, the phenomena of remembering and forgetting are intimately related—that is, we often forget precisely because we *have remembered* some other information. What we ultimately remember and forget is influenced both by our prior mnemonic experiences as well as the functioning of neurobiological mechanisms that guide mnemonic retrieval. In particular, the frontal lobes—which are known to play an important role in goal-directed attention and behavior—are central to the ability to direct retrieval toward those memories that are relevant and away from those that are irrelevant.

We consider two broad classes of forgetting and their corresponding relations to frontal lobe function. First, we review evidence that our ability to remember is often complicated by interference from competing memories, and that these situations (a) increase the likelihood of forgetting and (b) increase demands on the prefrontal cortex (PFC). Second, we consider situations in which our mnemonic activities require selecting against, or avoiding, particular memories, describing evidence that such acts of selection (a) increase the likelihood of later forgetting selected-against memories and (b) are supported by the PFC. We conclude by situating the relationship between the PFC and forgetting within the broader context of the PFC and the control of cognition and behavior.

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GROSS ANATOMY AND CONNECTIVITY OF THE PREFRONTAL CORTEX

In this chapter, we primarily focus on the role of the PFC in regulating episodic retrieval and forgetting. Thus, before considering specific classes of forgetting and their relation to the PFC, it is worth briefly describing the gross anatomy of the frontal lobes—namely, subregions within the PFC that putatively support distinct functional mechanisms.

The prefrontal cortex is generally divided into ventrolateral, dorsolateral, frontopolar, and medial subregions (Figure 30.1). In the human, the ventrolateral PFC (VLPFC; Figure 30.1A) corresponds to the inferior frontal gyrus, which includes, from the caudal to rostral extent, inferior frontal pars opercularis (Brodmann Area [BA] 44), inferior frontal pars triangularis (BA 45), and inferior frontal pars orbitalis (an area Petrides & Pandya, 2002, term area 47/12). Although Petrides and Pandya (2002) refer to area 47/12 and BA 45 collectively as the mid-VLPFC, distinguishing these regions from caudally situated BA 44, in this review, we highlight functional dissociations between area 47/12 and area 45. Thus, we refer to inferior frontal pars orbitalis (area 47/12) as the anterior VLPFC, pars triangularis (BA 45) as the mid-VLPFC, and pars opercularis (BA 44) as the posterior VLPFC. The VLPFC is separated from the dorsolateral PFC (DLPFC) by the inferior frontal sulcus in humans (in monkeys, the principal sulcus marks this boundary). Although DLPFC has been used to refer to a broad range of lateral PFC regions, we use DLPFC to refer to the middle frontal gyrus. As we discuss, episodic retrieval and forgetting have been linked with activity in BA's 46 and 9/46 (Figure 30.1A)—subregions of DLPFC that Petrides and Pandya (1999) refer to as mid-DLPFC. Rostral to DLPFC and VLPFC is the frontopolar cortex (FPC; BA 10; Figure 30.1A-B). A final area of interest for the present chapter is the anterior cingulate cortex (ACC; BA's 24 and 32; Figure 30.1B), which is situated along the medial wall of the PFC, immediately superior to the corpus callosum.

Importantly, PFC subregions are both interconnected and connected with posterior cortical sites, suggesting that

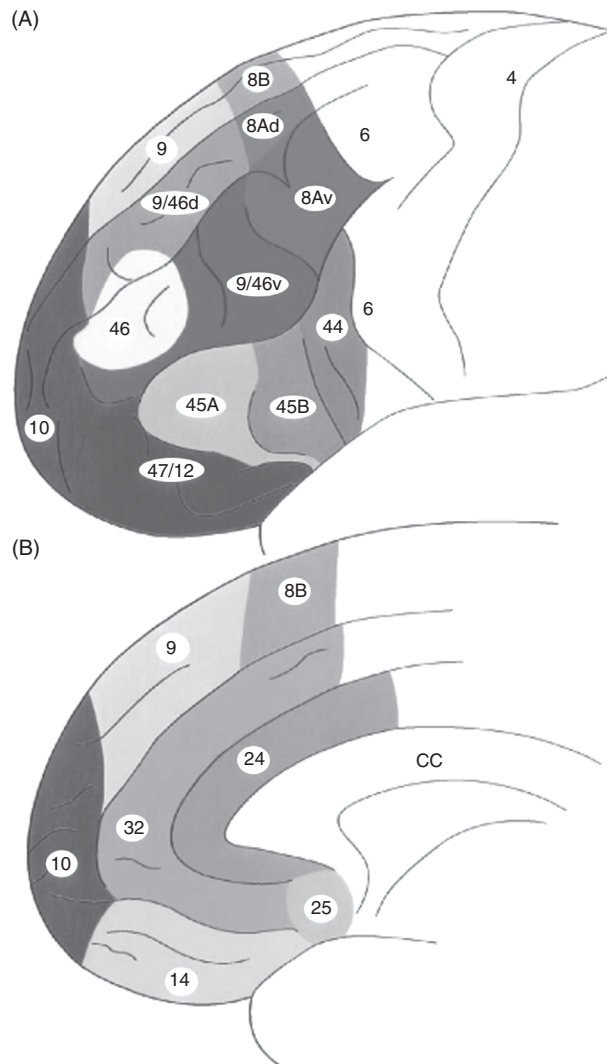


Figure 30.1 A: Lateral view of the PFC and corresponding cytoarchitectonic areas. B: Medial view of the PFC.

Note. (A) DLPFC = Areas 46 and 9/46. VLPFC = Areas 47/12, 45, and 44. FPC = Area 10. (B) ACC = Areas 32 and 24. From "Dorsolateral Prefrontal Cortex: Comparative Cytoarchitectonic Analysis in the Human and the Macaque Brain and Corticocortical Connection Patterns," by M. Petrides and D. N. Pandya, 1999, *European Journal of Neuroscience*, 11, pp. 1011–1036. Copyright 1999 by Blackwell Publishing. Reprinted with permission.

PFC subregions are well equipped to coordinate diverse cognitive operations. For example, the VLPFC is strongly connected with cortical areas in the lateral and medial temporal lobe, including (but not limited to) the inferotemporal cortex, superior temporal cortex, and, more medially, the perirhinal and parahippocampal cortex (Petrides & Pandya, 2002). The DLPFC has substantial reciprocal connections with posterior parietal cortex, superior temporal cortex, retrosplenial cortex, anterior and posterior cingulate cortex, as well as connectivity with VLPFC (Petrides & Pandya, 1999). Notably, through its connections with the

retrosplenial cortex, DLPFC may interact with hippocampal and parahippocampal structures (Petrides, 2005). The FPC is connected both with the DLPFC and VLPFC as well as with the superior temporal cortex, cingulate cortex, and retrosplenial cortex, suggesting that the FPC may be particularly well suited to incorporate diverse sources of information (Petrides, 2005; Petrides & Pandya, 2007). The ACC is also widely connected with cortical sites, including multiple lateral PFC sites (DLPFC, in particular), the posterior parietal cortex, and the medial temporal lobe cortex (Pandya, Van Hoesen, & Mesulam, 1981). Thus, whereas DLPFC and VLPFC have fairly distinct patterns of connectivity with the posterior cortical sites, the FPC and ACC may each interact with both DLPFC and VLPFC structures in coordinating goal-directed behavior.

INTERFERENCE AND MEMORY RETRIEVAL

Perhaps the most widely accepted and well-documented cause of forgetting is interference. Interference occurs whenever irrelevant memories compete with relevant memories (Mensink & Raaijmakers, 1988; for reviews, see M. C. Anderson & Spellman, 1995; Wixted, 2004). The extent to which interference contributes to forgetting is related both to the number of irrelevant memories that compete as well as the strength of these irrelevant memories. Most typically, interference is thought to occur during the act of retrieval, creating situations of *retrieval competition*. Retrieval competition has been particularly well studied in three classic behavioral paradigms. First, memories of past experiences often interfere with our ability to retrieve memories of more recent experiences—a situation termed *proactive interference*. Conversely, the ability to retrieve memories of past experiences is often subject to interference from more recent memories—*retroactive interference*. Finally, even when the order of learning is not relevant, the general principle that associates of a retrieval cue compete with each other during retrieval has been studied in the *fan effect* (J. R. Anderson, 1974). In the following sections, we briefly review first the classic behavioral evidence concerning these three situations of interference and then potential neurobiological mechanisms that serve to overcome interference.

Classic Interference Phenomena

Proactive interference (PI) and retroactive interference (RI) have been the subject of extensive behavioral research (for reviews, see M. C. Anderson & Spellman, 1995; Wixted, 2004), and have been best illustrated in classic A-B, A-C paradigms (Figure 30.2). In a standard A-B, A-C

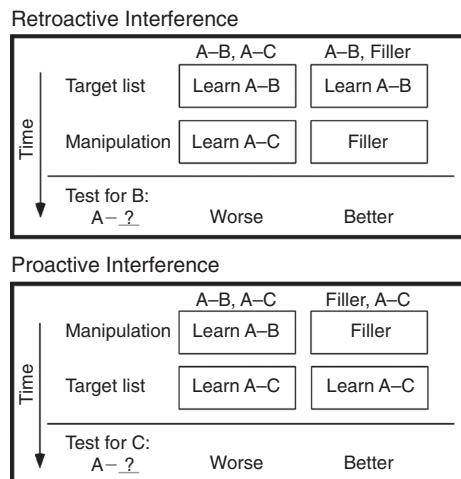


Figure 30.2 Schematic of retroactive interference and proactive interference paradigms.

