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A neural measure of behavioral engagement: Task-residual low frequency blood oxygenation level dependent activity in the precuneus

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Abstract

Brain imaging has provided a useful tool to examine the neural processes underlying human cognition. A critical question is whether and how task engagement influences the observed regional brain activations. Here we highlighted this issue and derived a neural measure of task engagement from the task-residual low frequency blood oxygenation level dependent (BOLD) activity in the precuneus. Using independent component analysis, we identified brain regions in the default circuit – including the precuneus and medial prefrontal cortex (mPFC) – showing greater activation during resting as compared to task-residuals in 33 individuals. Time series correlations with the posterior cingulate cortex as the seed region showed that connectivity with the precuneus was significantly stronger during resting as compared to task residuals. We hypothesized that if the task-residual BOLD activity in the precuneus reflects engagement, it should account for a certain amount of variance in task-related regional brain activation. In an additional experiment of 59 individuals performing a stop signal task, we observed that the fractional amplitude of low frequency fluctuation (fALFF) of the precuneus but not the mPFC accounted for approximately 10% of the variance in prefrontal activation related to attentional monitoring and response inhibition. Taken together, these results suggest that task-residual fALFF in the precuneus may be a potential indicator of task engagement. This measurement may serve as a useful covariate in identifying motivation-independent neural processes that underlie the pathogenesis of a psychiatric or neurological condition.

Keywords

motivation; default circuit; precuneus; low frequency fluctuation; fMRI

Introduction

Functional imaging is widely used to explore the neural processes of human cognition. An important question is whether motivation or behavioral engagement influences the degree brain

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regions activate during cognitive performance. For instance, this issue seems particularly critical in studies of patients with a neurological or psychiatric condition, who behaviorally were less engaged and frequently showed altered cerebral activation, as compared to healthy controls. Here we used imaging research of the endophenotypes of mental illnesses as an example to illustrate this issue.

In studies of the neural phenotypes of mental illnesses, a common approach is to compare regional brain activation in patients and healthy controls performing a behavioral task thought to be of pathogenetic importance, e.g., using working memory process to probe schizophrenia (Tan et al., 2006; Barch and Csernansky, 2007; Driesen et al., 2008; Koch et al., 2008; Lee et al., 2008; Schlosser et al., 2008). The results are typically described in two ways. In one scenario, patients showed less regional brain activation concomitant with altered behavioral performance, as compared to healthy controls (Barch and Csernansky, 2007; Lee et al., 2008; Schlosser et al., 2008). One criticism of this approach is that patients may not be as motivated or engaged during the task, hence their inferior performance and decreased cerebral activity (Fig. 1a). In a second approach, aimed to resolve this disparity, investigators compared patient and control subjects matched in task performance (Tan et al., 2006; Driesen et al., 2008; Koch et al., 2008). Thus, differences in regional brain activation cannot easily be attributed to discrepancy in task engagement (Fig. 1b). However, two arguments are often raised against this latter approach. First, some investigators suggest that patients simply employ different neural circuits and, as long as they do the task equally well, the differences in brain activation do not necessarily speak to underlying pathology. Second and perhaps more critically, indistinguishable behavioral performance could potentially result from a ceiling effect; namely, the task is not adequate to elicit veridical differences in performance as well as performance-related regional brain activation. On the other hand, once a task is used to “break” the ceiling, findings of between-group differences are subject to the issue of discrepancy in behavioral engagement. Here we proposed that a potential solution would be to obtain a neural measure of motivation or behavioral engagement, independent of task-related processes (Fig. 1c). The neural measure of behavioral engagement would facilitate the identification of motivation-independent differences in task-related process between patients and controls.

Brain regions in the “default” network are more active when individuals are in a resting state, compared to when they respond to an external environment or engage in mental effort (Raichle et al., 2001; Fox and Raichle, 2007). For instance, McKiernan and colleagues showed that task-induced deactivations in several of the default mode regions varied parametrically as a function of task difficulty (McKiernan et al., 2003). We hypothesized that activity in these default brain regions, including the precuneus, posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC) may signal the extent to which individuals are engaged in a behavioral task, independent of task-related processes. Such a neural signal would be useful in indexing whether individuals are adequately motivated in a laboratory test and whether comparison of task-related brain activation between patients and healthy controls is “legitimate.” However, the idea of task-independent deactivation of the default brain circuit has been challenged on a number of grounds, including evidence suggesting that the default brain regions activate rather than deactivate in response to task-related events (Morcom and Fletcher, 2007). This latter issue confounds its potential use as a neural signature of task-independent behavioral engagement.

We sought to overcome this confound by removing task-related activities from the time series to derive “task-residual” low frequency blood oxygenation level dependent (BOLD) activity (Fair et al., 2007). It is known that low frequency BOLD signal fluctuations that occur during rest reflect connectivity between functionally related brain regions (Biswal et al., 1995; Fair et al., 2007; Fox and Raichle, 2007). Recent studies of this “spontaneous” activity have provided insight into the intrinsic functional architecture of the brain, variability in behavior, and potential physiological correlates of neurological and psychiatric disease (Fox and Raichle, 2007). Notably, it was suggested that the spontaneous activity continues during a behavioral task and task-related brain activations represent a combination of the spontaneous activity and responses to stimulus input, behavioral output or attention (Arfanakis et al., 2000; Fox et al., 2006a; Fair et al., 2007). In particular, Fair and colleagues reported that the functional connectivity of low-frequency task-residual is similar to resting state (Fair et al., 2007). Therefore, we hypothesized that, by deactivating to a behavioral task, the default brain regions would show greater activity during resting state as compared to task-residual data. In addition, we hypothesized that, as an indicator of motivation or task engagement, the activity of the default brain regions would explain a certain amount of variance in task-related regional brain activations during fMRI.

