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Distinct neural mechanisms of risk and ambiguity: A meta-analysis of decision-making

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Converging evidence from human and animal studies suggests that decision-making relies upon a distributed neural network based in the frontal lobes. In particular, models of decision-making emphasize the involvement of orbitofrontal cortices (OFC) and the medial wall. While decision-making has been studied broadly as a class of executive function, recent models have suggested the differentiation between risky and ambiguous decision-making. Given recent emphasis on the role of OFC in affectively laden "hot" executive function and dorsolateral prefrontal cortex (DLPFC) in more purely cognitive "cool" executive function, we hypothesize that the neural substrates of decision-making may differ depending on the nature of the decision required. To test this hypothesis, we used recently developed meta-analytic techniques to examine the existent functional neuroimaging literature. An initial meta-analysis of decision-making, both risky and ambiguous, found significantly elevated probabilities of activation in frontal and parietal regions, thalamus, and caudate. Ambiguous decision-making was associated with activity in DLPFC, regions of dorsal and subcallosal anterior cingulate cortex (ACC), and parietal cortex. Risky decision-making was associated with activity in OFC, rostral portions of the ACC, and parietal cortex. Direct statistical comparisons revealed significant differences between risky and ambiguous decision-making in frontal regions, including OFC, DLPFC, and ACC, that were consistent with study hypotheses. These findings provide evidence for the dissociation of neural circuits underlying risky and ambiguous decision-making, reflecting differential involvement of affective "hot" and cognitive "cool" processes.

In recent years, there has been a growing interest in understanding the neural mechanisms underlying decision-making. In part, this reflects the increasing number of psychiatric disorders in which impaired decision-making has been noted, such as substance abuse/dependence, and disorders of conduct, attention, and anxiety. Converging evidence from neuropsychological, neuroimaging, and animal studies suggest that decision-making is supported by a distributed network of brain regions that includes orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), thalamus, parietal cortices, and caudate (see Ernst and Paulus, 2005 for a review). The OFC, in particular, has been identified as a key element of this network and, as a result, has received significant attention for its role in decision-making. Neurophysiological studies of rats and non-human primates suggest that OFC represents incentive information needed to guide performance (Schoenbaum and Setlow, 2001). Neuropsychological and neuroimaging studies of reward-based decision-making tasks in humans provide further support for OFC involvement in representing incentive information (Elliott et al., 2000). Furthermore, populations with impaired decision-making demonstrate abnormalities in OFC, further confirming a link between OFC function and psychopathological states (Bechara and Damasio, 2002; Blair et al., 2001; Bolla et al., 2003; Mitchell et al., 2002).

Neuroimaging studies of decision-making commonly compare decisions made under uncertain conditions with those made under certain conditions to identify underlying neural substrates. According to Bechara and colleagues (2005), decisions made under uncertain conditions can be divided into "decisions involving risk" and "decisions involving ambiguity." In decisions involving risk, the probability of each outcome is known and participants must decide between a safe choice and a risky choice. Safe choices have a high probability of gaining a reward, but the reward is relatively low in value. In contrast, risky choices have a low probability of gaining a reward, though the reward is substantially larger in value. Two examples of commonly used tasks that utilize decisions involving risk are the Iowa Gambling Task (Bechara et al., 1994, 1996) and the Cambridge Risk Task (Rogers et al., 1999).

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Decisions involving ambiguity are distinct from decisions involving risk in two ways. First, in ambiguous decisions, the probability of a specific outcome is either unknown or close to chance. Second, the two choices do not differ in reward value. For example, in the two-choice prediction task, the participant chooses on which side of a house a car will appear (Paulus, 1997). The probability of the car appearing on the left side of the house is identical to it appearing on the right side and there is no risk associated with choosing one side or the other.

