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Human Medial Frontal Cortex Activity Predicts Learning from Errors

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Learning from errors is a critical feature of human cognition. It underlies our ability to adapt to changing environmental demands and to tune behavior for optimal performance. The posterior medial frontal cortex (pMFC) has been implicated in the evaluation of errors to control behavior, although it has not previously been shown that activity in this region predicts learning from errors. Using functional magnetic resonance imaging, we examined activity in the pMFC during an associative learning task in which participants had to recall the spatial locations of 2-digit targets and were provided with immediate feedback regarding accuracy. Activity within the pMFC was significantly greater for errors that were subsequently corrected than for errors that were repeated. Moreover, pMFC activity during recall errors predicted future responses (correct vs. incorrect), despite a sizeable interval (on average 70 s) between an error and the next presentation of the same recall probe. Activity within the hippocampus also predicted future performance and correlated with error-feedback–related pMFC activity. A relationship between performance expectations and pMFC activity, in the absence of differing reinforcement value for errors, is consistent with the idea that error-related pMFC activity reflects the extent to which an outcome is "worse than expected."

Keywords: anterior cingulate cortex, associative learning, error processing, functional MRI

Introduction

Several studies have examined the neural mechanisms involved in error processing (Ridderinkhof, Ullsperger, et al. 2004), but it remains unclear how error-related neural activity influences posterror processes, particularly learning. Learning from errors, including specific arbitrary relationships, is critical to human cognition. Healthy adults learn remarkably quickly from their mistakes, often erring just once before successfully adapting their behavior (Noble 1957). Conversely, individuals with clinical disorders often experience difficulty in learning from errors (Barbarotto et al. 1998; Russell and Jarrold 1998), which causes significant complications with everyday functioning (Kern et al. 2003).

A range of evidence implicates the posterior medial frontal cortex (pMFC) in error processing (Gehring et al. 1993; Ullsperger and Von Cramon 2003; Ridderinkhof, Ullsperger, et al. 2004), including the finding that many clinical conditions are associated with dysfunctional pMFC responses to errors (Gehring and Knight 2000; Carter et al. 2001; Kaufman et al. 2003). The magnitude of neural activity in the pMFC has also been related to adaptive posterror changes in response behavior. Improvement in response speed that suggest increases in cognitive control (Gehring et al. 1993; Kerns et al. 2004) and generalized slowing of responding that is argued to reflect more cautious posterror behavior (Garavan et al. 2002; Debener et al. 2005) have both been associated with the magnitude of error-related pMFC activity. Such work has focused primarily on immediate posterror changes in executive control behavior, where there is close temporal proximity between the error and behavior change.

Several influential models have argued for a central role of the pMFC in associative learning (Holroyd and Coles 2002; Nieuwenhuis et al. 2004; Brown and Braver 2005), but direct evidence to support this claim is relatively scarce. Data from a probabilistic learning task has shown that the magnitude of error-related pMFC activity was reduced as the predictive value of a feedback signal was reduced. Similarly, Mars et al. (2005) found that error-related feedback activity in the pMFC was greatest during the early phase of learning a set of arbitrary visuomotor associations and gradually diminished later in the task.

The association between pMFC activity and learning has also been examined within the context of reward-based reinforcement learning. Evidence from monkey studies points to a crucial role for the pMFC in the use of rewards to guide choice behavior (Shima and Tanji 1998; Hadland et al. 2003; Matsumoto et al. 2003), including learning. For example, 2 recent studies found that during temporary disruption or after permanent lesions of the pMFC region, monkeys showed suboptimal decision-making strategies that suggested a failure to learn the value of their actions (Amiez et al. 2006; Kennerley et al. 2006). Given the practical limitation of training animals to perform some cognitive tasks, the role of the pMFC in nonrewarded associative learning tasks has received less attention. Much of human learning occurs when the value of errors is largely equivalent, so if the reward "value" of all erroneous responses is the same, is the magnitude of pMFC activity associated with which errors are learned from?

The literature supports an association between error-related pMFC activity and learning and highlights a relationship between the magnitude of pMFC activity and immediate adaptive changes in behavior. To date, however, no study has investigated pMFC activity during the learning of specific associations. For example, using a probabilistic reward task, Frank et al. (2004, 2005) demonstrated that individual differences in the magnitude of error-related pMFC activity correlated with a bias toward learning from negative outcomes (rather than positive outcomes). Participants with greater error-related pMFC responses were more likely to avoid a poorly rewarded stimulus (20% probability of reward) than to select a highly rewarded one (80% probability) during novel decision trials. However, no previous study has addressed whether pMFC activity during

a failed learning trial is directly related to correction of performance for the same stimulus upon a future presentation. For example, neural activity in the medial temporal lobes, a region widely implicated in memory and associative learning (Small et al. 2001), has demonstrated such a predictive relationship. Evidence from single-unit recording (Cameron et al. 2001) and functional magnetic resonance imaging (fMRI) (Strange et al. 2002) studies has shown that hippocampal activity during encoding predicts which paired associates are later recalled.

