

Role of Prefrontal and Anterior Cingulate Regions in Decision-Making Processes Shared by Memory and Nonmemory Tasks

Mathias S. Fleck^{1,2}, Sander M. Daselaar^{1,2}, Ian G. Dobbins² and Roberto Cabeza^{1,2}

¹Center for Cognitive Neuroscience, Duke University, Durham, NC 27708, USA and ²Department of Psychological and Brain Sciences, Duke University, Durham, NC 27708, USA

In the episodic retrieval (ER) domain, activations in right dorsolateral prefrontal cortex (DLPFC) are often attributed to postretrieval monitoring. Yet, right DLPFC activations are also frequently found during nonmemory tasks. To investigate the role of this region across different cognitive functions, we directly compared brain activity during ER and visual perception (VP) using event-related functional magnetic resonance imaging. In the ER task, participants decided whether words were old or new, whereas in the VP task, they decided which of the two colored screen areas was larger. In both tasks, each decision was followed by a confidence rating. The main finding was that right DLPFC (Brodmann area 46/10) activity was greater for low- than for high-confidence decisions in both tasks, demonstrating a general role in decision making. Even when reaction times (RTs) were included in the model, confidence remained the significant predictor of activity, suggesting that right DLPFC is involved in discontinuous evaluation rather than in continuous monitoring. In contrast, activity in anterior cingulate cortex was not only greater for low-confidence decisions but also increased with RT, reflecting a role in continuous conflict monitoring. Overall, the results demonstrate how direct cross-function comparisons clarify the generality and specificity of the functions of various brain regions.

Keywords: confidence, dorsolateral, episodic, parametric fMRI reaction time

Introduction

Functional neuroimaging has been used with growing frequency to explore the neural correlates of different cognitive functions (for a review, see Cabeza and Nyberg 2000). Typically, these functions are interpreted primarily within the focus of the laboratory conducting the research, such as emotion, language, or working memory. However, by restricting the explanation to one perspective of interest, there is a potential pitfall in overspecifying the cognitive processes driving observed activity. From an evolutionary perspective, it is more economic to presume some degree of flexibility and overlap in neural function. In support of this kind of shared functionality in prefrontal cortex (PFC), for example, Duncan (2001) notes that the extensive interconnectivity of this region suggests a broad cognitive role, which in turn may elicit activity in a number of diverse cognitive tasks. Thus, when examining neuroimaging data, it is critical to consider how very different tasks might generate very similar neural activity.

Meta-analyses of neuroimaging studies (Cabeza and Nyberg 2000; Fletcher and Henson 2001; Phan and others 2002; Wager and Smith 2003; Wager and others 2004) offer one method to characterize overlap in activations. Noting commonalities in cognitive tasks or stimulus types among different studies may

illuminate the general functionality of observed activations. However, the conclusions of these meta-analyses are limited by differences in participants, stimuli, paradigms, statistical thresholds, imaging parameters, and so on. Thus, to rigorously explore the role of brain regions activated by different cognitive functions, it is critical to compare these functions directly, within the same participants and within the same experiment.

This cross-functional approach has previously been used to determine the specificity of activations during episodic retrieval (ER), which refers to the recovery of memories for personally experienced past events (Tulving 1983). Cabeza, Dolcos, and others (2003) identified regions that were activated for both ER and visual attention tasks, including dorsal and ventral PFC, anterior cingulate, and medial temporal lobe. The overlap in these activations suggests that part of the typical episodic network might better be attributed to attentional rather than mnemonic processes. Nyberg and others (2003) found similar activations in PFC for episodic memory, knowledge-based semantic memory, and working memory, which the authors interpreted within a broader framework of cognitive control. Cabeza and others (2002) also revealed common activity in ER and working memory tasks in dorsolateral prefrontal cortex (DLPFC). The overlaps observed in these studies, particularly in PFC, motivated the current pursuit of determining what cognitive processes are shared across these differing tasks.

Several theories have been put forth to characterize the role of PFC in ER. In the case of the right PFC, it has been suggested that this region is involved in the evaluation of information recovered during retrieval with respect to task relevance and accuracy (Schacter and others 1996; Rugg and others 1998; Henson and others 2000; Allan and others 2000). This “postretrieval-monitoring hypothesis” is supported by lesion and functional neuroimaging evidence. As an example of lesion data, Schacter and others (1996) described a patient with a right PFC lesion who showed pathologically high false-alarm rates for lures related to the studied items, a deficit suggesting an inability to monitor and reject new items that seem old. Also, Stuss and others (1994) reported that subjects with right frontal lobe lesions repeatedly recalled the same items during a memory task, suggesting a deficit in monitoring previously retrieved items.

Functional neuroimaging data supporting the postretrieval-monitoring hypothesis include evidence that the right prefrontal activity increases with the number of targets included in the scan (Rugg and others 1998) and is greater for recognition than for recall (Cabeza, Locantore, and Anderson 2003), as well as for recombined versus identical associate pairs (Achim and Lepage 2005). The strongest functional neuroimaging evidence was provided by Henson and others (2000), who operationalized postretrieval monitoring using confidence ratings during

a recognition test. They proposed that postretrieval monitoring should be greater for low-confidence responses because they occur when the memory signal is close to the decision criterion and hence require additional evaluation. Consistent with the postretrieval-monitoring hypothesis, right DLPFC showed greater activity for low- than for high-confidence trials.