Materials and Methods

Subjects and behavioral task

Fifty-nine healthy adult adults (20-45 years of age, 30 men, right-handed) participated in four 10-minute sessions of a stop signal task (SST) during fMRI. Thirty-three of them were also scanned during a 10-minute resting session, in which they were instructed to relax and stay awake. All participants were without neurological or axis I psychiatric illnesses and reported no history of head injury or use of illicit substances. The SST was described in details in our earlier studies (Li et al., 2006; Li et al., 2007b; Di Martino et al., 2008).

Imaging protocol

Conventional T1-weighted spin echo sagittal anatomical images were acquired for slice localization using a 3T scanner (Siemens Trio). Anatomical images of the functional slice locations were next obtained with spin echo imaging in the axial plane parallel to the AC–PC line with TR = 300 ms, TE = 2.5 ms, bandwidth = 300 Hz/pixel, flip angle = 60°, field of view = 220 × 220 mm, matrix = 256 × 256, 32 slices with slice thickness = 4 mm and no gap. Functional, blood oxygenation level-dependent (BOLD) signals were then acquired with a single-shot gradient echo echoplanar imaging (EPI) sequence. Thirty-two axial slices parallel to the AC–PC line covering the whole brain were acquired with TR = 2000 ms, TE = 25 ms, bandwidth = 2004 Hz/pixel, flip angle = 85°, field of view = 220 × 220 mm, matrix = 64 × 64, 32 slices with slice thickness = 4 mm and no gap.

Imaging data preprocessing and general linear modeling

Brain imaging data were preprocessed using Statistical Parametric Mapping version 5 (Wellcome Department of Imaging Neuroscience, University College London, U.K.). Images from the first five TRs at the beginning of each trial were discarded to enable the signal to achieve steady-state equilibrium between RF pulsing and relaxation. Images of each individual subject were first corrected for slice timing and realigned (motion corrected). A mean functional image volume was constructed for each subject for each run from the realigned image volumes. These mean images were normalized to an MNI (Montreal Neurological Institute) EPI template with affine registration followed by nonlinear transformation (Friston et al., 1995; Ashburner and Friston, 1999). The normalization parameters determined for the mean functional volume were then applied to the corresponding functional image volumes for each subject. Finally, images were smoothed with a Gaussian kernel of 10 mm at Full Width at Half Maximum.

In general linear models (GLM) events of interest were employed as regressors to explain task-related data as described in detail in our previous work (Li et al., 2006; Li et al., 2007b; Di Martino et al., 2008). Of relevance to the current study are the findings of greater activation in the right inferior frontal cortex (MNI coordinate: x=44, y=48, z=−12) during stop success as compared to stop error trials and greater activation of the anterior pre-supplementary motor area (preSMA, x=−4, y=36, z=56) during stop success as compared to stop error trials in subjects with short as contrasted with those with long stop signal reaction time, estimated on the basis of the race model (Logan, 1994). Furthermore, we observed greater activation in the dorsal anterior cingulate cortex (dACC, x=−4, y=16, z=44) during stop error as compared to stop success trials.

Task-residual time series was obtained by removing task-related activity with the GLM. Based on previous studies that suggested a linear superposition of task activity and spontaneous BOLD fluctuations (Arfanakis et al., 2000; Fox et al., 2006b; Fox et al., 2006a), it was assumed that, if task induced variance was adequately removed, the remaining residual signal should represent the spontaneous signals (Fair et al., 2007).

Group independent component analysis (ICA)

Multivariate methods based upon ICA have been applied to examine functional connectivity between brain regions both during resting state and task performance (McKeown et al., 1998; Calhoun et al., 2001b, 2001a; Calhoun et al., 2004; Calhoun et al., 2008; Jafri et al., 2008). Here we applied group ICA to the preprocessed images of both resting state and task residual data using the informax algorithm (Bell and Sejnowski, 1995) as implemented in the GIFT (Group ICA of fMRI Toolbox, http://icatb.sourceforge.net/, version 2.0) software (Calhoun et al., 2001a). We used the minimum description length criteria, modified to account for spatial correlation to determine the number of independent components (Li et al., 2007c). The resting state and task residual data were each estimated to have 33 and 27 components. We focus on an average of 30 components in order to compare the two data sets. Single subject spatial maps were reconstructed, in which the aggregate components and the results from data reduction were used to compute individual subjects' components (Calhoun et al., 2001a). The default mode network components were selected and the calibrated component image map of individual subjects was computed according to percent signal change using the original fMRI data as a reference. These calibrated component image maps of all 33 subjects were applied to a paired t test comparing resting state and task residual data.

Low frequency BOLD signals

For both resting and task-related data, we reduced spurious BOLD variances that were unlikely to reflect neuronal activity (Rombouts et al., 2003; Fox et al., 2005; Fair et al., 2007; Fox and Raichle, 2007). The sources of spurious variance were removed through linear regression by including the signal from the ventricular system, the white matter, and the whole brain, in addition to the six parameters obtained by rigid body head motion correction. First-order derivatives of the whole brain, ventricular and white matter signals were also included in the regression.