In the present study, we sought to examine the influence of pMFC activity on learning from errors. We developed a multi-repetition, paired-associate learning task for use during fMRI data collection. The task required participants to learn sets of 8 number–location pairs (see Fig. 1); high-memory demands were imposed to induce a sufficient number of recall errors for an event-related fMRI analysis. Following an initial encoding period, a series of recall trials probed which 2-digit number was associated with each location. Feedback was provided after each recall response, indicating both the participant's accuracy and the correct response. Immediate feedback afforded participants an opportunity to "re-encode" the correct number–location association following failed recall, which was then tested several trials later during a subsequent recall probe. Our analyses focused on the comparison between brain activity for "corrected" and "repeated" errors. Recall error events were categorized into corrected and repeated on the basis of subsequent performance (see Fig. 2). A corrected error was a recall failure for which, on the next presentation of the same location probe (4–15 trials later), recall performance was now accurate. Conversely, a "repeated error" was a recall error for which performance on the next presentation of the same stimulus association was also incorrect.

Providing feedback on incorrect responses was expected to elicit significant blood oxygen level–dependent (BOLD) signals from the pMFC during all recall errors. We hypothesized that the magnitude of pMFC activity during initial recall errors would predict future performance, with significantly higher BOLD activity for corrected than repeated errors. Based on past research, we also hypothesized that hippocampal activity during error feedback, which afforded an opportunity to reencode the correct association, would be predictive of future performance.

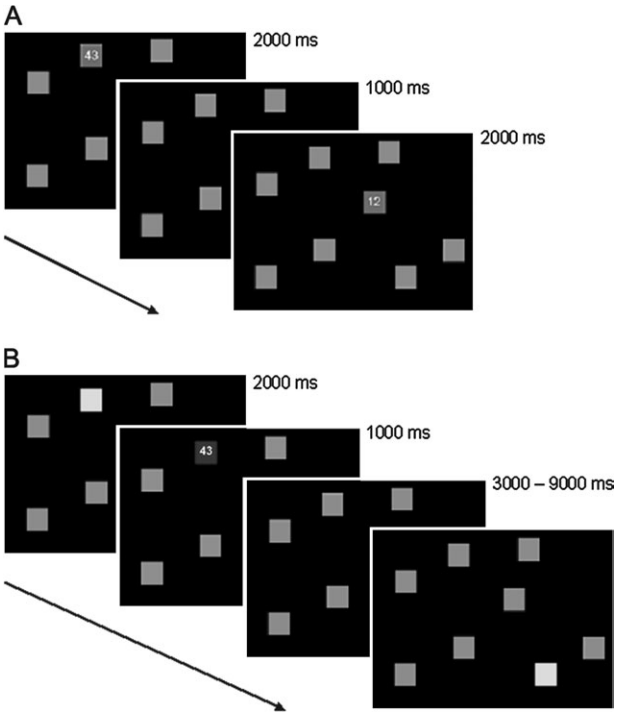

Figure 1. The spatial learning task used in the present study, with 8 location–number pairs. (*A*) Displays shown during the encoding phase. Two-digit numbers appeared, in random order, successively at each of the 8 gray locations. (*B*) Displays shown during the recall phase. A yellow location represents a cue to which the participant must respond. Feedback consisted of the correct number on a blue location for a correct response, or a red location for an error (not shown here).

