Neural Signatures of Economic Preferences for Risk and Ambiguity

Scott A. Huettel,[1,4,*] C. Jill Stowe,[2,4] Evan M. Gordon,[1]
Brent T. Warner,[1] and Michael L. Platt[3,4]
[1] Brain Imaging and Analysis Center
Duke University Medical Center
Durham, North Carolina 27710
[2] Fuqua School of Business
Duke University
Durham, North Carolina 27708
[3] Department of Neurobiology
Duke University Medical Center
Durham, North Carolina 27710
[4] Center for Neuroeconomic Studies
Duke University
Durham, North Carolina 27708

Summary

People often prefer the known over the unknown, sometimes sacrificing potential rewards for the sake of surety. Overcoming impulsive preferences for certainty in order to exploit uncertain but potentially lucrative options may require specialized neural mechanisms. Here, we demonstrate by functional magnetic resonance imaging (fMRI) that individuals' preferences for risk (uncertainty with known probabilities) and ambiguity (uncertainty with unknown probabilities) predict brain activation associated with decision making. Activation within the lateral prefrontal cortex was predicted by ambiguity preference and was also negatively correlated with an independent clinical measure of behavioral impulsiveness, suggesting that this region implements contextual analysis and inhibits impulsive responses. In contrast, activation of the posterior parietal cortex was predicted by risk preference. Together, this novel double dissociation indicates that decision making under ambiguity does not represent a special, more complex case of risky decision making; instead, these two forms of uncertainty are supported by distinct mechanisms.

Introduction

Decisions are often made in the presence of uncertainty about their outcomes. Uncertainty can refer to risk, which is present when there are multiple possible outcomes that could occur with well-defined or estimable probabilities (Bernoulli, 1738). To account for risk in decision making, early researchers developed models based on expected utility theory; specifically, the expected utility of a choice is the sum of probability-weighted utilities for each possible outcome (von Neumann and Morgenstern, 1944). The behavioral and neural correlates of decision making under risk have been frequently investigated: researchers have found that individuals differ in their preference for risk, and components of risk like probability and reward variance influence the activity of midbrain dopamine neurons as well as the activation of ventral prefrontal, insular and cingulate cortices (Bechara et al., 1999; Critchley et al., 2001; Fiorillo et al., 2003; Smith et al., 2002).

Uncertainty can also refer to ambiguity (also called Knightian uncertainty), which is present when there are multiple possible outcomes whose probabilities are unknown or are not well defined (Camerer and Weber, 1992; Ellsberg, 1961; Knight, 1921). Unlike risk in which individuals can compute the expected utility of different options, ambiguity renders the expected utility of different options incalculable directly because probabilities are unknown. Ambiguity poses a challenge for expected utility theory because people often prefer options with known probabilities to options with ambiguous probabilities, even when these choices contradict expected utility theory predictions (Becker and Brownson, 1964; Chipman, 1960; Heath and Tversky, 1991; Lauriola and Levin, 2001). Despite the prevalence of ambiguity in real-world decisions, the neural mechanisms supporting decision making under ambiguity—including whether risky and ambiguous contexts for decision making even evoke distinct neural processes—remain unknown (but see Hsu et al. [2005]).

We contrasted decision making in contexts with risk and ambiguity by examining choices between monetary gambles while human subjects were scanned by functional magnetic resonance imaging (fMRI). Each gamble involved a known outcome, a pair of outcomes with known probabilities, or a pair of outcomes with unknown probabilities (Figure 1A). We hereafter refer to these three types of gambles as "certain," "risky," and "ambiguous," respectively. The ambiguous gambles were resolved into risky or certain gambles following the subjects' overt choices; thus, they can be considered as having a second-order probability distribution (Camerer and Weber, 1992) rather than being of unknowable probability (Knight, 1921). On each trial, subjects viewed two gambles of similar expected value and chose between them (Figure 1B).

Critically for our planned analyses, we varied the probabilities and values of the gambles across trials, so that we could estimate our subjects' preferences for risk and ambiguity. Numerous studies have identified brain regions within prefrontal and parietal cortices whose activation increases during generalized decision making (Bunge et al., 2002; Platt, 2002), is greater when decisions involve risk (Paulus et al., 2001), and varies as a function of the risk in a decision (Huettel et al., 2005; Paulus et al., 2002; Volz et al., 2003). However, no prior study has heretofore linked subjective economic preferences held by individuals and their associated patterns of brain activation. Without evidence that activation in a particular region varies with subjective economic preferences, inferences about the causal mechanisms underlying risky and ambiguous decision making will be greatly limited. The goal of this study was to obtain such evidence.

*Correspondence: scott.huettel@duke.edu

A Trial Types

Risky - Certain
Ambiguous - Certain
Risky - Risky
Ambiguous - Risky

B Trial Structure

Decision (RT)

Expectation (4.5-6s)

Outcome (2s)

You won $20   You could have won $0
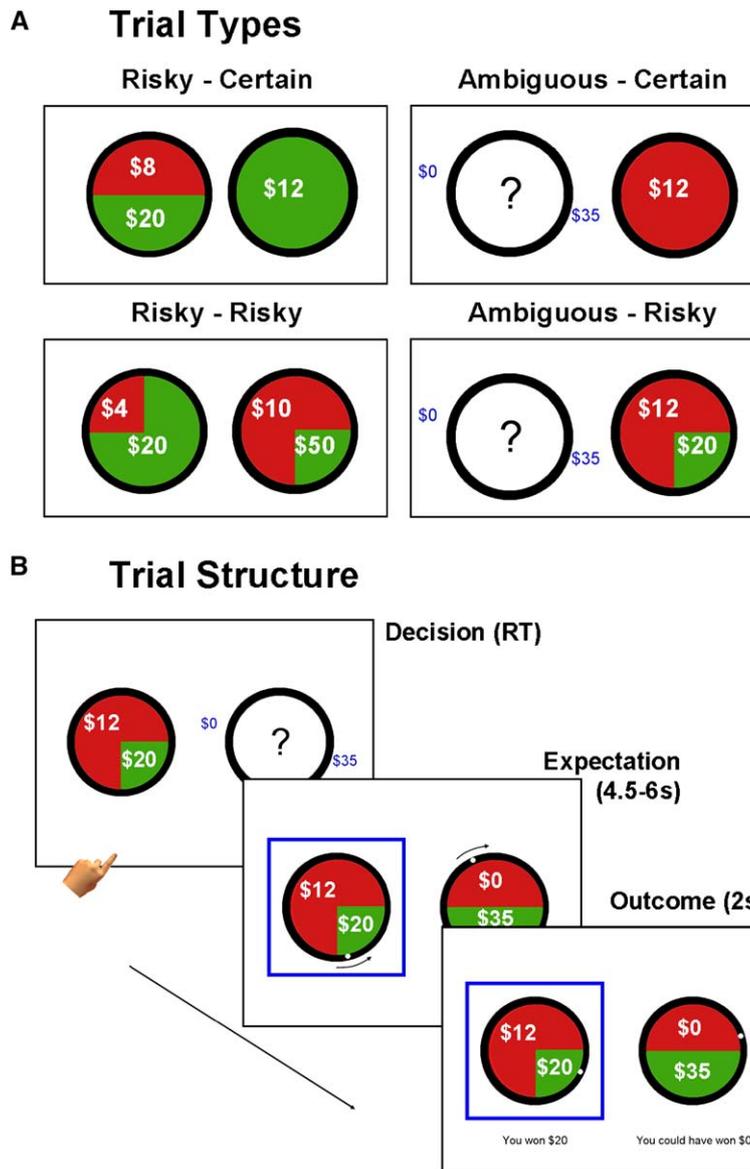
Figure 1. Experimental Design

(A) Subjects made decisions between pairs of gambles, drawn from the following types: *certain*, with a known outcome; *risky*, with two outcomes with known probabilities; and *ambiguous*, with two outcomes with unknown probabilities. Probabilities and reward values varied across trials, and expected value was roughly matched between the gambles.

