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Functional Connectivity with Anterior Cingulate and Orbitofrontal Cortices During Decision-Making

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Abstract

Recent neuroscience research has revealed much about the brain regions involved in decision-making under uncertainty, but little is known about whether or how these regions functionally interact with each other. Here, we used event-related functional magnetic resonance imaging to examine both changes in overall activity and changes in functional connectivity during risk-taking. Results showed that choosing high-risk decisions over low-risk decisions was associated with increased activity in the anterior cingulate and orbitofrontal cortex. Connectivity analyses revealed that several cortical and subcortical regions exhibited significant functional connectivity with both anterior cingulate and orbitofrontal cortices. Additionally, connectivity patterns in some regions, including the amygdala and nucleus accumbens, were modulated by the decision participants chose. These findings shed new light on the neurobiology of decision-making by demonstrating that expansive networks of brain regions are functionally connected with both anterior cingulate and orbitofrontal cortices during decision-making.

Theme I: Neural Basis of Behavior
Topic: Motivation and Emotion
Keywords: decision-making, FMRI, functional connectivity, orbitofrontal cortex, anterior cingulate, amygdala

1. Introduction

The ability to make decisions under uncertain conditions is arguably one of the most important functions of the brain. Current evidence suggests that ventromedial prefrontal areas including the orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) are critically involved in the process of evaluating and choosing between decision options when the outcomes of those decisions are unknown or uncertain [1-5]. For example, patients with damage to OFC show marked impairments in learning optimal decision-making strategies to avoid long-term monetary losses [4, 6], and are also impaired in adapting decision-making behavior to changes in stimulus-reward contingencies [7, 8]. Consistent with these observations, recent neuroimaging studies have demonstrated that regions including OFC and ACC become especially active during decision-making tasks that involve uncertainty or risk [9-11].

However, regions of the brain do not act in isolation of each other, but rather must work together as a system [5, 12]. For example, damaging anatomical connections between OFC and amygdala lead to similar impairments in learning and decision-making as those produced by damage to either region alone [13]. Thus, one challenge for understanding the neurobiological mechanisms of decision-making is to elucidate not only the brain regions that exhibit significantly heightened activity during decision-making, but also to understand how different regions of the brain interact on the functional-anatomical level during decision-making. To our knowledge, functional connectivity has not been examined in the context of decision-making, but based on known neuroanatomical connections with OFC and ACC, a number of candidate regions might exhibit functional connectivity during decision-making. For example, both OFC and ACC have extensive bilateral cortical connections within ventral and dorsal prefrontal cortex (PFC), insula, and parietal cortex, as well as with subcortical connections with amygdala,

striatum, and thalamus [14-16]. However, although broad anatomical connections within the brain are known, it is not clear whether these anatomical connections are mirrored in functional connections, and further, whether participants' decisions can modulate the strength and nature of these functional connections.

We designed an fMRI study that allowed us to experimentally separate neural activity related to choosing between high-risk and low-risk decision options from other processes engaged during decision-making, such as reward anticipation and evaluation. On each trial during the experiment, participants chose one of two uncertain gambles: a high-risk (40% chance of winning $2.50) or a low-risk (80% chance of winning $1.25) gamble. This decision was separated in time from learning whether they won money on that trial, which allowed us to identify regions of the brain specifically engaged when choosing between uncertain decision options, and then to further test for functional connectivity with these task-activated regions.

2. Materials and Methods

2.1 Participants

Sixteen participants (aged 20-27, 9 male) volunteered to be in the study in exchange for payment by the hour. All participants signed informed consent documents prior to the start of the experiment.