Yet, attributing right DLPFC activity during an ER task to postretrieval monitoring may be overspecifying the function of this region. Right DLPFC activity is found during many tasks that involve making decisions, even if they have no ER component (Badre and Wagner 2004; Yarkoni and others 2005). Even if one assumes like Henson and others (2000) that greater activity for low- than for high-confidence trials reflect additional monitoring processes, it is possible that these monitoring processes are not specific to ER decisions and may also occur for other kinds of decisions. In other words, rather than postretrieval monitoring, right DLPFC may be involved in general decision-making processes. Testing this alternative hypothesis was the primary goal of the present study. Our approach was to compare the effects of confidence on an ER task and on a cognitive task with no ER component using event-related functional magnetic resonance imaging (fMRI). If greater right DLPFC activity for low- than for high-confidence responses is found only in the ER task, the postretrieval-monitoring hypothesis would be supported, whereas if it is found in both tasks, the general decision-making hypothesis would be supported.

The paradigm is depicted in Figure 1. Participants studied a list of common words before scanning, and during scanning, they performed 2 different tasks: an ER task (word recognition) and a visual perception (VP) task (area size comparison). In both tasks, each decision (memory-based or perception-based) was followed by a confidence rating. An advantage of the area size comparison task is that its difficulty can be easily manipulated by varying differences in area size. By doing so across several pilot studies, we were able to find a set of stimuli that yielded accuracy rates and confidence ranges similar to those in the recognition task (Fig. 2). Using parametric fMRI analyses, we identified brain regions where activity increased as a function of decreasing confidence. Low-confidence activations (i.e., low > high) shared by both tasks were identified by conducting conjunction analyses. It is important to note that the focus of the present study was on similarities in process-related activations rather than on differences in activations. When finding similarities in process-related activations is the goal, using tasks involving different stimuli (e.g., verbal vs. nonverbal) is actually an advantage: if activation overlaps are found, they can be more safely attributed to similarities in processes rather than to similarities in stimuli. On the basis of a general decision-making hypothesis, we predicted an overlap in low-confidence activity in right DLPFC. On the basis of research linking anterior cingulate cortex (ACC) to conflict detection (Carter and others 1998; Botvinick and others 1999; MacDonald and others 2000; van Veen and Carter 2002), we also predicted shared low-confidence activity in this region. Finally, we expected shared low-confidence activity in regions associated with attention, such as the parietal cortex.

Assuming the validity of our decision-making hypothesis, the second goal of the study was to specify the nature of the decision-making processes mediated by right DLPFC, ACC, and other brain regions. We did so by measuring in ER and VP not only the effects of confidence on neural activity but also the effects of reaction time (RT). We assumed that decision making

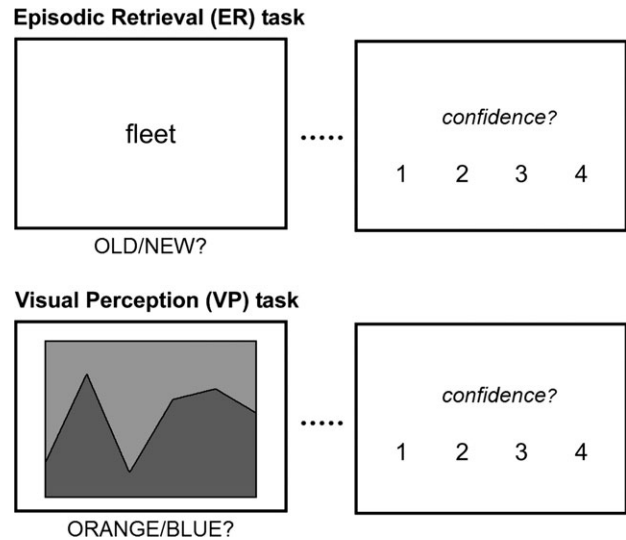


Figure 1. Participants studied a list of words before scanning and then performed 2 different tasks in the scanner: a recognition memory task and a VP task. On each trial of the memory task, participants decided whether a word was old (i.e., seen in the study phase) or new and then rated their confidence in the decision. On each trial of the area judgment task, participants decided which of the 2 differently colored screen areas was larger and then rated their confidence.

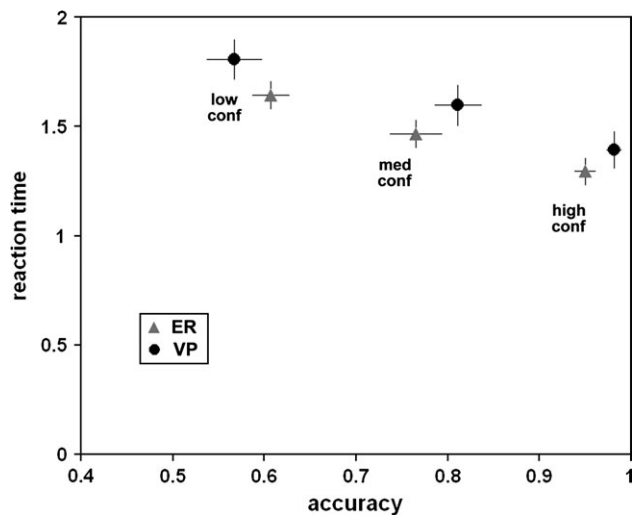


Figure 2. Behavioral data for both ER and VP tasks showing mean and standard error of RT and accuracy at each confidence level (high, medium, and low).

may be subdivided into processes with different temporal characteristics. Specifically, we considered 2 kinds of decision-making processes: processes that take place throughout the whole trial, such as the constant scrutiny of evidence arriving from memory or perception (online inspection), and processes that take place at a certain point during the trial, such as evaluating the accumulated evidence and choosing the appropriate action (response selection). Although both “online inspection” and “response selection” could explain greater activity for low- than for high-confidence trials, these 2 kinds of monitoring processes can be expected to have different effects on RTs. Given that online inspection accounts for a large proportion of the total RT, whereas response selection explains only a small proportion of the total RT, we assumed that only the

former type of decision-making process would have a significant impact on RT. Thus, we assumed that low-confidence activity that varies with RT reflects mainly online inspection, whereas low-confidence activity that is not affected by RT reflects mainly response selection.