(B) At the beginning of each trial, two gambles were presented and the subjects indicated their preference by pressing a joystick button. A square then appeared around the selected gamble and any ambiguity was revealed. Then, after a short delay, balls spun around the edge of the gambles like roulette wheels, and outcomes were indicated by their final position and by text below the gambles.

Results

Response Time and Economic Preference Parameters

Mean response time was fastest for decisions between ambiguous and certain (AC) gambles (mean ± st. dev.: 2.1 ± 0.5 s), intermediate for decisions between ambiguous and risky (AR) (2.5 ± 0.8 s) and between risky and certain (RC) gambles (2.7 ± 1.0 s), and slowest for decisions between risky gambles (RR) (3.4 ± 1.4 s). All differences between conditions were significant (pairwise t tests; all p values <0.01), except for the comparison of the AR and RC pairs (p > 0.1). Thus, decisions involving ambiguity were at least as fast as decisions involving only risk.

Using the choice history of each subject, we estimated subjects' preferences for ambiguity and risk, represented by the parameters α (Ghirardato et al., 2004) and β respectively (see Experimental Procedures). Values of α that are less than 0.5 indicate that a subject was ambiguity preferring, whereas values greater than 0.5 indicate ambiguity aversion. Similarly, values of β greater than 1 indicate risk preferring behavior, whereas values less than 1 indicate risk aversion. The values of these parameters were uncorrelated across subjects ($R_{12} = 0.26$, p > 0.1), indicating that for our subject sample and task, risk and ambiguity made independent contributions to the decision process. Furthermore, the estimated parameters accurately predicted our subjects' choices in the experiment, even given the near matching of expected value between gambles. The subjects' choices in the RC and RR conditions were consistent with expected utility theory because the estimates of β correctly predicted an average of 75% of the subjects' choices, with a minimum of 68% and a maximum of 86%. Likewise, subjects' choices in the AC and AR conditions were consistent with the theory of α-maxmin expected utility: the estimates correctly predicted an average of 79% of the subjects' choices, with a minimum of 71% and a maximum of 91%.

Table 1. Correlations between Cortical Activation and Behavioral Preferences

| Region | BA | MNI Coordinates | | | t Value | p Value | Correlation | | |
		x	y	z			Ambig. (1-α)	Risk (β)	Impuls.
Right pIFS	9	39	16	33	**7.2**	0.000006	**0.71**	−0.14	**−0.64**
		51	16	45	**6.8**	0.000009			
Right pIFS	8	40	6	44	**5.3**	0.000094	**0.70**	−0.20	−0.35
Right aINS	13	41	19	9	**5.5**	0.000066	0.16	−0.18	−0.47
Left pPAR	40	−36	−57	50	**7.3**	0.000004	0.16	**−0.62**	0.13

Shown are Brodmann Areas, stereotaxic coordinates, and significance values of frontal, insular, and parietal brain regions exhibiting significantly greater activation to decisions involving unknown probabilities (ambiguity) compared to decisions involving known probabilities (risk). Correlations are shown between differences in regression parameter estimates and the subjects' behavioral parameter estimates for ambiguity preference (1-α), risk preference (β), and impulsiveness (see also Figures 2 and 4). Boldface text indicates significance ($p \leq 0.01$, for correlations).

Identification of Regions Exhibiting Ambiguity Effects

We used event-related fMRI in conjunction with a general linear model analysis to identify regions within the brain that either exhibited activation to the decision phase of the task across all conditions or exhibited increased activation to decisions involving ambiguity compared to those involving only risk. Decision-related activation was observed in anterior and posterior lateral prefrontal cortices, medial frontal cortex, insular cortex, parietal cortex, the basal ganglia, and the thalamus. These regions are typical of those found in studies of decision making and executive processing (Huettel et al., 2005; Miller and Cohen, 2001; Paulus et al., 2001) and are not considered further in this manuscript.

However, a much more restricted set of regions (Table 1 and Figure 2A) showed a significantly different activation between gambles involving ambiguity and those involving risk. These regions included the posterior inferior frontal sulcus (pIFS) within lateral prefrontal cortex, the anterior insular cortex (aINS), and posterior parietal cortex (pPAR). Within pIFS, in particular, a dramatic effect of ambiguity was observed (Figures 2B and 2C). At the outset of each trial, when subjects considered their options and made a choice, activation was several times greater for decisions involving ambiguity than decisions involving risk. However, activation at the end of the trial, associated with viewing the outcome, showed a different dissociation: there was a greater response in AR and RR trials compared to those with a certain gamble. Thus, the modulatory consequences of ambiguity for pIFS were specific to the decision phase of the task. Within aINS and pPAR, in contrast, increased activation to trials with ambiguity was present but much less pronounced (Figures 2B and 2C).

Predicting Prefrontal and Parietal Activation from Economic Preferences

The results in Figure 2 demonstrate that activation within a selected set of regions, notably the lateral prefrontal cortex, increases when ambiguity is present. However, these activations are not themselves sufficient for assigning function to these regions, in the absence of any relation to behavior. Therefore, we next examined the correlations between ambiguity and risk effects on fMRI activation and subjects' economic preference parameters. To obtain a measure of decision-related activation, we determined the amplitude of the decision-phase regressors for each trial type within our analysis

model (see Experimental Procedures). These "fMRI parameter estimates" are not measures of absolute signal intensity, nor do they signal the goodness of fit of the model. Instead, they provide a measure of the relative strength of the neural response that can be attributed to each trial type during the decision phase.