Note. In both paradigms, the association between a cue (A term) and multiple associates (B & C terms) increases interference and, therefore, forgetting. In RI, the critical manipulation is whether an interfering second list is studied, whereas in PI the critical manipulation is whether an interfering prior list is studied.

paradigm, an initial list of A-B cue-associate pairs (e.g., SHOE-HOUSE) is studied, followed by a second list of A-C pairs in which some of the previously studied cues are paired with new associates (e.g., SHOE-ROPE). When memory for pairs from the second list is tested, the influence of proactive interference is reflected in poorer recall for those pairs that overlap with pairs from the first list, relative to pairs in the second list that are completely unrelated to pairs in the first list. Thus, learning of new information is impaired when previously learned information interferes. Retroactive interference, on the other hand, is evidenced by poorer recall of A-B pairs as a result of subsequently learning overlapping A-C pairs (e.g., memory for SHOE-HOUSE is impaired by learning SHOE-ROPE). Thus, in an A-B, A-C paradigm, either retroactive or proactive interference may occur, depending on which pairs (A-B or A-C) are tested.

Several features of PI and RI are of note. First, the magnitude of interference-related forgetting observed depends on the extent to which retrieval cues reference items from both study lists—an observation made in the earliest RI studies (Müller & Pilzecker, 1900). For example, RI is greater when A-B study is followed by A-C study than C-D study (i.e., a new cue and new associate). Second, PI and RI are maximally observed at different points in time. Specifically, PI is maximal when the lag between A-C study and A-C recall is long, and may be negligible when the delay is very short. RI, on the other hand, is maximal when the delay between A-C study and A-B recall is short,

with the magnitude of RI decreasing as the delay increases (Postman, Stark, & Fraser, 1968).

Importantly, both of these properties of PI/RI can be well explained in terms of retrieval competition that occurs during cued recall (McGeoch, 1942; Mensink & Raaijmakers, 1988). That is, an A-B, A-C paradigm elicits greater RI than an A-B, C-D paradigm because the A-B, A-C paradigm creates a situation in which a single retrieval cue (A) is linked to two associates—thereby enhancing retrieval competition and, therefore, the likelihood of forgetting. Similarly, changes in the relative magnitude of RI and PI at different delays can be explained in terms of changes in the relative salience of B and C terms and, therefore, changes in retrieval competition. For example, some models suggest differential decay rates for B and C terms following A-C study, meaning that the relative strengths of the associate terms change with time (J. R. Anderson, 1983b). Other models suggest that changes in the availability of contextual cues contribute to relative changes in the accessibility of B and C terms (Estes, 1955; Mensink & Raaijmakers, 1988). In either case, at very short delays following A-C study, A-C pairs are thought to be highly salient relative to A-B pairs, meaning that while RI will be high (if B terms are tested), PI will be low (if C terms are tested). At longer delays, the relative salience of A-C pairs decreases, thereby reducing RI, but increasing the potential for PI.

Retrieval competition has also been studied in the context of the fan effect (J. R. Anderson, 1974). The classic finding in fan effect paradigms is that as the amount of related information stored in long-term memory grows, the time it takes to verify that one recognizes a particular piece of that information increases (similarly, increases in fan size may also decrease accuracy). In a typical fan effect task, subjects study a series of propositions (e.g., “A doctor is in the bank,” “A fireman is in the park,” “A lawyer is in the park,” etc.). Importantly, individual elements may appear in multiple propositions (e.g., “park” is associated with both “lawyer” and “fireman”). When elements are associated with multiple propositions (a “fan”), the time it takes to recognize a proposition containing those elements (i.e., “high fan” propositions) increases (J. R. Anderson, 1983a). The fan effect has proven to be a highly consistent finding and has inspired influential models of human memory (J. R. Anderson, 1976). According to the standard account of the fan effect, during recognition memory a finite amount of activation is shared between all the elements in a fan. When the fan size is high, relevant elements receive correspondingly less activation, reflecting increased competition, and retrieval time is therefore slowed (J. R. Anderson, 1976, 1983a).

Thus far, we have considered a single mechanism—retrieval competition—to explain forgetting in RI and PI paradigms and to account for recognition memory slowing

in the fan paradigm. However, alternate accounts have been advanced for RI and PI (for reviews, see M. C. Anderson, 2003; Wixted, 2004). In an influential two-factor theory, Melton and Irwin (1940) argued that some factor in addition to response competition contributes to RI, noting that substantial RI is often observed even when there is little behavioral evidence that A-C pairs actually compete with retrieval of A-B pairs. They speculated that a second factor contributing to RI (in addition to response competition) is the *unlearning*, or direct weakening, of original (A-B) associations. While our focus on retrieval competition as the primary mechanism of interference-related forgetting reflects more recent arguments that classic interference phenomena can be fully accounted for by retrieval competition alone (Mensink & Raaijmakers, 1988), we later consider a mechanism of forgetting—*inhibition*—that bears many similarities to Melton and Irwin's (1940) unlearning mechanism. Specifically, inhibition shares with unlearning the idea that irrelevant memories may be directly weakened.

Neurobiological Mechanisms of Interference Resolution

A hallmark of frontal lobe damage is increased distractibility or perseveration upon irrelevant information. Consistent with this general observation, frontal lobe patients suffer an exaggerated susceptibility to PI (e.g., Shimamura, Jurica, Mangels, Gershberg, & Knight, 1995; Smith, Leonard, Crane, & Milner, 1995). Specifically, whereas frontal lobe patients typically learn list 1 items (e.g., A-B pairs) as well as controls, after studying a second list, their recall for list 2 items (e.g., A-C pairs) is impaired, relative to controls. The selective impairment for A-C pairs indicates that frontal lobe patients are relatively unimpaired at encoding information when interference is not present, but are particularly impaired when prior learning interferes with memory for subsequently encountered information. Indeed, during A-C cued recall, frontal lobe patients often show a greater tendency to generate B terms (intrusions), highlighting the sensitivity of frontal lobe patients to competition from prior learning (Shimamura et al., 1995).

While exaggerated susceptibility to PI has frequently been associated with frontal lobe damage, frontal lobe patients vary widely in the location and extent of their damage. As a result, initial studies of frontal lobe patients yielded considerable variability in the subregions of PFC implicated in resolving PI. For example, whereas some reports suggested a greater sensitivity to PI in patients with left frontal damage (Moscovitch, 1982), others revealed greater PI in patients with right frontal damage (Turner, Cipolotti, Yousry, & Shallice, 2007). Similarly, there were reports in which left and right frontal patients show comparable

increases in sensitivity to PI relative to controls (Smith et al., 1995), but also reports of frontal patients displaying relatively normal sensitivity to PI despite impairments on other "frontal tests" (Janowsky, Shimamura, Kritchevsky, & Squire, 1989). Thus, while initial studies of frontal patients highlighted that interference resolution likely depends on the integrity of the frontal lobes, this work yielded ambiguity regarding the specific PFC subregions that are critical for overcoming mnemonic competition.

Progress on this important issue has greatly accelerated over the past decade, largely because the higher resolution of functional neuroimaging methods—positron emission tomography (PET) and functional magnetic resonance imaging (fMRI)—has enabled researchers to begin to examine whether interference resolution is differentially associated with functional responses in specific PFC subregions. As we next review, considerable neuroimaging evidence, accumulated over the past decade, now indicates that at least some forms of interference resolution are associated with activation in the left ventrolateral PFC (VLPFC; Figure 30.1A). Moreover, recent neuropsychological investigations of patients with damage that specifically includes the left VLPFC also highlight the necessity of this region for overcoming mnemonic competition.

In a classic PET study of proactive interference (Dolan & Fletcher, 1997), subjects learned an initial set of word pairs (e.g., DOG-BOXER) followed by a second list that either contained completely new word pairs (e.g., CLOTH-VELVET), previously studied word pairs (e.g., DOG-BOXER), or word pairs that contained previously studied words paired with new associates (e.g., DOG-DALMATION or SPORTSMAN-BOXER). When list 2 contained completely new associates, relative to conditions that contained at least one old word, enhanced activation was observed in the hippocampus and medial temporal lobe cortex, suggesting that the medial temporal lobes preferentially respond to the novelty of to-be-learned information (Figure 30.3). In contrast, when list 2 contained previously studied words paired with new associates (a situation of interference equivalent to the A-C condition described previously), activation was observed in a region of the left lateral PFC that encompassed the mid/posterior VLPFC and DLPFC. Importantly, this left lateral PFC response was driven not by the novelty of individual words, but by the extent to which list 2 learning was complicated by interference from memory for list 1 pairs.

Subsequent neuroimaging work provided additional evidence that the left VLPFC, in particular, plays a critical role in resolving PI. For example, in an fMRI study of PI during episodic encoding (Henson, Shallice, Josephs, & Dolan, 2002), activation in the left VLPFC decreased as a word pair (A-B) was repeatedly studied, but increased

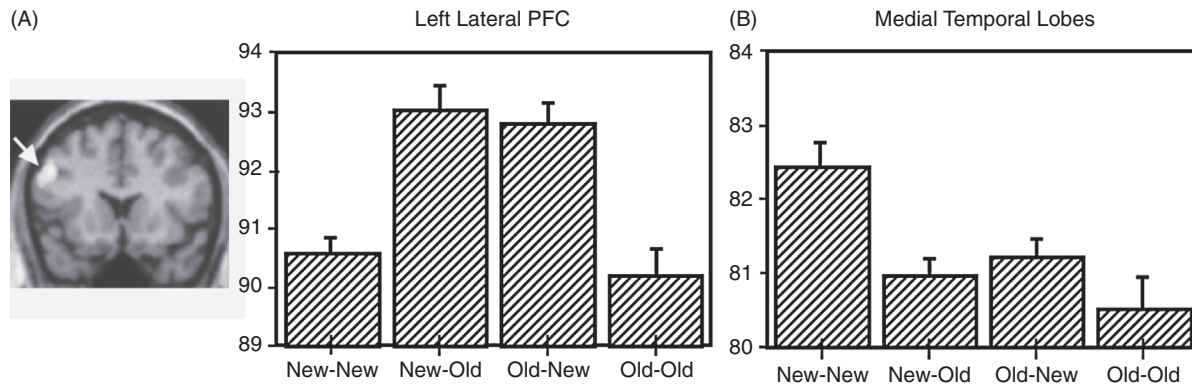


Figure 30.3 Activation in the left lateral PFC (A) and the medial temporal lobes (B) as a function of encoding condition.

