

Using fMRI to investigate a component process of reflection: Prefrontal correlates of refreshing a just-activated representation

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Using fMRI, we investigated the functional organization of prefrontal cortex (PFC) as participants briefly thought of a single just-experienced item (i.e., *refreshed* an active representation). The results of six studies, and a meta-analysis including previous studies, identified regions in left dorsolateral, anterior, and ventrolateral PFC associated in varying degrees with refreshing different types of information (visual and auditory words, drawings, patterns, people, places, or locations). In addition, activity increased in anterior cingulate with selection demands and in orbitofrontal cortex when a nonselected item was emotionally salient, consistent with a role for these areas in cognitive control (e.g., overcoming "mental rubbernecking"). We also found evidence that presenting emotional information disrupted an anterior component of the refresh circuit. We suggest that refreshing accounts for some neural activity observed in more complex tasks, such as working memory, long-term memory, and problem solving, and that its disruption (e.g., from aging or emotion) could have a broad impact.

A basic challenge for cognitive neuroscience is clarifying the neural substrates of the reflective cognitive operations that we call thought. Converging evidence from lesion and neurophysiological studies of animals, clinical observations and neuropsychological studies of brain-damaged human patients, and neuroimaging studies of neurologically intact humans indicates that the prefrontal cortex (PFC) plays a critical role in higher order processes of cognition: attention, memory, planning, problem solving, decision making, and so forth (for reviews, see, e.g., Cabeza & Nyberg, 2000; D'Esposito, Postle, & Rypma, 2000; Goldman-Rakic, 1987; Miller, 2000; Owen, 2000; Petrides, 1994; Shimamura, 1995; Smith & Jonides, 1997; Stuss & Levine, 2002).

Furthermore, investigators have raised the question of whether different PFC regions subserve different functional processes and/or different types of information. Logically, PFC could be organized in several ways: by type of process or type of information processed; by combinations of process and information; with no stable

organization but with PFC flexibly recruited to meet varying task demands; or with different areas organized in these different ways (Johnson, Raye, Mitchell, Greene, & Anderson, 2003). For example, it has been proposed that dorsolateral and ventrolateral PFC are associated, respectively, with manipulation/monitoring and maintenance/inhibition (D'Esposito, Postle, Ballard, & Lease, 1999; D'Esposito et al., 2000; Owen, Evans, & Petrides, 1996; Petrides, 2000; Smith & Jonides, 1999) or with spatial and nonspatial information (D'Esposito et al., 1998; Goldman-Rakic, 1987, 1995; Haxby, Petit, Ungerleider, & Courtney, 2000); that left and right PFC are associated, respectively, with encoding and retrieval (Habib, Nyberg, & Tulving, 2003; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994), systematic and heuristic processing (Nolde, Johnson, & Raye, 1998), or verbal and nonverbal information (Kelley et al., 1998; Raye, Johnson, Mitchell, Nolde, & D'Esposito, 2000; Wagner et al., 1998); that PFC is functionally organized by both process and type of information (Johnson et al., 2003); and that PFC is not functionally organized by type of information (Nystrom et al., 2000) or type of task (Duncan & Owen, 2000). Thus, although individual studies support one or another of these possibilities, there is no general consensus about the organization of functions within PFC (see, e.g., Goldman-Rakic, 2000; Miller, 2000; Owen, 2000).

Part of the difficulty in reaching consensus about the functional organization of PFC is the complexity of higher order cognition (see, e.g., Müller, Machado, & Knight, 2002). Assuming that higher order cognitive tasks require iterations and combinations of simpler component

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processes, it would be difficult to identify which neural activity is associated with which component process in a given complex task, even if specific PFC regions subserve specific component processes. For example, a commonly used working memory (WM) task, the *n*-back task (see, e.g., J. D. Cohen et al., 1997), minimally involves a combination of rehearsing the target set, noting whether the current item matches the target item, and updating the target and the rehearsal set by dropping the oldest item (the old target) and adding the current item to the rehearsal set. In addition, the more complex the task, the more likely it is that different people will perform the task in different ways. Such variability among participants in the strategies they use creates further uncertainty in associating brain activity with particular processes. Thus, clarifying the functional organization of PFC requires finding a level of analysis for characterizing processes that minimizes variability in strategies among participants as to whether the process is engaged and that captures commonalities across similar mental events. Such clarification may be difficult to accomplish using complex maintenance and manipulation tasks (see, e.g., Johnson, 1992, and Johnson et al., 2003, for further discussion).

Recent reviews of the neuroimaging literature (e.g., Cabeza & Nyberg, 2000; Duncan & Owen, 2000) show that the same PFC areas appear to play a role in tasks that seem, on the surface, quite different. The fact that many of the same regions of activation appear across studies may imply that these regions are flexibly deployed for quite different processes and types of information or, alternatively, may indicate some limited set of basic component processes that are recruited in different combinations for various tasks (Johnson, 1992; Wager & Smith, 2003). Work in our laboratory has focused on the latter possibility.

If we assume that there are component processes of cognition, what should be the criteria for identifying a component process? Reasonable cognitive neuroscience criteria might include (1) an operational definition that distinguishes the process from other processes; (2) identifying brain regions associated with the process; (3) distinguishing neural activity associated with the process from activity associated with other component processes; (4) demonstrating functional correlates of activity in these regions (e.g., improved memory); (5) showing behavioral disruption (loss of efficacy or efficiency) associated with damage to or dysfunction of the region(s) presumed to mediate the process; and (6) specifying how the process and its neural correlates change with changes in the situation (e.g., changes in the nature of the representations on which the process acts or changes in the context within which the process is carried out, such as changes in potential interference).

With these criteria in mind, we describe several previous studies and report six new experiments and a meta-analysis, all investigating a component process of reflection. This process is one of the most basic mental

acts, *refreshing*—that is, briefly thinking of something just after it is no longer present but while a representation is still active (Johnson, 1992; Johnson, Reeder, Raye, & Mitchell, 2002). The targets of refreshing can be recent thoughts or perceptions. Refreshing is an instance of reflective attention, which is different from perceptual attention in that the target is no longer externally available. It is a cognitive operation that is engaged and executed immediately, and can be conceptually and operationally distinguished from other processes, such as *rehearsing*, which typically involves one or more items cycled in a loop several times over several seconds (see, e.g., Baddeley & Hitch, 1974), or *reactivating*, by which information that is no longer active is activated (see, e.g., Johnson & Chalfonte, 1994; Johnson, Hashtroudi, & Lindsay, 1993; Johnson et al., 2002).

It may be useful to consider the relation among the concepts of iconic memory, working memory, and refreshing. *Iconic memory* refers to the idea that the processing of perceptual stimuli results in the creation or temporary activation of perceptual representations; this activation rapidly decays unless attention is allocated to the representations while they are “in” iconic memory (see, e.g., Sperling, 1960). Refreshing could be thought of as a specific process by which covert attention can be directed toward a representation in iconic memory or toward a representation of a just-previous thought (Johnson et al., 2002). Representations in iconic memory can also be rehearsed. Once items are in a WM rehearsal loop, refreshing is a process by which selective attention could be directed toward a specific WM representation. That is, we assume that the process(es) by which a representation is passively maintained briefly in iconic memory, by which it is actively maintained for a longer period in WM (e.g., rehearsing), and by which such active iconic or WM representations might receive focused or selective attention (e.g., refreshing) are different. The result of refreshing presumably is to briefly extend or augment the activity of a representation; thus, refreshing can be thought of both as a minimal maintenance process, in its effect of extending activity of a representation, and as a minimal manipulation process, in its effect of foregrounding a particular representation relative to others.

In each experiment described below, we directly compared the brain activity associated with refreshing a perceived item with that associated with perceiving the same item again or perceiving another item from the same class of materials. Our main focus was on refresh-related brain regions—that is, those areas in which activity was greater in the refresh than in a control condition. Thus, the nominal target was held constant across experimental conditions, and the brain regions identified presumably were involved in engaging and carrying out the reflective operation of refreshing an active representation. Across our experiments, we varied the type of information refreshed; we also varied the conditions under which the item was selected for refreshing in order to in-

investigate how refresh-related neural activity changes in different cognitive contexts that vary in their demands for cognitive control.

Converging Evidence for a Process of Refreshing

Raye, Johnson, Mitchell, Reeder, and Greene (2002) instructed young adults to read single words silently as they appeared on a screen. Event-related trials of three conditions were randomly intermixed. Participants read a word that was followed 550 msec later by either a different word (*read* condition), the same word (*repeat* condition), or a dot cue that signaled the participant to think of the just-previous word (*refresh* condition). Raye et al. (2002) identified a region in left dorsolateral PFC, middle frontal gyrus (GFm)¹ BA 9, where activity was significantly greater on refresh than on read or repeat trials (i.e., refresh-related activation). In addition, activation was greater in left BA 9 for items that were subsequently recognized than for items that were subsequently missed on a long-term recognition test. In a control experiment, refresh-related activity was again obtained in left GFm BA 9 when task-switching requirements were reduced by blocking refresh and repeat trials. In another control experiment, no significant refresh-related activity was seen in left GFm when participants were instructed to think “dot” whenever they saw the dot (rather than to refresh) or when they were presented with a symbol and instructed to think “up” when it was in one orientation or “down” when it was in another. These control experiments argue against the possibilities that activity observed in left dorsolateral PFC was a result of task switching, responding to a symbolic cue, or thinking any thought in response to a cue.

Other evidence supporting the specificity of a left-lateralized refresh process comes from a study in which the cognitive operation was changed (Johnson et al., 2003, Experiment 2). In that study, on each trial, an item was presented in black. It was followed after 550 msec by a different black item (a read trial similar to those in Raye et al., 2002) or by a red item that signaled the participant to silently *note* whether or not the item had been presented earlier (short-term old/new recognition). Across noting trials, there were three types of red items—an old item that was the same as the just-previous black item (*immediate* condition), an old item that was the same as a black item from two or three trials previously (for up to a 36-sec *delay*), or an item that had not been presented previously (*new* condition). Relative to read trials, these old/new recognition trials required a judgment from participants—to note whether the item was old or new. Noting whether an item is old or new after minimal encoding and very short retention intervals presumably involves primarily evaluation of familiarity/novelty or relative recency (see, e.g., Mitchell, Johnson, Raye, & Greene, 2004). Noting whether a word had been seen earlier was associated with activity in the GFm BA 9 area of right dorsolateral PFC. Johnson et al. (2003) suggested that the bilateral dorsolateral activity often observed in WM tasks such as the *n*-back task might be the

result, in part, of combinations of refreshing (left PFC) and noting whether the target was matched (right PFC).

If refreshing is associated with left dorsolateral PFC activity, then deficits in refreshing should be associated with reduced activity in this area. Two recent studies investigating age-related changes in refreshing provide relevant evidence. Johnson et al. (2002) reported a cognitive/behavioral study showing that in comparison with results from reading a new or repeated word, older adults took disproportionately longer than young adults to refresh a word and, unlike the young adults, did not get a significant benefit in long-term recognition memory from refreshing. In a subsequent fMRI study (Johnson, Mitchell, Raye, & Greene, 2004), this behavioral pattern was replicated with new groups of young and older adults, and older adults showed a refresh-related deficit in an area of left GFm that was within two voxels of the local maximum of the refresh area identified in Raye et al. (2002). These results comparing older and young adults provide converging evidence for the functional importance of refreshing and the involvement of left GFm in this process.

Refreshing Across Information Domains

With evidence for the first five of our criteria for identifying refreshing as a component process, we asked whether PFC regions associated with refreshing are different for different types of information. Is left PFC activity found when participants refresh information other than words, and if so, is the distribution of activity across left PFC the same or different depending on the type of information? In our first study investigating this question, participants refreshed words, outline drawings of objects, and abstract patterns in separate blocks of trials (Johnson et al., 2003, Experiment 1). Left GFm activity was associated with refreshing all three types of material, but the distribution of activity differed between words, on the one hand, and objects and patterns, on the other (activation was more dorsal and lateral for words and more anterior for objects and patterns).