2.2 Task Design

On each of 167 trials, participants first saw a visual cue on the screen that indicated that they needed to choose one of two decision options in attempt to win money: a low-risk decision, for which participants were 80% likely to win $1.25 and 20% likely to receive nothing ($0.00); or a high-risk decision, for which participants were 40% likely to win $2.50 and 60% likely to receive nothing. Participants indicated their decision by pressing one of two buttons on a

response box. Probabilities of winning on each trial were independent of the decisions and outcomes chosen in previous trials. Following the decision, a 7.5s anticipation period ensued before text appeared on the screen that indicated how much participants had won on that trial. The feedback was followed by a variable, 7-13s inter-trial-interval (ITI) before the next trial began. This design allowed us to deconvolve activity related to making the decision, anticipating the outcome, and evaluating the outcome on each trial [10, 17-20]. Participants were trained on this task prior to the start of the experiment, and were informed of the probabilities of outcomes associated with each decision option. This training minimized effects of learning and trial-and-error guessing strategies during the task. In addition to decision trials, control trials were included in which participants simply had to make a behavioral response in order to get a reward (with no decision required). These trials are not discussed in the present paper.

2.3 FMRI Acquisition

MRI data were collected on a 1.5T GE Signa scanner at the UC Davis Research Imaging Center. Functional imaging was done with a gradient echo EPI sequence (TR=2000, TE=40, FOV=220, 64x64 Matrix, voxel size=3.475 x 3.475 x 5 mm), with 24 oblique axial slices (tilt angle: ~ -15^0 from ac-pc line). Co-planar and high-resolution T1 weighted images were also acquired from each participant. EPI data were realigned to the first volume, corrected for slice-timing differences, co-registered with the anatomical scan, spatially normalized to the MNI space, resampled to 3.5 mm isotropic voxels, and spatially smoothed with an 8mm FWHM kernel using SPM99 software (Wellcome Department of Imaging Neuroscience, London, UK).

2.4 Statistical Analyses

Event-related blood oxygenation level dependent (BOLD) responses were estimated using multiple regression in VoxBo software (www.voxbo.org). Separate covariates modeled the

decision, anticipation, and outcome phases of each type of event, relative to the inter-trial-interval. All regression models incorporated empirically derived estimates of intrinsic temporal autocorrelation [21] and filters to attenuate frequencies above .25 Hz and below .01 Hz. BOLD responses to each event type were modeled with empirical hemodynamic response functions derived from each participant using BOLD responses in the central sulcus during a visuomotor response task [22, 23]. The mean of each scanning run, the global signal (orthogonalized with respect to the design matrix; [24], and an intercept were additionally included as covariates.

Following single-subject analyses, images of parameter estimates for each contrast of interest (e.g., high-risk minus low-risk decisions) were entered into a one-sample t-test in which the mean estimate across participants for each voxel was tested against zero. Significant regions of activation were identified using an uncorrected, two-tailed threshold of $p<.005$ and a cluster threshold of 6 contiguous voxels. In the figures, activations are overlaid on a single subject's T1 image, using MRIcro software [25] (convolved with an embossing filter kernel in matlab to produce the observed coloration).

2.4.1 Connectivity Analyses

To examine task-induced patterns of connectivity in our task, we used regression techniques to test for brain areas in which activity correlated significantly with activity in a seed region during a particular condition or task phase. To do this, we extracted the entire time-course of activity in a particular region (e.g., a cluster of voxels in OFC that showed significant activation during the task) for the whole experiment, and multiplied that time course with a condition vector that was ones for 6 TRs following an event of interest, and zeros otherwise, which allowed us to separately examine brain connectivity during the decision phases of the task independent of activity in other stages. These resulting vectors were then used as covariates in a

separate regression, which included the vectors as the independent variables of interest, as well as the nuisance covariates used in the original regressions, as described above. These independent variables are similar to the bilinear terms used in dynamic causal modeling of fMRI data [26], and similar analyses have been used previously to examine functional connectivity [27]. Group activation maps were created in the same way as with the standard regression analyses, described above. In these analyses, a positive activation indicates that activity in that region correlates more positively with activity in the seed region during the experimental condition relative to the inter-trial-interval, and a negative activation indicates that activity in that region correlates more negatively with activity in the seed region during the experimental condition relative to the inter-trial-interval.

3. Results

3.1. Behavioral Results

Participants were not more likely to choose the low-risk decision than the high-risk decision (48% ± 3.6 versus 52% ± 3.6, mean ± SEM, respectively, t_{15}=.53, *ns*), but took on average less time to indicate a high-risk relative to a low-risk decision (538ms ± 83 and 594ms ± 94, mean ± SEM, t_{15}=5.18, p<.01).