We investigated the relationship between neural activity and behavioral response by conducting a mixed-effects multiple regression analysis. Specifically, we examined the predictive value of confidence and RT to activity within regions of interest on a trial-by-trial basis. Regions were chosen from those showing a parametric effect of low confidence from our primary analysis. Based on evidence that DLPFC is involved in response selection (Hadland and others 2001; Bunge and others 2005), we predicted that RT should not predict activity in this region. In contrast, given that ACC has been associated with conflict detection, a process likely to be continuously active throughout the trial, we predicted that RT should be a significant predictor of activity in this region.

Materials and Methods

Participants

Fourteen right-handed young participants (7 females) with an average age of 21.0 years (standard deviation [SD] = 2.4) were recruited from the Duke University community and paid for their participation. All participants gave informed consent to a protocol approved by the Duke University Institutional Review Board.

Stimuli

The stimuli were words in the memory task and split rectangles in the perception task (see Fig. 1). Critical words consisted of 240 five-letter words that were selected from the medical research council psycholinguistic database (<http://www.psy.uwa.edu.au/MRCDataBase/mrc2.html>). The words were of moderate frequency (mean: 39), concreteness (mean: 504), and imageability (mean: 510). Perceptual stimuli were created by dividing 4.5" × 6" rectangles with a jagged line (6 variable points) into 2 areas, which were, respectively, colored blue and orange. The points of the jagged line were moved up or down in order to create many different versions of the split rectangles. Given that difficulty of the area size judgment is a direct function of the difference between the 2 areas, this difference was manipulated across several pilot studies in order to match the difficulty of the perception task to that of the memory task, and a final set of 120 rectangles of varying difficulty was selected.

Behavioral Paradigm

About 20 min prior to scanning, subjects viewed an intermixed list of 120 English words and 80 pronounceable pseudo-words, presented at a rate of 2 s per item. For each item, participants decided whether or not it was a real word (lexical decision task). They were also informed that memory for the words would be tested later. The lexical decision task was chosen because it leads to an intermediate level of recognition performance (between that of shallow and deep tasks), which is necessary in order to obtain a sufficient number of both low- and high-confidence recognition responses. Participants were also administered practice trials for the perceptual task. During the scan session, participants performed an ER task (recognition memory) and a VP task (area judgment). There were 4 ER scans and 2 VP scans, with the order counterbalanced across subjects. During ER scans, subjects were presented a randomized list of old words (from the lexical decision task) and new words (60 total words per scan, presented on-screen for 3.4 s each). Subjects used a four-key fiber-optic response box (Resonance Technology, Inc., Northridge, CA) to perform an "old/new" judgment on the presented stimuli. Subjects then were prompted to report their confidence (1.7 s) for their answer from 1 (lowest confidence) to 4 (highest confidence), followed by an intertrial interval of 0.2–5.4 s. The area judgment involved subjects viewing rectangles divided into 2 differently colored areas (blue and orange) by a jagged

line (see Fig. 1). Subjects had to determine which color had the greater surface area and then rate their confidence on this judgment. The timing was identical to the memory task.

fMRI Procedure

Subjects were scanned on a 4-T GE scanner. High-resolution T_1 -weighted structural images (256 × 256 matrix, repetition time [TR] = 12 ms, time to echo [TE] = 5 ms, field of view [FOV] = 24 cm, 68 slices, 1.9-mm slice thickness, 0-mm spacing) were collected first. Coplanar functional images were subsequently acquired utilizing an inverse spiral sequence (64 × 64 matrix, TR = 1700 ms, TE = 31 ms, FOV = 24 cm, 34 slices, 3.8-mm slice thickness, 0-mm spacing, 254 images). Scanner noise was reduced with earplugs, and head motion was minimized with foam pads. Stimuli were presented with liquid crystal display goggles (Resonance Technology, Inc.). Preprocessing and data analysis were performed using statistical parametric mapping software implemented in Matlab (SPM2; Wellcome Department of Cognitive Neurology, London, UK). After discarding initial volumes to allow for scanner stabilization, images were slice-timing and motion corrected, and then they were spatially normalized to the Montreal Neurological Institute template and smoothed using a Gaussian kernel of 8-mm full width half maximum. For each subject, trial-related activity was assessed by convolving a vector of stimulus onset time points with a canonical hemodynamic response function (HRF). A general linear model was specified for each participant to model the 2 trial types of interest, successful ER of studied memory items and successful visual perceptual judgments (VP). All other trial types, including incorrect trials, novel retrieval items, and no-response trials, were also included in the model but not used in the analyses.

Confidence Analysis

Using the first-order parametric option within SPM2, trial types were modulated inversely by the confidence reported on each trial, scaling the predicted HRF upward as confidence decreased. Because several subjects did not use the lowest confidence response (1), the 2 lowest confidence levels were collapsed within subjects for both tasks in the present analyses, leading to 3 modulated levels of confidence: low (1–2), medium (3), and high (4). This change did not significantly impact group level statistics. In this fashion, statistical parametric maps showing activity increasing with low confidence were generated for each subject on each of the 2 tasks. A second-level analysis was conducted for each task separately, treating subjects as a random effect. Finally, using the 2 resulting random-effects maps of low confidence within ER and VP, we performed a conjunction to find common, task-independent regions of low confidence. We report regions of interest containing voxels surviving $P < 0.005$ (uncorrected) with a minimum cluster size of 10 voxels in each and both tasks, leading to a joint probability of $P < 0.00025$ (i.e., 0.005×0.005).

