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A Specific Brain Structural Basis for Individual Differences in Reality Monitoring

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Abstract

Much recent interest has centered on understanding the relationship between brain structure variability and individual differences in cognition, but there has been little progress in identifying specific neuroanatomical bases of such individual differences. One cognitive ability that exhibits considerable variability in the healthy population is reality monitoring, the cognitive processes whereby one introspectively judges whether a memory came from an internal or external source (e.g., whether an event was imagined or actually occurred). Neuroimaging research has implicated the medial anterior prefrontal cortex (PFC) in reality monitoring, and here we sought to determine whether morphological variability in a specific anteromedial PFC brain structure, the paracingulate sulcus (PCS), might underlie performance. Fifty-three healthy volunteers were selected on the basis of MRI scans and classified into four groups according to presence or absence of the PCS in their left or right hemisphere. The group with absence of the PCS in both hemispheres showed significantly reduced reality monitoring performance, and ability to introspect metacognitively about their performance, compared with the other participants. Consistent with the prediction that sulcal absence might mean greater volume in the surrounding frontal gyri, voxel-based morphometry revealed a significant negative correlation between anterior PFC gray matter and reality monitoring performance. The findings provide evidence that individual differences in introspective abilities like reality monitoring may be associated with specific structural variability in the PFC.

INTRODUCTION

Remembering a previous experience often involves distinguishing information that was generated by internal cognitive functions (e.g., thought and imagination) from information that was derived from the outside world, an ability termed ‘reality monitoring’ (Johnson and Raye, 1981). A number of neuroimaging studies have investigated the brain basis of reality monitoring processes, with an emerging consensus that medial regions of anterior prefrontal cortex (PFC) are among the brain areas involved (Mitchell and Johnson, 2009). For example, activity in this area differentiates between recollection of whether stimuli were previously seen or imagined by a participant (Kensinger and Schacter, 2006; Simons et al., 2006), as well as whether a task was previously performed by the participant or another person (Simons et al., 2008; Lagioia et al., 2011).

Although we may feel that our reality monitoring abilities are reliable, there is evidence of substantial variability in accuracy across individuals. This is most apparent in the reality monitoring impairments often observed in patients with clinical disorders such as schizophrenia (Keefe et al., 2002), but variability in performance is also seen in apparently healthy volunteers (Hyman and Billings, 1998). As an illustration, Figure 1 shows the performance of 146 healthy young adult volunteers who undertook one of a number of reality monitoring tasks. As can be seen, reality monitoring accuracy varied considerably between individuals.

The relationship between brain structure variability and individual differences in cognitive function is an area of considerable interest currently (Kanai and Rees, 2011), but little is known about the specific brain basis of the reality monitoring variability in healthy individuals. An obvious place to look is for anatomical structures in the vicinity of anteromedial PFC that exhibit morphological variation in the normal population, such as the paracingulate sulcus (PCS). Located dorsal and parallel to the cingulate sulcus, the PCS is among the last sulci to develop *in utero* and for this reason varies greatly in size between individuals (Vogt et al., 1995; Paus et al., 1996). A prominent PCS can be observed in some healthy volunteers using structural MRI, whereas in others the PCS can appear to be absent (Figure 2). Its presence can have a dramatic effect on the cytoarchitecture, gray matter volume, and thickness of surrounding cortex, with possible implications for cognition (Vogt et al., 1995; Fornito et al., 2008).

Specific PCS reductions have been observed in schizophrenia (Noga et al., 1995; Fornito et al., 2006b) with one study, for example, reporting complete absence bilaterally in 44% of schizophrenia patients, compared with 27% of controls (Yucel et al., 2002a). As schizophrenia is associated with impaired reality monitoring (Keefe et al., 2002), PCS reductions may have functional significance for discriminating internally- from externally-generated information. Here, we investigate whether PCS structural variability can be used to explain the individual differences in reality monitoring observed in healthy individuals, using both visual classification and data-driven, voxel-based morphometry methods. On the basis of the schizophrenia findings described above, we predicted that PCS absence in both hemispheres would be reflected in relatively poorer reality monitoring performance.