3.2. FMRI Results

Our first set of analyses concerned brain regions that exhibited a significant difference in activity when participants chose the high-risk decision versus when they chose the low-risk decision. As seen in Figure 1, significantly greater activity was observed during high-risk vs. low-risk decisions in right OFC (BA 11), ACC (BA 24/32), bilateral dorsolateral PFC (BA 45), ventral striatum, parietal cortex (BA 40), and temporal cortex (BA 37). We note that the ACC and OFC activations were also significant at p<.001. No areas of the brain exhibited greater

activity during low-risk compared to high-risk trials. MNI coordinates of these and all other activations reported in this paper are presented in Table 1.

Our next set of analyses concerned functional connectivity. Based on the importance of the ACC and OFC in decision-making, we used these clusters of activation as seed regions. For each region, we first examined connectivity during high-risk and low-risk trials separately, and then tested whether there was a significant difference between connectivity during these two conditions.

We first examined connectivity with the ACC. As seen in Figure 2a, similar patterns of connectivity with the ACC emerged during both high- and low-risk decisions, including the extent of the cingulate gyrus (extending into medial PFC), bilateral striatum, parietal cortex (BA 39), and dorsolateral PFC (BA 45 and BA 9). We also observed significant deactivations with the ACC in right amygdala, supplementary motor area (BA 6), parietal cortex (BA 7), and cerebellum. We next examined regions that showed a significant difference in correlation with ACC during high- vs. low-risk trials. We observed several regions that showed enhanced connectivity with ACC during high- vs. low-risk decisions including right amygdala, left nucleus accumbens, medial and lateral OFC, supplementary motor area (BA 6), and cerebellum (see Figure 2b).

We next tested for areas of the brain in which activity correlated significantly with activity in OFC. As seen in Figure 3, during both high- and low-risk decisions, we observed significant correlations in PFC regions including bilateral OFC (BA 11), frontopolar PFC (BA 10/46), dorsolateral PFC (BA 44/9), and dorsomedial PFC (extending into ACC; BA 24/32), as well as in parietal cortex (BA 40/7) and temporal cortex (BA 20/37). We additionally observed negative correlations with bilateral superior temporal gyrus (BA 41 and BA 21). During high-

risk but not low-risk decisions, we observed significant correlations in posterior cingulate (BA 23). However, when directly comparing connectivity during high- and low-risk decisions, no significant differences emerged.

4. Discussion

In the present study, we sought to identify patterns of connectivity with the ACC and OFC during the performance of a decision-making task. Consistent with previous reports, we found that both ACC and OFC exhibited significantly greater activation when subjects made high-risk relative to low-risk decisions [9, 11]. Furthermore, these regions exhibited changes in functional connectivity with networks of cortical and subcortical regions during these decisions. We describe these results and their implications in more detail below.

4.1. Anterior Cingulate

Our finding that ACC was more active during high- compared to low-risk decisions is consistent with other reports of the ACC and decision-making [9, 11, 28]. We note that in our study, as well as in that of Rogers et al. [11], the activation in ACC was more ventral than reported in Bush et al. [28]. In the present study and the study of Rogers et al., participants chose between relatively risky options to obtain rewards. In contrast, subjects in the study of Bush et al. did not have to choose between relatively risky options, but rather had to learn to quickly change their decision-making strategies in light of changes in rewarding reinforcements. Thus, we speculate that decisions involving risk may recruit a more ventral region of ACC than decisions involving little or no risk. Indeed, as seen in the time course of activity in ACC (Figure 1) choosing the low-risk decision (in which participants were 80% likely to receive a reward) did not elicit any discernable activity changes in ACC. Such a distinction in function between risk-related decision-making in ventral ACC and non-risk-related decision-making in dorsal ACC

would be consistent with the suggestion that anterior ACC processes emotional information whereas dorsal ACC processes more cognitive information [29, 30].