RT Analysis

To further investigate the function of regions showing low-confidence activity, an additional analysis was conducted to disentangle the effects of confidence and RT. We conducted a regression analysis, simultaneously investigating the influence of confidence and RT on individual-trial activity within DLPFC and ACC, in turn. This analysis involved 3 steps. 1) To obtain activity for individual trials, we modeled every trial as a different condition in SPM. This procedure has been used in a previous fMRI study (Rissman and others 2004), and we confirmed its validity by checking that contrasts based on collapsing all trials/conditions of the same kind yielded the same activation maps as standard contrasts based on the same trials. 2) Activity for each trial and for each participant was extracted for regions of interest, namely, right DLPFC and ACC. As in the primary analysis, only successful retrieval and successful perceptual trials were included in the subsequent model. 3) A mixed-effects linear regression analysis treating subjects as a random effect was conducted using S-Plus 7.0 (Insightful Corp., Seattle, WA), with confidence and RT on each trial as the independent variables and with individual-trial activity within those 2 regions each in turn as the dependent variable. In this fashion, the effects of both confidence and RT were simultaneously entered into a single model to determine how well they independently or jointly predicted activity within either DLPFC or ACC.

Results

Behavioral Data

ER and VP performances were very similar overall. The proportion of correct trials was 0.75 (SD = 0.09) in the ER task and 0.74 (SD = 0.05) in the VP task. This difference was not significant ($P > 0.9$), confirming that accuracy was comparable in the 2 tasks. In both tasks, accuracy increased and RTs decreased as a function of confidence (Fig. 2, low-, medium-, and high-confidence levels shown). These impressions were confirmed by separate analyses of variance showing significant effects of confidence on accuracy ($P < 0.001$) and RTs ($P < 0.001$).

fMRI Data

Table 1 lists regions showing greater activity with decreasing confidence in both ER and VP tasks (conjunction analysis). Within these task-general regions, the location of local maxima peak voxels for each task individually is reported along with the associated t statistic. Consistent with our predictions, activated regions included right DLPFC (Brodmann area 46/10) and ACC/medial PFC. The latter cluster was a large activation with peaks within dorsal anterior cingulate and a peak within superior frontal gyrus. As illustrated by the line graphs in Figure 3, activity in both DLPFC and ACC regions increased as confidence decreased from high to low in a quasi-linear fashion. The finding that right DLPFC showed low-confidence activity not only for ER but also for VP indicates that the role of this region is not specific to postretrieval monitoring and is instead related to decision-making processes shared by memory and nonmemory tasks. The finding of shared low-confidence activity in ACC is consistent with the presumed role of this region in ongoing conflict detection. Finally, Table 1 lists other regions also showing low-confidence activity for both ER and VP, namely, in precuneus, insular, and right parietal regions.

To investigate differential effects of confidence and RT, we conducted a mixed-effects linear regression analysis with confidence and RT as the independent variables and individual-trial activity within DLPFC and ACC each in turn as the dependent variable. We found a significant effect of both confidence ($P < 0.0001$) and RT ($P < 0.005$) on activity within ACC, suggesting that both behavioral parameters independently

contribute to observed activations in this region during low-confidence decision making. However, when both parameters were entered into the regression model predicting DLPFC activity, only confidence ($P < 0.0001$), not RT ($P < 0.49$), was a significant predictor. To illustrate this finding, Figure 4 shows the regression lines for right DLPFC and ACC activity in individual trials as a function of RT and confidence in 2 representative subjects. Consistent with these graphs, both confidence and RT predict signal change within ACC, but only confidence, not RT, varies with signal change in right DLPFC. This finding supports the hypothesis that ACC is involved in continuous online inspection, whereas DLPFC is involved in a discontinuous response selection.

Finally, to ensure that these findings applied to both tasks, we conducted the same analysis separately for ER and VP trials. For the ER task, both confidence ($P < 0.0001$) and RT ($P < 0.04$) had a significant effect on activity within ACC, but only confidence ($P < 0.0001$), not RT ($P < 0.99$), was a predictor of activity within right DLPFC. For the VP task, again both confidence ($P < 0.0001$) and RT ($P < 0.004$) significantly predicted ACC activity, whereas confidence ($P < 0.0001$), not RT ($P < 0.68$), predicted activity within right DLPFC. These separate analyses confirm that the reported dissociation of confidence and RT within ACC and DLPFC is common to both of the tasks.

Discussion

The present study yielded 3 main findings. First, right DLPFC showed greater activity for low- than for high-confidence responses not only in the ER task but also in the VP task. This finding suggests that the functional role of this region is not specific to postretrieval monitoring and is instead related to general decision-making operations shared by memory and nonmemory tasks. Second, ACC also showed low-confidence activity, but this activity was additionally modulated by RT, an effect not shown in right DLPFC. This dissociation suggests that these 2 regions are involved in different kinds of decision-making processes, possibly online inspection in the case of ACC and response selection in the case of DLPFC. Finally, low-confidence activity shared by ER and VP was also found in insula and parietal regions, possibly reflecting a role of these regions in emotional and attentional processing. These 3 findings are discussed in separate sections below.