MATERIALS AND METHODS

Participants

53 participants (23 males, 30 females) were recruited from a pool of healthy volunteers who had received an MRI scan as part of ongoing research projects at the MRC Cognition and Brain Sciences Unit, Cambridge. Participants were selected for recruitment on the basis of structural MRI scan classification of the PCS identifying clear presence or absence in the left or right hemisphere. The mean age was 26.9 years, $SD = 9.25$, and participants had a mean of 16.8 years of education, $SD = 2.65$. After a complete description of the study, written informed consent was obtained in a manner approved by the University of Cambridge Psychology Research Ethics Committee.

Reality Monitoring Task

The computer-based reality monitoring memory task was adapted from that used by Simons et al. (2006; 2008). The stimuli consisted of 160 well-known word pairs (e.g., 'Jekyll and Hyde', 'Yin and Yang'). There were five blocks in total, each block containing a study and test phase. In the study phase, the first word to appear at the top of the screen was "SUBJECT" or "EXPERIMENTER", indicating who was to read out loud the word pair that would subsequently be presented in the centre of the screen. After 500ms either a word-pair

("Jekyll and Hyde": perceive condition) or the first word in the word-pair and a question mark ("Jekyll and ?": imagine condition) were shown. In the perceive condition, the subject or the experimenter read the word-pair aloud. In the imagine condition, the subject or experimenter imagined the word that completed the pair and vocalized the whole word-pair. Stimuli assignments to subject/experimenter and perceive/imagine conditions were counterbalanced between subjects and the trial order was pseudorandomized such that no more than three consecutive trials were of the same condition.

Immediately following each study phase, participants' reality-monitoring ability was assessed in a test phase. To test participants' recollection of whether they themselves or another person had read each word-pair out loud, the following cue was presented: "Did either you or the experimenter read this word pair aloud?" Participants were then shown the first word of the word pair (e.g. "Jekyll") in the centre of the display with a reminder instruction underneath, and were instructed to press '1' on the keyboard if they thought they themselves had read the pair in the study phase, and '2' if they believed the experimenter had read it aloud. To test participants' ability to discriminate between perceived and imagined information, they were first shown the cue: "Was the accompanying word either perceived or imagined?" and were told to press '1' if they believed that the second word was presented, or '2' if they thought that the accompanying word had been imagined. For each response, participants indicated how confident they were by holding down the response key as a confidence bar at the bottom of the screen increased in size. Participants had 4.5 sec to start making their response. The type of recollection cued for each item and the ordering of test conditions was systematically counterbalanced between subjects.

Classification of Sulcal Variability

T1-weighted SPGR structural MRI scans were obtained using a 3-T Siemens TIM Trio system. The PCS classifications were undertaken based on a protocol devised by Yücel and colleagues (2001) using freely available software (<http://surfer.nmr.mgh.harvard.edu>). An individual's PCS was identified as 'prominent' if there was a salient horizontal sulcus running dorsal and parallel to the cingulate sulcus for at least 40mm, and was observable for at least three contiguous sagittal slices. A PCS was classified as 'absent' if there was no indication of a PCS in the relevant slices (see Figure 2 for examples). Each PCS was classified by two independent raters (M.B. and A.F.), with any disagreements resolved by discussion. Subjects with either a 'prominent' or 'absent' PCS in each hemisphere were selected for recruitment to the current study. This resulted in four PCS groupings: prominent in the left and right hemispheres (p-p; $n = 16$), prominent left-absent right (p-a; $n = 11$), absent left-prominent right (a-p; $n = 13$), and absent in both hemispheres (a-a; $n = 13$). The groups did not differ significantly in terms of age, $F(3, 52) = 1.42$, $p = 0.25$, sex, $F(3, 52) = 0.29$, $p = 0.83$, or years of education, $F(3, 52) = 0.37$, $p = 0.78$. Participants were selected for inclusion without any knowledge of their cognitive profile, other than that there was no history of neurological or psychiatric disorder.