While it is possible that risky and ambiguous decisions may rely on the same underlying neural mechanisms, as both require a choice without certain knowledge of the outcome, it is equally possible that different neural circuits may support these two qualitatively distinct forms of decision-making. A recent model of executive function proposed by Zelazo and Muller may provide some insight into possible differences in the neural substrates underlying these two types of decision-making (Zelazo and Muller, 2002). They theorize that executive functions (EF) such as decision-making can be divided into "hot" and "cool" subtypes. Hot EF relies on affective inputs and is associated with the OFC, whereas cool EF is characterized by more purely cognitive processes that are served predominantly by the DLPFC. Hot decision-making paradigms are those that involve risks and rewards, such as gambling tasks (Kerr and Zelazo, 2004). Evidence from lesion and neuroimaging studies using these tasks demonstrate the role of the OFC in making risky decisions, thereby providing support for the hot EF theory (Bechara, 2001; Ernst et al., 2002). Conversely, ambiguous decision-making tasks that require a selection from among responses of equal valence and do not involve risk may be considered cool. This is supported by neuroimaging studies of 'willed action' which demonstrate DLPFC activation when subjects are making a choice from among several responses without an explicit risk or reward (Hyder et al., 1997; Frith et al., 1991).

To date, no studies have sought to directly compare the neural correlates of these similar yet distinct cognitive processes. Understanding the similarities and differences may allow us to

Table 1
List of studies included in meta-analysis

Article	Imaging modality	*N*	Task	Contrasts	Foci
Risky DM					
Bolla et al., 2003	PET	13	IGT	Task vs. Control	1
Bolla et al., 2004	PET	20	IGT	Task vs. Control	7
Bolla et al., 2005	PET	11	IGT	Task vs. Control	3
Cohen et al., 2005	fMRI	16	Decision game with low-risk and high-risk choices	High risk > low risk	5
Ernst et al., 2002	PET	20	IGT	Task vs. Control	22
Ernst et al., 2004	fMRI	20	Wheel of Fortune	Task vs. Control	27
				High reward/risk > low reward/risk	28
Ersche et al., 2005	PET	15	CRT	Task vs. Control	9
Fishbein et al., 2005	PET	14	CRT	Task vs. Control	11
Fukui et al., 2005	fMRI	14	IGT	Risky vs. Safe decisions	2
Matthews et al., 2004	fMRI	12	Lane Risk Taking Task	Risky vs. Safe responses	4
Paulus et al., 2003a,b,c	fMRI	17	Risky-Gains Decision-Making Task	Risky vs. Safe responses	5
Rogers et al., 1999	PET	8	CRT	Task vs. Control	17
				Risky vs. Safe	3
Rubinsztein et al., 2001	PET	10	CRT	Task vs. Control	5
Uncertain DM					
Blackwood et al., 2004	fMRI	8	Balls in a bottle, Personality survey	Uncertain > Certain	6
Critchley et al., 2001	fMRI	8	Two-choice card task	Parametric modulation of activity by degree of uncertainty	4
Elliott et al., 1999	fMRI	5	Card-playing task	Predicting vs. Reporting	12
O'Doherty et al., 2003	fMRI	15	Choice reversal task	Choice vs. Imperative	12
Paulus et al., 2001	fMRI	12	Two-choice prediction task	Prediction > Response	8
Paulus et al., 2002a	fMRI	10	Two-choice prediction task	Prediction > Response	11
Paulus et al., 2002b	fMRI	16	Two-choice prediction task	Prediction > Response	6
Paulus et al., 2002c	fMRI	15 SZ, 15 NC	Two-choice prediction task	Prediction > Response	29
Paulus et al., 2003a	fMRI	14 MA, 14 NC	Two-choice prediction task	50% error rate vs. 20% and 80% error rates	2
Paulus et al., 2003b	fMRI	17 SZ, 16 NC	Two-choice prediction task	Task × Error rate	16
Paulus et al., 2004	fMRI	26	Two-choice prediction task	Task × Error rate	5
Paulus et al., 2005	fMRI	12	Rock, paper, scissors	Action selection > Outcome	5
Verney et al., 2003	fMRI	17	Two-choice prediction task	Task × Error rate	12
Yarkoni et al., 2005	fMRI	28	Card decision task	Uncertain > more certain	10