Table 1

fMRI activations of decreasing confidence in both tasks

Region	BA	Voxels	episodic retrieval (ER)					visual perception (VP)				
			L/R	x	y	z	T	L/R	x	y	z	T
DLPFC	10/46	23	R	23	34	27	4.42	R	30	38	15	4.58
ACC/medial PFC	32	136	L	-11	19	38	7.02	R	11	19	34	4.35
	32		R	15	23	30	5.71	L	-11	15	49	4.49
Insula	8	66	L	-15	8	57	4.69	L	-19	11	57	4.79
	47		L	-19	19	4	4.38	L	-23	23	4	5.50
	47		R	34	15	4	3.90	R	34	11	4	4.40
Dorsal precuneus	13	130	R	42	-19	19	6.36	R	34	-23	19	5.15
	7		L	-11	-61	53	5.52	L	-15	-53	42	7.19
Superior parietal	19	24	R	23	-76	42	4.88	R	27	-80	42	5.60
Central cingulate gyrus	23	26	L	-23	-27	38	4.30	L	-27	-23	38	3.95
Cerebellum		23	R	0	-53	-42	3.64	R	4	-49	-38	5.71

Note: Regions showing significant activation in both tasks related to decreasing confidence, described in terms of laterality (left/right) and Brodmann area (BA) using Montreal Neurological Institute coordinates. T refers to the statistical t value at the peak voxel within SPM maps parametrically modulated by decreasing confidence, thresholded within each task at $P < 0.005$, with a 10-voxel minimum cluster size.

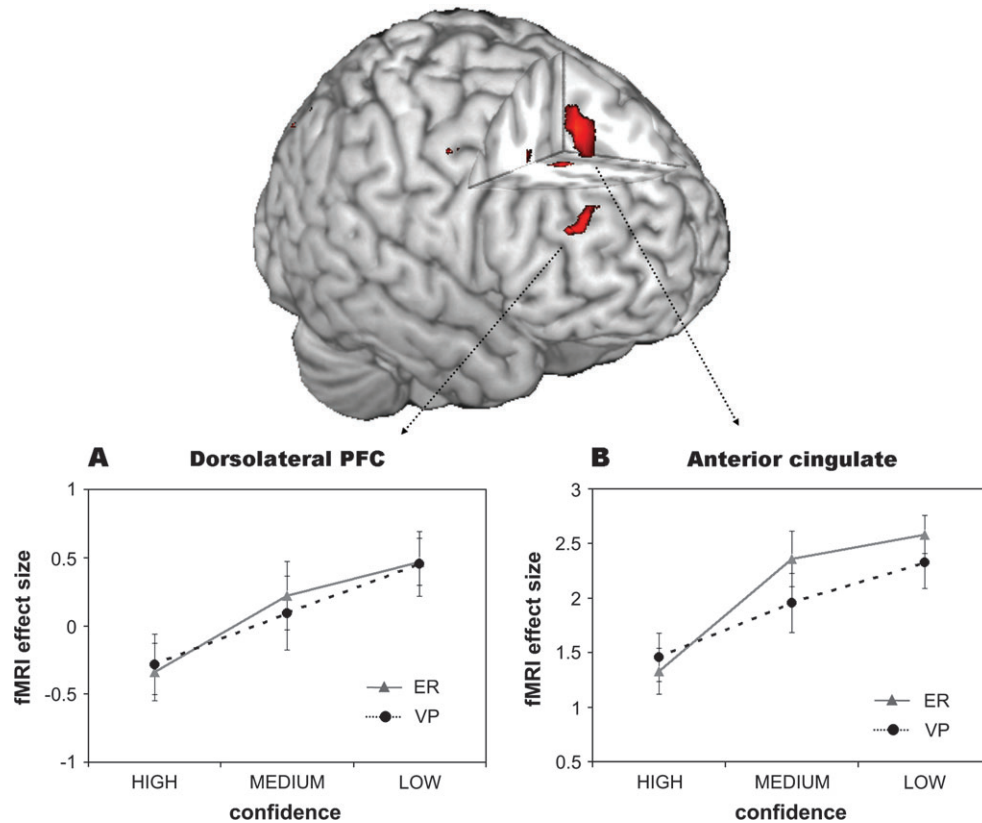


Figure 3. Render on 3-dimensional brain shows overlapping activity parametrically increasing as a function of decreasing confidence in both the recognition and the perceptual tasks. Also shown are effect sizes for each confidence level (high, medium, and low) for the retrieval task (solid line) and the perceptual task (dashed line) within (A) right DLPFC and (B) ACC.

Right DLPFC

The present study utilized a cross-functional approach to ascertain common cognitive components of 2 disparate tasks. By examining the same set of subjects within a single scan session, by matching difficulty and confidence reports, and by analyzing the same manipulations (confidence and RT) for the 2 tasks, we were able to directly compare 2 very different tasks. This cross-function approach contrasts with the within-function approach used by most neuroimaging studies, which typically investigate a single cognitive function (e.g., ER) and interpret the activated regions only in relation to this function. Within-function studies in the ER domain have attributed right DLPFC activation to postretrieval monitoring, and they have confirmed this hypothesis by showing greater activity in this region for low- compared with high-confidence recognition responses. To investigate whether this effect was specific to postretrieval monitoring, we used a cross-function approach to directly compare the effects of confidence on memory and nonmemory tasks.

The results of our study clearly show that low-confidence activity in right DLPFC is not specific to memory tasks but is shared for memory and nonmemory tasks. This finding indicates that the function of this region is therefore not specific to postretrieval monitoring and is instead related to general decision-making processes. A domain-general interpretation accords with models positing a general-purpose role of DLPFC in controlled processing and response, independent of task type and materials (Chein and Schneider 2005). Given that postre-

trieval monitoring is a subclass of decision-making operations, the general decision-making interpretation supported by the present findings can easily accommodate all data supporting the postretrieval-monitoring interpretation. For example, increased false alarming in patients with right DLPFC damage (Stuss and others 1994; Schacter and others 1996) may be explained as a general deficit in evaluative processes, and neuroimaging studies that have attributed right DLPFC activity to ER monitoring (Henson and others 2000; Achim and Lepage 2005) can also be interpreted in a broader framework involving making any low-confidence decision.