Cordes and colleagues suggested that BOLD fluctuations below a frequency of 0.1Hz contribute to regionally specific BOLD correlations (Cordes et al., 2001). The majority of resting state studies low-pass filtered BOLD signal at a cut-off of 0.08 or 0.1 Hz (Fox and Raichle, 2007). Thus, we applied a temporal band-pass filter ($0.009\text{Hz} < f < 0.08\text{Hz}$) to both resting and residual time course in order to obtain low-frequency fluctuations (Lowe et al., 1998; Fox et al., 2005; Fair et al., 2007; Fox and Raichle, 2007).

Seed region-based linear correlation

We utilized the masks from the Automated Anatomic Labeling (AAL) atlas as seed regions (Tzourio-Mazoyer et al., 2002). The BOLD time courses were averaged spatially over each seed region. We computed for individual subjects the correlation coefficient between the averaged time course of each seed region and the time courses of all other brain voxels.

To assess and compare the task-residual and resting state “correlograms,” we converted these image maps, which were not normally distributed, to z score maps by Fisher’s z transform (Jenkins and Watts, 1968; Berry and Mielke, 2000; Charles F. Bond and Richardson, 2004): $z\ 0.5\log_e[(1+r)/(1-r)]$. The z maps were used in group, random effect analyses.

Fractional amplitude of low frequency fluctuation (ALFF)

The amplitude of low-frequency fluctuation (ALFF) is a measure of power spectrum density. For instance, it was reported that the root mean square (RMS) of the LFFs in white matter was lower than that in gray matter by about 60% (Biswal et al., 1995; Li et al., 2000). Kiviniemi et al. used relative power of the peak over the noise fit to generate “resting activation” map in the visual cortex, and the results were similar to that obtained from correlation analysis (Kiviniemi et al., 2000). Using a discrete cosine basis set containing 120 regressors that spanned the frequency range of 0–0.1 Hz, Fransson found strong spontaneous fluctuation within the default mode network (Fransson, 2005). Furthermore, he showed that the mean power spectral density of intrinsic LFFs in the default mode network was significantly decreased during a working memory task compared to rest (Fransson, 2006). In the latter study, the investigator estimated the power spectrum of a signal by obtaining the discrete Fourier Transform and computing the squared magnitude of the Fourier coefficients.

Based on the these studies, Zang et al. developed an index – amplitude of LFFs (ALFF) – in which the square root of power spectrum was integrated in a low-frequency range, in order to examine the regional intensity of spontaneous BOLD fluctuations (Zang et al., 2007). Since the ALFF appeared to be sensitive to the physiological noise, Zou et al. proposed a fractional ALFF (fALFF) approach (Zou et al., 2008). The results showed that fALFF may effectively suppress non-specific signals and significantly improve the sensitivity and specificity in detecting regional spontaneous brain activity.

We carried out the fALFF analysis on both resting and task-residual data, as recently described in the literature (Yang et al., 2007; Zang et al., 2007; Zou et al., 2008). Briefly, filtered task-residual and resting state time series were transformed into the frequency domain using the fast Fourier transform (FFT). Since the power is proportional to $[\text{amplitude}]^2$ at a given frequency, the power spectrum obtained by FFT was square rooted to obtain amplitude. A ratio of the amplitude averaged across 0.009–0.08 Hz to that of the entire frequency range (0–0.25 Hz) was computed at each voxel to obtain the fALFF, creating an amplitude map for the whole brain, which was then normalized: normalized fALFF = (fALFF – global mean fALFF)/ standard deviation of global mean.

Results

Group independent component analysis (ICA)

Group ICA identified similar independent network components for resting state and task-residual data (Supplementary Results and Supplementary Figures 1-3). Using paired-t tests we compared components involving the default circuit brain regions including the precuneus, posterior cingulate cortex, and the medial prefrontal cortex (mPFC), and the results showed greater activation in both the precuneus and mPFC during resting state, as compared to task residuals ($p<0.05$, corrected for family-wise error of multiple comparisons; Fig. 2).

Time series correlation with default and anti-correlated brain regions

We further examined whether the pattern of functional connectivity of low frequency activity differs between resting state and task residuals. Using the posterior cingulate cortex (PCC) and primary motor cortex (PMC) as seed regions, we examined how functional connectivity of a default and anti-correlated region differs between resting state and task residuals (see Supplementary Results and Supplementary Figures 4 and 5 for the correlation maps of individual seed regions). The results showed that the PCC and PMC showed a complementary pattern of functional connectivity, with the PCC connected to other brain regions in the default circuit and the PMC connected to brain regions outside the default circuit (Fox et al., 2005;Fox et al., 2006b;Fransson, 2006;Fox and Raichle, 2007;Di Martino et al., 2008). Furthermore, the PCC showed significantly greater connectivity with the precuneus during resting state as compared to task residuals while the PMC showed the opposite pattern of results with greater connectivity to the precuneus during task residuals as compared to resting state (Fig. 3).

Fractional amplitude of low frequency fluctuation (fALFF)

The results from the ICA and seed region based correlation analyses suggested the precuneus as a key brain region whose activity may reflect the extent of task engagement. To derive a measure of task engagement, we computed the fALFF of BOLD signals for the whole brain. Replicating earlier studies (Gusnard et al., 2001; Raichle et al., 2001; Fransson, 2006; Fox and Raichle, 2007; Buckner et al., 2008), the default brain regions including the precuneus, posterior cingulate cortex (PCC), inferior parietal cortex (IPC), and medial prefrontal cortex (mPFC) showed greater fALFF and the anti-correlated brain regions showed less fALFF both for resting state and task-residual data (Supplementary Results and Supplementary Figure 6). Furthermore, in region of interest analyses, the precuneus ($p<0.001$, two-tailed paired t test) but not the PCC, IPC, or mPFC, showed greater fALFF during resting state, compared to task residuals (Fig. 4). In fact, the IPC ($p<0.001$) as well as mPFC ($p<0.001$) showed significantly greater fALFF and the PCC ($p<0.1$) showed a trend toward significantly greater fALFF during task residuals, as compared to resting state.