We first used the single (mean) preference parameter value for each subject that best predicted choices (Figure 3). Note that for ambiguity we plot the quantity 1-α, rather than α, so that increasing values indicate increasing ambiguity preference (as for risk). Across subjects, the ambiguity effect in the fMRI signal ([AC + AR] − [RC + RR]) in pIFS was significantly and positively correlated with the best-fit ambiguity preference quantity 1-α ($R_{12} = 0.71$, $p = 0.003$); that is, ambiguity evoked the greatest increase in pIFS activation in those subjects who had the greatest preference for ambiguity. No other region's activation was significantly correlated with behavioral preferences for ambiguous options (all p's > 0.1). We found the opposite effect in pPAR, for which there was a significant correlation between the risk effect ([RC + RR] – [AC + AR]) and the best-fit risk preference parameter β ($R_{12} = 0.61$, $p = 0.01$). That is, increased preference for risk predicted a relative increase in pPAR activation on risky trials. No other region's activation was significantly correlated with risk preference (all p's > 0.1). We additionally evaluated whether these significant correlations might have been influenced by outliers by removing each of the subjects in turn and repeating the correlation analysis with the remaining 12 subjects. In every case, the correlation was significant at the p < 0.05 level ($R_{11} > 0.47$).

To verify the robustness of these brain-behavior relations, we used a resampling procedure, as described in the Experimental Procedures. The results of the resampling analysis (Figure 4) completely confirmed the pattern observed when only using the mean parameter values. Across all iterations, activation in the right pIFS was significantly correlated with the ambiguity preference quantity 1-α at p < 0.001 on 30.8% of iterations, at p < 0.01 on 99.1% of iterations, and at p < 0.05 on 100% of iterations. A nonsignificant correlation (p > 0.05) was never observed across 10,000 samples. Similar analyses for ambiguity preferences were also conducted for aINS and pPAR, but no samples were observed with significant correlations (p < 0.05). When examining samples of risk preference parameters, we found that activation of the pPAR was significantly correlated with risk preference parameters on every sample

A Ambiguity effects

A Ambiguity Preference   B Risk Preference

Figure 3. Subjective Economic Preferences Predict Changes in Brain Activation

Each subject's mean preference value and fMRI parameter value is indicated by a single square. Crosses indicate the point of neutral ambiguity/risk preference (x axis) and the mean fMRI parameter estimate in that region (y axis). (A) Ambiguity effects were defined by subtracting activation parameters associated with risk from activation parameters associated with ambiguity. In pIFS, we found a significant positive correlation between the neural ambiguity effect in pIFS and the ambiguity preference parameter 1-α ($R_{12} = 0.71$, p < 0.01); no significant ambiguity correlations were observed in aINS or pPAR. (B) Risk effects were defined by subtracting activation parameters associated with ambiguity from activation parameters associated with risk (i.e., the opposite of the ambiguity effects). Within pPAR there was a significant negative correlation between the ambiguity effect and the risk preference parameter β ($R_{12} = -0.61$, p = 0.01). There were no significant risk correlations for pIFS and aINS.

Figure 2. Neural Substrates of Decision Making under Ambiguity Revealed by fMRI

(A) During the decision phase of the task, increased activation when ambiguity was present was found in the posterior part of the inferior frontal sulcus (pIFS) of lateral prefrontal cortex, in anterior insular cortex (aINS), and in posterior parietal cortex (pPAR). Slice locations are indicated via y coordinates.

(B) Hemodynamic time courses in the pIFS region (centroid: 39, 16, 33), aINS region aINS (centroid: 41, 19, 9), and pPAR (centroid: −36, −57, 50). Orange lines indicate decisions between ambiguous and certain gambles (AC), red lines indicate decisions between ambiguous and risky gambles (AR), cyan lines indicate decisions between risky and certain gambles (RC), and blue lines indicate decisions between risky and risky gambles (RR). The timing and mean durations of the three task phases are indicated schematically along the x axis: deciding between the gambles (solid line), expectation of the outcome of the gambles (dashed line), and reward presentation (dotted line). For illustrative purposes, the time period at which the maximum fMRI effect would be expected is indicated via shading with border indicating task phase. Visible is the large effect of ambiguity in pIFS upon the decision phase.

(C) Bars indicate the amplitude of the regression parameter (± standard error; expressed in arbitrary units) associated with the subjects' decision on each trial, for each of the four decision types (same colors as in [B]). Activation in pIFS was significantly greater for decisions involving ambiguity, with lesser but significant effects found in aINS and pPAR.

(p < 0.01, 4.3%; p < 0.05, 100%), and there were no samples in which pIFS or aINS activation correlated with risk preference parameters.

The above analyses allow us to conclude that activity in the lateral prefrontal cortex was predicted by ambiguity preferences and activity in the posterior parietal cor-

tex was predicted by risk preferences, across the entire range of possible preference parameters derived from our subject sample. However, they do not address the question of whether the observed correlations were greater in those regions than in other regions, e.g., that ambiguity preferences had a stronger relation with pIFS activation than aINS or pPAR activation. We conducted two additional tests to address this question. First, we set up a multiple regression analysis that examined the contributions of each of these three regions' activation toward predicting ambiguity or risk preferences. We found that pIFS made a significant contribution (t_9 = 2.9, p = 0.02) toward predicting ambiguity preferences, but the other regions did not. For predicting risk preferences, the contribution of pPAR approached significance (t_9 = 2.19, p = 0.06), but no other region contributed. Second, we conducted Hotelling-Williams tests to compare the relative significance of pairs of correlated correlation coefficients. For ambiguity, we found that the correlation with ambiguity preferences (i.e., 1-α) was greater for pIFS than for either the aINS or pPAR (both t_{10} = 1.8; p < 0.05, one-tailed). For risk, however, there was only a trend toward a significant difference, such that the correlation with β trended toward
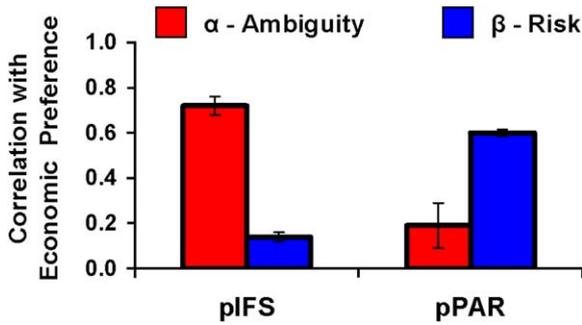
Figure 4. A Double Dissociation between Economic Preferences and fMRI Activation

To evaluate the robustness of the relations between ambiguity and risk preferences and fMRI activation, we conducted a resampling analysis in which we selected preference values randomly from each subjects' range of estimated values for both risk (β) and ambiguity (1-α). Shown are the correlations (mean ± standard deviation) obtained across 10,000 samples. A clear double dissociation was observed: ambiguity preferences correlate with changes in brain activation within pIFS, but not pPAR; risk preferences correlate with changes in brain activation within pPAR, but not pIFS.

Figure 5. Behavioral Impulsiveness Predicts Ambiguity Effects in pIFS

(A) We additionally correlated behavioral impulsiveness, as indexed by the Barratt Impulsiveness Scale (BIS), to ambiguity effects. Impulsiveness significantly predicted activation in pIFS ($R_9 = -0.64$, p = 0.01), with a trend toward significance observed in aINS, and no effect at all in pPAR.

