

Selective activation of the nucleus accumbens during risk-taking decision making

Scott C. Matthews,^{1,2,CA} Alan N. Simmons,^{1,2} Scott D. Lane and Martin P. Paulus^{1,2,3}

¹Department of Psychiatry; ²Laboratory of Biological Dynamics and Theoretical Medicine, University of California San Diego, La Jolla, CA 92093-0603; ³Veterans Affairs San Diego Health Care System; ⁴Psychiatry and Behavioral Sciences, The University of Texas Health Science Center-Houston, TX, USA

^{CA}Corresponding Author and Address: scmatthews@UCSD.Edu

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This study implemented a risk-taking task during fMRI to probe the brain circuitry involved in risk-taking decision-making in 12 healthy control subjects. Partially supporting the initial hypotheses, deliberation prior to selection of safe relative to risky responses generated greater activation in the inferior frontal cortex, superior temporal gyrus, and middle temporal gyrus; and deliberation prior to selection of risky relative to safe responses generated greater activation in medial frontal cortex, occipital cortex, nucleus

accumbens and caudate. Additionally, accumbens activation correlated positively with the harm avoidance subscale of the Temperament and Character Inventory (TCI) I25. These findings may provide target neural systems to study in subjects who exhibit problematic risk-taking behaviors and may partially explain why certain risky behaviors occur. *NeuroReport* 15:2123–2127 © 2004 Lippincott Williams & Wilkins.

Key words: Anticipation; Decision-making; fMRI; Harm avoidance; Nucleus accumbens; Reward; Risk-taking

INTRODUCTION

One approach for examining risk-taking attitudes is to present subjects with a choice between a sure thing and a gamble. By varying the expected value of the gamble, one can determine whether subjects are risk-seeking (i.e. selecting the gamble even when the expected value is lower than the sure thing) or risk-averse (i.e. selecting the sure thing even when the expected value of the gamble is higher). In these studies one frequently observes the flection effect in which preferences are typically risk-averse in the gain domain, but risk-seeking in the loss domain [1]. When this occurs, differences between the expected value of a gamble and its certainty equivalent can be reduced if risks are aggregated over time. Consistent with this finding is the observation that anticipating gain promotes risk aversion, whereas anticipating loss promotes risk-seeking during decision-making tasks [2]. It also appears that subjects are less sensitive to uncertainty than to risk [3].

Functional neuroimaging studies have shown that risk-taking decision-making is critically dependent on the activation of inferior prefrontal cortex [4], ventromedial and ventrolateral frontal cortex [5,6], anterior cingulate [5], insula [7], and parietal cortex [4]. Particular structures within this network appear to be differentially involved in specific processes of decision-making such as assessment, execution, and evaluation. For example, the anterior cingulate appears to play an evaluative role and is differentially activated during decision-making when the outcome is uncertain relative to when there is a well-defined right or wrong [8]. This structure has also been implicated in the execution of action in reward-related decision-making [9]. In comparison, striatal structures such as the nucleus

accumbens [10] are important in the assessment of outcomes in decision-making and have been implicated in processing alterations of reward magnitude and/or anticipation of reward. Additionally, the nucleus accumbens has been implicated in the calculation of an error signal due to the difference between expected and received reward [11].

The current study implemented a novel task to examine the neural substrates underlying risk-taking decision-making. We hypothesized that the neural substrates important for risk assessment would activate differentially during a deliberation period in a simple risk-taking decision-making paradigm. Specifically, we hypothesized that risk-taking may be rewarding and that the nucleus accumbens, a structures that is critically involved in the anticipation of reward [10], would show increased activation during risky *vs* safe response selection. Additionally, in accordance with prior studies describing activation in the insula [7,12] and ventromedial prefrontal cortex [13] related to risk-taking behavior, we hypothesized that these structures would show increased activation during risky relative to safe response selection. Support for these hypotheses would link risk-taking decision-making to specific activations in the brain and provide target neural systems to assess in subjects who exhibit problematic risk-taking behaviors.