We posited that if the task-residual activity in the precuneus reflects behavioral engagement, it would account for certain amount of variance in *task-related* regional brain activation. We sought to verify this hypothesis in 59 healthy adults who participated in four 10-minute sessions of a stop signal task (Li et al., 2006; Li et al., 2007b; Di Martino et al., 2008; Li et al., 2008). In these previous studies we isolated activation of the right inferior frontal cortex (rIFC) during attentional monitoring (stop success > stop error trials) (Li et al., 2006) and the pre-supplementary motor area (preSMA) (Li et al., 2006) during response inhibition (short > long stop signal reaction time), as well as the dorsal anterior cingulate cortex (dACC) (Li et al., 2008) during error detection (stop error > stop success trials). Results of the regions of interest analysis based on this current, larger cohort of subjects are shown in Supplementary Figure 7. We hypothesized that the task-residual fALFF in the precuneus would be inversely correlated with these task-related regional brain activities. The results confirmed the hypothesis: fALFF of the precuneus is inversely correlated with rIFC ($p<0.01$, $\rho=-0.34$; Spearman regression) and pre-SMA ($p<0.03$, $\rho=-0.30$) activation and with a composite measure of the two ($p<0.004$, $\rho=-0.38$; Fig. 5). The fALFF of the precuneus was not correlated with dACC activation during error detection ($p>0.5$). Furthermore, fALFF of the IPC ($p=0.6$, rIFC; $p=0.8$, preSMA; $p=0.8$, composite), PCC ($p=0.7$; 0.2; 0.2), or mPFC ($p=0.7$; 0.2; 0.6) is not associated with any of these regional brain activations.

Discussion

The current findings suggest that task-residual low frequency activity in the precuneus may represent a neural surrogate of task engagement. The fractional amplitude of low frequency fluctuation (fALFF) is inversely correlated with task-related regional brain activation and provides a neural measure allowing investigation of motivation-independent neural processes. As such the precuneus appears to be functionally distinct from other default brain regions (Buckner et al., 2008). While the posterior cingulate, medial prefrontal, and inferior parietal cortices mediate self-referential and other self-related mental activities, activity of the precuneus reflects how well individuals are engaged in responses to an external task. Previous studies have provided ample evidence showing that greater activation of the default brain regions may "disengage" participants from an external task such that they were slower in responding to a stimulus or vulnerable to making mistakes (Weissman et al., 2006; Li et al., 2007a; Eichele et al., 2008). The current results thus add to these findings by delineating a specific role of the precuneus in task engagement and describing quantitatively how activity of the precuneus is related to task engagement. Note that the fALFF of the precuneus explained only about 10% of the variance, indicating that the regional brain activations largely reflected task-specific cognitive processes that are not influenced by behavioral engagement. On the other hand, the 10% variation may be sufficient to obscure a less salient, otherwise observable signal which, for instance, reflects differences between young and elderly adults or between patients and healthy control subjects.

One would predict that, if activation of the precuneus reflects decreased task engagement, it would show decreased activation in situations where greater attention is required of task performance. Indeed, in working memory tasks where the memory load was systematically manipulated, decreased precuneus activation is associated with greater memory load, as we briefly discussed in the above (McKiernan et al., 2003; Pallesen et al., 2009). More recently, it was shown in a visual motion discrimination task that the default brain regions deactivate, in an event-related fashion, in inverse association with the percentage of coherence of the moving dots composing the stimulus (Singh and Fawcett, 2008); the more difficult the stimulus to discriminate, the greater the deactivation of default brain regions. In another study where subjects responded to a visual stimulus that appeared in predictable or unpredictable locations, Hahn and colleagues observed that BOLD responses in the precuneus and other frontal and parietal areas increased linearly with the location predictability (Hahn et al., 2006). The authors suggested that the precuneus along with these fronto-parietal structures are engaged in top-down attentional control. In light of the current findings, an alternative explanation would be that increased precunues activity reflects decreased effort and engagement of the participants once the target location became predictable.

If the activity of precuneus reflects task engagement, psychological manipulations that influence task engagement may impact task performance and task-related brain activation through their effects on the precuneus. A previous study supported such a general mediating role of the precuneus (Seminowicz and Davis, 2007). Healthy participants were engaged in a cognitive interference task parametrically modulated by task difficulty while receiving pain stimulation of varying intensity. As expected, the activity of a task-positive network of brain regions increased and a task-negative network of (mostly default) brain regions including the precuneus decreased in response to greater interference. Furthermore, pain intensity additively modulated both task-positive and task-negative activities in a parametric manner. Notably, spectral analysis showed that the "energy" of the task-negative network appeared to concentrate on the low frequency band (<0.05 Hz). These investigators suggested that task difficulty (or interference load) and pain intensity synergistically modulate attention required for adequate task performance, with decreased activation in task-negative regions indicating greater attention to the task. Thus, although not unique to the precuneus, these findings are in accord with our current findings. More specifically, the concentration of this BOLD signal in the low frequency band further supports the utility of the low frequency task-residual activity in evaluating task engagement.