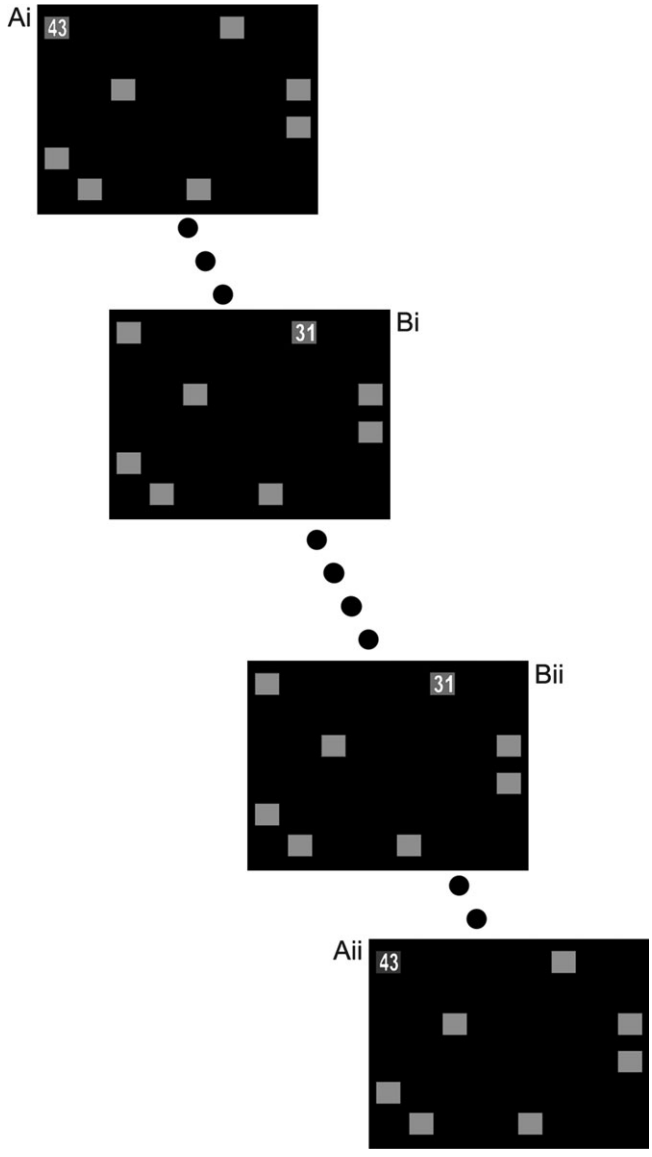

Figure 2. Method used to classify corrected and repeated errors. Feedback for a participant's response involved presentation of the correct number on either a red background, indicating an error, or a blue background, indicating an accurate recall response. Categorization as either a corrected or repeated error was determined by the participant's performance for the same trial during the next round. In example A, the participant correctly responded with the number 43 during the next recall probe of the top-left location (*Aii*), and so the initial error (*Ai*) is categorized as a corrected error. In example B, the participant incorrectly responds to the next presentation of the top-right location (*Bii*), and therefore the initial error (*Bi*) is categorized as a repeated error. Dots represent the intervening trials.

Materials and Methods

Participants

Seventeen healthy volunteers (11 females; mean age = 24.4 years; range = 21–29 years) participated in the experiment. All participants provided written informed consent, which was approved by ethics committees at The University of Queensland and St Vincent's Hospital, Melbourne.

Experimental Protocols

A spatial learning task was administered to participants, which consisted of an array of location–number associations that were to be learned by participants (see Fig. 1). All aspects of stimulus delivery and response recording were controlled by E-Prime software (version 1.1, Psychology Software Tools, Pittsburgh, PA), running on a laptop PC (Celeron 2-Ghz, 128-mb Nvidia Video Card) which was interfaced with the magnetic resonance (MR) scanner during acquisition of fMRI data. The task began with an encoding phase in which 8 locations designated as gray squares were presented simultaneously on a black background. The locations of the squares on the background were selected in a quasirandom fashion from an 8 × 8 matrix, with 2 locations randomly chosen from each of the 4 quadrants of the display.

At the commencement of the encoding phase, each location in turn had superimposed upon it a 2-digit number. The number remained visible for 2 s, and was followed by an interstimulus interval of 1 s. The digits of each number consisted of 1, 2, 3 or 4, and participants identified the number by entering each digit using the appropriate buttons on a pair of MR-compatible response boxes (Fibre-Optic response pads, Current Designs, Philadelphia, PA). Two-digit numbers were used to reduce the probability of guessing the correct answer to 6%. The encoding phase lasted 24 s in total and was followed by a 6-s interval prior to the start of the recall phase.

Following the encoding phase in which numbers were shown for each of the 8 locations, a series of recall trials was presented. During a recall trial, 1 of the 8 locations was highlighted in yellow, cueing the participant to respond with the 2-digit number associated with that location. Participants were required to respond within 2 s, after which feedback was presented for 1 s. Feedback provided both the validity of the response and the correct number. The location square turned blue to indicate a correct response or red to indicate an incorrect response, and the correct number was shown upon the colored background. Therefore, the participant received immediate response feedback and had another opportunity to encode the correct response. Following feedback, a variable delay of 3–9 s was introduced prior to the next recall trial, during which all 8 location squares remained on the screen. This variable delay had the effect of jittering the onset of each recall trial, which is necessary for event-related fMRI designs in which BOLD changes are modeled for single trials. Each location in the array was highlighted once, before being highlighted a second and third time, all in different pseudorandom orders. This created 3 rounds of 8 recall trials within each block. Six blocks of the encoding/recall cycle were administered to each participant, with each block involving a different array of locations and 2-digit numbers. No location in the array was used more than once throughout the 6 runs, and the 2-digit numbers were not repeated on consecutive blocks.

Image Acquisition

The fMR images were acquired at St Vincent's Hospital, Melbourne, using a whole-body 1.5-Tesla Siemens MAGNETOM Vision scanner with a gradient-echo echo-planar imaging (EPI) sequence. The scanner was equipped with a standard radio frequency birdcage head coil for signal transmission and reception. Lateral head stabilizers were used to minimize head movement. EPI images were acquired using a gradient-echo pulse sequence and sequential slice acquisition (T_R = 3,000 ms, T_E = 40 ms, flip angle = 78°, 32 contiguous slices of 4-mm thickness, no gap, in-plane resolution of 2.1 × 1.7 pixels in a field of view of 240 mm). Each functional run began with 2 volume acquisitions that were later discarded, to allow for steady-state tissue magnetization. A total of 86 EPI volumes were collected for each functional run, and a total of 6 functional runs were performed for each participant. Activation data were registered to high-resolution T_1-weighted isotropic (1 mm^3) structural MPRAGE images to localize the pattern of physiological changes associated with the task.