To clarify more specifically the role of right DLPFC in decision making, we investigated how confidence and RT individually or collectively predicted activity in this region. Our single-trial analysis entering both confidence and RT simultaneously into a mixed-effects model showed a significant effect of confidence, but not RT, on right DLPFC activity. This finding constrains the interpretation of the role of DLPFC in monitoring and favors a role for this region in the evaluation of accumulated information and response selection (Bunge 2004; Bunge and others 2005). We assume that this evaluation and selection-for-action is a discontinuous, relatively brief segment of a trial. That we observe right DLPFC for low- greater than for high-confidence trials supports the notion that more difficult trials might involve a greater evaluative component, and that this region is insensitive to RT fits with the idea that the actual amount of time spent on task should be independent of a final evaluative step.

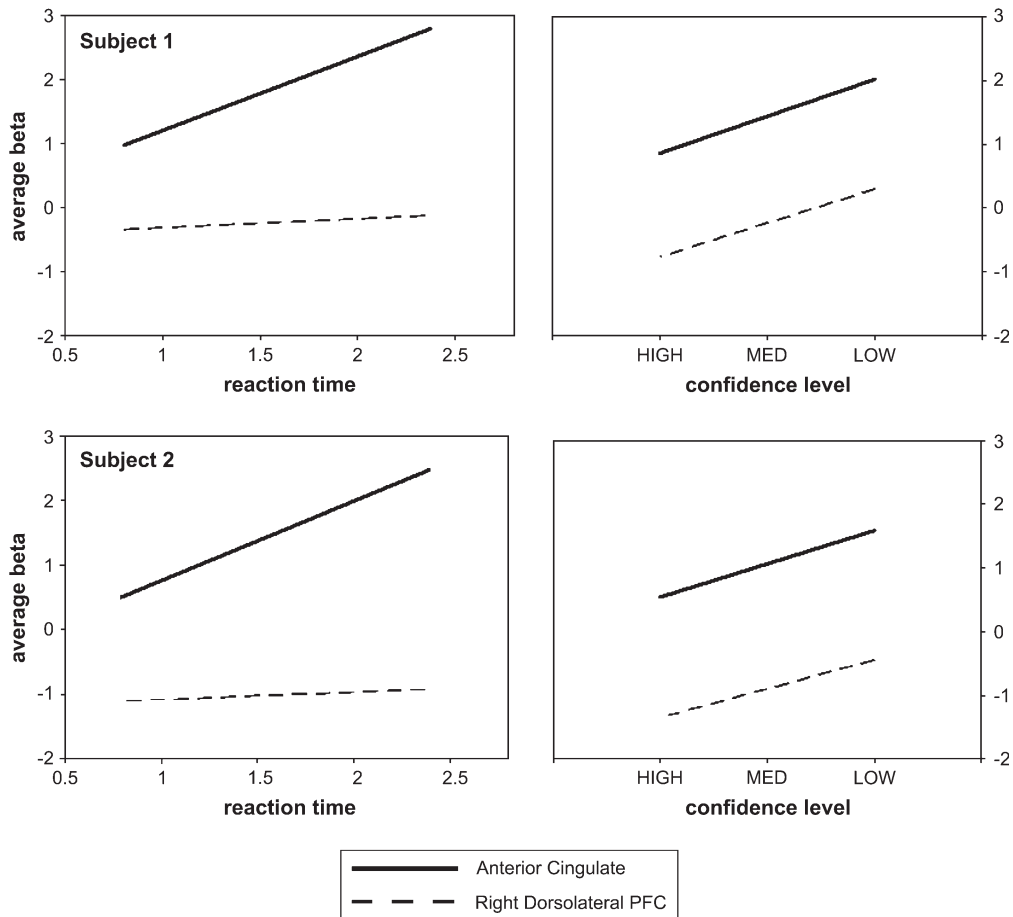


Figure 4. Two example subjects' regression functions for single-trial beta weights extracted from 2 regions of interest, right DLPFC (dashed line) and anterior cingulate (solid line), displayed as a function of RT and confidence. ACC and DLPFC both vary with subjects' confidence report, but RT varies only as a function of ACC, not DLPFC.

Our data support Rowe and others (2000) and Hadland and others (2001) studies that explored the role of DLPFC in working memory tasks and suggested that selection of a response, rather than online maintenance of information, yielded DLPFC (area 46) activity. As Rowe suggested, this explanation fits the observation that DLPFC is often activated within working memory studies and many other kinds of tasks (as in Cabeza and others 2002) because most studied tasks involve response selection.

Anterior Cingulate Cortex

ACC also yielded a significant effect of low confidence in both tasks, as we predicted. The ACC has been theorized to support or index online conflict detection (Botvinick and others 1999; Banich and others 2000), affective processing of conflict (Gehring and Fencsik 2001), and conflict resolution (Weissman and others 2005). Our single-trial analyses demonstrated a significant effect of both confidence and RT within ACC, suggesting independent contributions of each. Sensitivity to RT is consistent with the conflict detection hypothesis as detection should be ongoing throughout the trial, and hence, increased demands on this process can be expected to correlate with longer RTs.

The ACC and DLPFC coactivation observed in the present study has been reported as well in a number of working memory and conflict studies (for review, see Duncan and Owen 2000),

implicating a tightly related frontal network. The co-occurrence of activity in these areas has made distinguishing the functions of each a challenging endeavor but remains an important goal. MacDonald and others (2000) reported that DLPFC was engaged during a response preparation period and supporting cognitive control, whereas ACC is more engaged during the actual trial period and particularly during high conflict, in support of ongoing resolution of tasks at hand. Our single-trial analysis (Fig. 4) suggests that when confidence and RT are entered simultaneously into a mixed-effects regression model, both factors make a significant contribution to changes in measured signal within ACC. This contrasts with our findings within DLPFC, which demonstrated no such sensitivity to RT. These data contribute to evidence for a dissociation between these regions similar to MacDonald and others (2000). The differential effect of RT we observed in these 2 regions suggests that ACC is active throughout a trial as some index of task-related conflict, whereas DLPFC may ultimately evaluate the product of ongoing activity for task relevance and selection of a response.