Many investigations into the functions of the ACC concern cognitive control and monitoring behavior for response conflicts [31, 32]. Findings from these studies might lead one to conclude that our participants simply felt more conflict when they chose high-risk decisions over low-risk decisions. Although we did not collect online or post-experimental measures of whether participants experienced any differential levels of conflict during the experiment, several considerations suggest that increased response conflict cannot completely account for the ACC activation observed here. First, the locus of our activation is relatively ventral compared with the more dorsal (i.e., closer to SMA) ACC activations typically reported in studies of conflict monitoring [32, 33]. Second, response times for high-risk decisions were shorter than those for low-risk decisions, which is the opposite of what would be expected if high-risk decisions were associated with increased conflict. Third, it is likely that low-risk decisions were also associated with some amount of conflict, both because participants still had to make a decision under uncertain conditions. The conflict monitoring would therefore predict some amount of ACC activation even during low-risk decisions. However, the ACC cluster identified in the high- vs. low-risk contrast was not significantly active when comparing low-risk trials versus the inter-trial-interval (see time course and bar graph plots in Figure 1). This pattern of ACC activation also is not consistent with a role for this region in considering or debating between decision options, because these processes would have occurred during low-risk trials as well). Thus, the ACC activation was likely driven largely by representations of uncertain but large rewards. Given that ACC was not more active during low-risk decisions than during the ITI, it seems that ACC doesn't simply represent reward magnitude or reward uncertainty, but factors related to the

decision to choose a highly uncertain large reward.

Connectivity analyses using ACC activation as a seed region revealed that, consistent with known neuroanatomical connections of ACC, an extensive network of regions including the striatum, amygdala, cingulate gyrus, medial and lateral PFC, and parietal cortex exhibited activity that correlated significantly with that in ACC [15, 16]. Several regions of the brain exhibited significantly increased connectivity with ACC during high-risk compared to low-risk decisions, including the amygdala, OFC, and nucleus accumbens. Available evidence strongly implicates the ACC in behavioral inhibition and cognitive control [29, 31, 33], and it is possible that one mechanism for this control is through modulating the activity of neural populations in other regions of the brain. Specifically, the amygdala, nucleus accumbens, and OFC are all involved in motivation, reward seeking behavior, and emotion attentional modulation [34-37]. Given that high-risk decisions elicit increased physiological responses [38], and that ACC activity correlates with these physiological changes during risk-taking [10], increased functional coupling in regions such as amygdala, OFC, and nucleus accumbens with ACC may reflect a control mechanism by which ACC regulates emotional, attentional, and physiological processes during decision-making [10]. Further studies will need to be conducted to more closely examine the relationship between connectivity among these regions, levels of uncertainty, and attentional and physiological arousal.

4.2. Orbitofrontal Cortex

Our finding that OFC was significantly more active during high- vs. low-risk decisions is consistent with a growing literature on the link between OFC functioning and reward-related decision-making [6, 7, 9, 39]. For example, patients with lesions to OFC tend to prefer risky decision strategies, even when those strategies are associated with long-term losses [6, 40]. This

finding is sometimes interpreted to mean that OFC is critical for relearning reward-based associations when reward contingencies change [7, 41], or that OFC is involved in dynamically updating behavior according to ongoing reinforcements [42]. As with the ACC, no activity was observed in OFC during low-risk decisions, relative to the ITI baseline, suggesting that OFC is involved in decision processes related to representing and choosing high-risk rewards. Thus, OFC patients, in addition to difficulties with reward-based reversal learning, may also have difficulties representing the uncertainty or risk associated with certain rewards.

We note that our OFC activation was slightly more lateral than that reported by O'Doherty (2001), in which they demonstrated that whereas medial OFC represents information about monetary rewards, lateral OFC represents losses. However, other discrepancies regarding this finding have emerged. For example, in addition to our finding, lateral OFC activation was reported in another study involving risk-taking [11], as well as in contrasts of reward > no reward in other studies [2, 39]. However, methodological differences may partly explain some of these inconsistencies. For example, in O'Doherty's study [1], medial OFC activation was elicited by comparing rewarded with nonreward trials, here we compared activity during decisions about differently sized potential and uncertain rewards. However, we have observed a more medial OFC region to be activated when directly comparing receiving vs. not receiving a reward [43]. Such a distinction between OFC subregions representing rewards and decisions related to risky rewards would further support the idea of functional heterogeneity within the OFC [39].