A recent study suggested an interesting role of the precuneus that may be relevant to the current findings (Cojan et al., 2009). The authors studied a patient with conversion paralysis, who was unable to move her left hand, in a go/no-go task. The patient as well as healthy control participants showed greater activation in the left-hemispheric motor cortex when instructed to execute a movement with the right hand. However, while healthy control subjects activated the right-hemispheric motor cortex, the patient failed to show such activation, when instructed to move with the left hand. Instead, the precuneus showed greater activation at the “go” signal to move. Although of a lesser magnitude, greater activation of the precuneus was also observed during no-go trials involving the “paralyzed” hand, concomitant with a lack of inferior frontal activation characteristic of healthy control participants. Thus, one possible explanation for these findings is that greater activation of the precuneus disengaged the cerebral structures from being involved in the execution of a go or no-go response. Given that increased precuneus activation occurred both during go and no-go trials, the findings suggested “motivation” as the source of deficits in conversion paralysis, providing a clinical scenario in accord with the current results.

We observed that the fALFF of precuneus was not correlated with error-related activity in the dACC. An ad-hoc explanation is that error detection is relatively automatic and thus less likely to be influenced by task engagement (Klein et al., 2007; O’Connell et al., 2007). Consistent with this account is a recent study that investigated the neural processes underlying the generation of automaticity of sequential movements (Wu et al., 2008). Scanning participants who have “over-learned” a sequence of movements, these investigators found that, although regional brain activations associated with the movements decreased, the functional connectivity among the motor areas increased, as compared to a learning phase. Notably, the connectivity of the precuneus with motor networks decreased (became more negative) at this automatic stage. It was suggested that automaticity of movements developed along with decreased interaction with the attention networks. These findings thus also appeared to be consistent with a role of precuneus activity in task engagement: participants were less engaged in the behavioral task once movements became automatic. Thus, in the current results, if error detection as mediated by dACC activation is relatively automatic, the extent of dACC activation would not be influenced by precuneus activity. Warranting replication, these findings suggest that fALFF of the precuneus may also indicate the degree of automaticity of a cognitive process.

In summary, we have identified task-residual fALFF of the precuneus as a neural measure of task engagement. This neural surrogate could help investigators identify motivation-independent cerebral processes critical to the pathogenesis of a mental condition.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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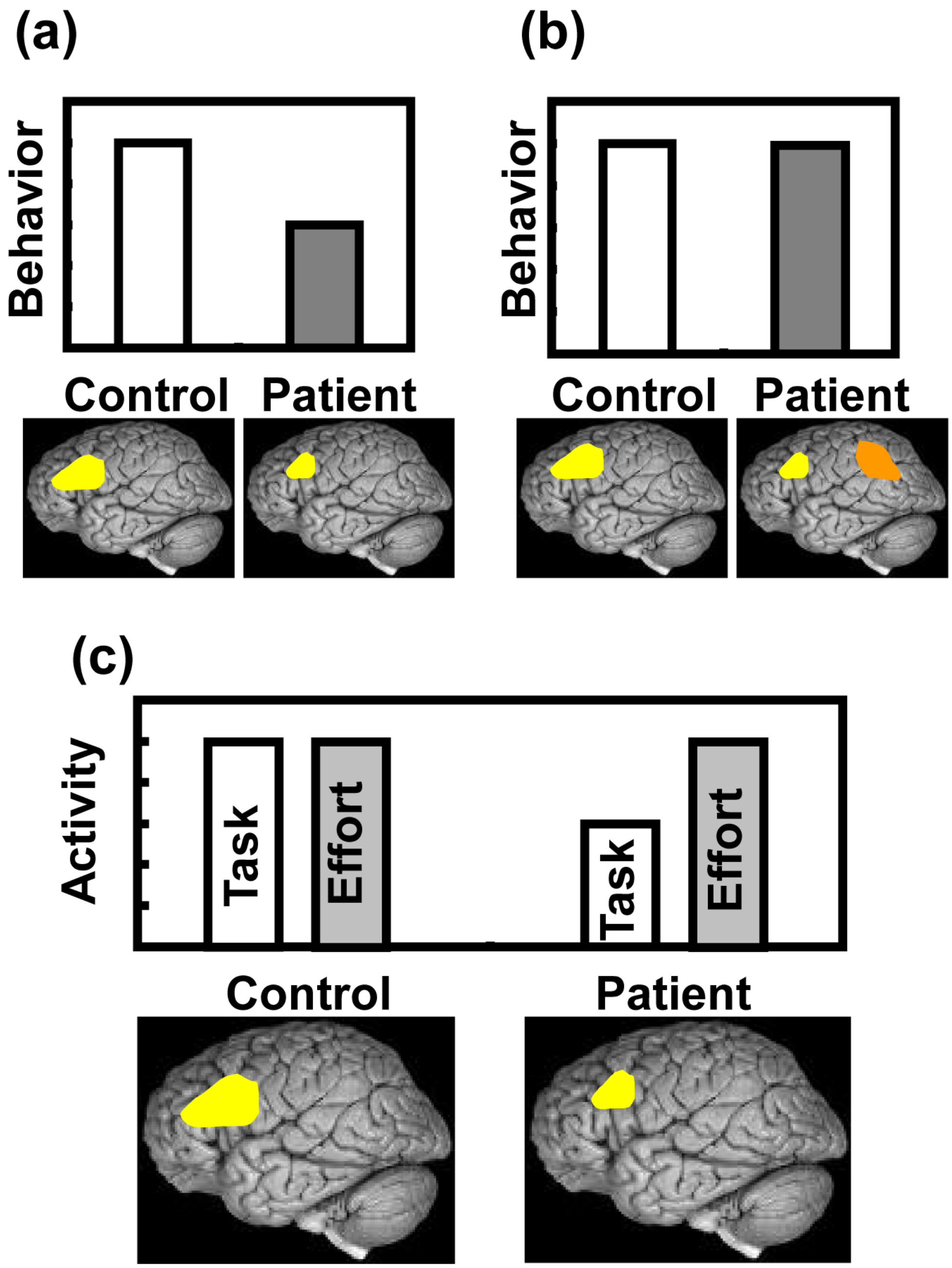

Figure 1.