Insula and Parietal Cortex

The present study also yielded significant low- greater than high-confidence activity in bilateral insula. Other decision-making studies have attributed insular activations to unfairness (Sanfey and others 2003), uncertainty (Huettel and others

2005), and violations of expectancy (Casey and others 2000), and in recognition memory, insular activity has been attributed to more effortful retrieval (Buckner and others 1998). Such findings are difficult to reconcile, but one possibility is that insular cortex activations may generally indicate a negative emotional reaction to task or stimuli. Accordingly, Paulus and others (2003) suggest that insular activity may reflect an internal somatic signal that may guide decision-making behavior.

Low-confidence activity was also observed in right superior parietal cortex. It has been proposed that posterior parietal cortex plays a role in allocating attentional resources (Colby and Goldberg 1999), which may be necessary in the present study during trials involving low-confidence decisions. This explanation is also in line with the findings of other cross-functional studies (Cabeza and others 2002), which found coactivation in this region for both a working memory and an ER task.

Finally, an additional medial parietal region was observed as an effect of common low confidence in left dorsal precuneus. Although precuneus has frequently been reported in successful ER (Kapur and others 1995; Krause and others 1999; Cabeza and others 2002), the region we report is more dorsal than in typical neuroimaging studies of ER. Indeed, when we examined only the retrieval confidence maps, we observe a shift to greater activity for high-confidence trials in a more ventral region of precuneus and into retrosplenial cortex, which has been associated with recollection and detailed retrieval (Yonelinas and others 2005). The dorsal region reported here showing the common low-confidence effect is closer to the region reported by Cabeza and others (2002) as showing greater activity for working memory than for ER, suggesting a cross-functional role for this region in working memory processes or attention-modulated online processing.

Conclusions

We investigated the specificity of right DLPFC activations by directly comparing activity during episodic memory retrieval and VP tasks using fMRI. We examined whether right PFC activity during low-confidence decisions would be specific to ER or shared with the VP task, and the present study revealed our predicted overlap: a right DLPFC region showing greater activity for low- than for high-confidence trials during both tasks. This finding suggests that right PFC activity during demanding decisions is not memory specific (i.e., postretrieval monitoring) and is instead related to a more general decision-making process. Subsequent analyses simultaneously incorporating both confidence and RT in a mixed-effects regression model provided evidence that right DLPFC activity is predicted by confidence, not RT, and thus may support response selection rather than ongoing conflict resolution. Regions involved in ongoing conflict resolution should yield an effect of RT, which we found in ACC, and a conflict-monitoring interpretation for this region fits well with studies from the attention and working memory domains. Overall, the results demonstrate how the neural components of cognitive processes potentially common to differing tasks can only be explored through direct cross-function comparisons.

Notes

This work was supported by a National Institutes of Health grant (AG19731) to RC. The authors would like to thank Amber Baptiste Tarter for assistance in subject recruitment, Rakesh Arya for analysis

support, and Steve Prince, Nancy Dennis, and Peggy St. Jacques for comments.

Address correspondence to Roberto Cabeza, PhD, Center for Cognitive Neuroscience, Duke University, PO Box 90999, Levine Science Research Center Building, Room B203, Durham, NC 27708, USA. Email: cabeza@duke.edu.

References

- Achim AM, Lepage M. 2005. Neural correlates of memory for items and for associations: an event-related functional magnetic resonance imaging study. *J Cogn Neurosci* 17:652-667.
- Allan K, Dolan RJ, Fletcher PC, Rugg MD. 2000. The role of the right anterior prefrontal cortex in episodic retrieval. *Neuroimage* 11:217-227.
- Badre D, Wagner AD. 2004. Selection, integration, and conflict monitoring; assessing the nature and generality of prefrontal cognitive control mechanisms. *Neuron* 41:473-487.
- Banich MT, Milham MP, Atchley R, Cohen NJ, Webb A, Wszalek T, Kramer AF, Liang ZP, Wright A, Shenker J, Magin R. 2000. fMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. *J Cogn Neurosci* 12:988-1000.
- Botvinick M, Nystrom LE, Fissell K, Carter CS, Cohen JD. 1999. Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature* 402:179-181.
- Buckner RL, Koutstaal W, Schacter DL, Wagner AD, Rosen BR. 1998. Functional-anatomic study of episodic retrieval using fMRI. I. Retrieval effort versus retrieval success. *Neuroimage* 7:151-162.
- Bunge SA. 2004. How we use rules to select actions: a review of evidence from cognitive neuroscience. *Cogn Affect Behav Neurosci* 4:564-579.
- Bunge SA, Wendelken C, Badre D, Wagner AD. 2005. Analogical reasoning and prefrontal cortex: evidence for separable retrieval and integration mechanisms. *Cereb Cortex* 15:239-249.
- Cabeza R, Dolcos F, Graham R, Nyberg L. 2002. Similarities and differences in the neural correlates of episodic memory retrieval and working memory. *Neuroimage* 16:317-330.
- Cabeza R, Dolcos F, Prince SE, Rice HJ, Weissman DH, Nyberg L. 2003. Attention-related activity during episodic memory retrieval: a cross-function fMRI study. *Neuropsychologia* 41:390-399.
- Cabeza R, Locantore JK, Anderson ND. 2003. Lateralization of prefrontal activity during episodic memory retrieval: evidence for the production-monitoring hypothesis. *J Cogn Neurosci* 15:249-259.
- Cabeza R, Nyberg L. 2000. Imaging cognition II: an empirical review of 275 PET and fMRI studies. *J Cogn Neurosci* 12:1-47.
- Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD. 1998. Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science* 280:747-749.
- Casey BJ, Thomas KM, Welsh TF, Badgaiyan RD, Eccard CH, Jennings JR, Crone EA. 2000. Dissociation of response conflict, attentional selection, and expectancy with functional magnetic resonance imaging. *Proc Natl Acad Sci USA* 97:8728-8733.
- Chen JM, Schneider W. 2005. Neuroimaging studies of practice-related change: fMRI and meta-analytic evidence of a domain-general control network for learning. *Brain Res Cogn Brain Res*. Forthcoming.
- Colby CL, Goldberg ME. 1999. Space and attention in parietal cortex. *Annu Rev Neurosci* 22:319-349.
- Duncan J. 2001. An adaptive coding model of prefrontal function. *Neuroimage* 13:S1300-S1300.
- Duncan J, Owen AM. 2000. Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends Neurosci* 23:475-483.
- Fletcher PC, Henson RN. 2001. Frontal lobes and human memory: insights from functional neuroimaging. *Brain* 124:849-881.
- Gehring WJ, Fencsik DE. 2001. Functions of the medial frontal cortex in the processing of conflict and errors. *J Neurosci* 21:9430-9437.
- Hadland KA, Rushworth MF, Passingham RE, Jahanshahi M, Rothwell JC. 2001. Interference with performance of a response selection task that has no working memory component: an rTMS comparison of the dorsolateral prefrontal and medial frontal cortex. *J Cogn Neurosci* 13:1097-1108.