Note. “New-New” corresponds to encoding of a novel word pair (equivalent to an A-B pair in a PI design); “New-Old” and “Old-New” correspond to a word pair in which one member of the pair is novel and the other was previously studied with a different word (equivalent to an A-C pair); “Old-Old” corresponds to a word pair that is repeated, intact (equivalent to repeated exposure to an A-B term). The left lateral

PFC is maximally engaged when the word pair being encoded partially overlaps with a previous pair (i.e., when interference is present). In contrast, medial temporal lobe activation is maximal when the word pair being encoded is completely novel. From “Dissociating Prefrontal and Hippocampal Function in Episodic Memory Encoding,” by R. J. Dolan and P. C. Fletcher, 1997, *Nature*, 388, pp. 582–585. Copyright 1997 by Macmillan Publishers. Adapted with permission.

when one of the pair members changed (A-C). Similarly, in another study (Fletcher, Shallice, & Dolan, 2000), left VLPFC activation increased when previously studied word pairs were rearranged, relative to their initial study configuration. While the relationship between PI and the left VLPFC has primarily been evidenced during *encoding* of A-C pairs, Henson et al. (2002) also observed greater activation in the left VLPFC, along with the anterior cingulate cortex (ACC), when *retrieval* occurred in the face of PI (neuroimaging data from the fan effect paradigm further implicate the left VLPFC in competitive retrieval, as described next).

Studies of retrieval from semantic memory and working memory also implicate the left VLPFC in guiding interference-laden mnemonic processing. Specifically, neuroimaging studies of semantic retrieval have consistently found greater engagement of the left VLPFC—particularly the left mid-VLPFC—when retrieval involves selecting between competing alternatives (e.g., Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997; for review, see Badre & Wagner, 2007). Moreover, when PFC damage includes the left mid-VLPFC, the ability to retrieve relevant semantic representations from among competitors is impaired (Martin & Cheng, 2006; Metzler, 2001; Thompson-Schill et al., 1998), establishing the necessity of this region for interference resolution during semantic retrieval. Similarly, within working memory, imaging studies have consistently implicated the left mid-VLPFC in overcoming PI that accumulates across trials (for review, see Jonides & Nee, 2006). Moreover, PFC lesions that include damage

to the left mid-VLPFC (Thompson-Schill et al., 2002) and focal transient disruption of the left mid-VLPFC with transcranial magnetic stimulation (Feredoes, Tononi, & Postle, 2006) impair working memory performance in the face of PI. Collectively, these convergent findings across episodic, semantic, and working memory contexts indicate that the left mid-VLPFC contributes to interference resolution.

While the left mid-VLPFC appears to play a critical role in resolving interference, there remains the question of *how*, in mechanistic terms. A prominent hypothesis, derived primarily from neuroimaging and patient data, is that the left mid-VLPFC supports the *selection* of task-relevant representations when competition is present (Thompson-Schill et al., 1997, 1998). That is, when multiple semantic—or episodic—representations become simultaneously active, a left mid-VLPFC bias mechanism is posited to favor relevant representations over irrelevant representations (Badre & Wagner, 2007). Accordingly, when viewed through this light, many instances of forgetting may reflect failures of mnemonic selection, as opposed to retrieval, *per se*.

Notably, within semantic and working memory paradigms, selection has typically been studied—and left mid-VLPFC activation has typically been observed—during *retrieval* (of either semantic information or working memory contents). Within episodic memory, however, left mid-VLPFC activation has most frequently been observed in PI paradigms during A-C *encoding*. Thus, it has been argued that A-C encoding engages the same selection mechanism that is observed during semantic and working memory retrieval (Henson et al., 2002). However, it should be noted that left mid-VLPFC activation during encoding

might also be recast in terms of retrieval-related activation. That is, A-C associations may become differentiable from A-B associations through an elaborative encoding process in which semantic properties unique to A-C associations are selectively favored during A-C study—a process that would amount to competitive semantic retrieval. In either case, competition from irrelevant associations drives left mid-VLPFC activation during A-C encoding.

During episodic retrieval, left mid-VLPFC engagement has also been observed when competition is present. In particular, the link between left VLPFC engagement and retrieval competition has been well established in studies of the fan effect. In fan paradigms, the increase in reaction time that is associated with “high fan” recognition is thought to directly correspond to prolonged engagement of mechanisms that guide retrieval in the face of competition (Sohn, Goode, Stenger, Carter, & Anderson, 2003). Consistent with this perspective, a pair of fMRI studies revealed that high fan, relative to low fan, recognition is associated with increased engagement of a region of the left lateral PFC, inclusive of the left mid-VLPFC (Sohn et al., 2003, 2005). This neural correlate of the fan effect provides a compelling link between recent neuroimaging work and classic interference theory, indicating that direct manipulations of retrieval competition increase the engagement of the left mid-VLPFC. Moreover, left mid-VLPFC engagement has been observed in other situations of competitive episodic retrieval, such as when the retrieval task requires recollection of specific (criterial) details of an encoding event (Dobbins, Foley, Schacter, & Wagner, 2002; Dobbins & Wagner, 2005; Kostopoulos & Petrides, 2003; Lundstrom, Ingvar, & Petersson, 2005).

Summary

Initial observations of increased sensitivity to interference following frontal lobe damage have now been complemented by substantial evidence that the left mid-VLPFC, in particular, plays a fundamental role in resolving interference. From a mechanistic perspective, the left mid-VLPFC is thought to resolve interference by selecting goal-relevant representations in the face of competition from irrelevant representations. This putative selection mechanism—and the many situations in which left mid-VLPFC-mediated selection has been observed—accords well with the perspective from classic interference theory that forgetting is well accounted for in terms of retrieval competition. In other words, retrieval competition powerfully influences the likelihood of forgetting, and it is in precisely these situations of enhanced retrieval competition that left mid-VLPFC selection resolves interference.

INHIBITION AS A CAUSE OF FORGETTING

In the previous section, we highlighted the potential for retrieval competition from irrelevant memories to obscure access to currently relevant memories and thereby produce retrieval failures, or forgetting. However, overcoming competition from irrelevant memories can also have consequences for what is remembered in the future. That is, when competing memories are selected against, there is a decreased likelihood that these memories will later be remembered (if they later become relevant). This form of forgetting is related to retrieval competition—it is a reaction to, and consequence of, competition from irrelevant memories—but the mechanism of forgetting is thought to reflect the direct weakening, or inhibition, of competing memories. We next consider two situations in which the relationship between forgetting and memory inhibition has been studied: (1) when the act of remembering a target memory requires selecting against closely related, but irrelevant, memories, and (2) when there is an explicit intention to forget or to keep out of mind individual memories or sets of memories. In each case, we consider the behavioral evidence supporting the occurrence of inhibition as well as the neurobiological mechanisms through which inhibition may occur.

Retrieval-Induced Forgetting

Competition that is present during the act of retrieval can compromise successful retrieval of target memories. Although we previously emphasized the demand to resolve competition such that successful retrieval, or selection, may occur, it has also been argued that retrieval competition is resolved through the inhibition of those memories that compete with the target memories (M. C. Anderson, Bjork, & Bjork, 1994; M. C. Anderson & Spellman, 1995; for reviews, see M. C. Anderson, 2003; Levy & Anderson, 2002). Functionally, the inhibition of irrelevant, competing memories is thought to be adaptive in that it reduces competition during the retrieval of target memories (M. C. Anderson, 2003; Bjork, 1989). However, to the extent that previously irrelevant memories later become relevant, the inhibition that they suffered increases the likelihood that they will be forgotten (for review, see Levy & Anderson, 2002).

That the retrieval of target memories can produce forgetting of related memories has been termed *retrieval-induced forgetting* and has been demonstrated in a variety of situations (for review, see Levy & Anderson, 2002). In a standard retrieval-induced forgetting paradigm, participants study a series of cue-associate pairs with multiple associates studied with each cue (e.g., “FRUIT-banana,”

“FRUIT-apple,” “DRINK-whiskey,” “DRINK-scotch”). After study, participants engage in selective *retrieval practice* of some of the associates of some of the cues. For example, participants might receive “FRUIT-a_” as a probe to remember “apple.” Typically, half of the associates of half of the cues are practiced, three times each, in this manner. Finally, all associates—both practiced and unpracticed—are tested in a final, cued recall phase where cues are presented along with the first letters of individual associates.

Not surprisingly, practiced associates (e.g., “apple”; referred to as RP+ items) are better remembered during the final test than unpracticed associates (Figure 30.4). However, some of the unpracticed associates are related to practiced associates (e.g., “banana”; RP– items), whereas other unpracticed associates are related to a cue for which none of the associates were practiced (e.g., “scotch” is related to “DRINK,” but none of the associates of “DRINK” receive practice; NRP items). Of critical interest, RP– items—the associates that are related to practiced items—are more poorly remembered than NRP (baseline) items (Figure 30.4). In other words, practice retrieving “apple” can make it more difficult to remember “banana”—evidence for retrieval-induced forgetting. This forgetting is thought to occur precisely because “banana” is related to “apple”—that is, during retrieval of “apple,” “banana” competes and is subject to inhibition as a means of reducing this competition. This inhibition is manifested, behaviorally, in an increased rate of forgetting.

That RP– items are more likely to be forgotten than NRP items does not, on its own, indicate that RP– items are necessarily inhibited. Instead, given that RP– items are tested using the same cues (e.g., “FRUIT-”) as RP+ items,

it is possible that the strengthening of RP+ items creates enhanced retrieval competition during RP– recall, thereby blocking or occluding access to RP– items (Mensink & Raaijmakers, 1988). Evidence of memory inhibition comes from the critical observation that retrieval-induced forgetting also occurs even when RP+ items are tested using novel cues (e.g., “MONKEY-b” for “banana”; Aslan, Bäuml, & Pastotter, 2007; Johnson & Anderson, 2004; Levy, McVeigh, Marful, & Anderson, 2007; MacLeod & Saunders, 2005; Saunders & MacLeod, 2006) or even when RP– items are tested in simple item recognition tests (Hicks & Starns, 2004). Importantly, both of these tests avoid the problem of retrieval competition between RP– and RP+ items, as the cue that they share in common is eliminated during the test procedure. This property of retrieval-induced forgetting is referred to as *cue-independence*.