(B) When considering only the Cognitive Impulsiveness subscale of the BIS, the correlation increased slightly in pIFS but was completely absent in the other regions. These results are consistent with the interpretation that pIFS supports the consideration of multiple interpretations of an ambiguous decision option, given that reduced pIFS activation was found in subjects who are highly impulsive and consider fewer decision options.

being larger for pPAR than for pIFS or aINS (both p's < 0.10, one-tailed).

We thus can make two conclusions about the relations between economic preferences and brain activation. Preferences for ambiguity are predicted by activation in pIFS, and this relation is stronger in pIFS than in any other region tested. Conversely, preferences for risk are predicted by activation in pPAR; however, our data do not rule out the possibility that the other regions identified may similarly contribute to risk preferences.

Predicting Prefrontal Activation from Behavioral Impulsiveness

The ambiguous stimuli used, by their very nature, are associated with a set of possible interpretations that might range from very favorable to very unfavorable. Differences in individuals' responses—whether neural or behavioral—to ambiguity might reflect their relative tendency to consider these options. When subjects act impulsively, failing to consider multiple contexts for a decision stimulus, controlled decision making may be impeded, and maladaptive outcomes may be more likely (Leland and Paulus, 2005). Inhibiting impulsive behavior is perceived to be central to decision making (Chapman and Niedermayer, 2001) and may be a cardinal function of prefrontal cortex (Miller, 2000). We therefore hypothesized that the behavioral trait of impulsiveness would be more associated with the neural processing of ambiguity than of risk.

To evaluate this potential relation, we collected psychometric data with the Barratt Impulsiveness Scale (BIS), 11th edition (Patton et al., 1995). The BIS comprises three subscales—Cognitive, Non-Planning, and Motor—which together provide an overall measure of impulsiveness. Normalized BIS values in educated young adults are about 60 ± 10 (mean ± SD), with increasing values indicating greater impulsiveness. Across subjects, impulsiveness was not significantly correlated with either ambiguity or risk preference parameters (p's > 0.1). As expected, we found that sub-

jects who were more impulsive, as evinced by increased BIS values, had faster response times than subjects who were less impulsive ($R_9 = -0.54$, p = 0.05). This negative correlation was present for all four trial types: AC, $R_9 = -0.61$; AR, $R_9 = -0.54$; RC, $R_9 = -0.50$; and RR, $R_9 = -0.49$.

However, impulsiveness was significantly and negatively correlated (Figure 5) with the ambiguity effect in pIFS ($R_9 = -0.64$, p = 0.02). Examination of subtests of the BIS revealed that the pIFS ambiguity effect most strongly correlated with cognitive impulsiveness ($R_9 = -0.70$, p = 0.01), compared to nonplanning impulsiveness ($R_9 = -0.47$, p = 0.08) and motor impulsiveness ($R_9 = -0.52$, p = 0.06). No other region's ambiguity effect was predicted by behavioral impulsiveness at the p < 0.05 level (Figures 4B and 4C). However, within the anterior insula, there was a trend toward a negative correlation between the ambiguity effect and behavioral impulsiveness ($R_9 = -0.47$, p = 0.08). Examination of the subtests of impulsiveness indicated that this effect was driven by motor impulsiveness ($R_9 = -0.60$, p = 0.03) because the cognitive and nonplanning effects were nonsignificant (p's ≥ 0.2).

We examined whether these significant correlations might have been influenced by outliers by removing each of the subjects in turn and repeating the correlation analysis with the remaining 12 subjects. For the correlation between pIFS activation and the total BIS score, removing the subject with the greatest BIS score caused the correlation to drop below significance ($R_8 = -0.41$,

p > 0.1); this was not the case for any other subject (all R_8 > −0.59, all p < 0.05). However, the correlation between pIFS activation and cognitive impulsiveness was robust to removal of any one subject (all R_8 > −0.59, all p < 0.05). Regression analyses demonstrated that activation of the pIFS ($t[6]$ = 2.73, p < 0.05), but not of the aINS or pPAR, predicted cognitive impulsiveness. No region's activation predicted a significant and independent component of the variance in total BIS score (i.e., overall impulsiveness). Note that the Hotelling-Williams test is not meaningful for these data, given the relatively few degrees of freedom. We conclude that activation in pIFS, unlike in other regions, mediates processes that counter cognitive impulsiveness in decision making.

Discussion

Understanding how the brain deals with uncertainty and how subjective economic preferences are represented neurally are two of the central motivating problems of the emerging discipline of neuroeconomics (Glimcher and Rustichini, 2004). Our study provided three novel results with implications for addressing these problems. First, we identified brain regions that showed a selective increase in activation to decision making under ambiguity, compared to decision making under risk. We demonstrated that ambiguity modulates activation in a subset of those regions generally activated by economic decision making: the pIFS, the aINS, and the pPAR. Second, we related, across subjects, changes in brain activation to calculated parameters representing economic preferences. We demonstrated, for the first time, that activation of specific brain regions is predictable based on subjects' economic preferences for ambiguity and risk. Furthermore, different regions' activations are modulated by different parameters: the lateral prefrontal cortex was modulated by preferences for ambiguity and the posterior parietal cortex was modulated by preferences for risk. Finally, we showed that behavioral impulsiveness also modulated activation in lateral prefrontal cortex, with greater activation to ambiguous decisions observed in less-impulsive subjects. Together these latter two results tell a simple and convergent story: that the lateral prefrontal cortex supports processes related to the successful resolution of ambiguity in decision making.

The Role of the Lateral Prefrontal Cortex in Resolving Uncertainty

The prefrontal cortex has been long considered to contribute to abstract thought, higher cognition, and the executive control of behavior. As evidence from cognitive neuroscience has refined this broad conception, there has been increasing recognition that executive control processes are specifically supported by regions along the lateral surface of the frontal lobe that are anterior to premotor regions and posterior to frontopolar cortex. These regions have been proposed to support a primarily regulative role, that of instantiating executive control processes to support achievement of task goals (Koechlin et al., 2003; Miller, 2000; Ridderinkhof et al., 2004).

Further, parsing the lateral prefrontal cortex into functional regions has been an area of active and ongoing research, and several frameworks for its functional topography have been advanced. Shared by most is a distinction between two types of executive control processes: contextual control, or the construction of rules for behavior based upon the current context; and episodic control, or the selection and initiation of the appropriate behavior based upon the specific stimuli presented. In these frameworks, contextual control processes are assigned to posterior regions and episodic control processes are assigned to anterior regions. For example, Koechlin and colleagues compared task cuing, which was presumed to be primarily contextual, and response cuing, which was presumed to be primarily episodic (Koechlin et al., 2003). Activation to the contextual cuing was observed in posterior lateral prefrontal cortex (centroid x, y, z: 36, 8, 28), which overlaps with the pIFS activation from the present study, although their region tends to be more inferior and more left lateralized. A similar conclusion was reached by Brass and von Cramon (2004), who investigated the brain systems involved in the selection of task context (i.e., what information is relevant for a decision and in what context that information should be evaluated). Although our economic decision-making task differs greatly from the perceptual cuing task of Brass and von Cramon, our activation foci in pIFS and pPAR mirror theirs (pIFS: −41, 18, 26; pPAR: −36, −57, 50), save that their pIFS activation was lateralized to the left hemisphere.