Connectivity analyses using OFC as the seed region revealed that, consistent with known anatomical pathways, OFC activity during decision-making was significantly correlated with activity in dorsal and medial PFC (extending into ACC), parietal and temporal cortices, as well as the striatum [14, 44]. Although patients with damage to OFC are often observed to perservate

in risk-taking behavior despite ongoing losses, a few reports have noted that patients with more extensive damage to dorsal PFC regions (sparing OFC) show similar impairments in risk-taking tasks [45-47]. Given the tight anatomical and functional connections between OFC and dorsal PFC, it is possible that damage to dorsal PFC regions additionally disrupts processes in OFC, thus causing the observed impairments.

We additionally observed that the posterior cingulate exhibited significant connectivity during high-risk but not low-risk trials. Several experiments have shown that the posterior cingulate is involved in making semantic or categorical decisions about emotionally-laden words and images [48, 49]. Our finding suggests that this region may participate in other kinds of decisions as well, and increased correlations in posterior cingulate with OFC may reflect addition emotion processing related to high-risk decisions. However, we note that this effect was not significant in a direct comparison between connectivity during high- and low-risk decisions. Indeed, no areas of the brain exhibited significantly different correlations with OFC between high- and low-risk decisions, in contrast to the corresponding analysis using ACC as the seed region. Although this seems to suggest that activity in OFC distinguishes high- from low-risk decisions yet its connectivity with other regions is relatively constant across these two types of decisions, one should be cautious when interpreting null findings, and it is also possible that changes in connectivity with OFC during different decision are more subtle than those associated with ACC, and therefore more difficult to detect.

4.3. Caveats and conclusions

We acknowledge a few caveats and limitations of the present study. First, as with many types of fMRI analyses, our connectivity data are inherently correlational, and therefore no strong claims can be made about the directions of influence. Further, although correlations

between activities in different brain regions suggest functional connectivity, it is possible that distinct brain regions could exhibit correlated time courses without being anatomically-functionally connected. However, we note that, at our threshold, activity in primary visual or motor cortices was not significantly correlated with activity in OFC and ACC, demonstrating that this analysis procedure is not modeling general task-related activity changes, and is therefore not redundant with the standard GLM approach to modeling increased activity in one condition over another. Second, our experiment focused on a decision between economically equivalent choices in order to obtain rewards. It is unclear whether our findings would generalize to other decision-making situations, such as those that involve losses or reward-based learning [6]. Finally, there are several ways of assessing functional connectivity using fMRI data [50], and it is not known whether other methods would reveal similar results. However, our methodology has been used previously [27], is similar to other methods of functional connectivity [26], and our findings are consistent with known anatomical connections of OFC and ACC [14, 16, 44].

In conclusion, we have demonstrated that ACC and OFC are significantly engaged when choosing high-risk over low-risk decisions. Further, additional techniques that allowed us to examine functional connectivity revealed that activity in other brain regions correlated highly with activity in ACC and OFC, and that some of these regions exhibited changes in connectivity as a function of participants' behavioral choices. These findings provide further evidence that neuroanatomical pathways are mirrored in functional connections, and shed new light into how regions of the brain interact with each other during decision-making.