The predominance of left lateralized activity during refreshing even for nonverbal materials was surprising, given previous reports that associate right PFC with processing pictorial material (Kelley et al., 1998; Raye et al., 2000; Wagner et al., 1998; see also a recent TMS study by Floel et al., 2004). However, previous studies used more complex tasks and did not clearly separate perceptual and reflective processes. It may be that perception is more strongly lateralized with respect to materials than is reflective thought. Alternatively, the materials we investigated might not have been the kind most likely to recruit right PFC during refreshing. Because the outline drawings were all nameable objects, participants may have refreshed their names, and the patterns may have been difficult to refresh pictorially.

To further investigate the issue of PFC organization by type of information given a specific process, we compared the refreshing of words with the refreshing of places, people, and spatial locations. In a fourth experiment, we compared refreshing of visually and auditorily

presented words. In two additional experiments, we held type of information constant (words) and varied the amount of control required in refreshing by manipulating the number of active representations (Experiment 5) or their relative salience (Experiments 6A and 6B). After describing these individual experiments, we will report the results of a meta-analysis across studies that provides converging evidence regarding the PFC areas associated with refreshing.

EXPERIMENT 1

Refreshing of Words–People–Places

Method

Participants. The Human Investigation Committee of Yale University Medical School approved all protocols used. In all cases, the participants were healthy, right-handed young adult volunteers from the Yale University community who gave written informed consent. Table 1 presents *N*s, gender distributions, and age information for each experiment.

Procedure and Materials. In all experiments, stimuli were projected during scanning onto a screen at the foot of the scanner; the participants viewed the screen through a mirror mounted on the head coil. The refresh procedure followed that in Raye et al. (2002) and is described in detail for Experiment 1; variations from this procedure are noted as each subsequent experiment is presented.

Each event-related trial was 12 sec long (see Figure 1.1); the structure and timing of trials were the same for each type of material. For word trials, the participants were instructed that whenever they saw a word on the screen, they should just read it silently to themselves. All words appeared in the center of the screen for 1,550 msec. On read trials, the initial word was followed 450 msec later by a new word; on repeat trials, the initial word was followed by a repetition of the word; and on refresh trials, the initial word was followed by a dot (•) that signaled the participants to think of (refresh) the just-preceding word. Duration of the second stimulus was also 1,550 msec. For the pictures of people and places, the participants were told to only look at each stimulus as it appeared on the screen. Trials with these stimuli on which an item was followed by a new item are called “read” trials for consistency, but of course the participants simply looked at the people and place pictures on these trials. As in the word condition, a third of the people and place pictures were followed by a new item (read), a third by the same item (repeat), and a third by a dot that signaled the participants to think of the picture that preceded the dot (refresh).

The word stimuli consisted of 84 common one- to three-syllable words (e.g., *knee*, *canoe*, *professor*). The people stimuli (see Figure 1.1 for examples) consisted of 84 grayscale photographs of individuals (males and females from a broad range of ages, in various poses and against different backgrounds), and the place stimuli were 84 color photographs of indoor and outdoor places (e.g., a living room or office building) taken from Henke, Buck, Weber, and Wieser (1997) and from similar materials readily available on the

Internet. In each of seven runs, 9 trials of each material type (3 from each condition—read, repeat, and refresh—randomly intermixed) were presented in a blocked fashion (e.g., Run 1 = 9 word trials followed by 9 person trials followed by 9 place trials, Run 2 = person/word/place, etc.). Thus, per participant, there were 63 trials per material type (21 trials in each condition, 126 fMRI images per condition/material type). Order of the three material types was pseudorandomly varied across runs for a single participant, and different orders were used across participants to ensure that each material type appeared nearly equally often in each ordinal position across runs and participants. As in all experiments presented here, each item occurred equally often in each of the three conditions across participants for all material types.

At the end of each trial, the participants saw a series of three arrows presented sequentially for 1,400 msec each (600-msec interstimulus interval), followed by 2,600 msec of blank screen. The participants responded to the arrow task using a fiberoptic response pad (Current Design, Philadelphia, PA) with their right hand. They were told that they should push the left button with their index finger if the arrow pointed left or push the right button with their middle finger if it pointed right. (In subsequent experiments, the participants had a response pad for each hand and pressed a button with their left hand for the left arrow or another button with their right hand for a right arrow.) This arrow task was used in all experiments presented here; it provided an 8-sec intertrial interval (ITI) task, common to all conditions, to allow for the hemodynamic response associated with reading/looking or refreshing. We used this procedure rather than a rest period to reduce variability among participants from uncontrolled mental activity (Raye et al., 2002). Note that the arrow task was not used as a baseline against which each experimental condition was contrasted, but rather as a common activity across conditions to space out the trials. In all experiments reported here, statistical analyses compared fMRI signals during the experimental conditions (e.g., read, repeat, refresh), as described in the fMRI analyses section.

Imaging details. The imaging details were the same for Experiments 1–4. T1-weighted anatomical images were acquired for each participant using a 1.5T GE SIGNA scanner at the Yale University School of Medicine. Functional scans were acquired with a single-shot echoplanar gradient-echo pulse sequence (TR = 2,000 msec, TE = 35 msec, flip angle = 80°, FOV 24). Experiment 5 was run on a 1.5T Siemens Sonata scanner, and Experiment 6B was run on a 3T Siemens Magnetom Trio scanner, both at the Magnetic Resonance Research Center at Yale University. These experiments used the same scanning parameters as in Experiments 1–4, except that for Experiment 6B the anatomical images were T2-weighted and the TE for the functional scans was 25 msec. In all experiments, 24 axial slices (slice thickness = 3.8 mm, resolution = 3.75 × 3.75 mm in plane) were aligned with the AC–PC line. Each run began with 12 blank seconds to allow tissue to reach steady-state magnetization, and each was followed by a 1-min rest interval. One volume was collected every 2 sec, or six full-brain scans for each trial.

fMRI analyses. Data were motion corrected using a 6-parameter automated algorithm (AIR; Woods, Cherry, & Mazziotta, 1992). A

Table 1
Number and Mean Age of Participants for Each Experiment

Experiment	<i>N</i>	Females	Males	Mean Age (Range)
1: Word–people–places	14	8	6	22.6 years (19–28)
2: Words–locations	12	5	7	20.8 years (18–29)
3: Locations	17	9	8	20.8 years (19–27)
4: Words (visual–auditory)	15	7	8	21.5 years (18–30)
5: Selective refreshing: Words (1 of 1 vs. 1 of 3)	15	10	5	23.2 years (18–26)
6: Words (neutral–emotional)				
A. Behavioral	23	14	9	20.4 years (18–30)
B. fMRI	14	11	3	20.6 years (18–28)

Word, Person, or Place	Delay	New Item (Read) Same Item (Repeat) or • (Refresh)		<		>		>		Blank
1,550 msec	450	1,550	450	1,400	600	1,400	600	1,400	600	2,000

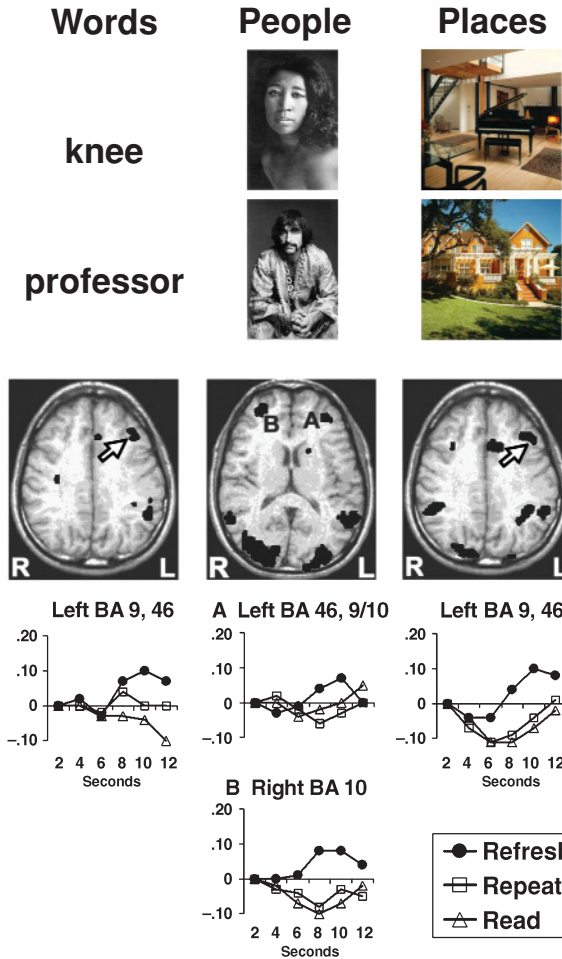


Figure 1.1. Trial event time line for Experiment 1, some example stimuli, and PFC areas and associated average within-trial time courses showing a significant condition \times time interaction for each material type: words, people, or places. For time courses in all figures, the x -axis represents time within a trial (in seconds), and the y -axis represents mean percent signal change from the first within-trial time point. Abbreviations of brain areas follow Talairach and Tournoux (1988; see note to Table 2). BAs and anatomical areas are listed in descending order of approximate size, with approximately equal areas of activation indicated by a slash. Slices in all figures were chosen to show representative activations, but the Talairach coordinates in Table 2 are for local maxima.

12-parameter AIR algorithm was used to co-register each participant's images to a common reference brain. Data were mean normalized across time and participants and spatially smoothed (3-D, 8-mm FWHM Gaussian kernel).

The data were analyzed using the NeuroImaging Software package (NIS; Laboratory for Clinical Cognitive Neuroscience, University of Pittsburgh, and the Neuroscience of Cognitive Control Laboratory, Princeton University). For all studies, analyses of variance (ANOVAs) had participant as a random factor and other factors, such as condition (e.g., read, repeat, or refresh), material (e.g., word, people, or places), time within trial (volumes 1–6), and run

(e.g., 1–4), as fixed factors. Initial analyses were conducted for each material separately, and we will report regions identified in the condition \times time interaction that had a minimum of six contiguous voxels, each significant at least at $p < .001$ (Forman et al., 1995). Three-way interactions (e.g., material \times condition \times time) were evaluated at $p < .01$. Specific follow-up analyses contrasted percent change (from Scan 1) between conditions or materials at the critical period of the trial (e.g., Scans 4, 5) ($p < .05$). In all experiments, F maps were transformed to Talairach space using the AFNI software (Cox, 1996), and areas of activation were localized using Talairach Daemon software (Lancaster, Summerlin, Rainey,

Table 2
PFC and ACC Regions of Activation in Experiments 1–6 and Meta-Analysis,
Along With Talairach Coordinates (*x, y, z*) of Local Maxima and Maximum *F* Values
for the Relevant Comparison