PET = Positron Emission Tomography, fMRI = functional magnetic resonance imaging; IGT = Iowa Gambling Task, CRT = Cambridge Risk Task; SZ = schizophrenic patients, NC = normal controls, MA = methamphetamine-dependent patients.

generate more specific hypotheses regarding decision-making processes, and the ways in which they can be impaired in psychiatric populations. The present work utilizes recently developed meta-analytic techniques to examine the existent functional imaging literature to determine if decisions involving risk and those involving ambiguity rely on the same underlying neural circuitry. We conducted a quantitative meta-analysis of studies of both types of tasks, ambiguous and risky decision-making, to provide an overview of the regions commonly found to be active during these tasks. Then, we conducted individual meta-analyses of each type of task alone. This allowed us to examine regions which may be associated with each distinct type of decision-making and to make direct comparisons using subtraction methods. Based on the hot–cool EF distinction, we hypothesized that risky tasks would be associated with more OFC activation while ambiguous tasks would show more DLPFC activity.

Methods

Research papers were found primarily by searching the PUBMED database (http://www.pubmed.org) using the keywords: *neuroimaging*, *fMRI*, *PET*, and *brain* cross-referenced with *gambl** and *decision making*, where * indicates a wild-card. We then reviewed the reference lists of each of these articles to obtain additional papers. Only articles that reported activation foci as 3D coordinates (x, y, z) in stereotactic space were included. Studies of clinical populations were only used if coordinates were available for the normal controls or for the total sample (controls and patient population combined).

The 27 studies identified (see Table 1) were split into two groups: risky decision-making (risky DM) and ambiguous decision-making (ambiguous DM) based on the following criteria. Studies were categorized as risky if they used a task that required a choice between high risk and low risk options. Studies of the Iowa Gambling Task and the Cambridge Risk Task were included in this group. Coordinates were included from within-task comparisons of risky vs. safe decisions and between-task comparisons (e.g., gambling vs. control tasks). Papers were selected for the ambiguous DM group if they utilized a task in which the choices in the condition of interest (i.e., the ambiguous condition) did not differ markedly in either probability or magnitude of the outcome. Coordinates were selected from between-task contrasts comparing activity while decisions were being made with activity during a motor control task. Additional within-task coordinates were included from contrasts examining activation across levels of uncertainty or error rate. Coordinates from studies that used the Montreal Neurological Institute (MNI) system were transformed to Talairach coordinate space (Brett, 1999).

All meta-analyses were carried out using the activation likelihood estimation (ALE) technique (Turkeltaub et al., 2002) implemented in BrainMap (Laird et al., 2005). Our primary meta-analysis included the coordinates from all studies of decision-making. Activation likelihood estimates were calculated for each voxel by modeling each coordinate with an equal weighting using a 3-D Gaussian probability density function with FWHM = 10 mm. We next carried out a permutation test to determine the voxel-wise significance of the resulting ALE values. More specifically, we made use of a non-parametric statistical approach previously described by Turkeltaub et al. (2002), in which 5000 permutations were generated using the same number of foci and FWHM as used to generate the ALE map. As such, no assumptions were made with respect to the distribution or spatial separation of these random foci (Laird et al., 2005; Turkeltaub et al., 2002). Resulting statistical maps were corrected for multiple comparisons using false discovery rates (FDR), and then thresholded at $p < 0.05$, corrected, with a cluster extent threshold of 8 voxels.

Next, separate meta-analyses were conducted with the ambiguous DM and risky DM groups using the same approach described above. To directly compare these groups, we used the ALE maps generated for each group to calculate ALE difference maps, risky-ambiguous and ambiguous-risky. Each of these difference maps was entered into a permutation analysis to generate voxel-wise statistical scores, as was previously done for the individual meta-analyses.