Further evidence for memory inhibition comes from the finding that retrieval-induced forgetting is most likely to occur when mnemonic competition is high. Specifically, if competing memories are weak they are *less* likely to be forgotten (inhibited); whereas competing memories that are strong are *more* likely to be forgotten (M. C. Anderson et al., 1994; Bäuml, 1998). Similarly, if retrieval practice of RP+ items is replaced with noncompetitive extra study exposures, forgetting of “competitors” (i.e., RP– items) does not occur (M. C. Anderson, Bjork, & Bjork, 2000). Together, these data provide strong support for the argument that retrieval-induced forgetting is a response to retrieval competition—a property we refer to as *competition-dependence*. Thus, the observation that retrieval-induced forgetting is cue-independent provides important evidence that competing memories are actually inhibited, while the observation that retrieval-induced forgetting is competition-dependent provides a constraint on when inhibition should occur.

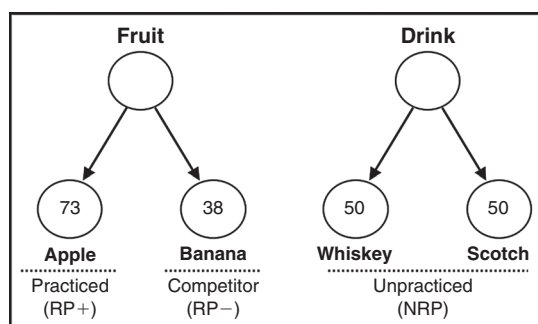


Figure 30.4 Schematic of retrieval-induced forgetting.

Note. Practiced items (RP+) are typically better remembered than baseline (NRP) or competing (RP–) items (numbers reflect percentage recall). Critically, RP– items are typically more poorly recalled than NRP items. The recall impairment for RP– items, relative to NRP items, reflects the magnitude of retrieval-induced forgetting. From “Rethinking Interference Theory: Executive Control and the Mechanisms of Forgetting,” by M. C. Anderson, 2003, *Journal of Memory and Language*, 49, pp. 415–445. Copyright 2003 by Elsevier Press. Adapted with permission.

Neurobiology of Retrieval-Induced Forgetting

Previously, we discussed the role of PFC in guiding retrieval in the face of competition. With respect to retrieval-induced forgetting, there is an additional phenomenon to explain: the weakening or inhibition of competing memories. On the one hand, inhibition may be a by-product of PFC control mechanisms that guide attention toward task-relevant representations—a form of biased competition (Miller & Cohen, 2001). On the other hand, inhibition may be a distinct form of control, implemented by an independent PFC control mechanism that directly weakens competing representations (M. C. Anderson et al., 2004; Levy & Anderson, 2002). Although current evidence does not clearly favor one of these possibilities over the other, both perspectives emphasize that PFC influences what is retrieved and what

is inhibited; we therefore review general evidence that the PFC is engaged during retrieval in situations that ultimately result in inhibition.

The key behavioral properties of retrieval-induced forgetting are well captured in a detailed neural network model developed by Norman, Newman, and Detre (2007). Central to the model is an algorithm in which oscillations in memory activation levels allow for the identification of target memories that are weak and competitors that are strong. Although the details of the model are beyond the scope of this chapter, it is of note that the model involves feedback mechanisms through which weak targets can be strengthened and strong competitors can be weakened. Of particular interest, the model does not contain a layer representing the contribution of the PFC. Rather, inhibition is explained in terms of local learning through feedback within memory-dedicated systems (i.e., within the medial temporal lobes). As long as competition exists, feedback mechanisms will punish competing memories. The model accounts for cue-independent forgetting in that individual items that compete for retrieval are directly weakened, and it accounts for competition-dependence in that competing items are only weakened if they become active (i.e., if they compete) during target retrieval.

While the Norman et al. (2007) model does not contain a layer representing PFC—and therefore does not explain inhibition, itself, in terms of PFC cognitive control operations—the authors argue that the PFC nonetheless plays an important role in retrieval-induced forgetting. By their view, the critical role of the PFC is that it supports the selection of relevant memories—a function that is particularly needed when competition is high. More specifically, they suggest that when a retrieval cue leads to the co-activation of both relevant and irrelevant memories, competition occurs, which is detected by ACC. The ACC then triggers the engagement of other PFC mechanisms that selectively increase the activation of goal-relevant memories, or increase attention to goal-relevant features, thereby resolving competition. By detecting competition and guiding retrieval toward target representations, the PFC can select target memories to be strengthened and, as a consequence, the PFC influences which memories are weakened. Thus, the Norman et al. (2007) model explains inhibition as a by-product of PFC-mediated biased competition (Miller & Cohen, 2001).

The relationship between retrieval competition, inhibition, and the PFC was recently addressed in an fMRI study of retrieval-induced forgetting (Kuhl, Dudukovic, Kahn, & Wagner, 2007) that focused on the neural responses within the PFC during selective retrieval practice (i.e., across the three retrieval practice attempts of each RP+ item). Of critical interest was whether PFC engagement across retrieval practice is related to the inhibition of competing (RP−) memories, as revealed by behavioral performance on the

final test of all items. As Norman et al. (2007) suggest, the PFC should be differentially necessary when competition is high. Thus, the PFC should be maximally engaged during initial retrieval practice attempts (i.e., before targets are strengthened and competitors are weakened), with PFC engagement decreasing as targets are repeatedly practiced and competitors are suppressed.

Consistent with this prediction, Kuhl et al. (2007) observed robust decreases in PFC engagement during repeated (third) relative to initial (first) retrieval practice trials. To directly test for a relationship between these decreases in PFC engagement and the phenomenon of competitor weakening (inhibition), the relative magnitude of competitor weakening was computed for each participant $[(\text{NRP accuracy} - \text{RP} - \text{accuracy}) / \text{NRP accuracy}]$ and then regressed upon the magnitude of PFC disengagement that each participant displayed across retrieval practice trials. If the weakening of competing memories reduces the demands on PFC, then the decrease in PFC engagement across retrieval practice trials should be positively correlated with the amount of competitor weakening. Indeed, such a relationship was observed in two PFC foci: the ACC and right anterior VLPFC (Figure 30.5).

The finding that ACC disengagement was related to the weakening of competing items is consistent with the hypothesis of Norman et al. (2007) that the ACC should serve to detect competition between target and competing memories, and is also consistent with a much broader literature implicating the ACC in detecting conflict between competing representations (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Braver, Barch, Gray, Molfese, & Snyder, 2001; MacDonald, Cohen, Stenger, & Carter, 2000; van Veen & Carter, 2002). In other words, the relative strength of target versus competing memories should increase as a function of retrieval practice repetition, meaning that with successive retrieval practice repetitions, to the extent that competitors are successfully weakened, there should be less retrieval competition and thus less ACC engagement.

The right anterior VLPFC was also clearly sensitive to the weakening of competing memories, with this sensitivity potentially taking two forms. On the one hand, the right anterior VLPFC may serve to increase activation of target memories or features of target memories—a function Norman et al. (2007) ascribe to PFC—with this function maximally required when competition is highest. On the other hand—and in contrast to the role of the PFC suggested by Norman et al. (2007)—the right anterior VLPFC may serve to directly inhibit competing memories. While these possibilities are difficult to disambiguate, we later return to potential mechanistic contributions of the right anterior VLPFC.

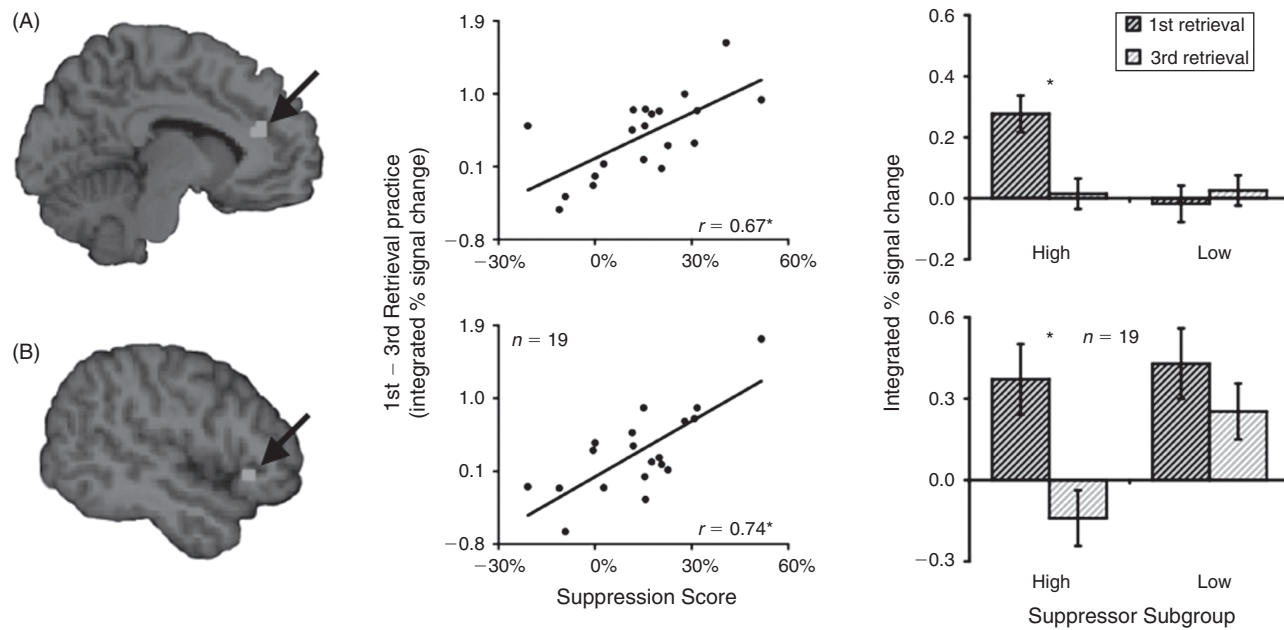


Figure 30.5 Neural activation reductions in the ACC (A) and the right anterior VLPFC (B) during retrieval practice correlated with behavioral measure of retrieval-induced forgetting.