These prior results suggest that the pIFS plays a particularly important role in assessing the context for decision making. But, why should this process (and not other aspects of executive control) differ for ambiguous and risky trials? We suggest that the cardinal requirement for successfully dealing with ambiguity is behavioral flexibility: when faced with an ambiguous situation, one must resolve its multiplicity of interpretations into a context that facilitates decision making. No such context needs to be constructed in risky decision making because all information is specified by the decision problem. Although the need for contextual analysis differentiates decision making under ambiguity and risk, other processes are likely to be common across all forms of decision making under uncertainty. These include episodic selection, which relies on anterior regions of lateral prefrontal cortex (Huettel et al., 2002; Rowe et al., 2000); performance monitoring, for which anterior cingulate cortex may be critical (Kerns et al., 2004); and learning stimulus-response contingencies, which depends upon medial prefrontal cortex (Volz et al., 2003). As noted briefly in the results, although our study was designed to elucidate differences not commonalities, activation in these regions was found for all trial types in the decision phase.

We emphasize that further distinctions may be possible between subregions of posterior lateral prefrontal cortex. Also observed was ambiguity-related activation in a second, more posterior focus within the inferior frontal sulcus; this region has been labeled the inferior frontal junction (IFJ) and has approximate coordinates (44, −1, 38) (Brass and von Cramon, 2002). Comparisons across studies have suggested that this region supports task preparation, as needed when there are multiple tasks in an experiment that are signaled by different cues (Brass and von Cramon, 2002, 2004; Bunge et al.,

2002). Increased activation in this region to decision making under ambiguity might reflect the subjects' treatment of ambiguity as signaling a different decision task than (the default) risk. However, it is notable that unlike in the anterior pIFS, activation of this more-posterior region did not track ambiguity preferences across our subjects, so that it does not appear to be linked with processes specific to ambiguity resolution.

Finally, activation of the lateral prefrontal cortex frequently co-occurs with that of posterior parietal cortex, suggesting that the two regions may each contribute to executive control (at least in the form required for most neuroimaging experiments). We observed two notable differences between these regions. First, although activation in pPAR was greater on ambiguous trials than nonambiguous trials, the differences were small compared to those in pIFS. Second, the ambiguity effect in pPAR was correlated with subjects' risk preferences, not their ambiguity preferences. That pPAR mediates the evaluation of risky decisions is consistent with single-unit studies in monkeys (Dorris and Glimcher, 2004; Sugrue et al., 2004), although the functional homologies between monkey and human posterior parietal cortex have not yet been established. Whether the observed risk effects in pPAR reflect differential demands for spatial response selection (Brass and von Cramon, 2004), activation of response rules (Bunge et al., 2002), analog calculation (Piazza et al., 2004), or another factor remains an avenue for future study.

Ambiguity and Risk as Distinct Forms of Uncertainty
Ambiguity is of particular interest to economists and decision scientists for several reasons: it is present in most real-world decisions, it presents choice paradoxes for which standard expected utility theory has difficulty accounting, and it is specific to human-decision making, in that its resolution requires communication or assessment of a second-order expectation about probabilities. In particular, understanding why and how people treat subjective probabilities differently from objective probabilities are central questions in economic thought (Camerer and Weber, 1992; Knight, 1921). Distinctions in neural function—and by inference, mental process—may lead to their answers.

There have been two prior neuroscience studies that manipulated ambiguity and risk in decision making, both with positron emission tomography (PET). Smith and colleagues evaluated how brain activation is influenced by gain and loss contexts in ambiguous and risky decisions (Smith et al., 2002); data are also reported in (Dickhaut et al., 2003). Because of the temporal limitations of PET, the same trial condition was presented repeatedly within individual blocks and thus analyses collapsed across all phases of the task. A second study from the same group overcame this limitation by withholding feedback until after the experiment, which allows analysis of data associated with the choice phase of the task (Rustichini et al., 2005). Across these two studies, they found two primary differences between decision making under risk and under ambiguity: that effects of gain/loss context, as found in the ventromedial prefrontal cortex, were more pronounced for risky decisions than ambiguous decisions; and that both ambiguous and risky decisions evoke activation in parietal cor-

tex, but not in lateral prefrontal cortex. These latter results stand in opposition to those of the present study, which showed clear evidence for lateral prefrontal cortex activation in decision making under uncertainty and for greater prefrontal activation when ambiguity was present, and to the large prior literature documenting the role of lateral prefrontal cortex in risky decision making. Thus, ours is the first study to link a specific region within prefrontal cortex, the pIFS, to decision making under ambiguity.

Even given a clear dissociation between ambiguity and risk, as operationalized in our task design, some consideration must be paid to confounding factors. Decisions under ambiguity and under risk might systematically differ in some secondary process—such as attention, motor preparation, or rule induction—that differentially drives activation in prefrontal and parietal cortices. It is possible, for example, that that attentional effects preferentially recruit lateral prefrontal cortex compared to posterior parietal cortex, accounting for the observed differences between ambiguity and risk. However, we believe this to be unlikely. Both regions exhibit attentional effects (with posterior parietal cortex more typically implicated), and any story about attentional differences associated with task difficulty and complexity would be difficult to reconcile with the faster response times observed on ambiguous trials.

Another potential explanation for the differences between prefrontal and parietal cortices could be that the former supports motor preparation processes, which might be more active for ambiguity than risk and might be deficient in our impulsive subjects. This conjecture is reasonable, given the contributions of premotor cortices to motor execution and preparation and the suggestions that posterior lateral prefrontal cortex supports task planning (Brass and von Cramon, 2002; Dove et al., 2000; Sohn et al., 2000). Nevertheless, the observed results argue against such an interpretation, for three reasons. First, if motor preparatory processes were engaged more rapidly and/or of more limited duration on trials with ambiguity, one would observe decreased activation in motor preparatory regions. However, we found a more than 2-fold increase in pIFS activation when ambiguity was present. Second, there were no significant effects of ambiguity in regions that are commonly implicated in motor preparation, such as the premotor cortex. Third, the amplitude of the BOLD response in the pIFS across conditions (i.e., Figure 2B) perfectly tracks the presence/absence of ambiguity (AC = AR > RC = RR) but is inconsistent with the ordering of response time across conditions (RR > RC = AR > AC).