MATERIALS AND METHODS

Subjects: Twelve healthy subjects (seven males and five females) gave written informed consent and completed the functional imaging portion of the study. One subject did not complete personality questionnaires (described below) and was not included in the correlational analyses. The mean

age of participants was 34 years (range 20–56) and the average education level of the population was 14.4 years (range 13–18). All subjects completed the structured clinical interview for DSM IV and had no lifetime history of any Axis I DSM IV disorder. The University of California San Diego (UCSD) Human Research Protection Program approved this study.

Task: The Lane Risk Taking Task presents both risky and safe responses and forces subjects to make a choice between the two (Fig. 1). For safe responses, subjects are assured of winning a relatively small monetary award. Conversely, for risky responses, there is a chance of winning a large monetary award, but also a chance of losing a relatively large amount of money. This task has been described elsewhere [14].

Personality questionnaires: Eleven of the 12 subjects completed a Temperament and Character Inventory (TCI) 125, which consists of 125 true/false statements to assess harm avoidance, reward dependence, novelty seeking, persistence, self-directiveness, cooperativeness, and self-transcendence [15].

Functional magnetic resonance imaging: All 12 subjects completed the fMRI portion of the study. Each scanning session lasted ~1 h. Sessions consisted of a three-plane scout scan (10 s), a high-resolution anatomic scan covering the whole brain, a series of T2* weighted echo-planar imaging (EPI) scans to measure blood oxygen-level dependent (BOLD) functional activity, and an EPI-based field map to correct for susceptibility induced geometric distortions. Imaging experiments were performed on a 1.5T Siemens

(Erlangen, Germany) scanner (T2*-weighted echoplanar imaging, TR=2000 ms, TE=40 ms, 64 × 64 matrix, twenty 4 mm axial slices). Each run was acquired in sessions of 256 repetitions and lasted 8 min 32 s. During the same experimental session, a T1-weighted image (MPRAGE, TR=11.4 ms, TE=4.4 ms, flip angle=10°, FOV=256 256, 1 mm³ voxels) was obtained for anatomical reference.

All structural and functional image processing and analysis was performed with the Analysis of Functional Neuroimages (AFNI) software package [16]. In order to minimize motion artifact, echoplanar images were realigned to the 128th acquired scan. Additionally, data were time corrected for slice acquisition order. Time series data for each individual were analyzed using a multiple regression model. For each regression, seven regressors were entered into this model including two task conditions (risky and safe), three motion parameters (yaw, pitch, and roll), one linear drift regressor, and the baseline condition (fixation cross). Prior to inclusion in the regression model, the task-related regressors were convolved with a modified gamma variate function [17] to account for the hemodynamic delay and the slow rise and fall of the hemodynamic response. Percentage signal difference was calculated from the ratio of the beta weight for the risky, non-risky, motor, and outcome regressors and the baseline regressor. A 6 mm full width-half maximum Gaussian filter was applied to the voxel-wise percentage signal difference data to account for individual variations in anatomical landmarks. Each subject's data were normalized to Talairach coordinates [18] and a whole-brain mask was applied to screen out non-brain voxels and voxels falling within the artifact region.

The voxel-wise percentage signal difference data for all subjects were entered into a mixed-model 2-way ANOVA with condition (risky/safe) as a fixed factor and subjects as a

