

# Prefrontal, Parietal, and Temporal Cortex Networks Underlie Decision-Making in the Presence of Uncertainty

Martin P. Paulus,\*†‡ Nikki Hozack,\* Blanca Zauscher,\* Jennifer E. McDowell,†  
Lawrence Frank,‡§ Gregory G. Brown,†‡ and David L. Braff †

\*Laboratory of Biological Dynamics and Theoretical Medicine, †Department of Psychiatry, §Department of Radiology, University of California San Diego, San Diego, California 92093-0603; and ‡San Diego Veterans Administration Medical Center, San Diego, California

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**Decision-making in the presence of uncertainty, i.e., selecting a sequence of responses in an uncertain environment according to a self-generated plan of action, is a complex activity that involves both cognitive and noncognitive processes. Using functional magnetic resonance imaging, the neural substrates of decision-making in the presence of uncertainty are examined. Normal control subjects show a significant activation of a frontoparietal and limbic neural system during a two-choice prediction task relative to a two-choice response task. The most prevalent response strategy during the two-choice prediction task was “win-stay/lose-shift,” where subjects will repeat the previous response if it successfully predicted the stimulus and switch to the alternative response otherwise. Increased frequency of responses that are consistent with this strategy is associated with activation in the superior temporal gyrus. In comparison, increased frequency of response inconsistent with win-stay/lose-shift is associated with parietal cortex activation. These results support the hypothesis that subjects use a frontoparietal neural system to establish a contingency based decision-making strategy even in the presence of random reinforcement.** © 2001

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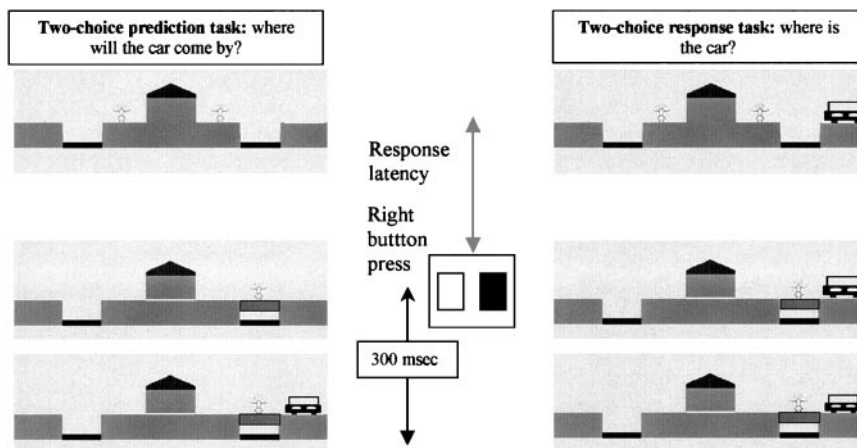
## INTRODUCTION

The prefrontal cortex is an essential brain substrate for a variety of neuropsychological processes including executive functioning, planning, reasoning, working memory, and context maintenance. Neuroimaging studies in humans have shown that tests of executive functioning are associated with activation of dorsolateral, ventromedial-orbitofrontal prefrontal, and cingulate cortex (Mellers *et al.*, 1995; D’Esposito *et al.*, 1995; Robbins, 1996; Cohen *et al.*, 1997; Owen *et al.*, 1998; Smith, Jonides, 1999; Mellers *et al.*, 1995). One key function of the prefrontal cortex is decision-making, i.e., selecting a response in the presence of a number of

response alternatives. Decision-making involves a set of cognitive and noncognitive processes, such as attention, working-memory (Bechara *et al.*, 1998), contingency approximation (Elliott and Dolan, 1998; Tversky *et al.*, 1988), hypothesis testing (Elliott and Dolan, 1998), and rule generation (Seale and Rapoport, 1997). In some decision-making situations involving judgments, the ventromedial prefrontal cortex appears to be a critical neural substrate that provides unconscious biasing steps to guide the subject to find an advantageous response (Bechara *et al.*, 1997). In other decision-making situations, i.e., when there is no *a priori* correct response and subject is using different rules to guide responses in the presence of uncertainty, the critical neural systems involved are not well understood.

Several decision-making tasks have been developed recently to examine the neural substrate underlying strategic decision-making. Specifically, a two-choice prediction task has been used by several investigators (Frith and Done, 1983; Elliott *et al.*, 1999; Lyon *et al.*, 1986) to examine decision-making in the presence of uncertainty. Central to this task is that the subject does not know which response is “correct” and does not know that each response is reinforced randomly. However, despite the random reinforcement, subjects do not select their sequences of responses randomly (Paulus, 1997; Paulus *et al.*, 1994). Instead, nonrandom sequences of responses support the basic hypothesis that subjects use rules that govern the decision-making process even in the presence of randomness. Remarkably, similar behavior has been observed in rodents on an animal analog of this task (Evenden, 1988).