The need of a neural measure of task engagement: (a) Patients typically show impaired behavioral performance and brain activation when compared to healthy control subjects. One concern is that this "deficit" may simply reflect less task engagement on the part of the patients. (b) To address this issue, investigators have compared brain activations between patient and control subjects who are matched in performance. However, in this case one might argue that, short of eliciting between-group differences, the behavioral task may not speak to the core characteristics of the mental illness. (c) We propose that an ideal solution would be to obtain a neural measure of task engagement, which, when covaried for task performance and related brain activation, would facilitate the identification of motivation-independent cerebral processes specific to the mental condition.

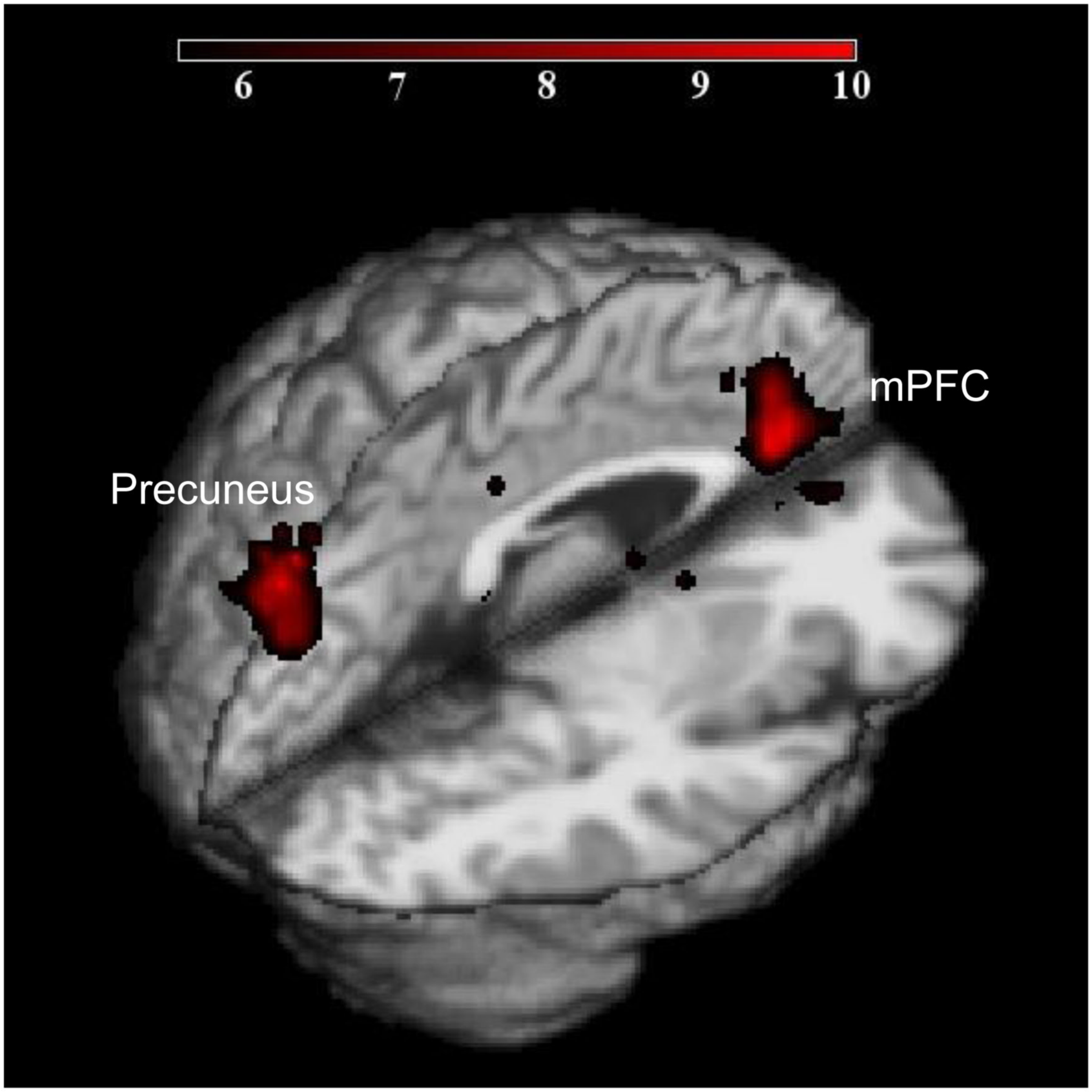

Figure 2.

Results of group independent component analysis showed that the precuneus (two peaks; x, y, z = 4, −84, 48; voxel Z=6.73; x, y, z = −4, −80, 40; voxel Z=5.58; 6,144 mm^3) and medial prefrontal cortex (three peaks; x, y, z = 0, 48, 8; Z=6.79; x, y, z = −4, 60, 4; Z=6.43; x, y, z = 8, 40, 12; Z=6.29; 8,960 mm^3) showed greater activity during resting state, compared to task-residuals (n=33; $P < 0.05$, corrected for family-wise error or FWE of multiple comparisons). Color bar represents voxel t value.