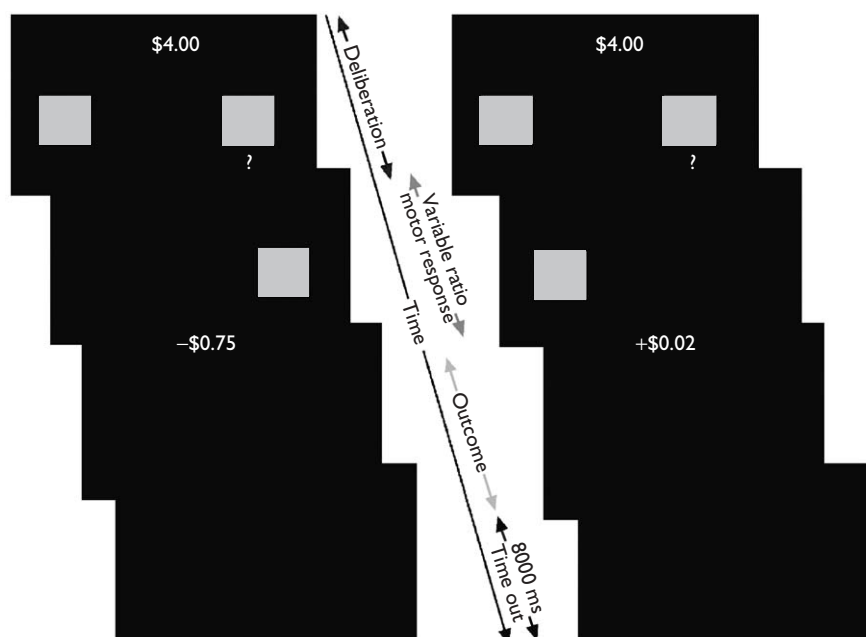


Fig. 1. This figure shows the main components of the Lane Risk-Taking task. First, subjects viewed two gray squares indicating the two possible response options. The "risky" option, i.e. the response that could either result in a gain or loss of \$0.25, \$0.50, \$0.75, or \$1.00 was indicated by a question mark. After selection, subjects had to press the mouse button multiple times (on a variable ratio schedule) before they were informed about the outcome. The outcome was presented for 2500 ms, followed by an 8000 ms time out period, then the next trial. The left and right panels of the figure represent risky loss and safe win trials respectively.

random factor. To determine areas that significantly activated with risk, a within subjects contrast was computed between the risky and safe stimuli. A threshold/cluster method was then applied. This threshold adjustment method was based on Monte-Carlo simulations and was used to guard against identifying false positive areas of activation [19]. Based on these simulations, it was determined that a voxel-wise a-priori probability of 0.05 would result in a corrected cluster-wise activation probability of 0.05 if a minimum volume of 1000 μl and a connectivity radius of 4.0 mm was considered. The average percentage signal difference for each subject during each task condition was extracted from regions of activation that were found to survive this threshold/cluster method.

In a separate analysis, the impulse response function was computed for the functional region of interest, which included the nucleus accumbens. Specifically, a one-repetition time (TR) delta function was included as a regressor of interest in the 3ddeconvolve program and shifted seven times by 1 TR. Percentage signal change was obtained by dividing the regressor coefficients by the baseline regressor.

RESULTS

Behavioral: Significant behavioral differences were not observed between risky and safe responses (Fig. 2). Specifically, a significant difference in response latency, i.e. the deliberation time between stimulus presentation and the selection of a risky or safe response, was not observed for risky relative to safe responses ($F(1,11)=0.00$, N.S.). In addition, the number of risky responses did not differ significantly from the number of safe responses ($F(1,11)=1.08$, N.S.).

Brain activation: Two important results were observed. First, several brain regions were differentially activated during performance of the Lane Task (Table 1, Table 2). Specifically, in the inferior frontal cortex, superior temporal gyrus, and middle temporal gyrus, deliberation prior to selection of a safe response generated a larger activation than did deliberation prior to selection of a risky response.

In contrast, in the medial frontal cortex, occipital cortex, nucleus accumbens and caudate, more activation was found during deliberation prior to a risky response relative to deliberation prior to a safe response (Fig. 3). Second, extracting the functional time series revealed that, for risky but not safe responses, the left nucleus accumbens showed a time-locked increase in activation that subsided once the decision was made (Fig. 4).

Brain-behavior relationships: A significant positive correlation was observed between BOLD signal in the nucleus accumbens and the harm avoidance subscale of the TCI (Spearman's $\rho=0.67$, $p<0.05$).