Finally, we consider the possibility that the pIFS activation reflects processes associated with rule induction, such that our ambiguity-preferring subjects were those who devoted the most energy to uncovering a hidden rule. Rule induction has been associated with the lateral prefrontal cortex, although reported activations are typically in the left hemisphere and in regions anterior to pIFS (Goel and Dolan, 2004). To control for the possibility that ambiguity-preferring subjects were spending more time making decisions when ambiguity was present, as would support this interpretation, we tested whether there were positive correlations across

subjects between ambiguity preference and response time. Instead, there were nonsignificant negative correlations both when combining across all trial types and for every trial type independently (all Rs between -0.26 and -0.32). Likewise, as noted in the results, response time decreased when ambiguity was present and there was no correlation between ambiguity preference and impulsiveness. We note that our subjects were well practiced in the task, had substantial experience with the distribution of probabilities, and received the same information about rules regardless of their decision. Together, these results and design features reduce the tenability of arguments that invoke an additional process like rule induction that is expressed more in ambiguity-seeking subjects.

Yet, although our results do not support the direct substitution of another cognitive process for ambiguity, we cannot make a positive and definitive statement about what processes together constitute decision making under ambiguity. Defining what is meant by "attitudes toward ambiguity" has been and remains a challenge for economic theorists because no two individuals necessarily perceive the same ambiguity in a decision problem (Ghirardato et al., 2004). Whereas risk can be defined in terms of certainty equivalents and expected values, there is no analog in ambiguous choice. This lack of a precise way to measure ambiguity attitudes even suggests that one may go so far as to interpret ambiguity preferring (averse) behavior as optimism (pessimism) about true probabilities. As discussed in the following section, a salutary effect of neuroeconomic research will be to provide evidence for or against the involvement of particular processes in complex forms of decision making.

Neuroeconomics: Predicting Brain Activation from Economic Preferences

The present results demonstrate how neuroscience data can inform theoretical perspectives in economics (Glimcher and Rustichini, 2004). Although behavioral experiments have demonstrated that individuals treat ambiguity differently from risk (Camerer and Weber, 1992; Luce, 2000), current theories proposed to accommodate decision making under ambiguity make several assumptions: that an individual's beliefs about the probabilities of each outcome are represented by a set of (possibly subjective) probability distributions, that the individual evaluates the expected utility of a choice according to each possible distribution, and that the individual then chooses one of the alternatives based on some objective. These assumptions predict that the processes evoked by risky decisions are subsumed within those evoked by ambiguous decisions. Our fMRI and response time results contradict this notion. We suggest that ambiguous decision making does not represent a special, more complex case of risky decision making; instead, these represent two types of decision making that are supported by distinct mechanisms.

The demonstration that activation of particular brain regions tracks specific economic preferences heralds a novel and potentially powerful approach for neuroeconomic studies. Although it is readily apparent that individuals differ in their preferences for risk and ambiguity, among other decision parameters (e.g., delayed versus immediate rewards), there is no necessity that such differences must be measurable by fMRI. Decision preferences might be variable or diffuse, not matching cleanly to economic models. In this vein, a strength of the current results was the use of both "best-fit" and "resampling" approaches to verify that our results are robust to uncertainty in the model used to calculate economic preferences. Nor must preferences manifest in changes in neural activity at the scale used by fMRI: recent work in monkeys has indicated that activity of neurons within parietal and posterior cingulate cortices tracks the relative value and risk of decision options (Dorris and Glimcher, 2004; McCoy and Platt, 2005a, 2005b; Sugrue et al., 2004). Thus, the finding of neural differences between preferences for ambiguity and risk provides a strong—and somewhat unexpected—grounding for future studies of their underlying mechanisms.

Of additional interest was the finding that behavioral impulsiveness covaries with pIFS activation, such that more impulsive individuals exhibited a smaller neural effect of ambiguity. That impulsiveness modulates prefrontal cortex activation is hardly surprising, given prior suggestions that a central function of prefrontal cortex is to inhibit impulsive or automatic behaviors (Miller, 2000) and that damage to prefrontal cortex (and/or neurotransmitter systems that modulate prefrontal cortex) is associated with increased behavioral impulsiveness (Best et al., 2002; Parrott, 2000; Walderhaug et al., 2002). However, the striking and novel result obtained here was that impulsiveness predicted activation in the specific region implicated for ambiguity preferences (but not in the other prefrontal regions or the parietal region implicated for risk preferences). We emphasize that the causal direction of this brain-behavior relation is not established by these data—it is equally plausible that the behavioral trait of impulsiveness is caused by reduced activity in pIFS and other brain regions that support considering multiple options in decision making. To identify the direction of causality, one would need to manipulate impulsiveness directly, as can be done with pharmacological methods like acute tryptophan depletion (Cools et al., 2005; Walderhaug et al., 2002).

Finally, we speculate that ambiguity aversion reflects the brain's implicit recognition of its computational limitations. Most people prefer to make decisions in domains in which they have prior knowledge (i.e., those in which alternative contexts can be readily brought to mind) compared to areas with which they are unfamiliar, even when probabilities are matched between the options (Heath and Tversky, 1991). Insufficient activation in pIFS could signify that uncertainty about probability has not yet been resolved, thus indicating to other brain systems that the value of an ambiguous decision option should be discounted.

Experimental Procedures

Subjects
Thirteen healthy volunteers (nine male; 18–33 years) participated in two sessions: one fMRI and one in a behavioral laboratory (order counterbalanced). All acclimated to the fMRI environment with a mock MRI scanner and participated in a 30 min practice session. All subjects gave written informed consent as part of a protocol approved by the Institutional Review Board of Duke University Medical Center.

Experimental Stimuli

Subjects chose between pairs of monetary gambles presented as pie charts (Figure 1A). *Certain* gambles showed only one monetary value, and thus their outcomes were known to the subjects. *Risky* gambles presented two monetary values and their associated probabilities. *Ambiguous* gambles presented two monetary values (one of which was always $0) but concealed their corresponding probabilities until a choice was made. Outcome probabilities of the ambiguous (risky) gambles ranged from 0 to 1 (0.25 to 0.75) in 0.25 increments. Expected values for the certain and risky gambles ranged from $5 to $25 (mean of $14), and expected value was matched within 20% for all gamble pairs. Four pairings of gamble types were presented with equal frequency: Ambiguous/Certain (AC), Ambiguous/Risky (AR), Risky/Certain (RC), and Risky/Risky (RR). The labels "certain," "risky," and "ambiguous" were never used within the experiment itself. The experiment was presented with the Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). Subjects indicated their choice on each trial via button press, whereupon the probabilities of any ambiguous gamble were revealed. The resolution of the gambles and the display of their outcomes were extended in time after the decision to allow isolation of decision-specific changes in brain activation.

Study Procedure

At the outset of each trial (Figure 1B), subjects were shown a pair of gambles. They were asked to select, by pressing a button with their right hand, the gamble they believed would best maximize their reward outcome on each trial. Upon selection, a blue box surrounded the chosen gamble, and probabilities were revealed for any Ambiguous gambles. Then, after a fixed delay of 2 s, the gambles were resolved by spinning small balls around their edges, much like roulette wheels, for a variable duration of 4.5–6 s. The balls' speed was randomized across trials to prevent inference about outcome from starting position. The outcomes of the chosen and unchosen gambles were indicated to the subjects both by the stopping positions of the balls and by text presented below each gamble for 2 s. The next trial began after a variable delay of 1.5–7.5 s. During each 9.5 min scan, approximately 28 trials were presented, and subjects participated in a mean of 7.2 scans. After completing both the fMRI session and a separate behavioral session, subjects were paid according to their choices on four gambles selected at random by rolling dice. Average payout over the four gambles was $60.50, which was then added to a guaranteed $30 for participation.