	Comp	L/R	BA	Anatomical Area	<i>x</i>	<i>y</i>	<i>z</i>	max <i>F</i>
Experiment 1	C × T							
Words		L	9, 46	GFm	-37	28	32	4.46
		L	46, 45	GFi, GFm	-36	37	3	3.41
People		L	46, 9/10	GFm	-33	42	16	3.70
		R	10	GFm/GFs	28	51	16	4.02
		R	13	ins	42	6	0	3.76
		Md	32/24	ACC	-2	21	26	5.05
Places		L	9, 46	GFm	-38	27	28	5.21
		L	13	ins, Cl, Pu	-36	14	1	8.83
		Md	32, 24	ACC	-5	14	30	6.53
	M × C × T	L	10, 46	GFm, GFs	-37	44	16	2.39
		L	13, 9, 47, 46, 45	ins, GFm, GFi	-36	23	9	3.04
		R	10	GFs, GFm	28	51	12	2.21
		Md	24	ACC	3	6	27	2.98
Experiment 2	C × T							
Words		L	6, 9, 44	GPrC, GFm, GFi	-44	2	34	5.53
		L	9/46	GFm	-45	18	31	4.09
		L	10/46	GFm/GFi	-40	41	10	3.61
		L	44	GFi, GPrC	-53	11	14	3.85
		R	44, 45	GFi	50	10	15	4.73
		Md	32, 24, 6	ACC, GFd	-6	20	39	7.26
Locations		L	9, 44, 6, 13	GFi, GFm/GPrC, ins	-53	6	34	6.64
		L	10/46	GFm, GFs, GFi	-34	50	23	6.01
		R	9/10	GFm	33	41	24	4.09
		R	6/9	GFi/GPrC	44	2	26	3.94
		R	13, 44, 22	ins, Cl, GPrC, GTs	42	10	3	5.34
		Md	32, 24, 6	ACC, GFd	-1	8	48	7.31
Experiment 3	C × T							
Locations		L	9, 10, 46	GFm	-33	58	22	6.69
		L	6/9/44, 47, 13, 45	GFi, GFm, GPrC, ins	-44	-4	38	8.79
		R	10, 46	GFm	28	44	22	4.15
		R	6, 9	GPrC, GFi/GFm	38	-1	40	4.25
		R	47, 44, 45, 13	GFi/ins	38	6	2	8.96
		Md	32, 6, 24	ACC, GFd	-2	13	43	12.97
Experiment 4	C × T							
Words: Visual		L	6	GPrC, GFm	-37	-4	35	4.01
		L	47, 44, 45	GFi, L Orb, GTs	-53	11	-1	8.32
		R	47, 13, 22	GFi, ins, GTs	46	10	-3	4.89
		Md	32, 24, 6	ACC, GFd	3	8	44	6.60
Words: Auditory		L	8	GFm, GPrC, GFs	-37	19	42	7.89
		L	8, 9, 6	GFd, GFs	-7	39	34	5.05
		L	44, 6	GFi, GPrC	-52	6	10	4.31
		L	47, 45, 13	L Orb, GFi, ins	-50	45	-9	6.89
	M × C × T	L	45/47	GFi	-40	30	3	3.09
Experiment 5	C × T							
Words		L	6	GPrC, GFm	-37	7	42	7.18
		L	13	ins/Cl	-36	7	6	9.18
		R	13, 44	ins/Cl, GPrC	46	10	3	8.53
		Md	32	ACC	2	12	39	8.57
	N × C × T	L	44, 9, 6	GFm, GFi, GPrC	-45	3	34	4.84
		Md	6, 32/24	GFd, GFs, ACC	-2	5	51	6.01
		L	45	GFi	-45	22	14	4.32
		R	6	GFm	34	-5	48	4.78
Experiment 6B	C × T							
Words		L	9/6	GFm	-33	0	40	6.14
		L	44, 6, 9	GFi, GFm, GPrC	-54	10	30	7.47
		L	13, 47	ins, GFi	-33	21	-5	8.73
		R	13	ins	38	17	-5	6.17
		Md	32, 6, 8	ACC, GFd	-2	16	40	6.24
	E × C × T	R	11	A Orb	24	67	-12	7.56

Table 2 (Continued)

	Comp	L/R	BA	Anatomical Area	x	y	z	max <i>F</i>
ω^2 Meta-analysis		L	9/6	GFm	-38	5	36	
		L	10, 46	GFm, GFs	-30	49	16	
		L	47, 45/13	GFi, ins	-37	23	-2	
		R	47, 45, 13	GFi, ins	45	16	-1	
		Md	32	ACC	± 3	19	31	
		L	6	SFs	-23	0	43	
		R	10, 46	GFm	36	52	14	
		L	45, 44	GFi	-45	19	16	

Note—Comp, comparison; C, condition; T, time; M, material; N, number; E, emotion; L, left; Md, medial; R, right; BA, Brodmann area; ACC, anterior cingulate; A Orb, anterior orbital gyrus; Cl, claustrum; GF, fusiform gyrus; GFD, medial frontal gyrus; GFi, inferior frontal gyrus; GFm, middle frontal gyrus; GFs, superior frontal gyrus; GL, lingual gyrus; GO, orbitofrontal gyrus; GOi, inferior occipital gyrus; GOM, middle occipital gyrus; GPrC, precentral gyrus; GTs, superior temporal gyrus; ins, insula; L Orb, lateral orbital gyrus; Pu, putamen; SFs, superior frontal sulcus. Abbreviations of brain areas follow Talairach and Tournoux (1988). BAs and anatomical areas are listed in decreasing order of approximate size, with approximately equal areas of activation indicated by a slash.

Freitas, & Fox, 1997) and manually checked against the Talairach and Tournoux (1988), Duvernoy (1999), or Mai, Assheuer, and Paxinos (1997) atlases. All refresh-related PFC and anterior cingulate (ACC) regions identified in each experiment are described in Table 2; some areas are also shown in figures. Time courses in figures show mean percent change in signal value from Time 1 within a trial.

Different posterior brain regions are involved in perceptually processing different types of information (e.g., visual vs. auditory or faces vs. scenes; see, e.g., Epstein & Kanwisher, 1998; Kanwisher, McDermott, & Chun, 1997) and in reflectively imagining or rehearsing different types of information (Druzgal & D’Esposito, 2003; O’Craven & Kanwisher, 2000). Thus, whereas we would expect different posterior regions to be involved when different materials are being refreshed, here we are primarily concerned with whether PFC component(s) of refreshing vary with materials and conditions (e.g., potential competition). Posterior regions associated with refreshing will be discussed in a separate article.

Results

As can be seen in Figure 1.1, when each type of material was analyzed separately, we found activity in left GFm associated with the refreshing of words, people, and places. As shown in Table 2, all three types of materials also showed activity in ventral areas (GFi or insula, left for words and places, right for people). Figure 1.1 (B) also shows that for people there was refresh-related activity in right anterior GFm/GFs that was contralateral to and somewhat larger in extent than the left GFm activity.

Including the three types of materials in the same analysis resulted in three areas of PFC that showed a material \times condition \times time interaction (see Figure 1.2). An area of left GFm (A) showed refresh-related activity for all three types of materials but varied in the shape of the refresh time lines (e.g., in time of peak, slope); a left area of largely insula (B) showed more sustained refresh-related activity for places; and, notably, an area of right anterior GFm/GFs (C) showed the most activity for people. These findings add to those we previously reported (Johnson et al., 2003), indicating the involvement of left GFm in refreshing across a range of types of information, with some differences in the distribution of activity in PFC as a function of the type of information refreshed.

Whereas frontal areas clearly showed greater activity for the refresh than for the read or repeat condition, more

posterior areas (e.g., GOM; see Figure 1.3) showed greater activity for the read and repeat than for the refresh condition. That is, as in previous studies (Johnson et al., 2003,

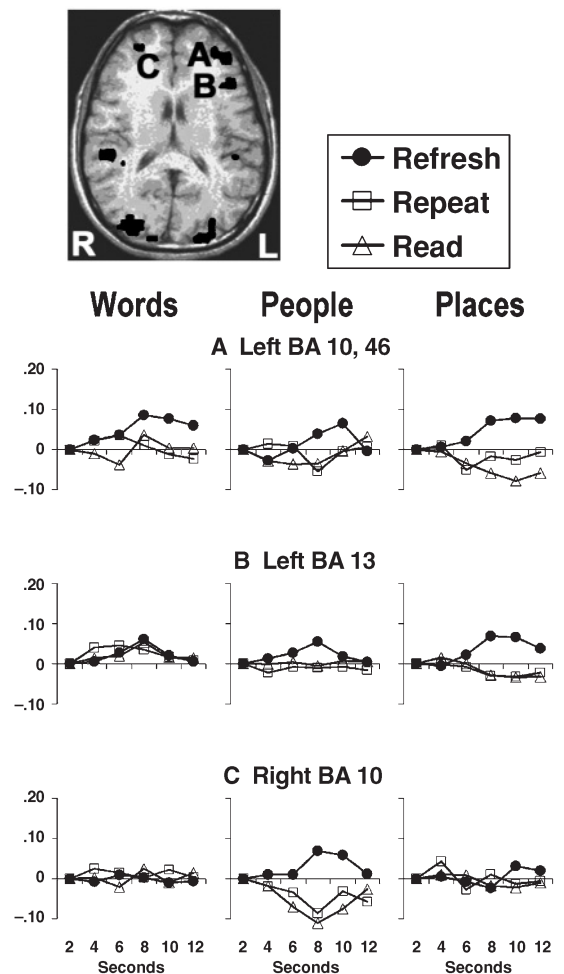


Figure 1.2. PFC areas in Experiment 1 showing a significant material \times condition \times time interaction and their within-trial time courses for each material (words, people, or places).

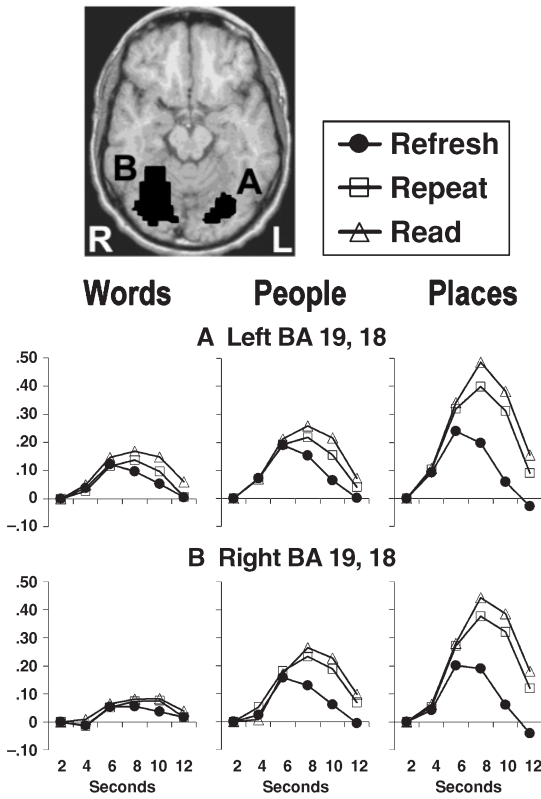


Figure 1.3. Posterior visual areas in Experiment 1 showing a significant material \times condition \times time interaction and their within-trial time courses for each material (words, people, or places).

Experiment 1; Raye et al., 2000, Experiment 1), activity in perceptual areas reflected perceptual properties of the stimuli (e.g., words or pictures > dot cue), as would be expected. Similar patterns were also seen in Experiments 2–6, with posterior perceptual processing areas (e.g., GOM, GOI, GF, GL) more active during read and repeat conditions than during the refresh condition. With the exception of Experiment 4, for which we show a comparison of auditory and visual areas activated in response to perception of auditory and visual stimuli, respectively, perceptual processing areas will not be discussed further. In Experiments 1–6, frontal areas showing less activity during refresh than during read and/or repeat conditions were infrequently observed, and all were medial or in the right hemisphere.² Because frontal activity associated with perceptual processing/ recognition is not our primary interest in this article, these areas will not be discussed further.

EXPERIMENT 2
Words Versus Locations

Several studies of working memory have reported evidence for organization of PFC by type of material, with left ventrolateral PFC associated with verbal WM and

right ventrolateral PFC with spatial WM (Reuter-Lorenz et al., 2000; Smith, Jonides, & Koeppel, 1996). It is of interest whether a similar lateralization by verbal versus spatial information occurs for dorsolateral PFC during refreshing. Given that these WM studies involved rehearsing several items over a delay, and that we postulate that refreshing and rehearsing are distinct processes (Johnson, 1992), refreshing may or may not be as lateralized as rehearsing. To examine this question, we compared the refreshing of words with the refreshing of spatial locations.

Method

In Experiment 2, the conditions (read, repeat, and refresh) were similar to those in Experiment 1, but the participants were asked to look at and think back to locations and words. Word trials were as in Experiment 1, except for a minor change in timing that paralleled the location trials described next. For location trials, stimuli were 10 possible locations where a black square could appear for 1,450 msec. The 10 pseudorandom locations were scattered about the visual field. Half of the locations were roughly in the upper visual field and half in the lower, and half were on the left and half on the right. The participants were told that when they saw a square they should just look at it. The first stimulus in each location trial was a square. After 550 msec, it was followed by either a square in a different location (read trial), a square in the same location (repeat trial), or a black dot in the center of the screen, which was the participants' cue to think of the location of the square that immediately preceded the dot (refresh trial). The second stimulus (square or dot) was presented for 1,450 msec.