DISCUSSION

This investigation yielded two main results that partially confirmed our initial hypotheses. First, a network of structures including the nucleus accumbens, caudate, medial frontal gyrus, and middle occipital gyrus showed greater activation during risky relative to safe responses. Second, activation in the nucleus accumbens correlated positively with the harm avoidance subscale of the Temperament and Character Inventory (TCI) 125. Although ventral striatum and associated areas have been implicated primarily in the processing [20] and anticipation of reward [10], the current investigation shows that this circuitry may also play an important role during the deliberation of risk-related behaviors. Thus, the activation of the nucleus accumbens is consistent with the idea that risk-taking behavior may be reinforcing because the anticipation of risky outcomes activates reward-related systems.

Risk and risk-related behaviors are not unitary constructs but are most likely complex phenomena with content and context specific characteristics, i.e. risk-taking in a particular situation may not generalize to an overall risk-taking attitude [21]. Anticipation of outcomes profoundly influences risk-taking behaviors [2]. The current study shows that brain structures critical for reward processing are activated when individuals deliberate about taking a risk, but are not activated when individuals select a safe

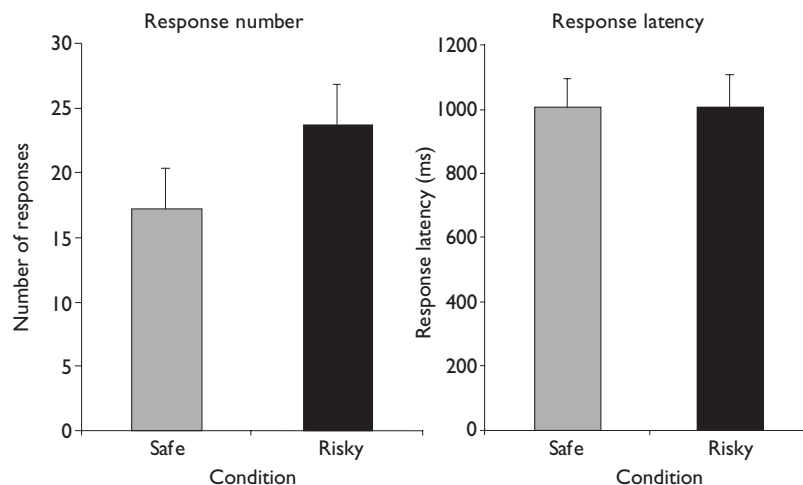


Fig. 2. As shown above, there was no significant difference between the latency to make a risky or safe response. Moreover, the number of risky responses did not differ significantly from safe responses.

Table 1. Active brain areas for safe minus risky responses in a whole brain analysis. All clusters contain at least 8 contiguous voxels all significant at $p < 0.05$.

Area (Brodmann Area)	Side	Vol. (ml)	x	y	z
Superior temporal gyrus (39)	L	2944	-47	-55	27
Middle temporal gyrus (39)	R	2560	35	-61	31
Inferior frontal gyrus (9)	L	1600	-63	12	24

Table 2. Active brain areas for risky minus safe responses in a whole brain analysis. All clusters contain at least 8 contiguous voxels all significant at $p < 0.05$.

Area (Brodmann Area)	Side	Vol. (ml)	x	y	z
Medial frontal gyrus (10)	R	1536	17	47	10
Nucleus accumbens	L	1152	-14	8	-4
Caudate tail	R	1152	23	-36	15
Middle occipital gyrus (18)	L	1088	-30	-83	-2