Voxel-Based Morphometry Analysis

For the VBM analysis, structural MRI scans for each participant were preprocessed in SPM5 (Wellcome Trust Centre for Neuroimaging, London UK) using a procedure based on the optimized VBM protocol (Good et al., 2001). All images were manually reoriented and spatially normalised into Montreal Neurological Institute (MNI) stereotactic space (Cocosco et al., 1997), before being segmented into gray matter, white matter, and CSF components. The four PCS groups did not differ in total intracranial volume, $F(3, 52) = 0.08$, $p = 0.97$, or in volume of any of the segmented components, all $F_s < 1$. The segmented images were spatially smoothed with an 8 mm full-width, half-maximum isotropic Gaussian kernel. Two *a priori* regions of interest were defined as 10 mm spheres centered on medial anterior PFC

coordinates from the two previous fMRI studies that involved our reality monitoring task (Simons et al., 2006; 2008). Multiple regression was used to identify clusters in which gray matter density correlated with reality monitoring performance at a threshold of $p < 0.05$, corrected for multiple comparisons within the regions of interest. Clusters outside the regions of interest were reported if they exceeded an uncorrected threshold of $p < 0.001$. Brain regions and Brodmann areas (BA) were estimated from the Talairach and Tournoux (1988) atlas, after coordinates had been transformed between atlas spaces.

RESULTS

Because our *a priori* prediction was that reduced reality monitoring would be seen in individuals with bilateral PCS absence, performance of participants in the a-a group was compared statistically with other participants using independent-samples t-tests (following the practice of, e.g., Stuss et al., 2005). Effect sizes were computed using Cohen's *d* (Cohen, 1988). Reality monitoring accuracy is displayed in Figure 3, from which it can be seen that as predicted, participants in the a-a group performed significantly worse overall than those in the other groups, $t(52) = 2.03$, $p < 0.05$, $d = 0.65$. Performance broken down by condition (see Table 1) indicated that this effect was significant for recollection of self/experimenter status, $t(52) = 2.08$, $p < 0.05$, $d = 0.66$, but not for perceived/imagined recollection, $t(52) = 1.56$, $p = 0.125$, $d = 0.5$, though there was no interaction, $F(1, 51) = 0.11$, $p = 0.75$. The reality monitoring accuracy reduction occurred despite no significant differences between the a-a group and other participants in reaction times, either across all trials or focusing just on correct responses, all $t(52) < 1$, $d < 0.13$.

There was no between-group difference in trial-by-trial rated confidence, as indicated by participants' response duration measure. This suggests that those individuals in the a-a group may not have been aware of their significantly reduced reality monitoring ability. To confirm this, a metacognitive awareness score was computed for each participant by calculating the difference in mean rated confidence for correct and incorrect trials, as a proportion of each participant's overall rated confidence level. This procedure produced a score between -1 and $+1$, with higher positive scores indicating a good correspondence between confidence and accuracy. Consistent with the idea that participants in the a-a group lacked introspective awareness of their reality monitoring deficit, their metacognition scores ($M = 0.18$, $SD = 0.14$) were significantly reduced compared with those in the other groups (p-p: $M = 0.23$, $SD = 0.1$; p-a: $M = 0.33$, $SD = 0.14$; a-p: $M = 0.26$, $SD = 0.14$), $t(52) = 2.18$, $p < 0.05$, $d = 0.70$.

As unequal group sizes can lead to violations of assumptions of the General Linear Model and thus increase statistical error, the observed a-a group differences were also assessed using a between subjects Monte Carlo permutation test, which is more robust against group size differences (Mewhort et al., 2009). Participant scores were randomly permuted without replacement and the mean difference between the smaller and larger groups was calculated. This procedure was repeated 100,000 times, producing a random distribution of differences against which to test the significance of the observed mean difference. The number of times the permuted mean differences exceeded the observed mean difference was computed, and this value was divided by the total number of permutation samples, giving confirmed probabilities of the observed reality monitoring and metacognition score differences of $p < 0.05$ at a two-tailed level.