There were six runs, each with 30 trials, in which word and location trials were pseudorandomly intermixed. Each run included 15 trials (5 each for the read, repeat, and refresh conditions) for each

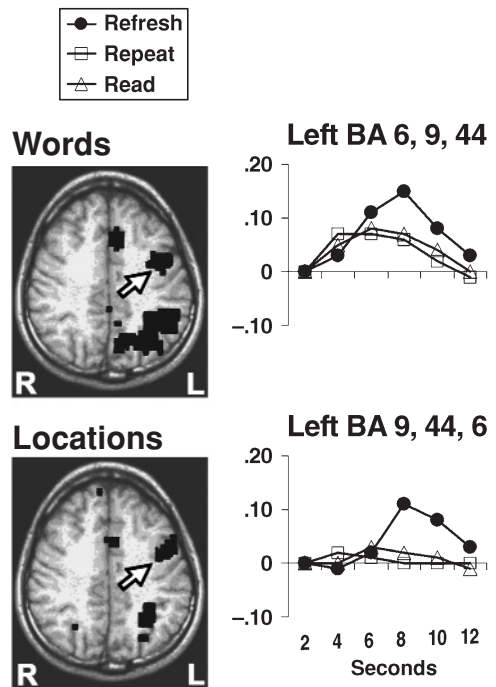


Figure 2. PFC areas in Experiment 2 showing a significant condition \times time interaction for each material type (words or locations) and their within-trial time courses.

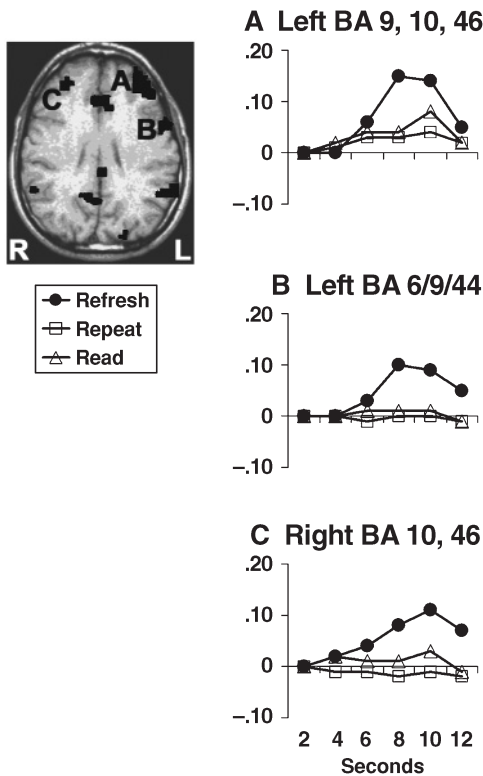


Figure 3. PFC areas in Experiment 3 (locations) showing a significant condition \times time interaction and their within-trial time courses.

material (words or locations). Altogether, there were 30 trials (180 images) in each condition for each material per participant.

Results

Figure 2 shows that for both words and locations, there was refresh-related left PFC activity in a region at the juncture of GFm and GPrC, extending into GFi. There were additional, smaller areas of left and right GFm and GFi for both types of material (see Table 2). There were no PFC areas showing an interaction of material \times condition \times time (which would have indicated a differential distribution of PFC activity associated with refreshing words vs. locations). These findings suggest that in comparison with rehearsing, refreshing is less likely to show laterality differences between PFC areas engaged in processing verbal and spatial information.

Together, the results of Experiments 1 and 2 indicate that it is unlikely that left PFC activity is uniquely associated with refreshing verbal information; rather, it is recruited during refreshing of currently active information of various types (including people, which also showed right PFC activity). On the other hand, both experiments included word trials. Perhaps processing words sensitizes left PFC or induces verbal processing even for non-verbal materials. Thus, Experiment 3 included only location trials.

EXPERIMENT 3 Locations

Method

There were four 30-trial runs of the spatial location task as described in Experiment 2. Ten trials each in the read, repeat, and refresh conditions were randomly intermixed per run, for a total of 40 trials (240 images) per condition for each participant.

Results

When only spatial trials were included, refresh-related activity was observed in a large area of left PFC in GFm and GFi extending superiorly into GPrC and inferiorly into insula (see Table 2 and Figure 3B), and in a more anterior area of left GFm (Figure 3A). There was also refresh-related activity in two areas of right PFC, which tended to be contralateral to the left PFC areas but smaller in extent (the time line for one of these is shown in Figure 3C).

EXPERIMENT 4 Visual Versus Auditory Words

A possibility consistent with the findings of Experiments 1–3 and with our previous findings (Johnson et al., 2004; Johnson et al., 2003; Raye et al., 2000) is that the left PFC activity we observed is specific to refreshing *visual* information (whether verbal, pictorial, or spatial). In order to test this hypothesis, Experiment 4 compared the refreshing of words that were presented visually with refreshing of words that were presented auditorily.

Method

The stimuli were 160 common one- to three-syllable words from the same pool used in Experiment 1; within-trial event timing was as in Experiment 2. Modality, visual or auditory, was blocked by run (two runs in each modality) presented in ABAB or BABA order across participants. Each run contained 30 trials (10 each for read, repeat, and refresh), pseudorandomly intermixed as in Experiment 1, for a total of 20 trials (120 images) per condition/modality for each participant.

The visual trials were like those described for Experiment 2. For auditory trials, individual words were recorded in a female voice as digital files using SoundEdit 16 software (Version 2, Macromedia, San Francisco, CA). The cue to refresh was an electronic beep and the words “left” and “right” were recorded in a male voice for the arrow task. Recorded words were spoken in a natural fashion, so the length of exposure of each spoken stimulus varied slightly but did not exceed the 1,450 msec allowed for visually presented words. The auditory stimuli were presented via headphones; for each participant, the volume was adjusted during the anatomical scans. All participants later reported being able to hear the words adequately to perform the tasks.

Results

As is shown in Figure 4.1, refresh-related activity was observed in an area at the juncture of left GPrC and GFm for visual words (A) and a near but more anterior and lateral area (primarily GFm) for auditory words (B). Additional refresh-related activation was seen for both visual and auditory words in more inferior areas (primarily left)

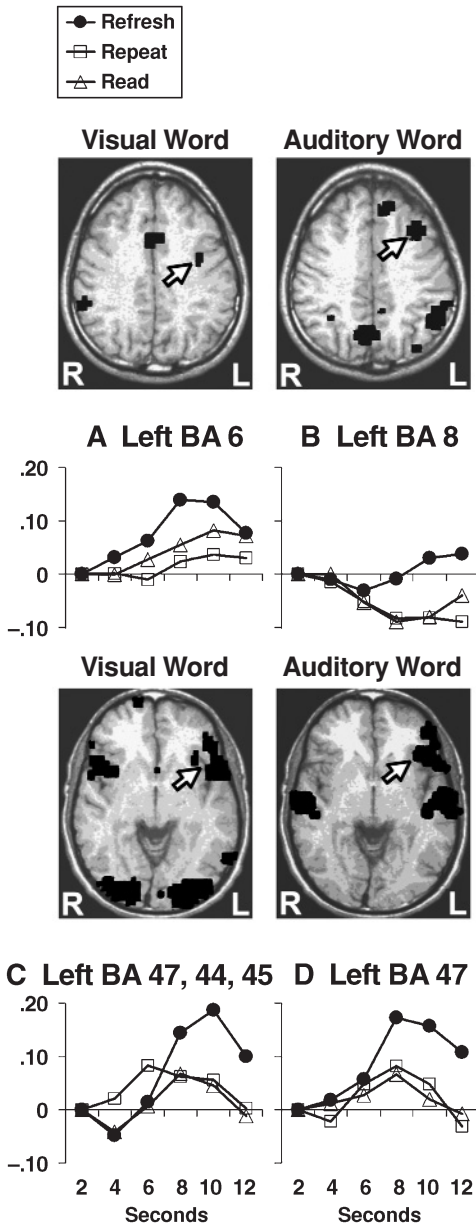


Figure 4.1. PFC areas in Experiment 4 showing a significant condition \times time interaction for each modality (visual or auditory words) and their within-trial time courses.

of GFi and lateral orbital gyrus (C, D). Thus, left PFC refresh-related activity is not limited to visually presented information. There was also a region of left inferior frontal gyrus showing a modality \times condition \times time interaction. As is shown in Figure 4.2, this region showed greater refresh-related activity when participants refreshed auditory rather than visual words.

Figure 4.3 shows that as one would expect, posterior visual areas were more active during visual trials, and auditory areas were more active during auditory trials. In addition, just as visual read and repeat trials here and in Experiment 1 showed greater activity than refresh tri-

als in visual areas, auditory read and repeat trials showed greater activity than refresh trials in auditory areas. A comparison of Figures 4.1 and 4.2 with Figure 4.3 emphasizes that PFC regions play a key role in reflective, as opposed to perceptual, processes (also cf. Figures 1.1 and 1.3).

Experiments 1–4, along with previously published studies (Johnson et al., 2003; Raye et al., 2002), support the idea that there is a cognitive process, refreshing (Johnson, 1992), that (1) involves left PFC, especially GFi; (2) can be distinguished from another cognitive operation—noting whether recently activated information is old or new—that recruits right PFC; (3) is associated with better long-term memory; (4) is disrupted in older adults; (5) is recruited across a range of information types; and (6) shows some differences in PFC distribution, depending on information type.

Differences in the type of information that is the target of a mental operation is only one way that the context for a process may vary; it may also vary in how much control is required to execute it (e.g., depending on amount of competition from other active representations). The issue of control was investigated in Experiments 5 and 6.

Refreshing and cognitive control. As noted in the introduction, reflective processes are sometimes categorized as maintenance and manipulation (see, e.g., D’Esposito, Postle, Ballard, & Lease, 1999), maintenance and monitoring (Petrides, 2000), or maintenance and control (Baddeley, 1992; Miller & Cohen, 2001). However, refreshing does not fall easily into any one of these categories. Refreshing is a process by which active information, which would otherwise quickly become less available (see, e.g., Sperling, 1960), is briefly maintained. At the

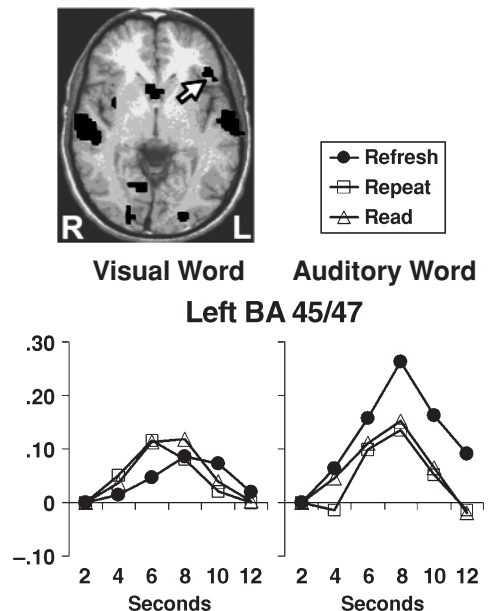


Figure 4.2. PFC area in Experiment 4 showing a significant modality \times condition \times time interaction and within-trial time courses for visual and auditory words.

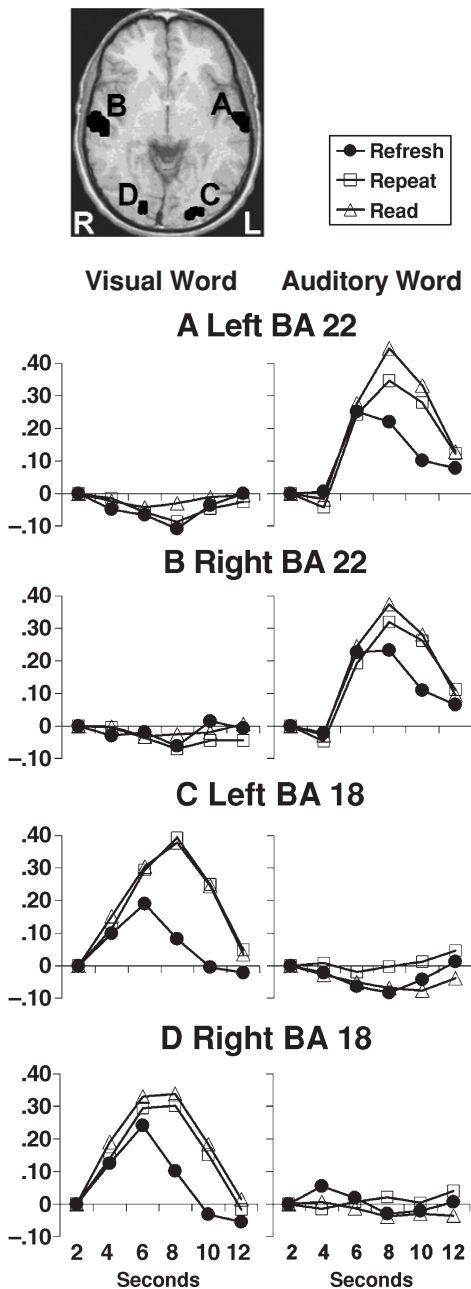


Figure 4.3. Posterior auditory (A, B) and visual (C, D) areas in Experiment 4 showing a significant modality \times condition \times time interaction and their within-trial time courses for each modality (auditory or visual).

same time, it is a process by which top-down control is executed as some stimuli are refreshed (e.g., the word on the just-previous screen) and some are not (e.g., the sounds of the scanner). That is, refreshing is one of the processes by which information is being selected during ongoing cognition—for example, in selective attention or WM tasks that require updating (J. D. Cohen et al., 1997), alphabetizing (D’Esposito, Postle, Ballard, & Lease, 1999), or other manipulations of information.