Note. Subjects that showed the greatest magnitude of suppression (of RP- items) displayed the greatest reductions in anterior cingulate cortex

and right anterior VLPFC activation during retrieval practice. From “Decreased Demands on Cognitive Control Reveal the Neural Processing Benefits of Forgetting,” by B. A. Kuhl, N. M. Dudukovic, I. Kahn, and A. D. Wagner, 2007, *Nature Neuroscience*, 10, p. 911. Reprinted with permission.

It remains ambiguous whether the right anterior VLPFC and ACC directly or indirectly contribute to the forgetting of competing memories, however, it also might be asked whether the forgetting observed by Kuhl et al. (2007) is best explained in terms of inhibition. As described previously, support for inhibition comes from evidence that retrieval-induced forgetting is cue-independent and competition-dependent. With respect to cue-independence, the key feature is that the forgetting of competing memories should not be accounted for in terms of strengthened, practiced memories interfering with RP- recall at test. Consistent with this prediction, the decreased engagement of the ACC and right anterior VLPFC across retrieval practice trials—which was correlated with RP forgetting—was not correlated with RP+ strengthening, suggesting that it was, in fact, the weakening of competing memories and not the strengthening of practiced memories, that reduced demands on these PFC subregions during retrieval practice.

With respect to competition-dependence, it should be predicted that, if the ACC indexes competition, the initial engagement of the ACC should be a signal that competition is present, thereby triggering competitor inhibition. Indeed, those participants that showed the most retrieval-induced forgetting demonstrated greater initial engagement of the ACC during retrieval practice. In support of

the claim that the ACC was driven by mnemonic competition and that mnemonic competition triggered inhibition, it was also observed that initial hippocampal activation was positively correlated with both initial ACC activation and the magnitude of inhibition. Thus, engagement of the hippocampus likely reflected successful retrieval of both target and competing memories, with robust hippocampal activation perhaps signaling inefficient, competition-laden retrieval—a situation that triggers competitor inhibition.

The competition-dependent role of the PFC in retrieval-induced forgetting is also supported by a recent event-related potential (ERP) study (Johansson, Aslan, Bäuml, Gabel, & Mecklinger, 2007). In this study, ERPs were compared during selective retrieval practice versus a control condition in which retrieval practice was replaced by extra study exposures. As noted earlier, behavioral data indicate that retrieval-induced forgetting is not observed when retrieval practice is replaced by extra study (M. C. Anderson et al., 2000), with the explanation being that extra study exposures are noncompetitive, or are at least much less competitive than retrieval practice. Replicating this dissociation, Johansson et al. (2007) observed that retrieval practice resulted in subsequently lower recall of competing memories than did extra study exposures. At the neural level, ERPs associated with retrieval practice were more positive-going than ERPs associated with extra study, with this

difference restricted to frontal electrode sites. Critically, the magnitude of this difference in frontal electrodes between retrieval practice and extra study was greater for participants who showed the most retrieval-induced forgetting, relative to those that showed the least retrieval-induced forgetting. These data are consistent with the theme that retrieval competition is associated with both the engagement of the PFC and the inhibition of competing memories. Moreover, these data, like those reported by Kuhl et al. (2007), demonstrate a coupling between the PFC's response to competition and the inhibition of competing memories.

While these findings support the relationship between the PFC and retrieval-induced forgetting, several researchers have also attempted to establish whether intact PFC functioning is *necessary* for retrieval-induced forgetting to occur. For example, retrieval-induced forgetting has been probed both in patients with frontal lobe damage as well as in older adults (a population in which frontal lobe dysfunction is common, e.g., Moscovitch & Winocur, 1992; Raz et al., 1997). In one such study, Conway and Fthenaki (2003) compared patients with frontal lobe damage (either left or right lateral PFC damage) to control participants. Although the PFC has frequently been implicated in inhibitory control, the frontal patients displayed a normal pattern of retrieval-induced forgetting, relative to controls. From these data, Conway and Fthenaki argued that retrieval-induced forgetting reflects a form of unintentional inhibition and that intact PFC functioning is not necessary for producing such inhibition. Paralleling these findings, Aslan and colleagues (2007) observed normal retrieval-induced forgetting in older adults, compared with younger adults. Although these observations perhaps suggest that normal PFC functioning is not necessary for retrieval-induced forgetting to occur, there are several issues complicating this conclusion.

As discussed earlier, in a standard retrieval-induced forgetting study, inhibition is not the only potential cause of forgetting. That is, if the test procedure allows the strengthened, practiced memories (RP+) to interfere with retrieval of competing memories (RP-), then retrieval-induced forgetting can be explained simply in terms of retrieval competition that arises at test. Moreover, as Norman et al. (2007) note, the PFC may be particularly important for resolving competition during the test phase of a retrieval-induced forgetting study, given that retrieval cues are linked to multiple associates and damage to the PFC is known to increase sensitivity to retrieval competition. While the potential contamination of retrieval competition during the test phase can be eliminated if an independent-probe test procedure is used (M. C. Anderson & Spellman, 1995), Conway and Fthenaki (2003) did not use such a procedure. Thus, their observation of normal retrieval-induced forgetting

in frontal patients may simply reflect robust sensitivity to retrieval competition at test, as opposed to the actual inhibition of competing memories.

Aslan and colleagues (2007), however, used both a standard test procedure as well as an independent probe test procedure, with older adults showing normal retrieval-induced forgetting in both cases. Although this result is intriguing, and, at first pass, may seem consistent with the hypothesis from Norman et al. (2007) that the PFC does not directly support inhibition, Aslan and colleagues did not explicitly address frontal lobe integrity among the older adults that were tested. Thus, it is unclear that these older adults suffered from any PFC dysfunction. Indeed, it is noteworthy that the older and younger adults tested by Aslan and colleagues demonstrated equivalent retrieval practice success. Given that the PFC is known to make necessary contributions to selective retrieval (Badre & Wagner, 2007; Dobbins & Wagner, 2005), this finding raises the possibility that the older adults tested may have had little, if any, PFC dysfunction.

Summary

Recent neurobiological evidence supports the claim that the PFC plays an important role in overcoming competition during selective retrieval and influencing what ultimately becomes inhibited. Moreover, the PFC is engaged in response to the presence of competition and the PFC directly benefits from the inhibition of competing memories. Thus, neurobiological evidence supports both behavioral evidence concerning when inhibition should occur (M. C. Anderson & Spellman, 1995; Levy & Anderson, 2002) as well as theoretical explanations of why inhibition is adaptive (M. C. Anderson, 2003; Bjork, 1989).

Although progress in understanding the functional neurobiology of forgetting has been made, a fundamental ambiguity that awaits further clarification concerns the precise mechanism through which inhibition occurs. As noted earlier, inhibition may occur because: (a) the PFC biases competition toward (selects) relevant memories (Miller & Cohen, 2001) and, as a consequence, competing memories are inhibited; or (b) the PFC directly weakens competing memories (Levy & Anderson, 2002). Disambiguating these possibilities is particularly difficult because both hypotheses predict that PFC function will be related to the phenomena of inhibition and selection. For example, if inhibition is a consequence of PFC selection, then damage to the PFC should impair the ability to select target memories and, as a consequence, competitors should not be inhibited. On the other hand, if the PFC directly contributes to inhibition as a means of facilitating selective retrieval (Levy & Anderson, 2002), then damage to the PFC should impair the ability to inhibit irrelevant memories, which should, as a consequence, compromise the ability to select target

memories. Thus, by either account, damage to the PFC should disrupt both the inhibition of irrelevant memories as well as the selection of relevant memories.

One approach to distinguish between the mechanisms of selection and inhibition is to examine whether distinct PFC subregions contribute to each. As will be recalled from the previous section, mnemonic selection has repeatedly been associated with the left mid-VLPFC (Badre & Wagner, 2007). In the study by Kuhl et al. (2007), right anterior VLPFC engagement, but not left mid-VLPFC engagement, was correlated with the inhibition of competing memories. Although this may suggest a dissociation between the left mid-VLPFC (selection) and right anterior VLPFC (inhibition), there remain alternative explanations. For example, the right anterior VLPFC may support the allocation of attention toward properties of the retrieval cue—a form of attentional selection—which is particularly necessary when competition is high. By this view, the right anterior VLPFC would support a form of selection that is distinct from the selection supported by the left mid-VLPFC, but would not directly support inhibition. As we describe in the following sections, there is, in fact, some evidence in support of a selective-attention account of the right anterior VLPFC. However, given the limited data at present, mechanistic dissociations between the left mid-VLPFC and right anterior VLPFC remain tentative.

Stopping Retrieval

While attempts to remember a target memory can trigger inhibition of competing memories, it has also been argued that inhibition can occur as a result of deliberate attempts to forget something or even deliberate attempts to simply keep something out of mind. For example, Bjork (1970) describes the predicament of a short-order cook, for whom it is highly advantageous to *forget* an order once it is complete. The advantage to forgetting a completed order, of course, is that it reduces confusion (proactive interference) when trying to remember a current order. The situation of deliberately trying to forget, or discard, something that has already been learned has been studied using the *directed forgetting* paradigm.

Directed forgetting studies are generally divided into two main classes. In the first type, the *list method*, there are typically two lists of stimuli, studied one after the other. In some cases, or for some participants, there is an instruction immediately following list 1 learning (and before list 2 learning) to forget the entire list that was just studied. After list 2 learning, memory is assessed for both list 2 items and list 1 items. When participants are instructed to forget list 1, there are typically two results of interest, relative to when a forget instruction was not issued: (1) recall of list 1 items is worse, and (2) recall of list 2 items is better.

The impaired recall of list 1 items suggests that recall for already learned material can be volitionally influenced, whereas the improved recall of list 2 items suggests that proactive interference can be reduced, as would be the goal of the short-order cook. The second procedure used in directed forgetting studies is the *item method*, in which individual items (e.g., single words) are presented one at a time, followed by an instruction to either remember or forget the item. Importantly, the remember/forget instruction typically does not appear until after the relevant item has disappeared, thus ensuring that the item is at least initially encoded. In item method directed forgetting studies, forget items are, again, more poorly recalled than remember items.