Although participants were selected for inclusion on the basis of their PCS classification, it is possible that the observed behavioral effects might be attributable at least as much to structural differences elsewhere in the brain. To address this issue, voxel-based morphometry (VBM) was used to identify any brain areas in which gray matter correlated

significantly with reality monitoring performance across participants. First, we examined whether VBM was sufficiently sensitive to elicit an effect in the vicinity of the PCS. Because the predicted between-group effect described above was a reduction in reality monitoring performance if the PCS was absent, we reasoned that less sulcus might equate to greater surrounding cortical gray matter (Fornito et al., 2006a) and that we would observe a negative correlation between gray matter and reality monitoring.

As displayed in Figure 4, VBM regression analysis did indeed reveal a significant negative relationship where greater gray matter in the anterior PFC region of interest was associated with lower performance on the self/experimenter reality monitoring task ($x = 22, y = 58, z = 2$; BA 10; $Z = 3.43$; $p < 0.05_{\text{svc}}$). Outside the region of interest, the only other areas to exhibit significant negative correlations with reality monitoring performance at a lower threshold of $p < 0.001_{\text{unc}}$ were in motor cortex. Positive correlations between gray matter and performance (at $p < 0.001_{\text{unc}}$) were observed in areas including right parahippocampal cortex, the dorsal striatum, and precuneus (see Table 2).

DISCUSSION

The principal finding of the present experiment was that there may be a distinct neuroanatomical basis for the individual differences in reality monitoring ability typically seen in the healthy population. Volunteers in the a-a group, whose structural MRI scans indicated an absence bilaterally of the paracingulate sulcus (PCS), a tertiary sulcus in the medial anterior prefrontal cortex (PFC), demonstrated significantly reduced reality monitoring ability compared with other participants. Moreover, the individuals in the a-a group appeared to lack introspective awareness of their reality monitoring deficit, scoring significantly lower in their metacognitive ability to discriminate correct from incorrect reality monitoring decisions, compared with those in the other PCS groups. Consistent with the prediction that PCS absence might mean greater volume in the surrounding frontal gyri, a data-driven, whole-brain analysis using voxel-based morphometry (VBM) revealed significantly greater anterior PFC gray matter in individuals who performed poorly on the reality monitoring task. It is important to note that all participants in this experiment were healthy adult volunteers with typical educational backgrounds and no reported history of cognitive dysfunction due to neurological or psychiatric disorder. In this context, the observed differences in performance and structural brain volume exhibited by the a-a group are particularly striking.

The identification of a neuroanatomical basis for reality monitoring in medial anterior PFC is consistent with much recent functional neuroimaging evidence. Activity in this area is differentially modulated when contrasting recollection of which encoding task was previously undertaken with stimuli against remembering where on the screen (Simons et al., 2005a; Gilbert et al., 2010) or when in time (Simons et al., 2005b) the stimuli were presented, or remembering their size on the screen (Dobbins and Wagner, 2005). Focusing more closely on the kinds of reality monitoring tasks used in the present experiment, the same PFC region is involved in remembering whether verbal phrases were previously presented in full on the screen (e.g., “bacon and eggs”), or whether a word was missing which participants had to imagine (e.g., “bacon and ?”) in order to complete the phrase themselves (Simons et al., 2006; Vinogradov et al., 2006; Turner et al., 2008). Likewise, activity in this area is seen when the task is to differentiate whether oneself or the experimenter previously read a word-pair out aloud (Simons et al., 2008; Lagioia et al., 2011).

In addition to exhibiting a reality monitoring deficit, individuals in the a-a group were significantly impaired in their metamemory, the introspective ability to make judgments

about their memory accuracy. Thus, their rated confidence in correct versus incorrect reality monitoring decisions was considerably less distinct than in the other participants. A number of previous neuroimaging studies have linked metamemory processes with regions of medial anterior PFC. For example, Schnyer, Nicholls, and Verfaellie (2005) used an episodic feeling-of-knowing (FOK) paradigm to elicit predictions from participants about their likelihood of successfully retrieving sought-after information. Activity in this area was observed during accurate retrieval predictions, regardless of actual retrieval success. Maril, Simons, Weaver, and Schacter (2005) compared FOK judgments with another intermediate retrieval state, tip-of-the-tongue, finding activity in a similar region that was sensitive to that kind of metacognitive judgment. Similarly, Chua, Schacter, and Sperling (2009) showed that the role for medial anterior PFC in metamemory generalized to making subjective confidence judgments about one's memory. Together, these findings are consistent with the proposal that the region plays a role in the introspective evaluation of stored memory contents (Moscovitch and Winocur, 2002).