Data Analysis

Behavioral data from each participant were used to categorize the recall events into successful responses, "corrected errors," and repeated errors. Errors were classified in this way according to the response made on the subsequent presentation of the same location–number pair (see Fig. 2). An incorrect response that was followed by another incorrect response for the same location in the subsequent round was classed as a repeated error, whereas an error that was followed by a correct response in the following round was classed as a corrected error. Errors in the third and final round of presentations could therefore not be included in this analysis because they did not precede another attempt at recall.

All analyses were conducted using AFNI software (http://afni.nimh.nih.gov/afni/). Following image reconstruction, the time series data were time shifted using Fourier interpolation to remove differences in slice acquisition times and motion corrected using 3D volume registration (least-squares alignment of 3 translational and 3 rotational parameters). Activation outside the brain was also removed using edge-detection techniques.

Separate hemodynamic response functions at 3-s temporal resolution were calculated using deconvolution techniques for corrected errors, repeated errors, final round errors, and correct recall events. A nonlinear regression program determined the best-fitting gamma-variate function for these Impulse Response Function as previously described (Garavan et al. 1999). The area under the curve of the gamma-variate function was expressed as a percentage of the area under the baseline. The baseline estimate was the mean activation recorded during the variable delay periods between recall trials. During this period, participants viewed the 8 gray locations on the screen while waiting for the next memory probe; thus, the baseline involved similar stimulus and memory load requirements as the experimental events of interest.

The percentage area (event-related activation) map voxels were resampled at 1-mm^3 resolution, then spatially normalized to standard Montreal Neurological Institute space (MNI 152 template), and spatially blurred with a 3-mm isotropic route mean square Gaussian kernel. Group activation maps for event type (corrected errors, repeated errors, correct recall, and final round errors) were determined with 1-sample *t*-tests against the null hypothesis of zero event-related activation changes (i.e., no change relative to baseline). Significant voxels passed a voxelwise statistical threshold ($t = 4.31$, $P \leq 0.001$) and were required to be part of a larger 142-μl cluster of contiguous significant voxels. Thresholding was determined through Monte Carlo simulations and resulted in a 1% probability of a cluster surviving due to chance.

The primary comparison of interest was to compare differences in activation between corrected and repeated errors. The activation clusters from whole-brain analyses of both corrected and repeated errors (see Table 1) were used to create an OR map for the purposes of an Region of Interest (ROI) analysis. An OR map includes the voxels of

Table 1

Regions of error-related activity differentiating corrected from repeated errors

Brain region	Volume (μl)	MNI coordinates		
		x	*y*	*Z*
Corrected errors > repeated errors				
L precentral gyrus	151	−27	−20	33
L anterior cingulate	190	−3	12	42
R insula	153	36	10	0
L middle temporal gyrus	175	−49	−42	−7
L hippocampus	306	−18	−20	−15
L superior temporal gyrus	204	−34	−13	−8
L cuneus	183	0	−83	11
L inferior frontal gyrus	231	−59	4	18
Repeated errors > corrected errors				
R Inferior Frontal Gyrus (pars opercularis)	170	26	3	34
L middle frontal gyrus	173	−22	32	22
R middle occipital gyrus	692	32	−87	4

Note: L, left; R, right.

activation, indicated as significant from either of the constituent maps. The mean activation for clusters in the combined map was then calculated for the purposes of an ROI analysis, deriving mean activation levels for corrected and repeated errors that were compared using repeated-measures *t*-tests, corrected via a modified Bonferroni procedure for multiple comparisons (Keppel 1991).

The post hoc analyses examining "expectancy" (expected vs. unexpected errors) followed the same steps as above. "Expected recall errors" were those in the second and third rounds of recall which had been preceded by failed recall performance during the same location–number pair in the previous round. "Unexpected errors" were preceded by accurate recall in the previous round. Both analyses involved a new multiple regression test to estimate percentage of event-related activation change based on the newly categorized canonical functions (determined by the participant's performance) for the events of interest. All analyses used the same measure of baseline activity (delay period between recall events). Due to the low number of events in the expectancy comparison, which has the capacity to confound the spatial extent of activity in whole-brain analyses (Murphy and Garavan 2005) and the fact that activity in the pMFC region was of primary interest, we chose to perform an ROI analysis comparing activity for the relevant events using the pMFC cluster of activity from the original corrected-versus-repeated event-related analysis. The mean activation for the pMFC region was then calculated using the voxel-level percentage change estimates for each event type, deriving mean activation scores for "expected" and unexpected errors, and error–error or error–correct event types. The estimates were compared using repeated-measures *t*-tests, corrected via the modified Bonferroni procedure for multiple comparisons (Keppel 1991).