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Region	BA	t	X	Y	Z
High>Low Risk					
R. orbital frontal	11	4.72	24	39	-12
R. cingulate	32	4.48	7	43	23
R. inferior frontal	45	4.47	52	33	20
L. middle frontal	46	4.06	43	-34	23
R. superior frontal	9	3.94	52	21	46
L. inferior parietal lobule	40	4.98	-63	-33	51
R. inferior parietal lobule	40	4.06	-45	-35	46
L. lateral temporal	37	5.23	-51	-54	-20
R. lateral temporal	37	3.82	-49	-53	-14
R. striatum		4.61	14	12	0
L. striatum		4.12	-16	16	-10
Connectivity with ACC: high-risk					
L. middle temporal	20	6.78	-56	-33	-14
R. middle temporal	21	8.82	53	-26	-6
medial OFC	11	10.94	0	50	-9
L. inferior frontal	47	5.99	-46.00	36	-19
R. inferior frontal	47	5.45	52	29	-3
L. striatum		9.19	-11	15	-4
R. striatum		10.40	7	15	3
Posterior cingulate	23	11.21	7	-54	29
L. inferior parietal	39	16.36	-49	-64	29
R. inferior parietal	39	12.61	57	-62	30
Anterior cingulate	24	44.15	3	46	25
L. precentral	43	5.10	-58	-9	33
L. middle frontal	44	3.91	-37	15	44
R. middle frontal	44	6.92	46	20	37
Dorsal cingulate	23	7.88	8	-18	47
L. cerebellum		-6.17	-38	-47	-40
R. cerebellum		-5.53	46	-54	-31
R. fusiform	19	-5.21	20	-50	-15
L. middle occipital	19	-5.10	-43	-65	-5
L. posterior insula		-3.92	-42	-20	0
L. temporal pole	48	-4.13	-61	6	2
L. posterior parietal	7	-4.56	-14	-72	51
R. posterior parietal	7	-7.35	18	-76	57
L. SMA	6	-4.99	-20	-3	59
R. SMA	6	-5.31	24	1	59
Connectivity with ACC: low-risk					
R. superior temporal	39	14.80	-52	-70	25
L. superior temporal	39	10.74	60	-70	32
R. orbitofrontal	11	7.13	-7	4	-17
R. inferior frontal	47	4.49	-52	18	-3
L. caudate	25	6.87	-10	14	-3
R. caudate	25	7.93	4	11	-3

L. cingulate	32	40.43	0	42	21
L. frontal operculum	44	5.69	-52	14	14
R. inferior frontal	38	6.06	46	28	-17
R. middle frontal	44	4.58	39	11	39
L. superior frontal	32	28.40	-3	53	21
R. insula	47	6.36	35	25	-17
R. middle occipital	39	13.47	49	-66	28
L. inferior temporal	20	4.78	-63	-38	-17
R. inferior temporal	20	5.93	56	-28	-17
R. parietal	7	-6.90	-14	-73	60
L. parietal	7	-6.82	11	-84	53
R. SMA	6	-6.73	32	-7	74
L. cerebellum		-8.55	-42	-35	-38
R. cerebellum		-9.29	42	-45	-42
L. postcentral	3	-4.50	-28	-31	49
R. postcentral	5	-6.32	11	-52	74
L. SMA	6	-5.76	-17	-7	60
R. superior frontal	6	-5.78	25	-3	60
L. precentral	6	-8.56	-28	-10	67
L. superior parietal	7	-6.45	-31	-66	56
R. superior parietal	7	-5.34	14	-59	70
R. precuneus	7	-4.54	7	-66	60
L. lingual	18	-6.43	-24	-73	-3
L. fusiform	36	-5.18	-28	0	-35
L. inferior temporal	37	-8.97	-45	-45	-24
L. inferior parietal	40	-4.90	-31	-38	42
Connectivity with ACC: High>Low risk					
medial orbital	11	4.40	0	53	-15
R. orbital frontal	11	3.99	25	43	-11
L. amygdala		4.44	21	-13	16
L. ventral striatum	-7	3.46	-7	10	-3
L. superior frontal	6	4.66	-18	0	52
L. inferior temporal	20	4.65	-48	-14	23
L. cerebellum		4.75	-38	-75	-27
R. fusiform	37	4.48	40	-42	-6
Connectivity with OFC: high-risk					
L. inferior temporal	20	5.73	-66	-45	-24
L. superior parietal	7	5.23	-24	-80	49
L. cuneus		5.71	-7	-77	39
L. cingulate	23	5.22	-3	-45	49
L. occipital	18	5.56	-3	-94	-21
R. caudate		4.72	7	21	4
R. precuneus		5.61	11	-56	53
R. paracentral	4	4.87	4	-21	74
L. angular	7	6.09	-38	-70	49
R. cuneus	7	5.05	11	-77	39
L. orbitofrontal	11	9.54	-24	39	-21
R. orbitofrontal	11	5.72	11	21	-7