Results

Decision-making

Using the search criteria specified above, we identified 27 studies of decision-making, yielding a total of 287 foci. Consistent with current models of decision-making, our meta-analysis revealed a distributed network of structures exhibiting significantly elevated probabilities of activation (see Table 2). These regions included OFC, DLPFC, insular cortex and ACC in the frontal lobes, precuneus and bilateral superior parietal lobules in parietal

Table 2
Decision-making ALE analysis

Region	Cluster size	*x*	*y*	*z*	BA	Mean *p*-value
Orbitofrontal/medial wall						
Lateral orbitofrontal (L)	972	−26	42	1	10/44	0.013
Superior frontal gyrus (R)	38	32	54	−4	10	0.010
Medial frontal gyrus (L)	883	−10	34	32	9	0.012
Lateral frontal						
Middle frontal gyrus (R)	65	28	4	58	6	0.011
Inferior frontal gyrus (L)	395	−36	21	7	13	0.013
Inferior frontal gyrus (R)	39	44	42	8	46	0.010
Insula (R)	16	34	17	2	–	0.010
Parietal						
Inferior parietal lobule (L)	367	−48	−43	51	40	0.011
Superior parietal lobule (L)	155	−30	−59	48	7	0.012
Superior parietal lobule (R)	141	30	−51	55	7	0.012
Superior parietal lobule (L)	82	−12	−66	57	7	0.012
Precuneus (L)	84	−4	−53	51	7	0.012
Precuneus (R)	48	12	−64	63	7	0.010
Postcentral gyrus (R)	26	54	−30	48	40	0.010
Postcentral gyrus (R)	21	20	−34	71	3	0.010
Other						
Caudate (L)	67	−6	20	−1	–	0.011
Caudate (L)	21	−6	2	19	–	0.010
Caudate (R)	15	14	9	6	–	0.010
Thalamus (L)	78	−8	−12	18	–	0.012
Cerebellum (L)	26	−4	−78	−16	–	0.010
Middle occipital gyrus (L)	24	−30	−83	1	18	0.010
Middle occipital gyrus (R)	14	32	−79	8	19	0.011
Fusiform gyrus (R)	106	42	−68	−8	19	0.012
Middle temporal gyrus (L)	20	−38	−80	23	19	0.010

*False Discovery Rate (FDR) corrected *p*-values.

Table 3
Ambiguous decision-making

Region	Cluster size	x	y	z	BA	Mean p-value
Medial wall						
Anterior cingulate (L)	217	−10	32	−2	32	0.008
Cingulate gyrus (L)	180	−4	22	37	32	0.009
Lateral frontal						
Superior frontal gyrus (L)	202	−30	45	26	9	0.010
Superior frontal gyrus (R)	9	40	40	30	9	0.007
Middle frontal gyrus (R)	102	28	2	60	6	0.009
Middle frontal gyrus (R)	8	46	15	44	8	0.007
Inferior frontal gyrus (L)	53	−46	16	19	45	0.009
Insula (R)	10	34	17	7	13	0.007
Insula (L)	119	−34	19	13	13	0.011
Parietal						
Precuneus (L)	308	−8	−59	53	7	0.010
Inferior parietal lobule (L)	115	−40	−47	47	40	0.009
Inferior parietal lobule (R)	43	46	−49	53	40	0.008
Inferior parietal lobule (R)	23	52	−26	44	40	0.007
Superior parietal lobule (R)	130	12	−66	61	7	0.009
Angular gyrus (R)	14	52	−54	33	40	0.007
Other regions						
Caudate (R)	8	4	9	10	–	0.007
Thalamus (L)	118	−8	−12	18	–	0.011
Postcentral gyrus (R)	56	20	−34	71	3	0.008

*False Discovery Rate (FDR) corrected p-values.

cortex, thalamus, and caudate. These results reflect the complex nature of decision-making, relying upon a variety of regions involved in response selection, response conflict, reward processing, and attentional control.