Although refreshing is a simple process, the conditions under which it occurs vary in potential distraction or competition; hence, refreshing can vary in the amount of control required. In Experiments 5 and 6, we investigated the neural correlates associated with refreshing under conditions that differ in the need for control. In Experiment 5, we varied selection demands by varying the number of items activated before the cue to refresh was presented, and in Experiment 6, we increased the requirement for control by varying the salience of the not-to-be-selected items (i.e., those selected against). Of interest is how the neural activity associated with the relatively simple process of refreshing changes as control demands are increased. Does activity increase in the left PFC areas usually associated with refreshing? Are different or additional areas engaged, thus increasing the functional complexity of a refresh circuit?

EXPERIMENT 5

Selective Refreshing (1 of 1 vs. 1 of 3)

In Experiment 5, we compared refreshing a single item that had just been perceived with refreshing one of three items just perceived. What should be the consequences of increasing the number of potential candidates or targets for the refresh operation? Because refreshing can be viewed as a method of selection, one possibility is that greater left dorsolateral PFC activity will be associated with selecting an item from among a number of possibilities; that is, refresh-related activity may increase with increased selection demands (as in a Stroop task; see, e.g., Banich et al., 2000; MacDonald, Cohen, Stenger, & Carter, 2000). Alternatively, other areas—for example, ventrolateral PFC (see, e.g., D’Esposito, Postle, Jonides, & Smith, 1999; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997)—may contribute to selection or inhibition of nonselected information. We might also expect an increase in activity in ACC associated with refreshing when three items versus one item are presented. ACC activity is associated with response competition created by having to overcome a prepotent response, as in the Stroop or go/no-go tasks (Carter et al., 1998; MacDonald et al., 2000; Milham et al., 2001). If ACC serves a general conflict-detection function, ACC activity should increase when selection from active representations is required, even when the options are all equally salient (i.e., there is no prepotent alternative).

Method

The trial structure was very much like the visual word conditions previously described, but the number of items in the first stimulus display was manipulated: For half of the trials, three words were presented in a column on the screen, and for the other half, a single word was presented in the upper, middle, or bottom position. In both cases, the first display was presented for 1,600 msec. After 400 msec, the participants saw, for 1,450 msec, either a single new word (read) or the dot (refresh) in one of the three locations. The dot, by its location, signaled the participant to think of (refresh) the word that had appeared in that position on the just-previous screen.

Thus, number of items (one vs. three) was orthogonally crossed with condition (read vs. refresh). Trials were pseudorandomly intermixed in six runs of 32 trials (8 trials for each number/condition combination per run, for a total of 48 trials, and 288 images per number/condition combination for each participant). For each combination, the critical item occupied each position in the column equally often.

Results

In this experiment, four regions similar to those found previously showed condition \times time interactions reflecting refresh-related activity (see Table 2). Of primary interest here were regions showing a number \times condition \times time interaction in which significantly greater activity occurred when participants refreshed one of three items than when they refreshed one of one item, and in which number of items presented did not affect the read condition. Three of these regions are shown in Figure 5: a dorsolateral area at the juncture of left GFm, GF_i, and GPrC; a ventrolateral area of left GF_i; and an area of medial frontal gyrus extending into ACC. A small region of right GFm also displayed this interaction (see Table 2). These results suggest a role for both dorsolateral and ventrolateral PFC in selection (cf. Barde & Thompson-Schill, 2002). In both dorsolateral and ventrolateral PFC areas, the two read conditions (which did not differ from each other) produced more activity than the refresh one-of-one condition, but less than the refresh one-of-three condition. This pattern suggests that even relatively passive reading may require some selection as the reader shifts attention to new items. More important for the present discussion, however, is that having to select one of several active mental representations without benefit of current perceptual support is especially likely to recruit areas of ventrolateral and dorsolateral PFC. The results further indicate that the need to select from a set of active mental representations is sufficient to increase ACC activity. Conflicting prior response tendencies (from earlier trials, or from prepotent responses as in the Stroop task) are not necessary.

EXPERIMENTS 6A AND 6B Neutral Versus Emotional Words

In Experiment 5, we varied selection demands by varying the number of items presented and showed that refresh-related activity increased in both left PFC and ACC when the item refreshed had to be selected from a set of three items rather than a single item. In Experiments 6A and 6B, we held the number of presented items constant at three, but instead of presenting three relatively neutral words as in Experiment 5, we presented either two neutral words (e.g., *square*, *coffee*) and one negative emotional word (e.g., *rape*) or three neutral words. We manipulated selection demands by varying whether participants were cued to refresh an emotional item or a neutral item. In a mixed set of emotional and neutral items, attention should be drawn to the more salient emotional item (*mental rubbernecking*), and thus partic-

ipants should have to exert more control to refresh a less salient neutral item. Experiment 6A was a cognitive/behavioral study performed in order to establish that it would take more control (as indexed by response time) to refresh a neutral rather than an emotional item in this context, and Experiment 6B was an fMRI study designed to identify associated brain regions.

EXPERIMENT 6A Behavioral Study

Method

The participants in this behavioral study were (accurately) told that we were interested in the time it takes people to read and to think about words. They were instructed that when they saw words, they should just read them aloud as quickly and accurately as possible. If they saw a black dot, they were to think of, and say out loud, the word that had appeared in the same position on the just-previous screen. The participants were informed that some of the words they would be reading would be unpleasant (e.g., *slime*, *morgue*, *divorce*), and they were given the option not to participate. As in Johnson et al. (2002), a voice-activated microphone was used to record responses and latencies.

The stimuli were composed of 324 words taken from Bellezza, Greenwald, and Banaji (1986; the full set of words and norms was

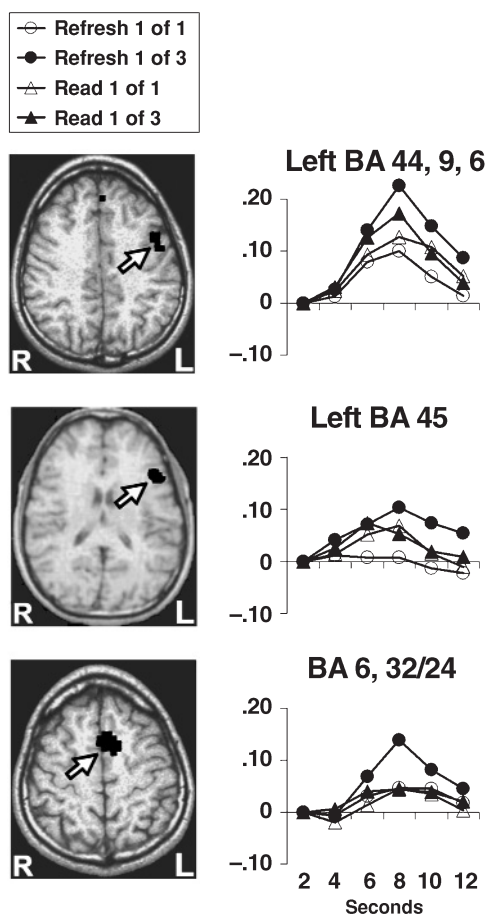


Figure 5. Areas in Experiment 5 showing a significant number \times condition \times time interaction and their within-trial time courses.

acquired from M. Banaji via personal communication, April, 2002). The emotion rating of each word was calculated by multiplying Bellezza et al.'s emotion and pleasantness ratings (with the pleasantness score reversed). The 216 neutral words ranged from 1.54 to 9.74 on this scale ($M = 5.08, SE = 0.10$), whereas the 108 emotional words ranged from 18.21 to 36.44 ($M = 25.31, SE = 0.45$). There were also 162 neutral words taken from the same pool used in Experiment 1 that were equated with the neutral words from the Bellezza et al. pool for length and frequency.

On each trial, the participants saw a column of three words (one emotional and two neutral [ENN trial] or three neutral [NNN trial]) presented for 1,625 msec and said the words aloud. The emotional word appeared in each position equally often. After 425 msec, either one of the three words appeared again in the same location and the participant said the word again (repeat), or a black dot appeared that by its location, signaled the participant to think back to and say again (refresh) the word that had appeared in that location on the just-previous screen. The second screen was presented for 1,450 msec, and a voice key recorded the time to initiate saying the critical word. This critical item was either emotional (ENN-E) or neutral (ENN-N or NNN-N). Thus, there was a 2 (condition: repeat or refresh) \times 3 (context/target combination: ENN-E, ENN-N, or NNN-N) design, with the different combinations randomly inter-mixed. The ITI was 3 sec. The participant completed six 27-trial runs, for a total of 27 trials in each cell of the design.

Results

We replicated previous findings (Johnson et al., 2002) indicating that it takes more time to refresh (624 msec) than to repeat (506 msec) a word [$F(1,22) = 92.54, MS_e = 5142, p < .0001$]. More important, there was a condition \times context/target interaction [$F(2,44) = 7.69, MS_e = 696, p < .002$]. On repeat trials, the context and the emotion of the target word did not matter (507, 512, and 503 msec for ENN-E, ENN-N, and NNN-N, respectively; $p > .20$), whereas they did matter for refresh trials (604, 652, and 618 msec for ENN-E, ENN-N, and NNN-N, respectively) [$F(2,44) = 14.78, p < .0001$]. Subsequent comparisons indicated that participants were slower to refresh in the ENN-N condition than in the other two conditions, which did not differ from each other. This pattern is consistent with the idea of mental rubbernecking: The presence of an emotional distractor interfered with selectively refreshing a neutral word.

**EXPERIMENT 6B
fMRI Study**

Method

Experiment 6B was an fMRI study using the materials and procedure from Experiment 6A, with the following changes: The arrow task, previously described, served as the filler task during an 8-sec ITI. The first screen of the trial was presented for 1,600 msec, followed by a 400-msec interstimulus interval. To limit the length of the overall procedure, only the ENN-E and ENN-N conditions were included. The participants did not speak; as in the previous fMRI experiments, they read words silently to themselves and silently thought back to the just-previous word on refresh trials.

Results

There were several areas showing greater activity in refresh than in repeat conditions, and these areas did not vary significantly with emotional content: left GFm, GFi

(Figure 6A) and ACC (Figure 6B), and left GFm and left and right insula (Table 2). Although there was some suggestion that ACC was more active when the neutral rather than the emotional item was refreshed (Figure 6B), the difference was not significant.