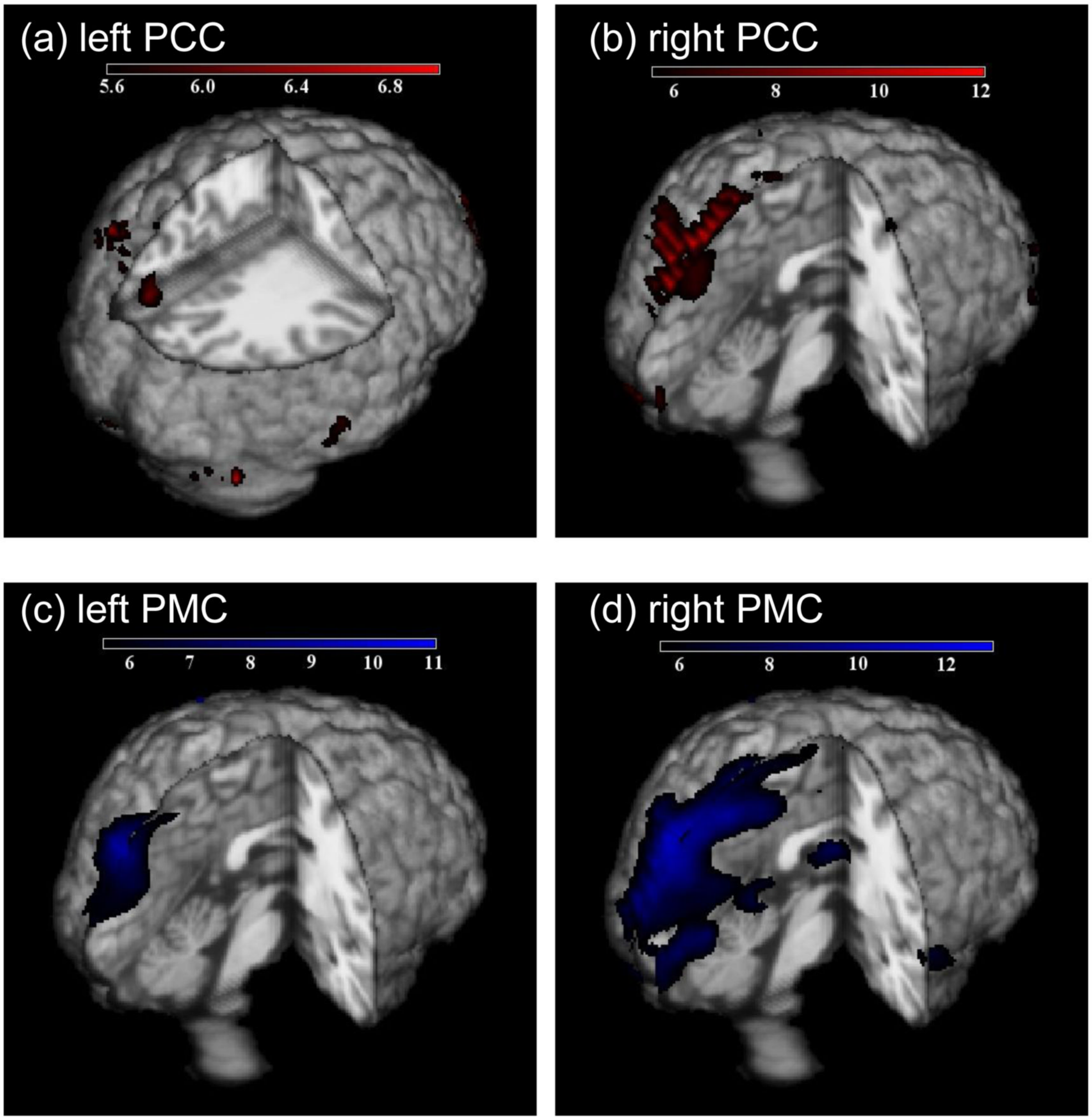

Figure 3.

Comparing resting state and task-residuals in voxelwise linear correlation of low frequency signals using the (a) left posterior cingulate cortex (PCC); (b) right PCC; (c) left primary motor cortex (PMC); and (d) right PMC as see regions. Overall, the results showed significantly greater PCC connectivity with the precuneus during resting state as compared to task residuals and greater PMC connectivity to the precuneus during task residuals as compared to resting state (n=33; $P < 0.05$, corrected for FWE). Color bars represent voxel t values. Red: resting > task-residual; Blue: task-residual > resting.