Results

Behavioral Results

Learning of the number–location associations occurred within the task blocks, with recall performance improving significantly across the 3 rounds, $F_{2,32} = 40.6$, $P < 0.05$. Participants successfully responded to 32.8% of recall trials in round 1, 46.8% in round 2, and 56.1% in the round 3. On average, 37.2% of recall trial errors were corrected on the next presentation, with 34.3% of round 1 recall errors and 38.7% of round 2 errors corrected upon their next presentation. Substantial variation was seen in error-correction rates across participants (range = 14–66%). The number of trials between a recall error and the next presentation of the same location did not differ for corrected (CorrErr) and repeated errors (RepErr) (8.0 and 8.1 trials, respectively); nor did mean reaction times (CorrErr = 1,810 ms; RepErr = 1,848 ms), $t_{16} = -0.93$, $P > 0.05$ or the percentage of errors resulting from nonresponses (CorrErr = 27.6%; RepErr = 26.2%), $t_{16} = 0.607$, $P > 0.05$. The latter result did not change if incomplete or partial responses were included (CorrErr = 34.4%; RepErr = 35.1%), $t_{16} = -0.25$, $P > 0.05$.

Corrected versus Repeated Errors

Feedback indicating erroneous recall was associated with significant activity in the pMFC (see Fig. 3*A*). The center of

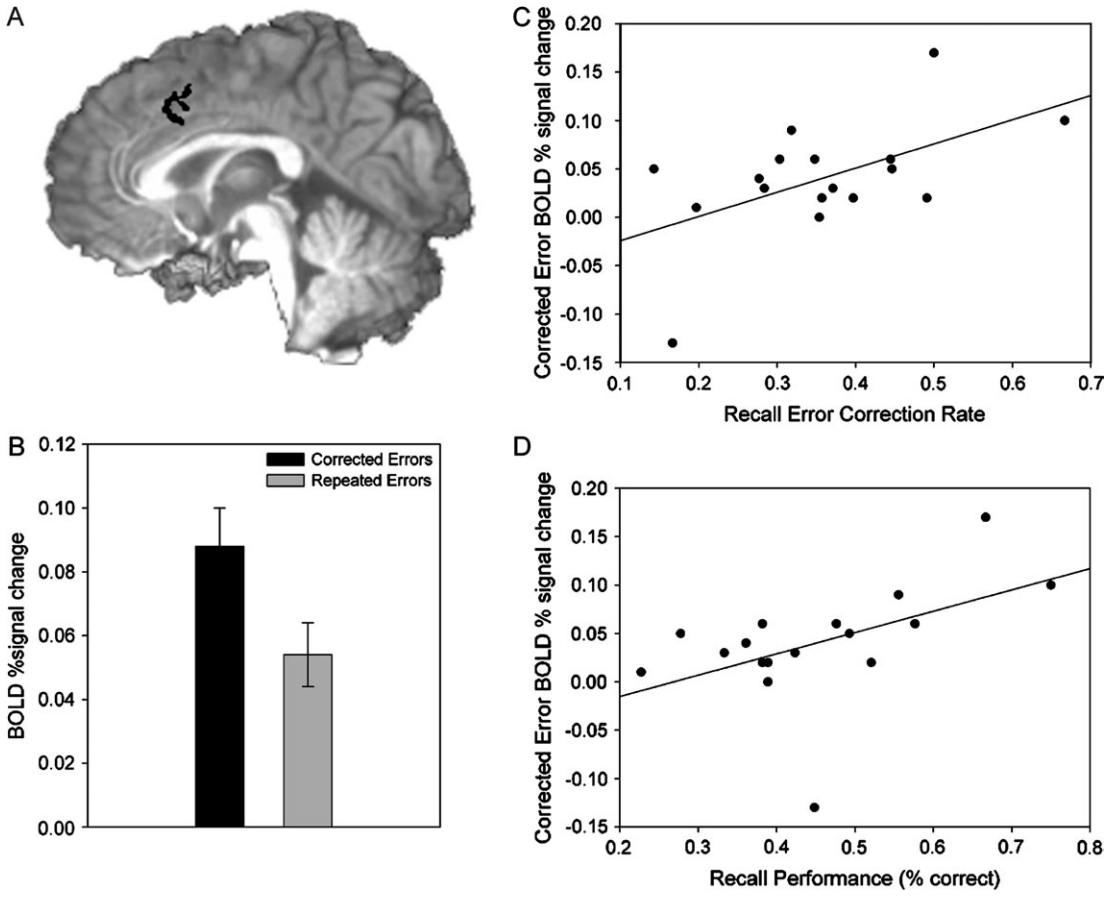

Figure 3. Corrected errors were associated with significantly higher levels of activity in the medial frontal cortex. (*A*) Axial view of the error-related cingulate cluster (MNI: $x = -3$; $y = 12$; and $z = 42$). (*B*) Amount of BOLD signal change (relative to baseline) in the error-related pMFC region during corrected and repeated error events. (*C*) Individual differences in the rate of error correction (accurate performance for a trial that had produced an error in the previous round), correlated positively with the amount of activity in the pMFC during corrected errors (relative to repeated errors). (*D*) Recall performance, indexed as the percentage of correct responses from all trials, correlated positively with BOLD activity in the pMFC during corrected errors.

mass for this cluster of activity was located in the left dorsal anterior cingulate cortex (MNI coordinates: $x = -3$; $y = 12$; $z = 42$), which falls within the rostral cingulate zone highlighted by the review of performance monitoring of Ridderinkhof, Ullsperger, et al. (2004). Within this functionally defined ROI, corrected errors were associated with significantly higher levels of BOLD activity compared with repeated errors (Fig. 3*B*) and with correct recall (activity during repeated errors and correct recall was not significantly different, $P = 0.562$). Activity in several other regions also differentiated corrected from repeated errors (see Table 1). Consistent with findings from the associate learning literature, activity in the left hippocampus was significantly higher during corrected errors than during either repeated errors (Fig. 4*B*) or correct recall. Participants with high levels of pMFC activity during corrected errors also had high levels of activity in the left hippocampus ($r = 0.55$, $P < 0.05$).