Although the two methods of directed forgetting are seemingly similar, the forgetting that is observed (of forget items) may have different causes. In the item method, evidence suggests that remember items benefit from preferential encoding, relative to forget items, with inhibition thought to play little role (Basden, Basden, & Gargano, 1993). In other words, remember items likely benefit from the remember instruction, but it is not clear that forget items actually *suffer* from the forget instruction. In the list method, however, preferential encoding in the control condition does not seem to account for the forgetting of list 1 items in the forget condition (Basden et al., 1993; Geiselman, Bjork, & Fishman, 1983). Rather, forgetting in the list method following a forget instruction has been explained in terms of either inhibition (e.g., Bjork, 1989) or an internal context change in response to the forget instruction (Sahakyan & Kelley, 2002). Although these two accounts of list-method directed forgetting are not mutually exclusive, the contextual change account has proven to hold substantial explanatory power (Sahakyan, Delaney, & Waldum, 2008).

Although directed forgetting has received considerable attention given its potential application to the control of real-life memories, the mechanistic ambiguity concerning the phenomenon creates challenges for studying memory inhibition. By contrast, a more recently developed paradigm—the Think/No-Think paradigm (M. C. Anderson & Green, 2001)—has allowed for a more direct assessment of the relationship between memory control and inhibition. In the Think/No-Think paradigm, participants first study a series of cue-associate pairs (e.g., “ordeal-roach,” “journey-pants”) and are trained to recall the associate word (e.g., “roach”) when presented with the cue (e.g., “ordeal”; Figure 30.6A). Next, participants engage in the Think/No-Think phase, in which they are presented with cues (the left-hand member of a cue-associate pair; e.g., “ordeal-”) from some of the previously studied pairs. For some of these cues, participants are instructed to retrieve (Think) of the corresponding associate. For other cues, participants are instructed to prevent the corresponding associate from

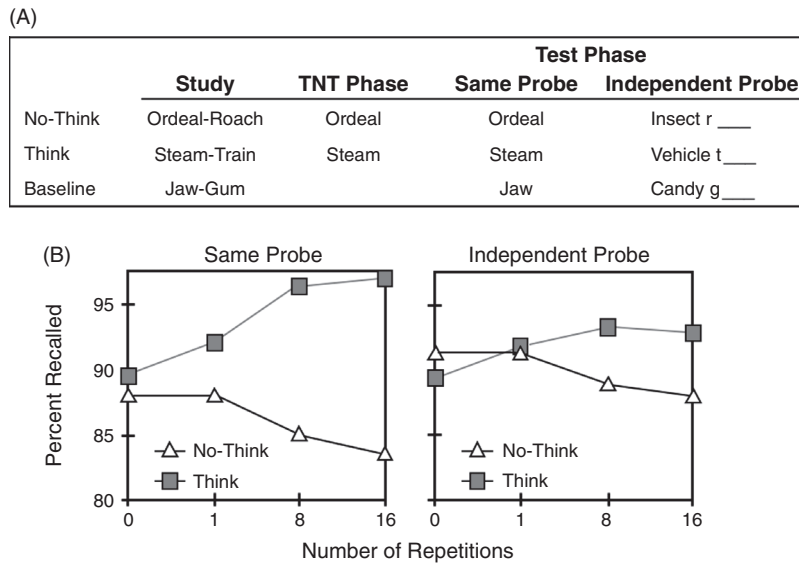


Figure 30.6 A: Outline of the Think/No-Think paradigm. **B:** Recall performance at test for “Think” items increases as a function of “Think” repetitions.

Note. (A) Critically, during the Think/No-Think phase, subjects are cued to think of the corresponding associate for “Think” items, but to avoid thinking of the response for “No-Think” items. Adapted from M. C. Anderson et al. (2004). (B) Recall performance for “No-Think” items decreases as a function of “No-Think” repetitions. This pattern is apparent both in the Same Probe and Independent Probe tests. From “Suppressing Unwanted Memories by Executive Control,” by M. C. Anderson and C. Green, 2001, *Nature*, 410, pp. 366–369. Copyright 2001 by Macmillan Publishers. Adapted with permission.

entering awareness (No-Think). Critically, participants are instructed that it is not enough to simply withhold a response on No-Think trials; rather, they are instructed to do their best to completely avoid thinking of the associate. Think and No-Think cues are repeated a varying numbers of times (e.g., 0, 1, 8, or 16 repetitions for each cue). Importantly, some of the cues never appear in the Think/No-Think phase, functioning as baseline items (0 repetitions). Finally, recall of all associates (Think, No-Think, Baseline) is tested.

Cued recall reveals that Think items are, not surprisingly, better remembered than No-Think items (Figure 30.6B). This result is essentially equivalent to the comparison of remember versus forget conditions in an item-method-directed forgetting study. However, to identify whether No-Think items actually suffered a cost, test-phase recall performance for No-Think items is compared to recall of Baseline items (i.e., items that were initially studied and trained, but that did not appear during the Think/No-Think phase). The Baseline condition provides a critical comparison condition (one that is not present in directed forgetting studies) for assessing whether No-Think items actually suffer a cost. That is, if No-Think instructions impair memory for No-Think items, then these items should be more poorly recalled than Baseline items. This is what is typically observed, with memory for No-Think items decreasing as a function of the number of No-Think repetitions that an item received (Figure 30.6B; M. C. Anderson & Green, 2001).

Although a cued-recall impairment for No-Think items relative to Baseline items is suggestive of memory inhibition, it is alternatively possible that the impaired recall of No-Think items simply reflects retrieval competition (interference) that arises at test—a concern that we considered above with respect to retrieval-induced forgetting. In

retrieval-induced forgetting, the concern over an interference explanation is perhaps more obvious, given that retrieval practice involves strengthening RP+ items that share a retrieval cue with RP– items. In the Think/No-Think paradigm, however, it is possible that when presented with No-Think trials, participants direct their thought away from the trained associate by thinking of something else; with repetition, this new, self-generated associate may be strengthened, relative to the originally trained associate. Accordingly, at test, the cue may elicit this self-generated memory, which would interfere with target recall.

As with retrieval-induced forgetting, the independent probe technique has been applied to the Think/No-Think paradigm in order to establish whether inhibition has actually occurred. For example, rather than testing the associate “roach” with the original cue “ordeal,” a new, independent probe such as “Insect-r” can be used. Critically, below-baseline forgetting of No-Think items is evident when independent probes are used at test (Figure 30.6; M. C. Anderson & Green, 2001; M. C. Anderson et al., 2004). Thus, although the Think/No-Think paradigm bears a procedural similarity to directed forgetting, the forgetting observed in the TNT paradigm has a clearer mechanistic cause—namely, deliberate attempts to keep a memory out of mind when presented with a reminder can result in inhibition of that memory. It should be noted, however, that, to the extent that participants approach No-Think trials in the Think/No-Think paradigm by actively remembering something else, the Think/No-Think paradigm and retrieval-induced forgetting may reduce to a common phenomenon. Consistent with this view, it has been demonstrated that inhibition in the Think/No-Think paradigm is most likely to occur when participants approach No-Think trials by generating diversionary thoughts (Hertel & Calcaterra, 2005).

Neurobiological Mechanisms of Stopping Retrieval

Given that the directed forgetting paradigm was developed 3 decades prior to the Think/No-Think paradigm, there have been considerably more attempts to understand the neurobiological basis of directed forgetting than inhibition in Think/No-Think. However, because the mechanisms of directed forgetting are more ambiguous, we briefly review several examples of the potential relationship between the PFC and directed forgetting before more fully considering the role of the PFC in the context of Think/No-Think paradigms.

Zacks, Radvansky, and Hasher (1996) compared directed forgetting between older and younger adults across multiple experiments, using both item- and list-method procedures, and consistently observed that older adults were poorer at directed forgetting than young adults, consistent with the hypothesis of an inhibitory deficit associated with aging. Specifically, relative to their baseline retrieval rate, older adults were more likely than young adults to retrieve items that had previously received a forget instruction. Although suggestive of an inhibitory deficit, there are, as the authors note, alternative accounts. For example, older adults might have been poorer at encoding remember/forget instructions, and/or as the experiment progressed, older adults may have had greater difficulty keeping track of which items were supposed to be remembered versus forgotten, potentially leading to inadvertent rehearsal of forget items. Thus, while the impairment of older adults in this context is in contrast to normal retrieval-induced forgetting among older adults (Aslan et al., 2007), it is not clear what accounts for this dissociation.

Directed forgetting has also been examined in frontal patients, but with somewhat variable results. For example, Conway and Fthenaki (2003) found impaired directed forgetting among frontal patients using both list and item method designs, with the impairment restricted to those patients with right frontal damage. However, Andrés, Van der Linden, and Parmentier (2007) reported normal item-method directed forgetting among frontal patients. Unfortunately, given the variability in the size and location of lesions across these studies, it is difficult to reconcile the discrepancies in the data or to draw conclusions about the mechanisms involved. Rather, it seems that, as with aging, frontal lobe damage may, at least in some cases, disrupt directed forgetting.

Finally, item-method directed forgetting has also been assessed using both ERPs and fMRI. In an ERP study, Paz-Caballero, Menor, and Jimenez (2004) observed an early (100 to 200 ms) frontal positivity for forget instructions, relative to remember instructions, that was only observed for those participants that showed a high amount of directed forgetting. The authors suggest that this frontal

positivity may reflect the engagement of the PFC in order to inhibit or stop processing of forget items. Although this interpretation involves an inhibitory component, it does not demand that forget items themselves are inhibited; rather, it could simply be that the processing of forget items is discontinued. Thus, this interpretation is compatible with the argument that item-method directed forgetting reflects preferential encoding of remember items. By contrast, Wylie, Foxe, and Taylor (2008) used an item-method-directed forgetting paradigm with fMRI and found that the right anterior VLPFC was more active for forget items that were actually forgotten, whereas a reverse pattern was observed for items that received a remember instruction. The authors argue that the positive relationship between the right anterior VLPFC and the forgetting of forget items suggests an active mechanism of forgetting, challenging the selective rehearsal account of item-method-directed forgetting. As previously described, activation in the right anterior VLPFC was also correlated with the forgetting of competing memories in the context of retrieval-induced forgetting (Kuhl et al., 2007), perhaps suggesting a common mechanistic contribution across these two contexts.