Ambiguity

Our review of the literature identified 14 studies of ambiguous decision-making that met our inclusion criteria, yielding a total of 138 foci. Consistent with our hypothesis, the ALE meta-analysis identified regions of DLPFC with significantly elevated probabilities of activity bilaterally (see Table 3). While there is clear evidence of DLPFC activity, there was no evidence of consistent orbitofrontal involvement across studies. Additional frontal areas of elevated probability of activity were noted within the dorsal and subcallosal regions of ACC (BA 32), as well as bilateral insular cortex.

Our ALE analysis suggested that posterior regions also play a role in ambiguous DM. In particular, multiple areas of parietal cortex showed significantly elevated probabilities of activity, including precuneus (BA 7), the lateral aspects of the inferior parietal lobule bilaterally (BA 40), and right superior parietal lobe (BA 7).

Risk

Our review of the literature identified 13 studies of risky decision-making that met our criteria for inclusion in the ALE meta-analysis, yielding a total of 149 foci. Consistent with our hypothesis, the ALE meta-analysis detected significant areas of activity bilaterally in OFC, centered in BA 10 (see Table 4). Of note, while clusters of OFC activity were detected in the right hemisphere, the most extensive activation was found in the left hemisphere, with a cluster of 1871 voxels extending from the anteriormost aspect of middle frontal gyrus (BA 10) caudally to insular cortex and dorsally to anterior cingulate (BA 8/ 9). Thus, overall, frontal involvement in risky decision-making appears to be primarily dependent upon orbitofrontal and medial frontal cortices.

Significantly elevated probabilities of activation found in parietal regions differed from those found in the ambiguous DM analysis. Risky DM was associated with activity in left inferior parietal lobe (BA 40) and lateral areas of the superior parietal lobe bilaterally (BA 7). Other notable activations were found in the left caudate, bilateral occipital cortex, and middle temporal gyrus (BA 21).

In light of the large number of PET studies in the risky DM group (5 out of 8), we compared activations in studies using PET to those using fMRI. While overall significance levels were lower due to decreased statistical power, there were no significant differences between the two techniques.

Risk vs. ambiguity

Overall, individual meta-analyses clearly suggest that the neural substrates for risky decisions are functionally dissociable from those involved in handling ambiguity. Direct statistical comparisons of the ALE maps for risk and ambiguity (risk > ambiguity, ambiguity > risk) provide further support for the presence of such dissociations (see Table 5, see Fig. 1). First, the comparison of risk > ambiguity revealed a significantly greater probability of activation in OFC, while ambiguity > risk revealed a greater probability of activation in DLPFC. Second, as suggested by the individual meta-analyses, functionally dissociable regions were noted within the medial wall. More specifically, in dorsal regions of ACC, the comparison of ambiguity > risk demonstrated greater probability of activation in caudal regions (BA 32), while risk >

Table 4
Risky decision-making

Region	Cluster size	x	y	z	BA	Mean p-value
Orbitofrontal/Medial Wall						
OFC/Anterior cingulate (L)	1871	−20	39	14	9	0.010
Middle frontal gyrus (R)	93	32	56	0	10	0.008
Inferior frontal gyrus (R)	48	46	42	6	46	0.008
Lateral frontal						
Middle frontal gyrus (L)	28	−32	18	61	6	0.007
Parietal						
Inferior parietal lobule (L)	273	−50	−41	53	40	0.010
Superior parietal lobule (R)	219	30	−51	55	7	0.011
Superior parietal lobule (L)	196	−30	−59	50	7	0.011
Other						
Caudate (L)	117	−12	18	−3	–	0.008
Thalamus (L)	9	−2	−2	16	–	0.007
Precentral gyrus (R)	11	40	5	36	9	0.007
Middle temporal gyrus (L)	29	−62	−44	−4	21	0.007
Middle occipital gyrus (R)	179	42	−68	−8	19	0.011
Middle occipital gyrus (R)	123	32	−82	12	19	0.008
Middle occipital gyrus (L)	55	−30	−83	1	18	0.009
Declive (L)	106	−4	−76	−16	–	0.008
Declive (R)	32	14	−80	−14	18	0.008

*False Discovery Rate (FDR) corrected p-values.