Considering medial anterior PFC structures more closely, the present findings indicate that the PCS may have a specific deterministic role in supporting reality monitoring ability. Though this is the first study to associate the PCS with reality monitoring, such a link is consistent with a number of converging lines of previous research. First, the medial PFC as a whole, and the region surrounding the paracingulate cortex in particular, exhibits considerable inter-individual variability in sulcal and gyral anatomy. The PCS which, when present, forms the superior and dorsal border to the paracingulate gyrus, is evident in 30-60% of the normal population, most frequently in the left hemisphere (Paus et al., 1996). Functional consequences of this variability have been observed in performance on tests of executive function and cognitive control, such as spatial working memory and verbal fluency (Fornito et al., 2004). Second, PCS reductions have been reported in schizophrenia (Noga et al., 1995; Yucel et al., 2002a; Fornito et al., 2006b), a disorder in which patients often exhibit impaired reality monitoring (Keefe et al., 2002). Functional imaging studies of schizophrenia have associated the reality monitoring deficit seen in the disorder with reduced activity in the medial anterior PFC (Vinogradov et al., 2008). The specific relationship between PCS reductions in schizophrenia and reality monitoring impairment has yet to be investigated, although previous research has linked PCS variability in the disorder with performance variations on working memory tasks (Fornito et al., 2006b).

The observed association between PCS variability and reality monitoring suggests that such structural variability may directly influence the functional capacity of the medial PFC, consistent with evidence that PCS cortical folding variations can affect local activation patterns (Crosson et al., 1999; Yucel et al., 2002b; Amiez et al., 2006). The correlation between anterior PFC gray matter and reality monitoring performance in our data suggests that this influence is mediated through the effects of PCS variability on the morphometry (e.g., grey matter volume, thickness, surface area) of surrounding cortex, consistent with past work demonstrating that the morphometric consequences of such variations are directly correlated with cognitive abilities (Fornito et al., 2008). Such changes may reflect alterations in neuronal or synaptic density, or differences in the degree of intra- vs inter-regional connectivity, given that cortical folds are thought to emerge as a product of gradients in the tension of axons linking proximal and distal areas (Van Essen, 1997). The precise relationship between variations in cortical folding and connectional anatomy are unclear, but could be further explored using diffusion-based imaging.

This is the first study we are aware of to investigate the structural basis of individual differences in reality monitoring in healthy individuals. However, a recent study used VBM to examine gray matter differences underlying performance variability in a non-memory task that might require the kind of metacognitive awareness needed for reality monitoring.

Fleming, Weil, Nagy, Dolan, and Rees (2010) asked participants to perform a simple perceptual decision task and rate their confidence in each decision that they made. Participants' ability to accurately link their confidence with their successful performance on the task was found to correlate positively with gray matter volume in anterior PFC. Consistent with this anatomical characterization, VBM analysis in the present experiment identified a closely-located region of anterior PFC in which gray matter correlated significantly with lower reality monitoring performance.

The negative correlation observed in the present data fits with the finding of the PCS analysis that sulcal absence and thus, perhaps, greater volume of the surrounding gray matter (Fornito et al., 2006a), was associated with reality monitoring impairment. Similar negative relationships between regional brain volume and performance have been reported in a number of previous studies (Hyde et al., 2007; Dumontheil et al., 2010; Kanai et al., 2011), including one that linked the ability to manipulate self-generated thoughts in adolescence with reduced anterior PFC gray matter density (Dumontheil et al., 2010). It should be noted, however, that participants in the present study were specifically selected because MRI scans indicated particularly clear PCS presence or absence; it remains to be seen whether a similar negative correlation is observed in a random sample of the normal population. The VBM analysis in the present experiment also identified positive correlations between gray matter and performance in regions that included right parahippocampal cortex, the dorsal striatum, and precuneus, all areas known for their roles in learning and memory (Poldrack and Packard, 2003; Cavanna and Trimble, 2006). The present findings suggest that future VBM studies and, for that matter, functional neuroimaging studies, should take account of whether their results could be influenced by structural morphological variations that may be present in participants.