L cerebellum	18	4.23	-17	-91	-21
L. superior occipital	19	4.86	-21	-87	39
R. inferior temporal	20	5.43	53	-28	-24
L. posterior cingulate	23	4.93	-3	-38	28
R. middle cingulate	24	7.30	4	21	39
L. SMA	32	4.49	-7	11	46
R. SMA	32	6.99	4	14	49
R. inferior temporal	37	4.87	56	-66	-21
L. inferior parietal	40	5.39	-45	-49	42
R. angular	40	7.70	39	-56	42
R. middle frontal	46	9.74	32	53	28
L. superior temporal	41	-5.98	49	-38	17
L. middle temporal	21	-4.90	-50	-2	-17
R. middle temporal	20	-4.97	40	4	-24
Connectivity with OFC: low-risk					
L. cerebellum		5.17	-7	-84	-24
L. superior parietal		7.46	-28	-80	49
R. precuneus		4.60	0	-56	74
R. superior frontal	6	5.91	18	7	56
L. precentral	6	4.69	-52	4	42
L. SMA	6	4.68	0	0	70
R. SMA	6	7.17	4	18	53
L. middle occipital	7	6.20	-24	-63	42
R. superior parietal	7	7.21	25	-73	49
L. middle frontal	8	8.60	-31	7	60
L. middle frontal	8	6.34	0	25	46
R. middle frontal	9	7.10	35	28	46
L. middle frontal	10	5.99	-35	60	11
L. orbitofrontal	11	10.45	-21	39	-21
R. orbitofrontal	11	50.80	18	42	-21
L. inferior temporal	20	5.45	-59	-35	-24
R. inferior temporal	20	6.09	56	-38	-21
R. angular	39	6.95	39	-59	42
L. inferior parietal	39	6.19	-45	-52	39
R. inferior parietal	40	6.29	46	-49	49
L. middle frontal	44	6.20	-49	28	35
R. inferior frontal	45	5.10	49	42	-3
R. inferior frontal	45	7.96	49	35	28
R. middle frontal	45	7.11	42	42	21
L. middle frontal	46	9.15	-45	49	14
L. superior temporal	48	-5.19	-41	-23	16
R. superior temporal	48	-5.50	42	-16	19

Table 1. List of peak voxels for activation clusters. L.=left hemisphere; R.=right hemisphere. BA=brodmann's areas.

Figure 1. Regions of the brain exhibiting significantly greater activity during high-risk compared to low-risk decisions. Top right shows a bar graph depicting the parameter estimates for high- and low-risk decisions in ACC and OFC. Error bars represent standard errors about the mean. Bottom left and right show time course plots of activity from ACC and OFC, respectively. Y-axis represents percent signal change. Gray bars indicate expected time of HRF following decision.

Figure 2. Connectivity with the ACC. (**a**) Connectivity with the ACC is shown during high-risk decisions, although during low-risk decisions, the topographical distribution of connectivity was very similar (see Results and Table 1). Yellow voxels indicate that activity correlated more positively with ACC during the decision than during the ITI, blue voxels indicate that activity correlated more negatively during the decision than during the ITI. (**b**) Top right and lower left: Areas that showed significantly greater connectivity with ACC during high-risk compared with low-risk trials.

Figure 3. Areas that exhibited significant connectivity with OFC during high-risk (left) and low-risk (right) decisions.

Figure 1.