While the discussed ERP and fMRI studies of item-method-directed forgetting suggest an active mechanism is involved in stopping retrieval and, potentially, in inhibiting competing memories, these possibilities have been more directly assessed in a pair of fMRI studies using the Think/No-Think paradigm. These studies used emotionally neutral word pairs (M. C. Anderson et al., 2004) or emotionally valenced images (Depue, Curran, & Banich, 2007), and yielded several convergent outcomes. A key theoretical claim of M. C. Anderson's is that inhibition reflects the engagement of active control processes supported by the PFC (Levy & Anderson, 2002). Thus, in each study it was predicted that No-Think trials would not simply reflect the failure to engage retrieval mechanisms, but rather that No-Think trials would engage PFC control mechanisms to a greater extent than Think trials. M. C. Anderson et al. (2004) observed greater activation during No-Think versus Think trials in several PFC subregions, including bilateral DLPFC, VLPFC (inclusive of right anterior VLPFC), and ACC. In contrast, Think trials were associated with greater activation in the hippocampus—consistent with the role of the hippocampus in retrieving episodic memories (e.g., Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Kirwan & Stark, 2004). Similarly, Depue et al. (2007) observed greater No-Think than Think activation in the right DLPFC, right frontopolar cortex, and right anterior VLPFC; greater Think than No-Think activation was again observed in the hippocampus. Thus, with respect to the contrast of No-Think versus Think, both studies revealed activation in the right DLPFC and right anterior VLPFC.

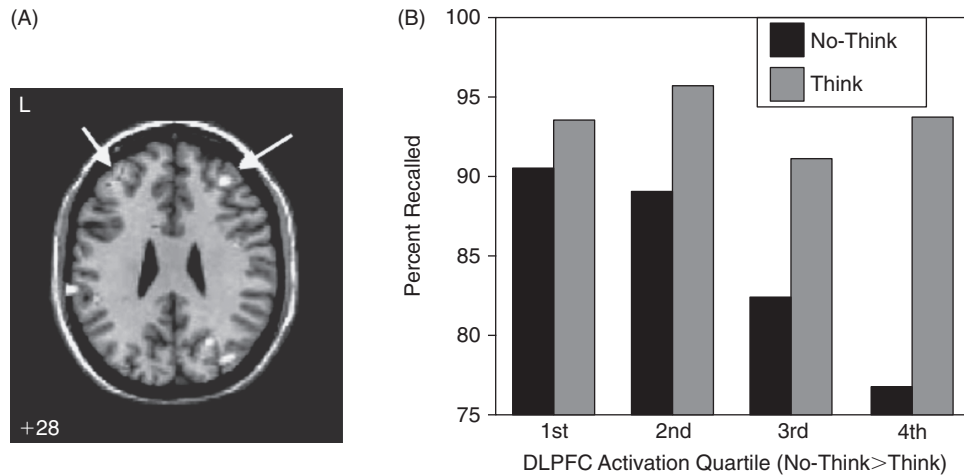


Figure 30.7 **A:** Activation in the bilateral DLPFC during “No-Think” trials was positively correlated with the inhibition score (i.e., forgetting of No-Think items at test). **B:** Participants who displayed the greatest DLPFC activation during No-Think trials were characterized by lower recall accuracy for No-Think items at test, relative to Baseline items.

Note. From “Neural Systems Underlying the Suppression of Unwanted Memories,” by M. C. Anderson et al., 2004, *Science*, 303, pp. 232–235. Copyright 2004 by the American Association for the Advancement of Science. Adapted with permission.

Strikingly, both studies also found that the engagement of the PFC during No-Think trials was related to the fate of the to-be-avoided memories. Specifically, the magnitude of activation in the DLPFC (bilateral in M. C. Anderson et al., 2004; Figure 30.7; right lateralized in Depue et al., 2007) positively correlated with the magnitude of inhibition (forgetting) of No-Think items. These data indicate that the DLPFC is recruited during attempts to stop retrieval, and that this recruitment is associated with a cost for those memories that are avoided.

Within the hippocampus, an intriguing pattern of data was observed. During Think trials, both Depue et al. (2007) and M. C. Anderson et al. (2004) observed that the hippocampus tended to be more active for items that were later remembered, relative to those that were later forgotten. By contrast, during No-Think trials, M. C. Anderson et al. (2004) reported a trend toward greater hippocampal activation for No-Think items that were later *forgotten*. This finding of greater hippocampal activation for No-Think items later forgotten compared to those later remembered was particularly robust among those participants who exhibited the most inhibition. If hippocampal activation is typically associated with remembering, then why is greater hippocampal activation on No-Think trials associated with forgetting? M. C. Anderson et al. suggest that such activation may reflect momentary intrusions of the to-be-avoided memories, noting that hippocampal activation during No-Think trials was also correlated with DLPFC engagement. Consistent with this interpretation, Depue et al. (2007) reported that hippocampal activation tended to

decrease across repetitions of No-Think items (presumably reflecting a practice-related decrease in intrusions), but increased across repetitions of Think trials. Moreover, this decrease in hippocampal activation across No-Think repetitions was apparent to a greater degree for the items later forgotten than those later remembered.

Together, these data suggest that hippocampal activation during No-Think trials may reflect inadvertent remembering, thereby triggering DLPFC-mediated control that results in the eventual inhibition of intruding memories. As such, these data are consistent with the competition-dependent property of retrieval-induced forgetting (i.e., that competition triggers inhibition) and are potentially compatible with the observation by Kuhl et al. (2007) that greater hippocampal activation during initial retrieval practice attempts was associated with greater inhibition of competing memories.

While M. C. Anderson et al. (2004) and Depue et al. (2007) found compelling evidence that the DLPFC was related to memory inhibition in Think/No-Think paradigms, Kuhl et al. (2007) observed a relationship between the right anterior VLPFC (and ACC) and memory inhibition in retrieval-induced forgetting. Although this apparent discrepancy in the foci of lateral PFC activations may, at first pass, suggest different mechanisms of inhibition in the two paradigms, there is a notable difference in the analyses reported by Kuhl et al. (2007) and those reported by M. C. Anderson et al. (2004) and Depue et al. (2007). Specifically, M. C. Anderson et al. and Depue et al. found that DLPFC activation, collapsed across all No-Think repetitions,

predicted memory inhibition, whereas Kuhl et al. (2007) found that activation *changes* in right anterior VLPFC activation (i.e., repetition-related reductions) predicted memory inhibition.

Although M. C. Anderson and colleagues (2004) did not consider their data as a function of repetition, Depue and colleagues (2007) separately considered activation in each of four quartiles (each quartile contained three repetitions of Think/No-Think items). Importantly, right anterior VLPFC activation during No-Think trials tended to decrease across repetitions—indeed, this region was engaged, above Baseline, only during No-Think trials in the first two quartiles. Although Dupue et al. did not report whether the magnitude of this decrease was related to the magnitude of inhibition, the data are at least consistent with the view that right anterior VLPFC engagement is decreasingly necessary as No-Think items are inhibited. By contrast, right DLPFC activation did not decrease across quartiles; in fact, right DLPFC only displayed above-Baseline activation during No-Think trials in the last three quartiles. Moreover, a negative correlation was observed between DLPFC and hippocampal activation that was maximal during the last quartile. Thus, while DLPFC activation was correlated with memory inhibition and hippocampal activation, the temporal profile of DLPFC activation raises interesting questions about its mechanistic contribution.

If intrusions during No-Think trials are most likely to occur during initial No-Think attempts, and these intrusions trigger DLPFC-mediated inhibition, as argued by M. C. Anderson and colleagues (2004), then why is the DLPFC most active during later repetitions, relative to initial repetitions? Moreover, why are hippocampal and DLPFC activation uncorrelated during initial No-Think repetitions (when intrusions are presumably highest), but strongly negatively correlated during late repetitions (when intrusions are presumably low)? These two aspects of the data seem to indicate that DLPFC engagement is highest when the *demand* for inhibition is actually lowest. Although not discussed by Depue and colleagues (2007), perhaps the increase in DLPFC activation across repetitions, and the increasingly negative relationship between the DLPFC and the hippocampus, reflects a practice-related improvement in the ability to engage the DLPFC. That is, during initial No-Think attempts, there may be a failure to engage the DLPFC to inhibit No-Think items; with practice, the DLPFC is successfully recruited and this is reflected in the down-regulation of the hippocampus. Importantly, this view suggests that DLPFC engagement is not an obligatory response to competition, but may be flexibly engaged to regulate competition.

Regardless of why DLPFC engagement onsets later than the right anterior VLPFC, the dissociation between

these regions is intriguing, particularly in light of evidence implicating each of these regions in other contexts that putatively involve memory inhibition. Moreover, it is also of note that the left mid-VLPFC, which has repeatedly been implicated in resolving mnemonic competition (for review, see Badre & Wagner, 2007), has not been implicated in the inhibition of episodic memories using either retrieval-induced forgetting or Think/No-Think paradigms. Although additional work is clearly necessary in order to better elucidate the relationship between these various PFC control mechanisms and the mechanisms of selective retrieval and inhibition, in the next section we attempt to synthesize the evidence reviewed thus far, situating this evidence in the broader context of how the PFC contributes to selective attention and goal-oriented behavior.