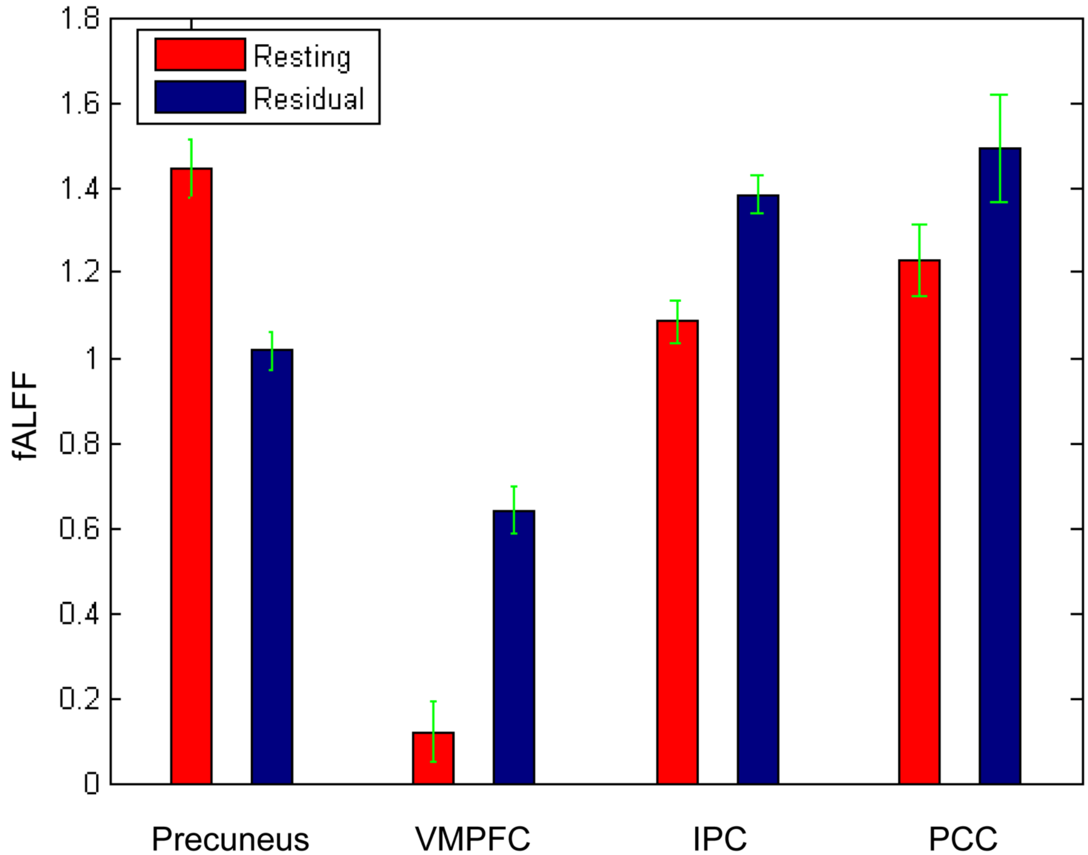

Figure 4.
The precuneus but not the PCC, IPC or mPFC, showed greater fALFF during resting state, compared to task residuals in region of interest analyses. Vertical bars represent standard error of the mean. See text for statistics.

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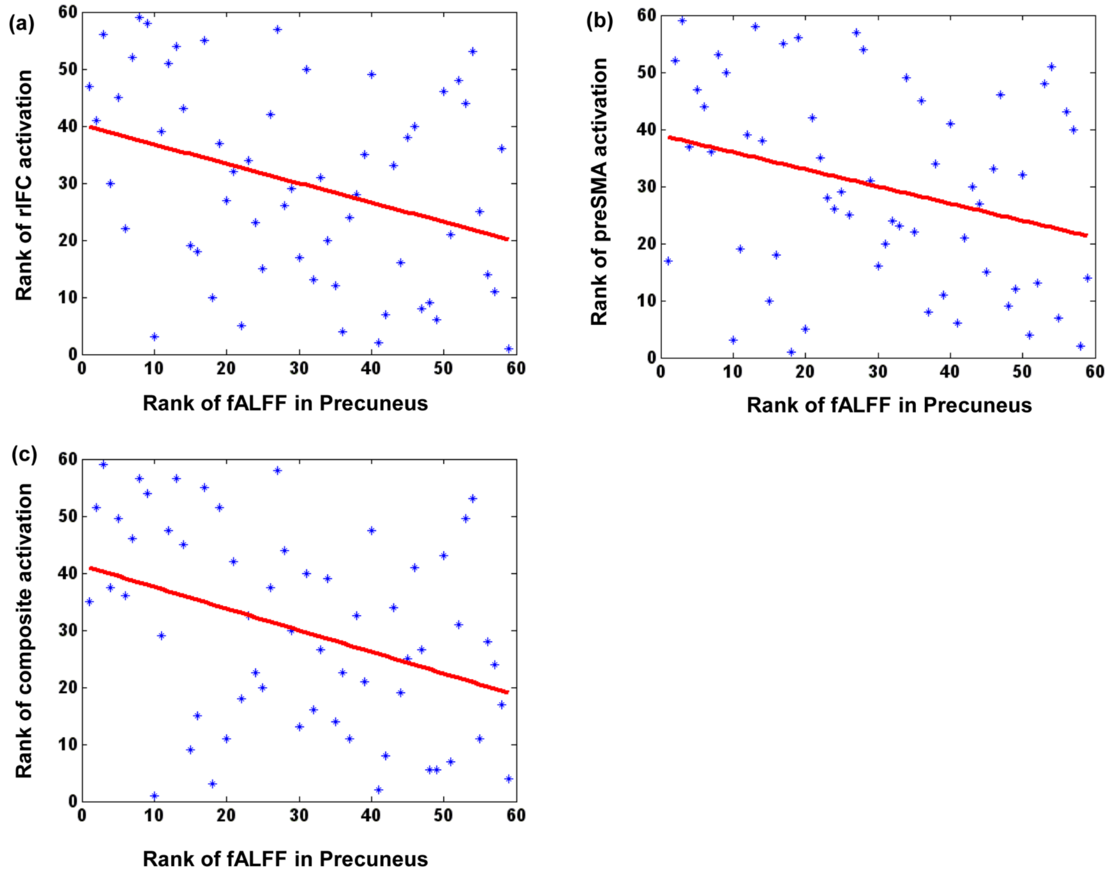

Figure 5.

Spearman regression (n=59) showed that the fALFF of the precuneus was inversely correlated with the activation of the (a) right inferior frontal cortex (rIFC) during attentional monitoring, (b) pre-supplementary motor area (preSMA) during response inhibition, and (c) a composite measure of the two (sum of rank orders). Each asterisk represents data of one subject.