Table 5
Differences between ambiguity and risk ALE maps

Region	Cluster size	x	y	z	BA	Mean p-value
Ambiguity > Risk						
Medial wall						
Anterior cingulate (L)	44	−4	32	−2	24	0.007
Cingulate gyrus (L)	87	−6	22	35	32	0.009
Lateral frontal						
Middle frontal gyrus (L)	137	−30	45	24	10	0.010
Middle frontal gyrus (R)	74	28	2	60	6	0.009
Middle frontal gyrus (R)	11	46	15	44	8	0.007
Inferior frontal gyrus (L)	17	−46	16	20	9	0.008
Superior frontal gyrus (R)	11	42	40	30	9	0.007
Insula (L)	27	−36	19	15	13	0.008
Parietal						
Superior parietal lobule (L)	301	−8	−59	53	7	0.010
Precuneus (R)	120	12	−66	61	7	0.009
Inferior parietal lobule (R)	44	46	−49	53	40	0.008
Other						
Thalamus (L)	111	−8	−14	18	–	0.010
Postcentral gyrus (R)	57	20	−34	71	3	0.008
Risk > Ambiguity						
Orbitofrontal/medial wall						
Medial frontal gyrus (L)	1080	−24	44	8	10	0.011
Middle frontal gyrus (R)	84	32	56	0	10	0.008
Inferior frontal gyrus (R)	34	46	40	6	46	0.008
Superior frontal gyrus (R)	231	2	29	44	8	0.009
Lateral frontal						
Middle frontal gyrus (L)	29	−32	16	61	6	0.007
Insula (L)	75	−32	21	4	13	0.009
Precentral gyrus (R)	8	40	3	36	6	0.007
Parietal						
Superior parietal lobule (R)	201	30	−51	55	7	0.011
Inferior parietal lobule (L)	190	−50	−41	54	40	0.010
Superior parietal lobule (L)	162	−30	−59	50	7	0.011
Other						
Caudate (L)	61	−12	18	−3	–	0.008
Middle occipital gyrus (R)	130	32	−82	14	18	0.008
Middle occipital gyrus (L)	63	−30	−83	1	18	0.009
Lingual gyrus (R)	17	14	−80	−15	18	0.008
Declive	113	−4	−76	−16	–	0.008
Fusiform gyrus (R)	179	42	−66	−8	19	0.010
Middle temporal gyrus (L)	29	−62	−42	−4	21	0.007

*False Discovery Rate (FDR) corrected p-values.

ambiguity showed more rostral activation (BA 8). Additional activity was found in the subcallosal portion of BA 24 in the ambiguity > risk contrast. Finally, direct comparisons verified the presence of functional dissociations in parietal cortices, with greater probability of activation being detected in bilateral superior parietal regions for risk > ambiguity comparisons, and precuneus for ambiguity > risk. Inferior parietal activity was greater in the left hemisphere for the risk > ambiguity contrast and greater in the right for ambiguity > risk.

To address the concern that the differences between risk and ambiguity may be in part the result of the different number of foci in the two ALE maps, we randomly selected and removed 9 foci from the risky DM meta-analysis and recalculated the difference map with the reduced set of foci. Permutation analyses yielded an identical pattern of results.

Discussion

Our findings suggest that the neural substrates of decision-making vary depending on the nature of the decision being made. Using recently developed meta-analytic techniques, we demonstrated dissociable patterns of neural activity in frontal and parietal cortices between decisions involving risk and those involving ambiguity.