Imaging Methods

fMRI data were collected with a gradient-echo spiral-in pulse sequence with imaging parameters (TR = 1500 ms, TE = 35 ms, 34 axial slices parallel to the AC-PC plane, 3.75 × 3.75 × 3.8 mm) on a GE 1.5T scanner with a volume head coil. High-resolution 3D full-brain SPGR images were acquired to aid in normalization and coregistration. Functional images were corrected for head motion and time of acquisition within a TR and were normalized into a standard stereotaxic space (Montreal Neurological Institute) for intersubject comparison with SPM (Wellcome Department of Cognitive Neurology, University College London). A smoothing filter of width 8 mm was applied after normalization.

To identify activated brain regions, we used event-related fMRI in conjunction with a multiple regression analysis. A multiple regression analysis was performed with regressors for each of three trial components: the decision phase, which spanned the interval between presentation of the decision stimulus and the subject's response; the expectation phase, which included the spinning of the gambles until their resolution; and the outcome phase, which was defined as the TR after resolution of the gambles. Within the decision phase, separate regressors were used for each of the gamble pair types and for each possible decision, to allow examination of trial-type effects. Hypothesized BOLD responses time locked to these components were modeled by convolution of a canonical hemodynamic response and its first-order time derivative. Covariates for head motion and run-mean effects were included in the analyses. Least-squares parameter estimates were used to construct statistical parametric maps for each subject, which were then entered into a second-order random-effects analysis across subjects. Voxel clusters were counted as significant if the cluster maximum exceeded a threshold of p < 0.0001, with ten or more contiguous voxels exceeding a threshold of p < 0.001.

Behavioral Data Acquisition and Analysis

Parameters for each subject's risk and ambiguity preferences were estimated with their history of choices in both the fMRI and behavioral sessions. For risk, we assumed that the subjects' preferences had an expected utility representation. The utility $u(x)$ of a monetary outcome $x \geq 0$ was modeled with a power function (Equation 1).

$$u(x) = x^\beta \tag{1}$$

Here, $\beta > (= , <) 1$ corresponds to risk-preferring (neutral, averse) behavior, respectively. For each subject, we calibrated the power function by finding the value of β that maximized the number of correct predictions in the RC and RR trials combined. Estimates of β spanned the range from risk averse to risk seeking, indicating considerable heterogeneity in risk preferences across subjects.

Using the value of β obtained for each individual, we then estimated a second parameter α representing the individual's ambiguity preferences. We assumed that individuals evaluate ambiguous gambles with an α-Maxmin Expected Utility function (Ghirardato et al., 2004). If subjects believe that both 0 and 1 are possible probabilities for the good outcome, this model reduces to Equation 2.

$$u(x_1, x_2) = (1 - \alpha)(u(x_1)) + \alpha(u(x_2)) \tag{2}$$

Here, x_1 and x_2 are monetary outcomes with $x_1 > 0$ and $x_2 = 0$. This model suggests that under ambiguity, the decision maker acts as if he places a weight of α on the expected utility of the choice under the worst probability distribution and a weight of $(1-\alpha)$ on the expected utility of the choice under the best probability distribution. We restricted $0 \leq \alpha \leq 1$, and consequently, $\alpha > (= , <) 0.5$ corresponds to ambiguity-averse (neutral, preferring) behavior, respectively. For each subject, we calibrated Equation 2 and found the value of α that maximized the number of correct predictions in the AC and AR trials combined. As in the case of risk, estimates of α spanned the range from ambiguity averse to ambiguity preferring behavior. (Note that we plot the quantity $1-\alpha$ in all figures so that increasing values indicate increasing ambiguity preference, as for risk.)

This procedure necessarily produces not simply a single parameter estimate, but one or more ranges of feasible parameter values (for each parameter, three subjects had disjoint ranges). To account for this potential analytical uncertainty about our subjects' true preference parameters, we calculated correlations between brain activation and preferences with both the mean parameter estimates and values drawn from the range of possible parameter estimates. For the latter analysis, we used a resampling approach with 10,000 iterations. On each iteration, we drew ambiguity and risk preference parameters from the ranges of possible values for each subject, sampled uniformly. We then calculated the correlations across subjects between each of the two sets of preference parameters and the fMRI data. We used the proportion of significant samples as an index of the robustness of the brain-behavior correlation for each brain region and preference parameter.

We additionally obtained a clinical measure of behavioral impulsiveness for ten of our 13 subjects with the Barratt Impulsiveness Scale, or BIS (Patton et al., 1995), for which increasing values indicate increasing impulsiveness. Typical values are approximately 60 ± 10 (mean ± standard deviation) for young-adult college students (Patton et al., 1995).

References

Bechara, A., Damasio, H., Damasio, A.R., and Lee, G.P. (1999). Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. J. Neurosci. *19*, 5473–5481.

Becker, S.W., and Brownson, F.O. (1964). What price ambiguity? Or the role of ambiguity in decision making. J. Polit. Econ. *72*, 62–73.

Bernoulli, D. (1738). Specimen theoriae novae de mensura sortis. Commentarii Academiae Scientarum Imperialis Petropolitanae *5*, 175–192.

Best, M., Williams, J.M., and Coccaro, E.F. (2002). Evidence for a dysfunctional prefrontal circuit in patients with an impulsive aggressive disorder. Proc. Natl. Acad. Sci. USA *99*, 8448–8453.

Brainard, D.H. (1997). The psychophysics toolbox. Spat. Vis. *10*, 433–436.

Brass, M., and von Cramon, D.Y. (2002). The role of the frontal cortex in task preparation. Cereb. Cortex *12*, 908–914.

Brass, M., and von Cramon, D.Y. (2004). Selection for cognitive control: a functional magnetic resonance imaging study on the selection of task-relevant information. J. Neurosci. *24*, 8847–8852.

Bunge, S.A., Hazeltine, E., Scanlon, M.D., Rosen, A.C., and Gabrieli, J.D. (2002). Dissociable contributions of prefrontal and parietal cortices to response selection. Neuroimage *17*, 1562–1571.

Camerer, C., and Weber, M. (1992). Recent developments in modeling preferences: uncertainty and ambiguity. J. Risk Uncertain. *5*, 325–370.

Chapman, G.B., and Niedermayer, L.Y. (2001). What counts as a decision? Predictors of perceived decision making. Psychon. Bull. Rev. *8*, 615–621.

Chipman, J.S. (1960). Stochastic choice and subjective probability. In Decision, Values, and Groups, D. Willmer, ed. (New York: Pergamon Press), pp. 70–95.

Cools, R., Blackwell, A., Clark, L., Menzies, L., Cox, S., and Robbins, T.W. (2005). Tryptophan depletion disrupts the motivational guidance of goal-directed behavior as a function of trait impulsivity. Neuropsychopharmacology *30*, 1362–1373.