In conclusion, the present study builds on previous work that has linked brain structure variability with individual differences in cognition, providing evidence that the variability in introspective abilities like reality monitoring typically seen in the healthy population may have a specific structural basis in the PCS. Because the defining morphological characteristics of the PCS are largely determined *in utero* (Chi et al., 1977; Armstrong et al., 1995), one speculation is that the observed differences reflect a constraint imposed by early neurodevelopmental processes on the subsequent emergence of reality monitoring. As with all correlational data, it is not possible to establish a causal direction from the present findings, but it can be surmised with some certainty that individual differences in reality monitoring appear to have a specific structural basis in medial anterior PFC.

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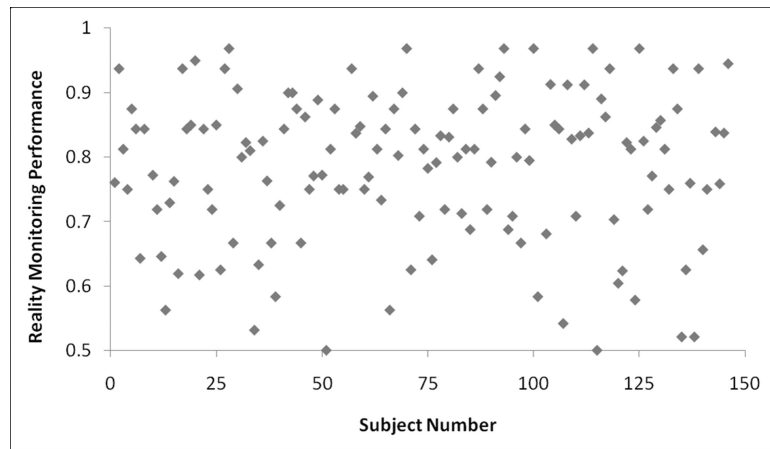


Figure 1.

Performance of 146 healthy young adult volunteers who had undertaken one of a number of different reality monitoring tasks, illustrating the substantial individual differences in performance even in such a young, healthy sample. All tasks were two-alternative forced-choice, so chance performance would be 0.5

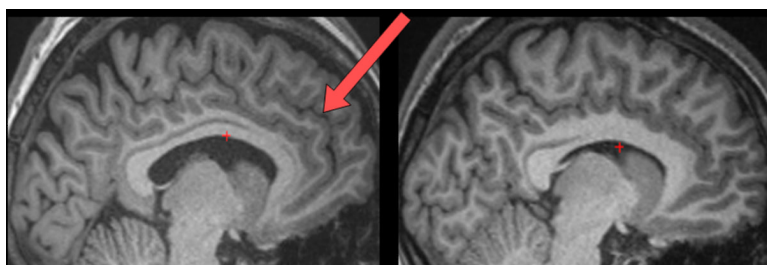


Figure 2. Examples of 'prominent' (left) and 'absent' (right) PCS classifications. In the left panel, the PCS is indicated by the red arrow.

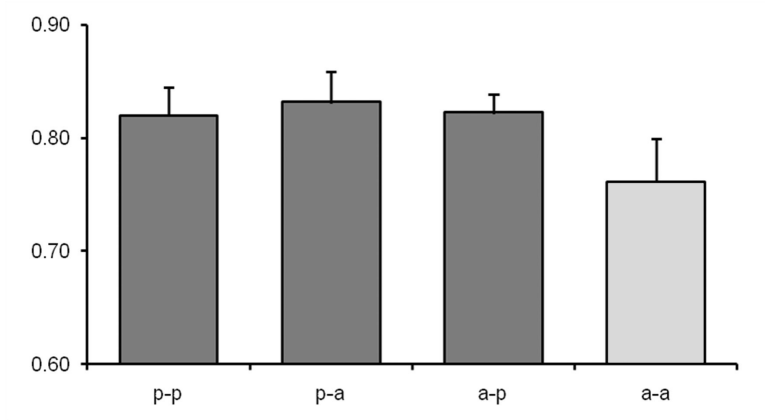


Figure 3.