The most notable distinction revealed by our analyses is the differential involvement of orbitofrontal and lateral frontal cortices in decision-making, with increases in OFC activity more likely to occur during tasks involving risk and those in DLPFC activity more likely to occur during tasks involving ambiguity. These findings are consistent with Zelazo and Muller's recently developed framework of executive function. Risky decisions, which possess a clear affective, or hot, component, were associated with activity in OFC, while ambiguous decisions, which are less affectively laden or cool, relied primarily on DLPFC.

Similar to recent studies of top-down cognitive control (Kiehl et al., 2000; Milham and Banich, 2005; van Veen et al., 2001), our examination of decision-making demonstrated the presence of functionally differentiated sub-regions within ACC. While both risky and ambiguous decision-making activate ACC, risky decisions were associated with activity in a more rostral portion of BA 32 as well as nearby areas of pre-supplementary motor area (BA 8/9). This distinction is consistent with a growing literature showing a greater involvement of rostral ACC areas in affective processes (e.g., error-related processing, conflict detection), and of more caudal portions in pure cognitive processes (e.g., response facilitation/inhibition) (Kiehl et al., 2000; Milham and Banich, 2005; van Veen et al., 2001). Of note, ambiguous decisions appear to activate a sub-callosal region of cingulate not seen with risky decisions. This may be somewhat surprising as this region is typically associated with psychiatric disorders characterized by emotional dysregulation, and is thought to be connected to OFC, a region not consistently activated for ambiguous decisions. While further examination and characterization of this sub-callosal region is needed, the present data suggest that this region can act independently of OFC despite their intimate connections. Furthermore, the activation of this region suggests the presence of a possible affective component in ambiguous decisions, though still markedly less than in risky decisions.

Parietal activation is common to many cognitive and sensory stimuli (Culham and Kanwisher, 2001). Regions of the parietal cortex, specifically BA 7, have been implicated in attentional processes, which may explain why clusters within this region were significant in both types of decision-making. However, risky decision-making was associated with greater activity in the left inferior parietal lobe, while ambiguous decision-making showed greater activation on the right. This dissociation may reflect the need for numeric evaluation and comparison in the risky decision-making tasks, which are processes associated with left parietal activity (Pesenti et al., 2000; Sandrini et al., 2004). In contrast, the ambiguous decision-making tasks do not involve explicit numerical computations.