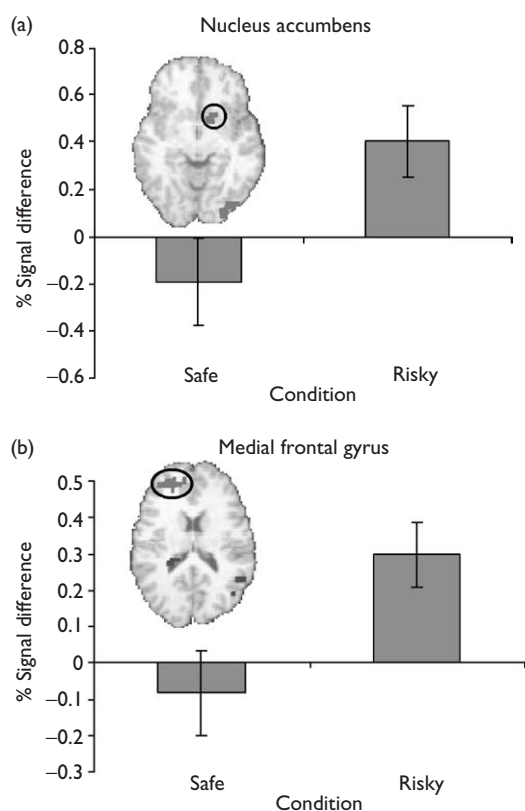


Fig. 3. Percent signal difference values during risky and safe responses in: (a) nucleus accumbens and (b) medial frontal gyrus.

response. In addition, the correlation between the harm avoidance subscale of the TCI and the degree of accumbens activation is consistent with the view that the magnitude of brain activations associated with risk-taking behaviors may predict overall risk-related personality and temperamental characteristics.

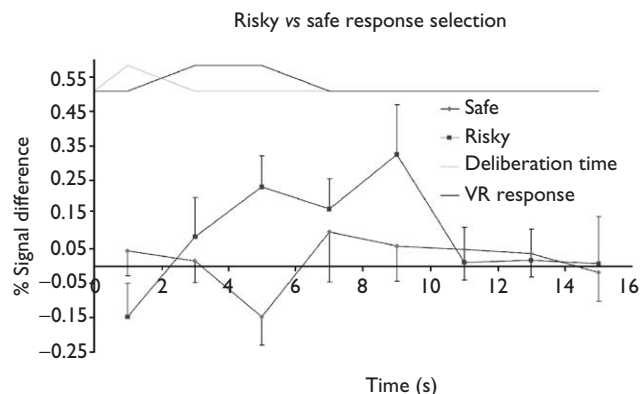


Fig. 4. Activation time course in the left nucleus accumbens during the deliberation of risky and safe responses. "VR response" in the figure above is the variable ratio response.

The nucleus accumbens has been found to be the key neural substrate for hedonic regulation for the prediction of forthcoming reward and for disruption by drugs of abuse [22,23]. Thus, the increased activation in the nucleus accumbens during the deliberation of risky responses, and the observation of increased risk-taking behaviors in individuals at risk for substance or drug-related problems, may point toward a common pathway for both risk behavior and reward processing. This view is consistent with the finding that the nucleus accumbens tracks the anticipation of a positive outcome [10]. If one assumes that activation of the nucleus accumbens is associated with a reinforcing behavior, one may speculate that certain risk-taking situations are reinforcing, i.e. lead to an increase in risky behaviors despite to potential for negative consequences. This hypothesis is consistent with previous interpretations of (a) drug-induced shifts in risky response patterns and (b) high levels of risk taking in individuals with conduct disorder and past substance dependence. Based on trial-by-trial analyses of risky response probabilities, these studies suggested that increased risk taking resulted from heightened sensitivity to reward and diminished sensitivity to aversive outcomes [14,24].

There are several limitations to this study. First, selecting risky responses is, when successful, always associated with a higher reward than selecting a safe response. Thus, one cannot completely eliminate the possibility that individuals process primarily the positive outcome but ignore the negative outcome. If that were the case, however, one would expect that harm avoidance would not be correlated with the amount of accumbens activation. Second, the deliberation time in this task was relatively short suggesting automatic processing of risky *vs* safe responses. In a future study, it may be of use to increase deliberation time by implementing response options that signal different degrees of risk, i.e. gains and losses.

CONCLUSION

The current study shows that the nucleus accumbens is critically involved in the deliberation of selecting a risky response. This activation is associated with the degree of harm avoidance. These findings support the notion that deliberation of a risky response is reinforcing and may partially explain why certain risk-taking behaviors occur.

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