The only PFC area showing a significant emotion \times condition \times time interaction was in anterior orbitofrontal cortex (OFC; Figure 6C). Activity was significantly greater when participants refreshed neutral rather than emotional items, whereas for repeat items, the difference between neutral and emotional items was in the opposite direction ($p < .06$). The overall pattern of these time lines is consistent with the idea that activity in this region of OFC may reflect processes engaged to control emotional responses that might interfere with an ongoing task. Specifically, activity was high in OFC when participants were to refresh a neutral item (N refresh) and presumably had to suppress or ignore emotional responses that would recruit attention to the (inappropri-

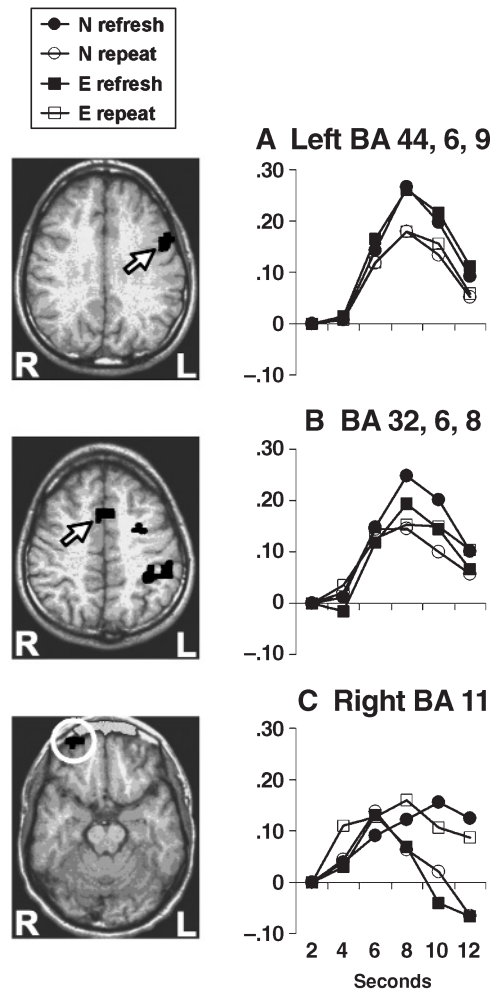


Figure 6. (A, B) Areas in Experiment 6B showing a significant condition \times time interaction. (C) Area showing a significant emotion \times condition \times time interaction. Within-trial time courses are shown for each area.

Table 3
Long-Term Memory d' Scores With Standard Errors of the Means

	Read		Repeat		Refresh	
	<i>M</i>	<i>SEM</i>	<i>M</i>	<i>SEM</i>	<i>M</i>	<i>SEM</i>
Experiment 1						
Words	1.34 ^{ab}	0.21	1.72 ^{bc}	0.22	2.02 ^{ac}	0.30
People	1.07 ^{b1, b2}	0.19	1.40 ^{b1}	0.15	1.36 ^{b2}	0.14
Places	0.59 ^c	0.13	0.65	0.14	0.80 ^c	0.16
Experiment 5						
1 of 1	0.72 ^a		0.08		1.02 ^a	0.11
1 of 3	0.76		0.10		0.87	0.15
Experiment 6A						
ENN_E			1.73	0.12	1.76	0.14
ENN_N			1.50 ^b	0.09	1.72 ^b	0.10
NNN_N			1.48 ^b	0.09	1.71 ^b	0.10
Experiment 6B						
ENN-E			1.57	0.15	1.59	0.17
ENN-N			1.20 ^a	0.16	1.48 ^a	0.17

Note—Means within a row with the same superscript are different (^a $p < .01$; ^b $p < .05$; ^c $.05 < p < .10$). In Experiment 1, a 3 (condition: read, repeat, or refresh) \times 3 (material: words, people, or places) ANOVA showed a main effect of condition [$F(2,26) = 10.55$, $MS_e = 0.16$, $p < .001$; refresh (1.39 mean) = repeat (1.26 mean) > read (1.00 mean)] and a main effect of material [$F(2,26) = 11.58$, $MS_e = 0.94$, $p < .001$; words (1.69) > people (1.27) > places (0.68)]. Although the interaction was not significant [$F(4,52) = 2.07$, $MS_e = 0.14$, $p < .10$], the advantage for refreshed items over read and repeat items showed a pattern of words > people > places (see the Long-term memory section for a discussion of why the impact of refreshing on LTM might vary across materials). In Experiment 5, a 2 (condition: read or refresh) \times 2 (number: one or three) ANOVA showed a main effect of condition [$F(1,14) = 8.31$, $MS_e = 0.07$, $p = .01$; refresh (0.94) > read (0.74)]; again, the interaction was not significant [$F(1,14) = 3.13$, $MS_e = 0.05$, $p < .10$]. Nevertheless, the advantage for refreshed items over read items was significant for the single-item trials [$t(14) = 4.23$, $p < .001$] but not for the three-item trials ($p > .10$). In Experiment 6A, a 3 (trial type: ENN-E, ENN-N, or NNN-N) \times 2 (condition: repeat or refresh) ANOVA showed only a main effect of condition [$F(1,22) = 7.12$, $MS_e = 0.12$, $p < .05$; refresh (1.73) > repeat (1.57)]; the interaction failed to reach significance [$F(2,44) = 1.96$, $MS_e = 0.07$, $p > .10$], but the advantage for refreshed items over repeated items was significant only for those trials on which a neutral item was selected for further processing [ENN-N, $t(22) = 2.55$, $p < .02$; NNN-N, $t(22) = 2.68$, $p < .02$] and not when the emotional item was selected (ENN-E, $p > .70$). This pattern was replicated in Experiment 6B, where a 2 (trial type: ENN-N or NNN-N) \times 2 (condition: repeat or refresh) ANOVA showed only a main effect of condition [$F(1,13) = 4.49$, $MS_e = 0.07$, $p \leq .05$; refresh (1.54) > repeat (1.39)]; the interaction was not significant ($p > .10$), but, as in Experiment 6A, the advantage for refreshed items over repeated items was significant only for ENN-N [$t(13) = 3.06$, $p < .01$], not for ENN-E ($p > .90$).

ate) emotional item from the set. The fact that OFC activity was also high on trials when the emotional item was presented again (E repeat) suggests that continued perceptual attention to an emotional item was aversive or disruptive, triggering control processes. Cuing participants to refresh the emotional item (E refresh) presumably allowed them to “complete” their processing of the emotional item, making additional control processes unnecessary. A neutral item presented for a second time (N repeat) may give the neutral item an advantage over the competing emotional item (seen only once), reducing the need for control processes. Although somewhat speculative, this reasoning offers testable predictions—for example, that a read control condition (i.e., read a new neutral item) might show more activity in OFC than a repeat control condition (i.e., read the same item again) because

a new neutral item would not be as successful as a repeated neutral item at competing with the emotional item. Of course, OFC activity is not specific to emotionally significant material; OFC activity is also observed in other tasks when the material is neutral (e.g., in a go/no-go task; Casey et al., 1997; Horn, Dolan, Elliott, Deakin, & Woodruff, 2003). Nonetheless, the results of Experiment 6B are consistent with the suggestion that OFC plays a role in cognitive control and/or emotional regulation (see, e.g., Rule, Shimamura, & Knight, 2002; Shimamura, 2000).

Refresh-related left PFC activity increased with the number of alternatives (Experiment 5) but not with the salience of the alternatives (Experiment 6). This suggests that lateral PFC subserves selection via increasing activation of a relevant representation, and that orbital

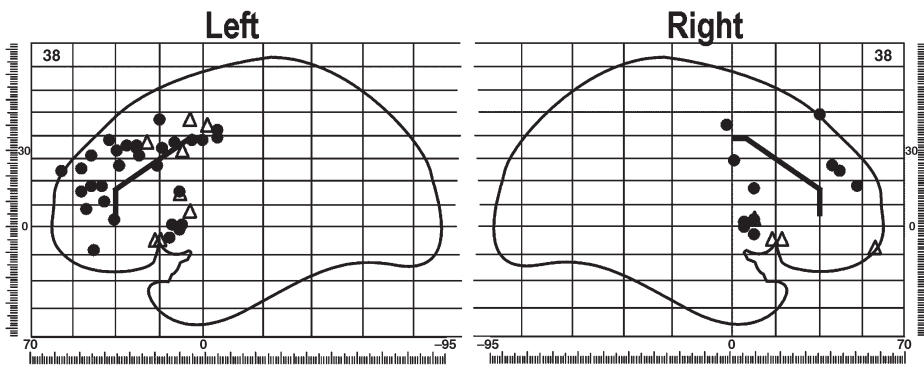


Figure 7. Sagittal schematic showing left and right refresh-related PFC local maxima from Experiments 1–6, together with maxima from Johnson et al., 2004; Johnson et al., 2003 (Experiment 1); and Raye et al., 2002 (Experiments 1 and 2). Circles are studies in which one item was presented and refreshed, and open triangles are studies in which participants refreshed one of three presented items. GfM is above and GfI below the gray line.

PFC subserves inhibition, perhaps by regulating emotion or inhibiting responses until agenda-related selection is complete. This is an intriguing potential dissociation between dorsolateral (and perhaps ventrolateral) PFC and orbital PFC during refreshing that warrants further study.

LONG-TERM MEMORY

Johnson et al. (2003) found that although long-term memory (LTM) of words (see also Johnson et al., 2004; Johnson et al., 2002; Raye et al., 2002) and LTM of line drawings of objects both benefited from refreshing an item relative to seeing it once (read) or seeing it again (repeat), LTM for abstract patterns was not greater for refresh than for repeat or read conditions (in fact, repeated items showed a slight numerical advantage over refreshed items). We suggested that people may be less successful in refreshing an abstract pattern than a word or simple line drawing. (Also, the distractors on a long-term recognition memory test may be more similar to their targets for some types of materials than for others.) Thus, a single refresh may be sufficient to allow people to later distinguish targets from distractors for some materials but not for others.

To explore further the relative consequences for LTM of seeing an item once, seeing it twice, or seeing it and refreshing it, postscan recognition memory data were collected for several of the present experiments (see Table 3). Old items were mixed with new items from the same class of materials. Participants indicated *old* or *new* for each item, and d' (Macmillan & Creelman, 1991) was computed as the measure of recognition memory. For each of these studies, an ANOVA showed a main effect of condition, with subsequent comparisons showing an LTM advantage for refreshed over read items and equal or greater LTM for refreshed than for repeated items (see the note to Table 3 for statistical details). It is

particularly interesting that a comparison of refresh and repeat conditions did not produce an LTM advantage for emotional words (Experiments 6A and 6B). The pattern of means for Experiments 6A and 6B suggests that greater attention may have been directed at repeated emotional rather than repeated neutral words; thus, the advantage of refreshing (relative to repeating) was less for emotional than for neutral words. It is also of interest that in Experiment 5, the advantage of refreshing over reading tended to be reduced when selection was required (one out of three items), suggesting that competition among potential candidates reduces the efficacy of refreshing any one of them.

META-ANALYSES

Descriptive Meta-Analysis

Figure 7 summarizes the left and right PFC local maxima of refresh-related areas we have found for different materials in 10 refresh studies (the present six fMRI experiments; Johnson et al., 2004; Johnson et al., 2003, Experiment 1; Raye et al., 2002, Experiments 1 and 2). The circles represent activations from studies in which participants were presented with and refreshed single items. The left PFC activations tended to be distributed along the middle frontal gyrus, with activations sometimes also seen in the inferior frontal gyrus. This is in contrast to studies of rehearsal, in which activity is more likely to be found in the inferior frontal gyrus—for example, for words in left BA 44/6 (Wagner, Maril, Bjork, & Schacter, 2001) or for letters in left BA 44 and locations in right BA 47 (Reuter-Lorenz et al., 2000). This difference between activity associated with refreshing and rehearsing is consistent with the proposal that they are different component processes; rehearsing is not simply repeated refreshing (see, e.g., Johnson, 1992).

The open triangles show activations from experiments in which participants refreshed one of three items they

had just seen. The activations associated with selective refreshing tended to be more posterior and inferior. This pattern suggests that there may be some difference in the distribution of PFC activity depending on the selection requirements of the task—for example, number of items and relative saliency of the selected and unselected information. The more posterior/inferior activations may reflect selection directly (see, e.g., Thompson-Schill et al., 1997) or, alternatively, may reflect the fact that when multiple items have been presented, participants tend to select from a rehearsal set (Poldrack et al., 1999).

Quantitative Meta-Analysis

Another way to compare neural activity across experiments is to assess refresh-related activity under different conditions in defined regions of interest (ROIs). This could be done by examining activity in each experiment using a “mask” of anatomically based ROIs—focused, for example, on dorsolateral or ventrolateral PFC (see, e.g., D’Esposito, Postle, Ballard, & Lease, 1999; Rypma & D’Esposito, 2003)—or using a mask that includes spherical regions (of several voxels radius) drawn around local maxima obtained in a prior study (e.g., Nelson, Reuter-Lorenz, Sylvester, Jonides, & Smith, 2003) or meta-analysis (e.g., Bishop, Duncan, Brett, & Lawrence, 2004). Both of these methods are useful, but they each have limitations as well: The first method may not be sensitive to potential differences within the same large anatomical region (e.g., Barde & Thompson-Schill, 2002). Although the second method is more functionally based and more specific, it may be too specific if it is based only on a single experimental outcome; spherical ROIs may also cross anatomical or functional boundaries, thus reducing sensitivity by including voxels not involved in the target process.