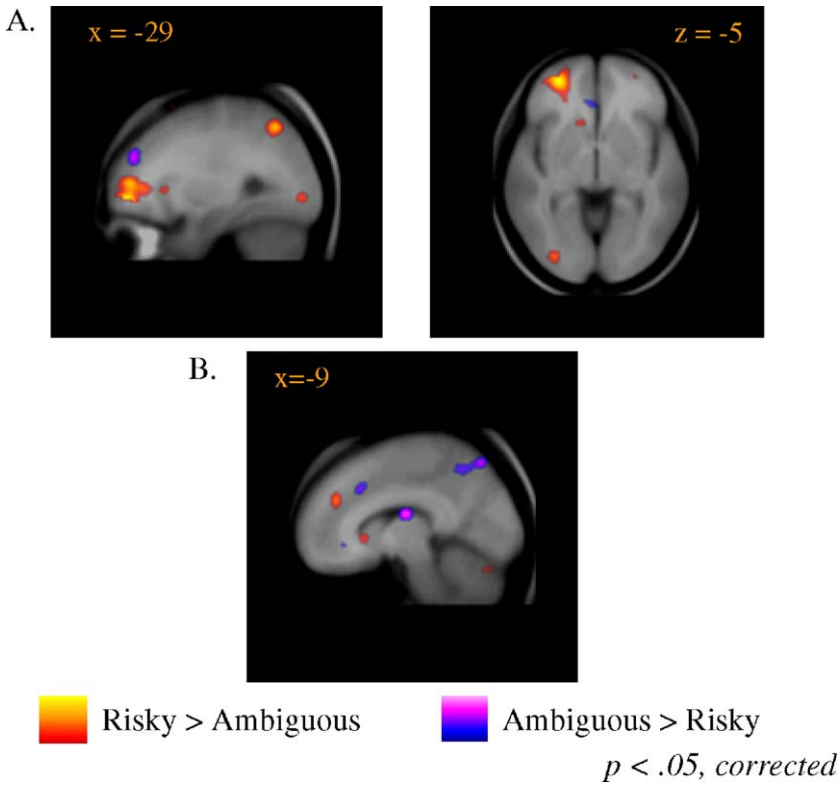

Fig. 1. Results of risky Dm vs. ambiguous DM contrast at a threshold of $p < .05$, corrected. (A) Significantly elevated probabilities of activation in orbitofrontal regions ($x = -29$, $z = -5$). (B) Significantly elevated probabilities of activation in medial wall ($x = -9$).

While the functional dissociations revealed by our meta-analyses are intriguing, some methodological limitations must also be considered. First, unlike other meta-analytic techniques, the ALE procedure does not take into account the number of foci contributed by each study, raising potential concerns about the relative contributions of each study. Though a valid concern, each comparison can only report a single focus once—as such, each comparison has equal weight in determining the likelihood of activation for a particular focus. A related issue is the use of tight comparisons (e.g., risky choice–safe choice) in some studies and loose comparisons (e.g., IGT-control) in others. While greater reliance on tight comparisons may result in detection of a more limited subset of regions for a particular group of studies, differences in the nature of comparisons would not account for the detection of functionally dissociable regions noted in our work. Additionally, the number of tight and loose comparisons did not differ systematically between groups in the current study.

Another source of potential bias is the inclusion of multiple studies from the same investigator(s), which is difficult to avoid when studying a highly specific cognitive construct. However, the use of different, and therefore independent, samples in each study helps to minimize this bias. Also, some studies reported data from patient and healthy control populations, as well as comparisons between them. In these cases, we only included those activations noted in both populations and those in healthy subjects alone. To address the concern that including patient populations may have biased our results, we repeated analyses without studies including patient populations. We confirmed the same pattern of activations, though the results were less robust due to the loss of statistical power.

The aim of this meta-analytic technique is to highlight the presence of *consistent* findings across studies; as a result, some foci, despite being significant in individual comparisons, are not detected. Clearly, individual studies have demonstrated involvement of OFC regions during ambiguous decision-making (Elliott et al., 1999; Paulus et al., 2001). The lack of significant ambiguity-related OFC activity found in our study may be explained by several factors. First, as discussed by Rolls (2004), OFC is a heterogeneous structure, similar to prefrontal and medial frontal cortices. The specific location of OFC activations associated with ambiguity may be highly variable across studies, limiting the ability of our meta-analytic technique to detect consistent significant activity in this region. Second, fMRI is limited in its ability to detect activations in medial OFC due to susceptibility artifacts; the extent to which the artifacts vary from study to study may also impact the ability to detect consistent OFC activations. This is especially true for medial areas of OFC, within which neither of our meta-analyses detected activation. Finally, OFC activation may be highly sensitive to design parameters, which suggests that greater attention to specific task components is needed when designing paradigms for the study of ambiguity.

In conclusion, these findings draw attention to differences in the neural substrates of decision-making depending on the nature of the decision being made. While risky decision-making relies on areas such as OFC and rostral portions of the medial wall, ambiguous decision-making relies on DLPFC and more caudal portions of ACC. These findings are consistent with recent models differentiating between affectively laden “hot” executive functions and more purely cognitive “cool” executive functions, as well as their neural substrates. This dissociation can inform our understanding of decision-making and of impairments in decision-

making found in various psychiatric disorders. Future studies of decision making in healthy and clinical populations should include both risky and ambiguous paradigms to delineate with greater specificity disruptions in these cognitive processes and their underlying neural circuits.

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