Individual differences in pMFC activity also correlated with behavioral performance. Participants who had high levels of activity during corrected errors (relative to repeated errors) had better overall recall performance ($r = 0.51$, $P = 0.03$) and higher error-correction rates ($r = 0.57$, $P = 0.02$) (Fig. 3*C*,*D*). Similarly, high levels of activity in the left hippocampus during corrected errors (relative to repeated errors) correlate with better recall performance ($r = 0.45$, $P = 0.06$) and error-correction rates ($r = 0.42$, $P = 0.09$) (Fig. 4*C*,*D*). The interrelationship between activity in the pMFC, hippocampus, and behavioral performance appeared relatively unique; none of the other "error-correction" regions showed activity patterns that intercorrelated or related to overall recall performance. The one exception was the right insula, whose activity levels during corrected errors significantly correlated with corrected error activity in both the pMFC ($r = 0.63$, $P < 0.05$) and the left hippocampus ($r = 0.57$, $P < 0.05$).

Three error-related regions showed greater activity for repeated errors when compared with corrected errors: right superior occipital, left middle frontal, and right inferior frontal gyrus (Table 1). The activity in these regions did not intercorrelate nor did it significantly correlate with behavioral performance.

Unexpected versus Expected Errors

Recent theories of error-related pMFC function have argued that error likelihood (Brown and Braver 2005), or the extent to which an outcome is "worse than expected" (Holroyd and Coles 2002; Nieuwenhuis et al. 2004), influences the magnitude of error-related pMFC activity. To test this hypothesis, we