With these considerations in mind, we conducted a quantitative meta-analysis defining ROIs by combining available per-voxel analyzed data (i.e., unthresholded F maps) across experiments (for quantitative meta-analysis methods that use only hotspots, see Chein, Fissell, Jacobs, & Fiez, 2002; Wager & Smith, 2003). We identified ROIs by averaging effect sizes across studies in which participants refreshed an item from a display containing only one item. There were 13 comparisons from seven independent studies that were similar in design and fMRI procedures. Using SPM2 (Friston et al., 1994), individual condition \times time unthresholded F maps were warped to our standard reference brain. Each of these warped F maps was then converted to an omega squared (ω^2) map (ω^2 is an unbiased index of effect size, corresponding to variance accounted for, that can be used for cross-study comparisons). We then calculated the mean ω^2 on a voxel-by-voxel basis and thresholded the resulting mean ω^2 map to identify regions with six contiguous voxels at $\omega^2 > .09$.³ This procedure identified three left PFC areas, one each in dorsolateral, anterior, and ventrolateral PFC; one right ventrolateral PFC area; and an area of ACC. Using a more liberal criterion

of two contiguous voxels, three additional small regions were identified, one each in left dorsal, right anterior, and left ventrolateral PFC. We used this set of eight ROIs as our “canonical” set of refresh-related PFC areas and applied this mean ω^2 map to the raw signal data from the experimental conditions in each individual study to obtain time lines associated with activity in the identified ROIs. These areas are shown in Table 2 and Figure 8.⁴ The figure also includes time lines for individual refresh conditions⁵ and averaged time lines for verbal (blue) versus nonverbal (red) materials. Ventral areas are shown in Figures 8A–8C, anterior and dorsal areas in Figures 8D–8G, and the ACC area is shown in Figure 8H.

Differentiation of regions within left PFC. Anterior (BA 47, 45/13) and posterior (BA 45, 44) areas of left ventrolateral PFC showed greater activity when participants refreshed verbal rather than nonverbal information ($ps < .05$; see Figures 8A and 8C). In contrast, right ventrolateral PFC (Figure 8B) did not show a difference in activation between verbal and nonverbal information. The greater activity for verbal than for nonverbal information in left ventrolateral areas is consistent with other findings showing that these areas are involved in verbal processing (McDermott, Petersen, Watson, & Ojemann, 2003; Poldrack et al., 1999). It is also notable that activity in ventrolateral areas was greater for refreshing auditory words than for refreshing other types of information. This finding suggests that auditory presentation of words may be more sensitive than visual presentation when fMRI is used to study language areas or to identify language areas preoperatively (see, e.g., Badre & Wagner, 2002; Carpentier et al., 2001; McDermott et al., 2003). Crottaz-Herbette, Anagnoson, and Menon (2004) recently reported greater activation in left dorsolateral cortex for auditory than for visual presentation in a 2-back WM task. The fact that we did not find an auditory versus visual difference in dorsolateral PFC (see Experiment 4 and Figure 8F), and that Crottaz-Herbette et al. did, may be related to the greater complexity of the n -back versus the refresh task.

Our meta-analysis also identified a region of left anterior PFC (BA 10, Figure 8D), along with a contralateral, and significantly ($p < .01$) less active, area of right BA 10 (Figure 8E). Neither of these anterior PFC regions showed an overall difference in activation associated with refreshing verbal versus nonverbal information, but interestingly, in left anterior PFC (Figure 8D) the *least* activity was associated with refreshing people, and in right anterior PFC (Figure 8E) the *most* activity was associated with refreshing people. The time courses associated with left BA 10 (Figure 8D) appeared to be quite similar, and a comparison of the variances of time courses within ROIs showed that BA 10 was significantly less variable than any of the other areas in the meta-analysis ($ps < .05$), with the exception of ACC (Figure 8H), from which it did not differ in variability. The relative homogeneity among time lines associated with activity in left BA 10 suggests that this area may be

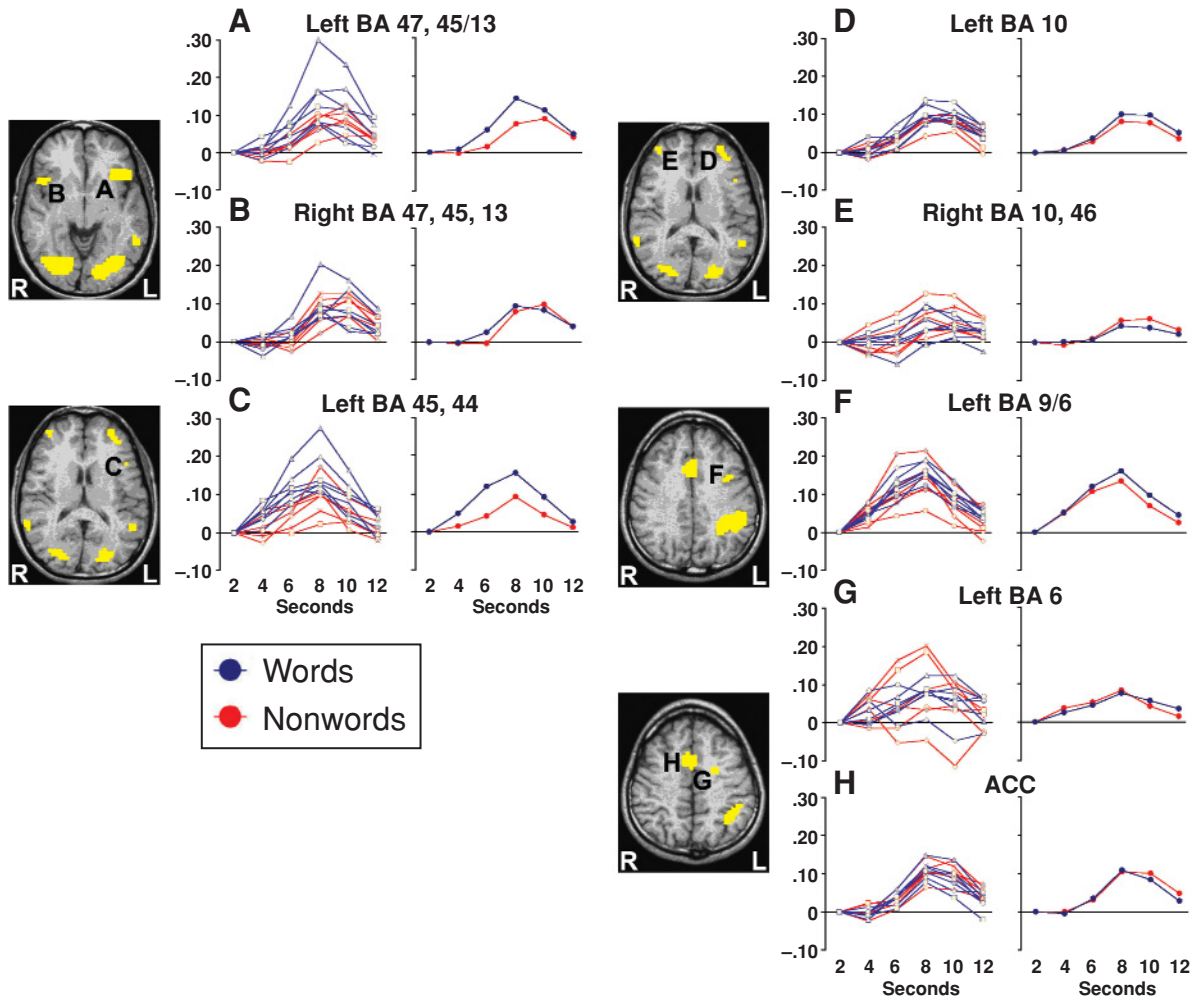


Figure 8. PFC and ACC areas identified in an ω^2 meta-analysis (see text). The time lines on the left of each panel represent the refresh-related activity in each of 13 comparisons across seven independent experiments (each material type presented separately for present Experiments 1–4; Johnson et al., 2004; Johnson et al., 2003, Experiment 1; and Raye et al., 2002, Experiment 1; blue lines represent words, including auditory words, and red lines represent nonwords). The time lines on the right represent the averages when words (blue) and nonwords (red) were refreshed.

playing a quite general role in refreshing, perhaps an “executive” role such as setting the agenda for, or initiating, the process of refreshing.

Although there was more variability in left dorsolateral BA 9/6 (Figure 8F) than in anterior BA 10, activity in this dorsolateral region also did not differ significantly between verbal and nonverbal information. This is consistent with the idea that differences in the distribution of dorsolateral PFC activity during refreshing different types of information (see, e.g., Johnson et al., 2003, and the present Experiment 1) arise from neurons that vary in sensitivity to different features (yet to be specified) and that are distributed probabilistically throughout the region rather than segregated categorically (e.g., Duncan, 2001; Miller & Cohen, 2001). By contrast, a small area of left superior frontal sulcus (BA 6, Figure 8G) showed greatest activation in the location conditions of Experiments 2 and 3. The relatively selec-

tive responsiveness of this area to refreshing locations that is apparent in the two independent replications shown in Figure 8G is consistent with findings from studies of spatial WM (Courtney, Ungerleider, Keil, & Haxby, 1996). It would be interesting to compare specific regions for refreshing and rehearsing spatial information in the same study. That is, are there additional regions that are recruited when spatial information has to be maintained over intervals of several seconds?

The differences in shape and variability among time courses in the various PFC regions shown in Figure 8 suggest that fluctuations in the locations of regions of activation in PFC across studies depend on the type of information individuals are refreshing, as well as other factors, such as the need for control (as shown in Experiments 5 and 6). In a recent review of studies of WM for spatial, nonspatial, and verbal information, Owen (2000) concluded that ventral and dorsolateral PFC are topo-

graphically organized according to process, not type of information. However, he also noted that there might be differences within regions that were not detected with the methods he used. Our meta-analysis of refreshing across different types of information suggests that organization of reflective processes by broad class of information, such as by verbal versus nonverbal information, may be most likely to be found in ventral PFC, and that other areas may show preferences for certain types of information as well (e.g., right anterior PFC for people, left dorsal superior frontal gyrus for spatial information).

Interaction between emotion and cognition. The mean ω^2 map can also be applied to new studies whose data did not contribute to it. For example, in Experiment 6B, we required participants to refresh either a negative or a neutral item from a set of three items. To examine further the interaction between this simple mental operation and the emotional salience of the information upon which it acts, we applied our averaged ω^2 map ROIs as a mask to the raw signal data from Experiment 6B in order to assess activity in the refresh-related ROIs derived from our meta-analysis. The ω^2 mask identified refresh-related activity in Experiment 6B in left BA 9/6 and BA 47, 45, but interestingly there was significant deactivation in anterior PFC (BA 10, $p < .001$), as is shown in Figure 9.

One possibility is that BA 10 deactivates whenever a stimulus includes multiple items; however, when the refresh-related ω^2 mask was applied to the data from Experiment 5, in which only neutral items were used, there was no such deactivation for the three-item trials. Elucidating the range of conditions under which one observes deactivations is an important topic beyond the scope of this article (see, e.g., Gusnard & Raichle, 2001). Nevertheless, the fact that this anterior PFC area deactivated when an emotional item was present suggests that the presence of a negative emotional item in the display may temporarily attenuate processing (e.g., initiation of refreshing) subserved by this area. The behavioral data of

Experiment 6A indicate that participants were slower to respond for neutral than for emotional items on the refresh but not on the repeat trials, a result consistent with the idea that emotion slows the initiation of refreshing, perhaps because it attenuates processing in left anterior PFC, which affects refreshing more than it does reading an item again. Previously, we found a behavioral age-related deficit in refreshing (Johnson et al., 2002) and evidence of dysfunction in older adults in left dorsolateral PFC (Johnson et al., 2004). Together, these findings provide converging evidence that left PFC is particularly important for efficient refreshing.

The possible impact of emotion on activity in BA 10 suggests the hypothesis that the relatively low activation of BA 10 when participants refreshed pictures of people (the lowest time line in Figure 8D) may have occurred because these stimuli were more emotionally engaging than other stimuli we have used. In agreement with this idea, in Experiment 1, we observed greater amygdala activity in the people condition relative to words and places ($p < .01$). It may be that emotional responses to perceptual stimuli sometimes inhibit the initiation or execution of PFC-mediated reflective processing (Experiments 1 and 6B), and in turn that PFC activity can modulate emotional responses (Cunningham, Johnson, et al., 2004; Cunningham, Raye, & Johnson, 2004; Gray, Braver, & Raichle, 2002; Ochsner, Bunge, Gross, & Gabrieli, 2002).