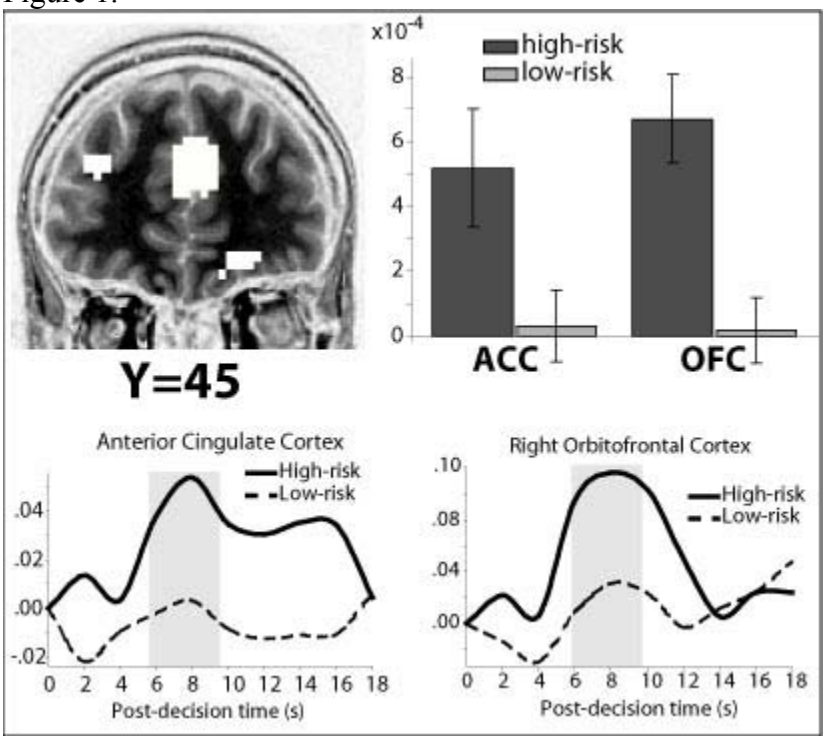
x10-4
high-risk
low-risk
8
6
4
2
0
ACC
OFC
Y=45
Anterior Cingulate Cortex
High-risk
Low-risk
.04
.02
.00
-.02
0 2 4 6 8 10 12 14 16 18
Post-decision time (s)
Right Orbitofrontal Cortex
.10
.08
.04
.00
High-risk
Low-risk
0 2 4 6 8 10 12 14 16 18
Post-decision time (s)

Figure 2.

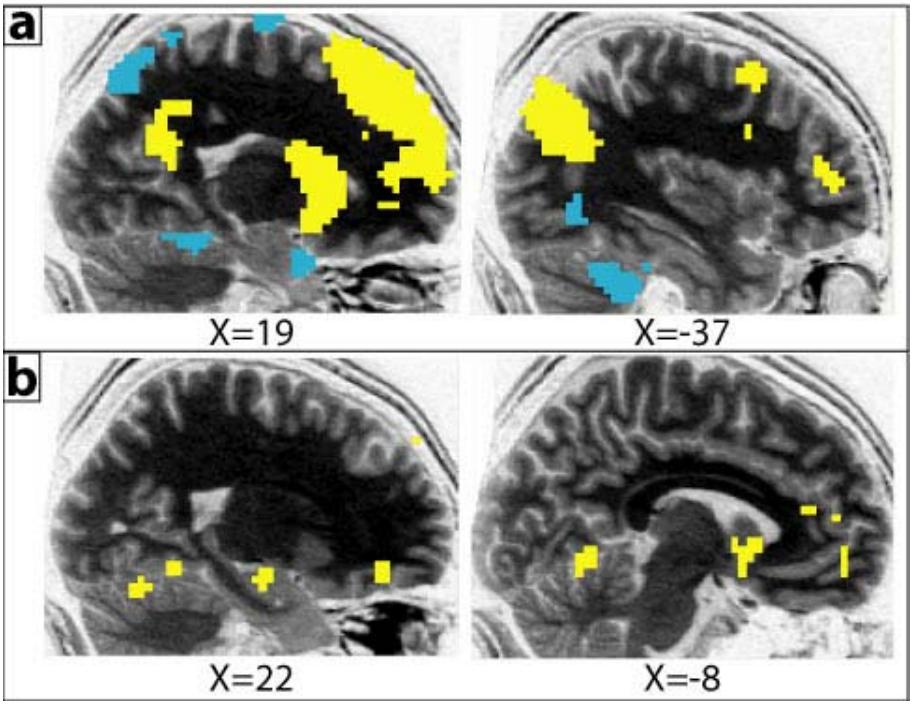

Figure 3.