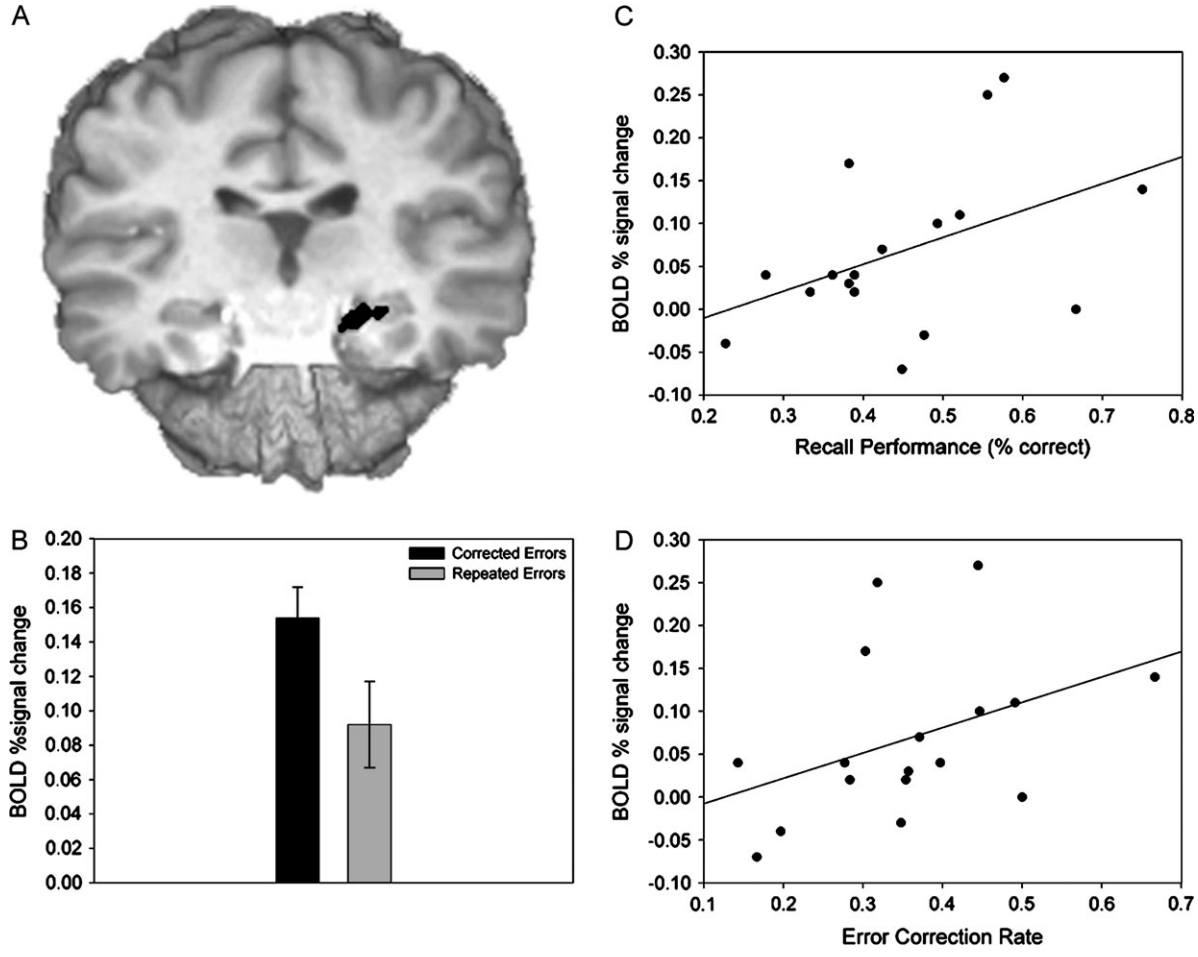

Figure 4. Corrected errors were associated with significantly higher levels of activity in the left hippocampus. (*A*) Coronal view of the error-related left hippocampal cluster (MNI: $x = -18$; $y = -20$; and $z = -15$). (*B*) Amount of BOLD signal change (relative to baseline) in the error-related hippocampal region during corrected and repeated error events. (*C*) Individual differences in the rate of error correction (accurate performance for a trial that had produced an error in the previous round), correlated positively with the amount of activity in the left hippocampus during corrected errors (relative to repeated errors). (*D*) Recall performance, indexed as the percentage of correct responses from all trials, positively correlated with BOLD activity in the left hippocampus during corrected errors.

performed an analysis that compared activity within our functionally defined pMFC ROI for expected and unexpected recall errors. Expected recall errors were those in the second and third rounds of recall that had been preceded by failed recall performance during the same location–number pair in the previous round. Unexpected errors were preceded by accurate recall in the previous round. Unexpected errors were relatively rare, with an average of only 8 events per participant; by contrast, there were on average 35 expected errors for each participant. Such a comparison can be confounded by the low number of unexpected error events, which may potentially underestimate BOLD activity for infrequent event types (Murphy and Garavan 2005). However, despite this potential problem, unexpected errors were associated with significantly higher levels of pMFC activity than expected errors, $t_{16} = -2.39$, $P < 0.05$.

Discussion

Error-related neural activity in the pMFC has been associated with immediate adaptive changes in response behavior. The results of the present study suggest that delayed adjustments to behavior, in the form of learning arbitrary associations, are also associated with the magnitude of error-related activity in the pMFC. We found that when recall errors were categorized by subsequent performance—essentially whether the failure to accurately recall a number–location association was corrected at the next presentation of the same trial—the magnitude of error-related pMFC activity predicted future correction. A higher level of pMFC activity was observed during feedback for corrected errors when compared with repeated errors, even though the interval between an error event and subsequent correction lasted on average 70 s (i.e., 8 trials). In support of this group effect, we also found that participants with high levels of activity during corrected errors (relative to repeated errors) had better overall recall performance and higher error-correction rates than those with low levels of activity during corrected errors.

The elevated levels of pMFC activity during corrected errors correlated with activity in 2 other regions, the left hippocampus and right insula. Although the hippocampus is not typically associated with error-related neural activity, the design of the current study combined response accuracy feedback with the opportunity to reencode the correct number–location association (see Fig. 3*B*). The hippocampus is critical to the successful encoding of arbitrary associations (Small et al. 2001). Thus, the higher levels of hippocampal activity we observed during corrected versus repeated errors may indicate a contribution to successfully "reencoding" the location–number association. Notably, participants with high levels of hippocampal activity during corrected errors also had better overall recall performance and higher error-correction rates, supporting a reencoding account. It is important to note that the *P* value for the individual difference correlations were nonsignificant (between $P = 0.06$ and 0.09). Our confidence in this pair of results is based on 3 factors: 1) the magnitude of the relationship or effect size (*r* value), which suggests a moderate relationship; 2) that they are consistent with our group-based findings, which also show that improved performance (learning from errors) was associated with greater activity in this specific region (corrected errors compared with repeated errors); and 3) consistency with previous findings of an associative relationship between greater hippocampal activity and learning (Small et al. 2001; Sperling et al. 2001, 2003; Stark and Okado 2003; Degonda et al. 2005; Law et al. 2005; Suzuki 2007).

Activity in the right insula, a limbic region consistently observed in studies examining error-related processing (Ullsperger and Von Cramon 2003; Hester et al. 2004), correlated with activity in both the pMFC and left hippocampus, but did not correlate with individual differences in behavioral performance. The insular cortex is known to be sensitive to performance feedback (Ridderinkhof, van den Wildenberg, et al. 2004), with activity in this region argued to reflect the level of emotional significance of a particular event or outcome (Elliott et al. 2000). Lesion studies in both rats (Nerad et al. 1996) and humans (Kornhuber et al. 1995) have also highlighted the insula's importance in learning, where it is thought to influence the attribution of salience and thus the allocation of attention (Dayan et al. 2000).

Several other regions differentiated corrected from repeated errors (see Table 1), but the interrelationship between activity in these regions and the association between brain activity and individual differences in learning were limited to the pMFC, left hippocampus, and right insula.