GENERAL DISCUSSION

Most investigations of the neural correlates of frontally mediated executive processing have used relatively complex cognitive tasks, such as delay WM tasks, the n -back task, or manipulation tasks (e.g., alphabetizing). Although a great deal has been learned using such relatively complex tasks, they are not ideal for isolating component processes, and thus may not be ideal for exploring the functional organization of PFC (see, e.g., Barde & Thompson-Schill, 2002, p. 1061). For example, what appears to be a straightforward approach of manipulating WM load to identify maintenance regions probably affects more than maintenance alone by increasing the chances that participants use elaboration or organizational strategies rather than just rehearsal (see, e.g., Rypma & D'Esposito, 1999), and thus that they engage combinations of different component processes (Johnson, 1992; Johnson & Hirst, 1993; for recent approaches to identifying brain areas associated with strategies, see, e.g., Huettel & McCarthy, 2004; Maestú et al., 2003; Rypma, Berger, & D'Esposito, 2002).

To increase control over the processes engaged, we have investigated the neural correlates of a relatively minimal reflective operation—refreshing. Our goal was to characterize similarities and differences in the PFC correlates of refreshing across different types of representations and under conditions differing in requirements for control. We focused on refreshing not only because it is relatively simple but because it is important

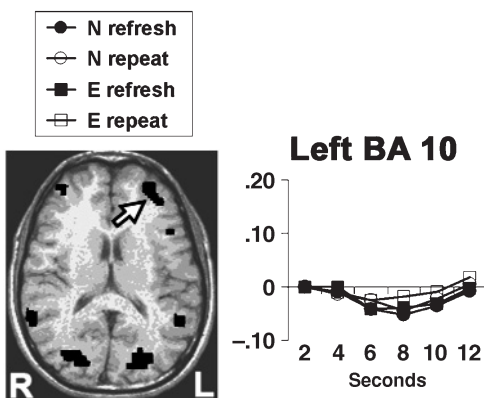


Figure 9. Time courses from Experiment 6B in an anterior PFC ROI identified in the meta-analysis (see the text, and compare time lines with those in Figure 8D).

cognitively: We propose that refreshing is a basic component of many more complex tasks and that disruptions in refreshing could have wide-ranging consequences for higher order cognition (Johnson et al., 2002). For example, refreshing may help keep agendas (i.e., goals, sub-goals, contexts, attentional templates, and rules) active; keep potentially relevant information active during comprehension or problem solving; and bridge between a thought and its expression or between intention and action. If so, deficits in refreshing would produce “senior moments” (Johnson et al., 2002; McDaniel, Einstein, Stout, & Morgan, 2003) and other potentially more serious cognitive dysfunctions. In this section, we will summarize our main findings and highlight some questions that remain.

Frontal Subcomponents of Refreshing

Our ω^2 meta-analysis across the present and previously published experiments (Johnson et al., 2004; Johnson et al., 2003; Raye et al., 2002) identified regions of dorsolateral, anterior, and ventrolateral PFC associated with refreshing (Figures 8A–8G). Activations in these general regions of PFC frequently occur in cognitive studies (Cabeza & Nyberg, 2000; Wager & Smith, 2003), as would be expected if refreshing is a basic component of attentional, executive, memory, and problem solving tasks. Other reflective processes (e.g., rehearsing, noting, reactivating, or retrieving; Johnson, 1992; Johnson & Hirst, 1993) presumably recruit different areas in dorsolateral, anterior, and ventrolateral PFC or use the same areas in a differently configured network. Specifying these differences among basic component processes remains a challenge (see, e.g., Johnson et al., 2003; Wager & Smith, 2003) that will require systematic comparisons between these processes under a range of conditions.

Does PFC Activity Change Depending on What Is Being Refreshed?

Within experiments that varied materials, we found evidence for differences in the distribution of activity in PFC associated with refreshing different types of information (Johnson et al., 2003 [pictures, textures, and words] and the present Experiments 1 [people, places, and words] and 4 [visual or auditory words]). This suggests that for refreshing, PFC differentiation by type of stimuli is most likely with contrasts that maximize differences in features or number of features (e.g., people vs. words, or different modalities). At the same time, it should also be noted that two of these studies included three classes of visual materials. If PFC flexibly reorganizes to meet task demands, there may be more need to organize by type of information when more types of information are being processed. Although we did not find evidence of a significantly different distribution of PFC activity by type of information refreshed in a direct comparison of locations and words (Experiment 2), our meta-analysis identified a small area of superior frontal sulcus, BA 6, that was particularly active when spatial locations were refreshed in two different studies. In ad-

dition, our meta-analysis showed that across experiments, differences in the magnitude of activation between refreshing verbal and nonverbal materials were more likely to be observed in left ventrolateral than in left anterior or dorsolateral PFC. In short, there was both within-experiments and across-experiments evidence for differences in distribution of PFC activity depending on materials.

It remains to be determined whether brain areas associated with a particular combination of process and type of information are constant or shift depending on the overall context (e.g., other types of information being refreshed in the same study). For example, are the areas that are active for refreshing of words and pictures when each is the only type of information the same as those that are active when some trials consist of words and some of pictures? Consistency in areas recruited for the same process/information combination across different contexts would provide strong evidence for stable functional PFC organization. Differences in areas active for process/information combinations in different contexts would imply flexibility in PFC organization, flexibility that perhaps serves to temporarily segregate mental functions in particular contexts. For example, across our experiments, it appears that the PFC area identified with refreshing words is quite consistent when the conditions are constant from experiment to experiment (e.g., compare Raye et al., 2000, with Johnson et al., 2004; the local maximum for left PFC activation was within two voxels in the two experiments). However, the area(s) associated with refreshing words appear to vary somewhat depending on whether words alone are refreshed and on what other types of information are being refreshed (compare the regions associated with refreshing words for Experiments 1 and 2 in Figures 1 and 2 and Table 2). New experiments that randomly assign participants to refresh the same information while varying the broader context will be needed in order to determine the extent to which PFC dynamically adjusts (see, e.g., Duncan & Miller, 2002) while ostensibly executing the same process in different contexts.

Cognitive Control: Selective Refreshing

As Miller and Cohen (2001) and many other cognitive neuroscientists have noted, cognitive control is “one of the great mysteries of the brain” (p. 193). The essence of control is agenda-governed selection among alternative possibilities—alternative perceptions, thoughts, memories, attitudes, emotions, or responses. From our studies of selective refreshing, we obtained findings consistent with those from other studies of cognitive control. We found that selective refreshing was associated with increased activity not only in left PFC but in ACC as well, consistent with the idea that PFC and ACC work together in a control circuit (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter et al., 2000; Casey et al., 1997; MacDonald et al., 2000; Milham et al., 2001; Miller & Cohen, 2001). We also found that orbitofrontal cortex was more active when selection was made in the face of

an emotionally salient alternative, consistent with the idea that OFC is recruited to regulate emotion and/or to withhold or inhibit initial responses (Casey et al., 1997; Horn et al., 2003; Rule et al., 2002; Shimamura, 2000). These findings suggest that the refresh task, because it is easy to explain to participants and easy to do, may be useful for studying disruptions in cognitive control in patient populations (see, e.g., Grillon et al., in press). In turn, converging evidence about the role of ACC and OFC in selective refreshing would be provided by studies of refreshing in appropriate patient populations in which cognitive control (e.g., schizophrenia; Braver, Barch, & Cohen, 1999) or the interaction between cognition and emotion (e.g., depression, posttraumatic stress disorder, or borderline personality disorder; Elliott, Rubinsztein, Sahakian, & Dolan, 2002; Krystal, Bennett, Bremner, Southwick, & Charney, 1995; Schmah, Vermetten, Elzinga, & Bremner, 2004) are disrupted.

Summary

We have identified areas of activation in PFC associated with the simple mental act of thinking of an item just experienced—that is, with refreshing. Our meta-analysis suggests that at least with respect to their role in the process of refreshing, different areas of left PFC are organized differently (Model 5 in Johnson et al., 2003). Across studies, refresh-related activity in left ventrolateral PFC (BA 47, 45; BA 45, 44) showed differences by type of information—that is, greater activity for verbal than for nonverbal materials (see Figures 8A, 8C). In contrast, in left BA 10 there was no significant difference in activation with verbal versus nonverbal materials and less overall variability in activity across types of materials than was found in other areas. Activity in left dorsolateral PFC (BA 9/6), although more variable than in anterior PFC, also did not show significant differences with verbal versus nonverbal materials. However, when type of information was manipulated within experiments, areas of dorsolateral and anterior PFC did show differences in activity associated with materials (Johnson et al., 2003, Experiment 1 and the present Experiment 1), suggesting that there may be local variations within these regions as a function of differential distributions of neurons related to different stimulus features. The degree of consistency versus flexibility in the distribution of refresh-related PFC activity for particular types of information as a function of varying cognitive context remains to be systematically determined. Increasing potential competition among representations increases activity in ACC and, when emotionally salient representations must be selected against, in OFC. The need for selection may also shift activity to more posterior/ventral regions of lateral PFC. Whether this shift to more ventral activation indicates that a rehearsal process (see, e.g., Smith & Jonides, 1999; Wagner et al., 2001) or selection/inhibition mechanisms (e.g., Thompson-Schill et al., 1997) are being engaged remains to be deter-

mined. Furthermore, there is evidence that the presence of an emotional item may selectively disrupt an anterior (BA 10) subcomponent of the refresh circuit. Reciprocal modulation between amygdala and prefrontal areas (e.g., Cunningham, Johnson, et al., 2004; Cunningham, Raye, & Johnson, 2004; Gray et al., 2002; Ochsner et al., 2002) begins to provide a neural account complementing social/cognitive accounts of emotion–cognition interactions (e.g., Fiske & Pavelchak, 1986; Johnson & Multhaup, 1992; Lazarus, 1982; Leventhal & Scherer, 1987; Ortony, Clore, & Collins, 1988; Zajonc, 1980). Finally, the fact that refreshing is likely to be a frequent component of more complex tasks may account for some of the commonality in the frontal regions identified across cognitive studies, and variation within this overall similarity may reflect differences in neural activity associated with differences in materials and/or control demands.

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NOTES

1. See the note to Table 2 for a list of anatomical abbreviations.
2. In the six fMRI experiments reported here, only six such areas were identified, all right or medial PFC and tending to show greater activity for repeat (and usually for read as well) than for refresh: Experiment 1, for places—GFm (BA 8); Experiment 2, for words—GO (BA 11) and GFs (BA 10); Experiment 3, for locations—GFs, GFm, GFd (BA 8) and GFs, GFm (BA 8); and Experiment 4, for visual words—frontal pole (BA 10). Greater right PFC activity in the repeat condition might reflect participants' noting of item familiarity (see, e.g., Johnson et al., 2003; Mitchell et al., 2004).
3. In comparison with eta squared, ω^2 has been shown to provide a relatively unbiased estimate of effect size (Keselman, 1975). Some researchers have suggested that effect size may be overestimated when conventional formulas devised for between-subjects comparisons are applied to repeated measures designs (Dunlap, Cortina, Vaslow, & Burke, 1996). Others have suggested that such estimates are only problematic when comparing between-subjects and within-subjects designs (Morris & DeShon, 2002). All of the studies reported here are repeated measures designs, using nearly identical methods. We selected a threshold of .09, which provided good differentiation among ROIs. Conventionally, an ω^2 of .06 is considered a medium effect size, and an ω^2 of .14 is considered a large effect size (J. Cohen, 1988). We are using ω^2 only as a method of combining data on a voxel-by-voxel basis across experiments while accounting for sample sizes; we do not attach any special importance to the absolute level of ω^2 that produced distinct ROIs.
4. Posterior areas identified by the ω^2 meta-analysis will be discussed elsewhere.
5. For clarity, time lines for the repeat and read control conditions are not shown. The average of the refresh time lines showed greater activity than did the average of the control time lines, confirming that these are indeed refresh-related areas.

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