- Henson RNA, Rugg MD, Shallice T, Dolan RJ. 2000. Confidence in recognition memory for words: dissociating right prefrontal roles in episodic retrieval. *J Cogn Neurosci* 12:913-923.
- Huettel SA, Song AW, McCarthy G. 2005. Decisions under uncertainty: probabilistic context influences activation of prefrontal and parietal cortices. *J Neurosci* 25:3304-3311.
- Kapur S, Craik FI, Jones C, Brown GM, Houle S, Tulving E. 1995. Functional role of the prefrontal cortex in retrieval of memories: a PET study. *Neuroreport* 6:1880-1884.
- Krause BJ, Schmidt D, Mottaghy FM, Taylor J, Halsband U, Herzog H, Tellmann L, Muller-Gartner HW. 1999. Episodic retrieval activates the precuneus irrespective of the imagery content of word pair associates. A PET study. *Brain* 122(Pt 2):255-263.
- MacDonald AW III, Cohen JD, Stenger VA, Carter CS. 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 288:1835-1838.
- Nyberg L, Marklund P, Persson J, Cabeza R, Forkstam C, Petersson KM, Ingvar M. 2003. Common prefrontal activations during working memory, episodic memory, and semantic memory. *Neuropsychologia* 41:371-377.
- Paulus MP, Rogalsky C, Simmons A, Feinstein JS, Stein MB. 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *Neuroimage* 19:1439-1448.
- Phan KL, Wager T, Taylor SF, Liberzon I. 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 16:331-348.
- Rissman J, Gazzaley A, D'Esposito M. 2004. Measuring functional connectivity during distinct stages of a cognitive task. *Neuroimage* 23:752-763.
- Rowe JB, Toni I, Josephs O, Frackowiak RS, Passingham RE. 2000. The prefrontal cortex: response selection or maintenance within working memory? *Science* 288:1656-1660.
- Rugg MD, Fletcher PC, Allan K, Frith CD, Frackowiak RS, Dolan RJ. 1998. Neural correlates of memory retrieval during recognition memory and cued recall. *Neuroimage* 8:262-273.
- Sanfey AG, Rilling JK, Aronson JA, Nystrom LE, Cohen JD. 2003. The neural basis of economic decision-making in the ultimatum game. *Science* 300:1755-1758.
- Schacter DL, Curran T, Galluccio L, Milberg WP, Bates JF. 1996. False recognition and the right frontal lobe: a case study. *Neuropsychologia* 34:793-808.
- Stuss DT, Alexander MP, Palumbo CL, Buckle L, Sayer L, Pogue J. 1994. Organizational strategies with unilateral or bilateral frontal lobe injury in word list learning tasks. *Neuropsychology* 8:355-373.
- Tulving E. 1983. *Elements of episodic memory*. New York: Columbia University Press.
- van Veen V, Carter CS. 2002. The timing of action-monitoring processes in the anterior cingulate cortex. *J Cogn Neurosci* 14:593-602.
- Wager TD, Jonides J, Reading S. 2004. Neuroimaging studies of shifting attention: a meta-analysis. *Neuroimage* 22:1679-1693.
- Wager TD, Smith EE. 2003. Neuroimaging studies of working memory: a meta-analysis. *Cogn Affect Behav Neurosci* 3:255-274.
- Weissman DH, Gopalakrishnan A, Hazlett CJ, Woldorff MG. 2005. Dorsal anterior cingulate cortex resolves conflict from distracting stimuli by boosting attention toward relevant events. *Cereb Cortex* 15:229-237.
- Yarkoni T, Gray JR, Chrsatil ER, Barch DM, Green L, Braver TS. 2005. Sustained neural activity associated with cognitive control during temporally extended decision making. *Brain Res Cogn Brain Res* 23:71-84.
- Yonelinas AP, Otten IJ, Shaw KN, Rugg MD. 2005. Separating the brain regions involved in recollection and familiarity in recognition memory. *J Neurosci* 25:3002-3008.