The function of error-related pMFC activity has been the subject of much debate. Within the context of learning, it has been discussed primarily within the framework of reinforcement learning (Schultz 2006). Animal research, which for practical reasons involves overt rewards for learning particular associations, suggests that the pMFC performs an evaluative role that is critical to learning and maintaining the value of actions (Amiez et al. 2006; Kennerley et al. 2006). Human research also points to a role for the pMFC in assessing the consequences of choices (Walton et al. 2004) but suggests that the pMFC is only somewhat sensitive to the value of an error. For example, errors that incur a monetary loss have been associated with more pMFC activity than those with no monetary penalty (Taylor et al. 2006), but errors that incur either small or large losses have not been found to yield different levels of pMFC activity (Yeung and Sanfey 2004). These results have been taken as support for theories that link error-related pMFC activity to expectations about an outcome (Holroyd and Coles 2002; Nieuwenhuis et al. 2004). For example, Holroyd and Coles argue that error-related pMFC activity may reflect a phasic decrease in midbrain dopamine activity (modulated by the basal ganglia), which indicates that an outcome was worse than expected. This dopaminergic signal is argued to contribute to reinforcement learning through stimulation of other regions in the mesencephalic dopamine system.

The results of the present study appear to support the evaluative role of the pMFC, by showing significantly greater activity for errors when compared with either the rehearsal activity baseline or correct recall feedback. Additionally, the magnitude of error-related pMFC activity was associated with learning from errors, despite the absence of any manipulation of error value. Activity in the pMFC was higher during corrected errors (when compared with repeated errors) and correlated with individual differences in both performance (error-correction rates and overall recall accuracy) and with hippocampal activity. The correlation of activity in the pMFC and (left) hippocampus is consistent with the hypothesis that the magnitude of activity in the pMFC, which reflects a phasic dopaminergic signal, will correlate with increased activity in other dopaminergically enervated cortical regions (Holroyd and Coles 2002).

Our findings also support the idea that outcome expectancy modulates pMFC activity. Human models, borrowing from the reward "prediction error" hypothesis popular in the animal literature, suggest that the magnitude of error-related pMFC activity reflects error expectancy (Brown and Braver 2005) or that the outcome was worse than expected (Holroyd and Coles 2002; Nieuwenhuis et al. 2004; Holroyd et al. 2005). In our study, a post hoc analysis of errors compared unexpected errors (i.e., number–location trials that had been answered correctly on the previous presentation) with expected errors (those preceded by failed recall). We found that pMFC activity was significantly higher for unexpected errors. Insufficient trials were available to examine the influence of expectancy on learning performance. Although the expected versus unexpected error's comparison was post hoc, and as such caution should be exercised in interpreting these results, the greater level of pMFC for unexpected errors appears consistent with the hypothesis that performance expectations drive pMFC activity, which in turn influences neural and behavioral measures of learning.

One limitation of the current study design was the absence of separate estimates of neural activity for feedback and reencoding. The absence of separate estimates was a pragmatic step because the temporal separation required for an event-related fMRI design would have increased the paradigm's length (by over 30 min) beyond a tolerable level for participants. Such separation would, however, have allowed clarification of which epoch pMFC activity most contributed to hippocampal activity and/or learning performance. In the absence of separate estimates, one alternative explanation for the corrected versus repeated error effect concerns the "effort" applied to information processing (Paus 2001; Critchley et al. 2003). The higher level of pMFC activity during corrected errors may reflect greater effort involved in reencoding S–R associations or a general increase in arousal during these trials. An arousal-related or "attention-related" account might also explain the correlation between pMFC activity and performance, if participants who paid more attention to the error feedback had better overall performance than those who paid less attention. The limitation of the effort' hypothesis is determining what characteristic of a corrected error trial instigates the need for increased effort. In the current task all associations, and by definition all errors, were of equivalent value, so for what reason would more effort be applied during some errors? For example, it could be argued that more effort would be made to reencode errors that were worse than expected, which is entirely consistent with finding of greater pMFC activity during unexpected (as compared with expected) errors. In the absence of such categorization, it could be argued that the differential levels of effort, and therefore error correction, is the result of random fluctuation and can therefore not be easily predicted? More definitive evidence to test these hypotheses could be obtained from separate pMFC activity estimates for feedback and reencoding.

To conclude, the current findings provide new evidence for an association between error-related pMFC activity and adaptive posterror behavior change. By examining delayed recall performance following an error, we have provided a neural marker for the hypothesized association between error-related neural activity and associative learning. Critically, and in contrast with previous studies, we have revealed this key role for the pMFC using a task that did not involve overt rewards or punishments for performance. Although the present results are consistent with animal-based work suggesting a role for the pMFC in evaluating and learning the value of actions, the absence of overt rewards or punishments for errors provides additional support to the human-based work implicating expectancy, or that the outcome was worse than expected, for modulating pMFC activity during errors. Future work will need to examine the dynamics of the relationship between pMFC activity and learning, and in particular how the evaluation of an error by the pMFC might translate to processes critical to learning, such as encoding.

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