PREFRONTAL CORTEX CONTRIBUTIONS TO RETRIEVAL AND FORGETTING

Although our treatment of forgetting is grouped into two main themes—interference and inhibition—it should be clear that these are not two, independent causes of forgetting. Rather, the presence of competition can directly interfere with retrieval, thereby causing forgetting, but competition can also trigger the inhibition of competing memories, again contributing to forgetting. In other words, both forms of forgetting are ultimately related to the presence of competition and the mechanisms through which competition is resolved. Understanding the way in which competition is resolved is not, of course, a question that is specific to the domain of memory, as several influential models of PFC function are principally focused on mechanisms of competition resolution (e.g., Desimone & Duncan, 1995; Miller & Cohen, 2001; Shimamura, 2000). Thus, understanding the control processes that guide retrieval and forgetting should benefit from a consideration of the ways in which the PFC guides attention and goal-directed behavior. In this final section, we briefly consider how attention and cognitive control may be implemented through coordinated, but distinct, contributions from the ACC, DLPFC, and VLPFC.

By some accounts, attentional control may be implemented via two distinct frontoparietal networks (Corbetta & Shulman, 2002). At a first level, attention-grabbing changes in sensory stimuli, across multiple modalities, tend to activate a network of ventral fronto-parietal regions, with the right VLPFC perhaps the most frequently activated PFC sub-region (e.g., Downar, Crawley, Mikulis, & Davis, 2000; for review, see Corbetta & Shulman, 2002). For example, right anterior VLPFC activation has been associated with the reorienting of attention in response to, and in order to overcome,

distraction (Weissman, Roberts, Visscher, & Woldorff, 2006). This ventral fronto-parietal attentional system has been dissociated from a dorsal fronto-parietal system that is thought to support top-down orienting of attention, perhaps integrating bottom-up inputs with attentional task sets (Corbetta & Shulman, 2002). Although the frontal component of this dorsal system most frequently involves the frontal eye fields, the DLPFC may also be a component of this same system, particularly when considering attentional control outside the domain of visual attention (e.g., Luks, Simpson, Dale, & Hough, 2007). For example, in a now classic study, the role of the DLPFC in implementing control in a modified Stroop task was contrasted with that of the ACC (MacDonald et al., 2000). Critically, during task preparation, the DLPFC, but not the ACC, was modulated by the task instruction. During the trial itself, the ACC—but not the DLPFC—was modulated by the level of conflict (greater ACC engagement for incongruent versus congruent trials). Conceptually, similar dissociations between the DLPFC and ACC have since been reported (e.g., Weissman, Warner, & Woldorff, 2004), and from these and other observations, it has been argued that the DLPFC supports the top-down implementation of control.

Thus, with respect to attentional control, the VLPFC appears to be engaged in response to distracting or unexpected stimuli or events and serves to reorient attention. In a complementary manner, the DLPFC appears to play a critical role in volitionally engaging attention; this top-down allocation of attention may occur in preparation for a demanding cognitive task, but may also occur during task execution, to the extent that attended information interacts with task goals (Corbetta & Shulman, 2002).

Distinctions between the VLPFC and DLPFC have also been drawn in other domains, where a putatively hierarchical relationship between the VLPFC and DLPFC has often been emphasized. For example, with respect to the use of rules, it has been argued that the VLPFC supports the retrieval and maintenance of task rules, whereas the DLPFC may support flexible rule use or rule selection (for review, see Bunge, 2004). This view is supported by evidence that the VLPFC tends to be continuously engaged during rule maintenance, whereas the DLPFC tends to be engaged in preparation for a response (Bunge, 2004). Within the context of working memory paradigms, the DLPFC has frequently been implicated in response selection and top-down control, as opposed to simply maintaining information (e.g., Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000; for review, see Curtis & D'Esposito, 2003). The higher-order role of the DLPFC in working memory has been contrasted with the role of the VLPFC, which is thought to support retrieval or simple maintenance of information (D'Esposito et al., 1998; D'Esposito, Postle,

Ballard, & Lease, 1999; Petrides, 1996). For example, the VLPFC is engaged during rote rehearsal and during elaborative rehearsal that requires the manipulation or updating of working memory contents, whereas the DLPFC is selectively engaged by elaborative rehearsal (Wagner, Maril, Bjork, & Schacter, 2001). Moreover, DLPFC activation may lag VLPFC activation, consistent with the idea that the DLPFC operates on the products of information maintained/retrieved by VLPFC (Wagner et al., 2001). Similarly, within episodic memory, the VLPFC has been implicated in maintaining and elaborating on retrieval cues, whereas DLPFC has been implicated in monitoring the products of retrieval and their relation to decision rules (Dobbins et al., 2002; Dobbins & Wagner, 2005).

Returning to the theme of this chapter, a central question is how do selective retrieval and forgetting relate to these PFC processing distinctions? As we review, retrieval competition has been associated with the engagement of the VLPFC—both the left mid-VLPFC (Badre & Wagner, 2007; Thompson-Schill et al., 1997) and the right anterior VLPFC (Kuhl et al., 2007). However, the VLPFC has also been implicated in stopping retrieval (M. C. Anderson et al., 2004; Depue et al., 2007; Wylie et al., 2008), suggesting that VLPFC is engaged in response to competition from irrelevant memories, rather than remembering, *per se*. Indeed, it is a critical point that VLPFC engagement appears to be more tightly coupled with retrieval competition than with the actual phenomenon of retrieval. For example, repeated successful retrieval of the same information—which is associated with behavioral facilitation—is associated with robust decreases in the engagement of the bilateral VLPFC, but relatively little modulation of the DLPFC; in contrast, the actual phenomenon of retrieval success is associated with robust engagement of the DLPFC, but more limited activation of the VLPFC (Kuhl et al., 2007). Similarly, when task demands explicitly require stopping the act of retrieval, the right anterior VLPFC is engaged during initial attempts, but is less engaged with practice, presumably reflecting decreasing competition from to-be-avoided memories; DLPFC engagement, on the other hand, does not decrease across repeated attempts to stop retrieval, and may even tend to increase (Depue et al., 2007).

These dissociations between the VLPFC and DLPFC are potentially compatible with dual-system theories of attention (Corbetta & Shulman, 2002). As discussed, the VLPFC is thought to support reflexive orienting to distracting stimuli. Compatible with this perspective, in the context of mnemonic control, competing memories may serve as distracting representations that help reorient attention via VLPFC engagement. The DLPFC, on the other hand, may support the top-down allocation of attention. In situations of mnemonic control, it may be that the DLPFC

is not directly engaged *in response to* mnemonic competition, but rather is engaged to help bias mnemonic processing such that mnemonic goals are achieved. For example, the DLPFC may evaluate retrieval products with respect to task goals (Dobbins et al., 2002; Henson, Rugg, Shallice, & Dolan, 2000), and may therefore be sensitive to retrieval success. Alternatively, or additionally, the DLPFC may implement attentional biases that, once in place, effectively reduce mnemonic competition. Although a distinction between the VLPFC and DLPFC based on reflexive versus top-down control, respectively, may hold some explanatory power, it should be noted that the left VLPFC has also been implicated in implementing top-down control during retrieval (e.g., Badre et al., 2005). Thus, further evidence is necessary in order to better specify the mechanistic distinctions between VLPFC and DLPFC control processes and their relation to mnemonic processing.

Although the distinction between the VLPFC and DLPFC has been of particular interest in theories of PFC-mediated control, it is worth emphasizing that these regions (a) act in concert with other prefrontal structures (e.g., ACC and frontopolar cortex), and (b) can likely be further subdivided into distinct functional units. With respect to other PFC control mechanisms, the ACC may support an initial component of cognitive control, in that it can detect competition between multiple, coactive representations (Botvinick et al., 2001; Braver et al., 2001; van Veen & Carter, 2002). Importantly, ACC engagement has frequently been shown to correlate with DLPFC engagement (Badre & Wagner, 2004; Bunge, Burrows, & Wagner, 2004; Kondo, Osaka, & Osaka, 2004), leading to the hypothesis that ACC-mediated competition detection triggers DLPFC-mediated control. Such couplings have been observed in the context of competitive remembering (Bunge et al., 2004; Kuhl et al., 2007), with one possibility being that the computation performed by the DLPFC, in response to ACC signaling, is to increase activation of goal-relevant memories (Miller & Cohen, 2001). The frontopolar cortex, on the other hand, may be situated at the top of the PFC processing hierarchy (Koechlin & Summerfield, 2007), coordinating VLPFC/DLPFC operations with specific subgoals (Braver & Bongiolatti, 2002). Consistent with a supervisory role of the frontopolar cortex, initial attempts to stop retrieval result in coupled activation between the right anterior VLPFC and frontopolar cortex, whereas later attempts are associated with coupling between the DLPFC and frontopolar cortex (Depue et al., 2007).

Finally, while the organizing principles of the VLPFC and DLPFC that we consider here may be useful in terms of constraining hypotheses of how the PFC implements control, both the VLPFC and DLPFC can likely be further decomposed into distinct functional units (e.g., Badre

et al., 2005; Dobbins et al., 2002; Gold et al., 2006). For example, within the VLPFC, the left mid-VLPFC has been implicated in selecting between multiple, active representations, whereas the left anterior VLPFC has been implicated in controlled retrieval of semantic information through direct interaction with posterior semantic stores (for review, see Badre & Wagner, 2007). In other words, there are likely multiple ways in which the VLPFC responds to competition and multiple ways in which the DLPFC coordinates mnemonic processing. Future work will undoubtedly advance understanding of both the specific mechanisms supported by PFC subregions as well as the way in which these mechanisms act in concert such that mnemonic competition is resolved.

SUMMARY

In this chapter, we highlighted the interrelated nature of remembering and forgetting, and the substantial impact that prefrontal function has on each. Specifically, the prefrontal cortex serves to guide retrieval toward goal-relevant memories and away from those memories that prove irrelevant. These prefrontal-mediated operations have important consequences both for what we presently remember as well as what we later forget. Moreover, multiple, functionally distinct prefrontal subregions are involved in coordinating these mnemonic operations, likely reflecting the engagement of broader cognitive control mechanisms that allow for the flexible allocation of attention. Accordingly, a complete telling of the story of forgetting and remembering will ultimately entail full specification of the many ways in which the frontal lobes shape acts of retrieval.

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604 Forgetting and Retrieval

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