Critchley, H.D., Mathias, C.J., and Dolan, R.J. (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. Neuron *29*, 537–545.

Dickhaut, J., McCabe, K., Nagode, J.C., Rustichini, A., Smith, K., and Pardo, J.V. (2003). The impact of the certainty context on the process of choice. Proc. Natl. Acad. Sci. USA *100*, 3536–3541.

Dorris, M.C., and Glimcher, P.W. (2004). Activity in posterior parietal cortex is correlated with the relative subjective desirability of action. Neuron *44*, 365–378.

Dove, A., Pollmann, S., Schubert, T., Wiggins, C.J., and von Cramon, D.Y. (2000). Prefrontal cortex activation in task switching: an event-related fMRI study. Brain Res. Cogn. Brain Res. *9*, 103–109.

Ellsberg, D. (1961). Risk, ambiguity, and the Savage axioms. Q. J. Econ. *75*, 643–669.

Fiorillo, C.D., Tobler, P.N., and Schultz, W. (2003). Discrete coding of reward probability and uncertainty by dopamine neurons. Science *299*, 1898–1902.

Ghirardato, P., Maccheroni, F., and Marinacci, M. (2004). Differentiating ambiguity and ambiguity attitude. J. Econ. Theory *118*, 133–173.

Glimcher, P.W., and Rustichini, A. (2004). Neuroeconomics: the consilience of brain and decision. Science *306*, 447–452.

Goel, V., and Dolan, R.J. (2004). Differential involvement of left prefrontal cortex in inductive and deductive reasoning. Cognition *93*, B109–B121.

Heath, C., and Tversky, A. (1991). Preference and belief: ambiguity and competence in choice under uncertainty. J. Risk Uncertain. *4*, 177–212.

Hsu, M., Bhatt, M., Adolphs, R., Tranel, D., and Camerer, C.F. (2005). Neural systems responding to degrees of uncertainty in human decision-making. Science *310*, 1680–1683.

Huettel, S.A., Mack, P.B., and McCarthy, G. (2002). Perceiving patterns in random series: dynamic processing of sequence in prefrontal cortex. Nat. Neurosci. *5*, 485–490.

Huettel, S.A., Song, A.W., and McCarthy, G. (2005). Decisions under uncertainty: probabilistic context influences activity of prefrontal and parietal cortices. J. Neurosci. *25*, 3304–3311.

Kerns, J.G., Cohen, J.D., MacDonald, A.W., 3rd, Cho, R.Y., Stenger, V.A., and Carter, C.S. (2004). Anterior cingulate conflict monitoring and adjustments in control. Science *303*, 1023–1026.

Knight, F.H. (1921). Risk, Uncertainty, and Profit (New York: Houghton Mifflin).

Koechlin, E., Ody, C., and Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. Science *302*, 1181–1185.

Lauriola, M., and Levin, I.P. (2001). Relating individual differences in attitude toward ambiguity to risky choices. J. Behav. Decis. Mak. *14*, 107–122.

Leland, D.S., and Paulus, M.P. (2005). Increased risk-taking decision-making but not altered response to punishment in stimulant-using young adults. Drug Alcohol Depend. *78*, 83–90.

Luce, R.D. (2000). Utility of Gains and Losses: Measurement-Theoretical and Experimental Approaches (London: Lawrence Erlbaum).

McCoy, A.N., and Platt, M.L. (2005a). Expectations and outcomes: decision-making in the primate brain. J. Comp. Physiol. [A] *191*, 201–211.

McCoy, A.N., and Platt, M.L. (2005b). Risk-sensitive neurons in macaque posterior cingulate cortex. Nat. Neurosci. *8*, 1220–1227.

Miller, E.K. (2000). The prefrontal cortex and cognitive control. Nat. Rev. Neurosci. *1*, 59–65.

Miller, E.K., and Cohen, J.D. (2001). An integrative theory of prefrontal cortex function. Annu. Rev. Neurosci. *24*, 167–202.

Parrott, A.C. (2000). Human research on MDMA (3,4-methylene- dioxymethamphetamine) neurotoxicity: cognitive and behavioural indices of change. Neuropsychobiology *42*, 17–24.

Patton, J.J., Stanford, M.S., and Barratt, E.S. (1995). Factor structure of the Barratt impulsiveness scale. J. Clin. Psychol. *51*, 768–774.

Paulus, M.P., Hozack, N., Zauscher, B., McDowell, J.E., Frank, L., Brown, G.G., and Braff, D.L. (2001). Prefrontal, parietal, and temporal cortex networks underlie decision-making in the presence of uncertainty. Neuroimage *13*, 91–100.

Paulus, M.P., Hozack, N., Frank, L., and Brown, G.G. (2002). Error rate and outcome predictability affect neural activation in prefrontal cortex and anterior cingulate during decision-making. Neuroimage *15*, 836–846.

Pelli, D.G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into movies. Spat. Vis. *10*, 437–442.

Piazza, M., Izard, V., Pinel, P., Le Bihan, D., and Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. Neuron *44*, 547–555.

Platt, M.L. (2002). Neural correlates of decisions. Curr. Opin. Neurobiol. *12*, 141–148.

Ridderinkhof, K.R., Ullsperger, M., Crone, E.A., and Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. Science *306*, 443–447.

Rowe, J.B., Toni, I., Josephs, O., Frackowiak, R.S., and Passingham, R.E. (2000). The prefrontal cortex: response selection or maintenance within working memory? Science *288*, 1656–1660.

Rustichini, A., Dickhaut, J., Ghirardato, P., Smith, K., and Pardo, J.V. (2005). A brain imaging study of the choice procedure. Games Econ. Behav. *52*, 257–282.

Smith, K., Dickhaut, J., McCabe, K., and Pardo, J.V. (2002). Neuronal substrates for choice under ambiguity, risk, gains, and losses. Manage. Sci. *48*, 711–718.

Sohn, M., Ursu, S., Anderson, J.R., Stenger, V.A., and Carter, C.S. (2000). The role of prefrontal cortex and posterior parietal cortex in task switching. Proc. Natl. Acad. Sci. USA *97*, 13448–13453.

Sugrue, L.P., Corrado, G.S., and Newsome, W.T. (2004). Matching behavior and the representation of value in parietal cortex. Science *304*, 1782–1787.

Volz, K.G., Schubotz, R.I., and von Cramon, D.Y. (2003). Predicting events of varying probability: uncertainty investigated by fMRI. Neuroimage *19*, 271–280.

von Neumann, J., and Morgenstern, O. (1944). Theory of Games and Economic Behavior (Princeton, NJ: Princeton University Press).

Walderhaug, E., Lunde, H., Nordvik, J.E., Landro, N.I., Refsum, H., and Magnusson, A. (2002). Lowering of serotonin by rapid tryptophan depletion increases impulsiveness in normal individuals. Psychopharmacology (Berl.) *164*, 385–391.