Reality monitoring performance of the four PCS groups. p-p = prominent-prominent, p-a = prominent-absent, a-p = absent-prominent, a-a = absent-absent.

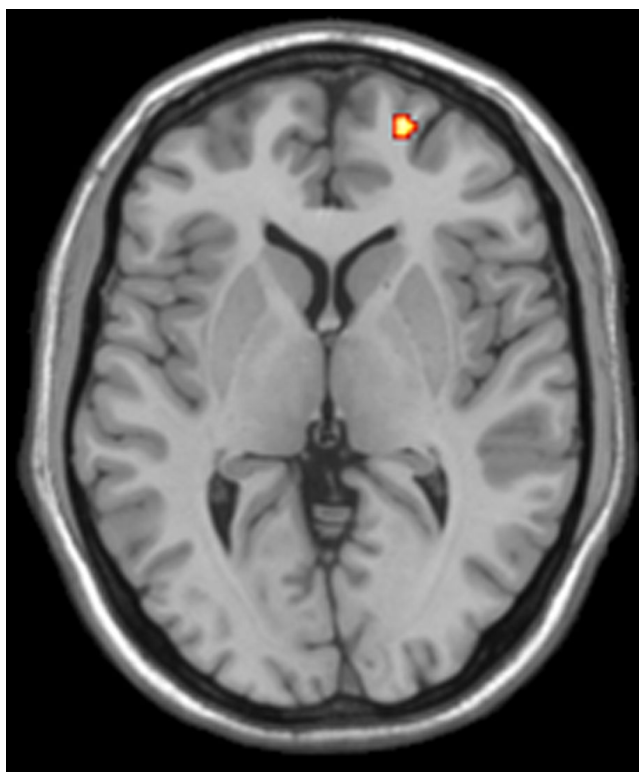


Figure 4.
Voxel-based morphometry analysis illustrating a significant correlation between greater anterior PFC gray matter and lower reality monitoring performance.

TABLE 1

Accuracy and reaction time (ms) data

Group	Accuracy		Reaction Time	
	P/I	S/E	P/I	S/E
p-p	0.77 (0.15)	0.87 (0.07)	1786 (240)	1505 (189)
p-a	0.78 (0.15)	0.89 (0.05)	1733 (317)	1558 (227)
a-p	0.78 (0.09)	0.86 (0.05)	1974 (243)	1648 (228)
a-a	0.71 (0.17)	0.82 (0.14)	1867 (261)	1583 (270)

Note: Data are means, with standard deviations in parentheses. P/I = perceived/imagined, S/E = self/experimenter, p-p = prominent-prominent, p-a = prominent-absent, a-p = absent-prominent, a-a = absent-absent

TABLE 2

Regions exhibiting significant correlations between gray matter volume and reality monitoring performance

Brain Region	Coordinates		
	x	y	z
<i>Negative Correlations</i>			
Right medial PFC (BA 10)	22	58	2
Right motor cortex (BA 6)	26	8	64
Right motor cortex (BA 6)	32	-6	64
<i>Positive Correlations</i>			
Left ventrolateral PFC (BA 44)	-42	16	12
Right putamen (BA 24)	28	14	0
Left putamen (BA 24)	-24	10	8
Right parahippocampal gyrus (BA 36)	28	-44	-8
Right temporal cortex (BA 39)	54	-68	12
Right occipital cortex (BA 18)	12	-76	-20
Right precuneus (BA 7)	14	-78	46

Note: Coordinates are in MNI atlas space (Cocosco et al., 1997)