A common decision-making strategy is called win-stay/lose-shift (Evenden and Robbins, 1983). When using this strategy, subjects select their current response based on the outcome of the previous situation. For example, if the previous response was reinforced, i.e., the subject was informed that the selected response was a “correct,” the subject chooses the same response



**FIG. 1.** Two-choice response task and two-choice guessing task. The subject sits in front of a computer. A house is shown in the center of the screen with a person to the left and right. Two-choice prediction task. The task is to decide whether a car will be presented on the left or the right side and to push a left or right button accordingly. After pressing a button, a bridge is shown on the left or right, respectively, and the car is presented for 300 ms on the left or right side by chance. Two-choice response task: the subject is instructed to press the Left or Right button depending on which side the car is shown. For both tasks, the computer randomly generates the location of the car. Both tasks are self-paced, i.e., the next trial is initiated after a brief (300 ms) time-out period.

again (win-stay). If the previous response was not reinforced, the subject switches to a different response (lose-shift). This investigation addressed the central question whether circumscribed neural substrates are activated when the subject is influenced by a specific strategy. Specifically, nonlinear assessment tools are used to quantify the degree to which sequences of responses during the two-choice prediction task are consistent with different possible strategies.

Previous neuroimaging studies support the notion that the neural substrate underlying the behavior observed in these tasks involves the both ventromedial and dorsolateral prefrontal cortex (Elliott and Dolan, 1998; Elliott *et al.*, 1999; Rogers *et al.*, 1999).

Therefore, the following hypotheses were examined. If the subject uses self-generated strategies while performing the two-choice prediction task and self-generated actions are associated with the activation of prefrontal cortex, then one would expect to see prefrontal activation confirming these previous reports. Moreover, if win-stay/lose-shift is the prominent strategy influencing the sequences of responses on this task and the prefrontal cortex is part of a neural network that underlies the behavior of this task, one would expect to see significant activation of the prefrontal cortex or associated areas with the fluctuating frequency of the win-stay/lose-shift rule during this task.

## METHODS

**Subjects.** This study was approved by the UCSD Human Subjects Committee. Twelve normal control, right-handed subjects (2 females and 10 males) age  $40.0 \text{ years} \pm 1.95$  (range 28–50) with an average education level of  $15.0 \pm 0.43$  years (range 12–18) partic-

ipated in this study. Subjects were screened for psychopathology using a structured clinical interview for DSM IV diagnosis and a MMPI-2 personality questionnaire. These subjects were given the two-choice response task and the two-choice prediction task prior to the experiment in the fMRI environment.

**Task.** The two-choice prediction task has been described in detail elsewhere (Paulus, 1997). A simple situation is presented graphically on a computer screen (see Fig. 1). The task for the subject is to predict the occurrence of a stimulus. The reinforcement schedule is determined beforehand such that 50% of the responses will be reinforced, i.e., each subject will “correctly” predict half of the presentations of the car. The two-choice response task requires the subject to select a response based on the presence of a stimulus. The duration of each trial for both the two-choice prediction and the two-choice response task depends on the latency between the presentation of the situation and the selection of the response. Therefore, the number of trials per experimental block depends on the subject’s average latency to select a response during the block. The key difference between these two tasks is that in the two-choice response task the subject knows the correct response before selecting a response and, therefore, does not have to invoke a strategy to select the correct response. In comparison, during the two choice prediction task, the subject does not know the correct response in advance and the sequence of previous responses and outcomes comprises the only information for the subject to guide the selection of the current response.

**Behavioral measures.** For both the two-choice prediction task and the two-choice response task, the fol-

lowing variables were recorded: (1) the choice selected by the subject (left or right), (2) the computer selected response (left or right), and (3) the latency to select a response or decision time (time from the presentation of the current situation to the selection of the response). Based on these variables, the strategies of decision making in the presence of uncertainty were assessed by two sets of measures: (1) General response biases: the number of left or right responses or stay (a left response followed by left response), versus switch (left followed by right response), responses. (2) The degree to which the current response is determined by the previous response, the previous stimulus, or a combination of both is quantified by mutual information measures. Mutual information functions (Herzfeld and Grosse, 1997) are based on the logarithmic likelihood ratio between the observed frequency of an event and the expected frequency of an event. These functions quantify the degree to which the co-occurrence of two observations is above chance level in units of bits. For example, if the subject selects the left response more often when the car was shown previously on the left side, the mutual information will quantify the bits of information contained in the response selection due to knowing the previous location of the car. The largest possible value of the mutual information is the number of bits necessary to predict the response. For example, if the subject chooses left 50% of the time, 1 bit is needed to determine any given response. If knowing the previous location of the car completely predicts the response then the mutual information between the location of the car and the response is 1 bit.

*fMRI protocol and image analysis pathway.* A standard fMRI protocol was used. Specifically, magnetic resonance images were obtained using a 1.5 Tesla whole body system (Siemens, Erlangen). Anatomical T1-weighted images of the whole brain (MPRAGE, TR/TE 11.4/4.4 ms, flip angle = 10°, FOV = 256 × 256 1 mm pixels, 1 mm slice thickness) were obtained sagittally to identify the anterior/posterior commissure, to coregister the functional image and to transform the images into Talairach space. Thirty-two slices of T2\*-weighted images were obtained in the transverse plane using echo planar imaging (TR/TE 60/40 ms, flip angle = 90°, 64 × 64 pixel FOV = 220 × 220 mm, 3-mm slice thickness) every 3000 ms for 112 repetitions. The in-plane resolution of the functional images was 3.43 × 3.43 × 3 mm. The slice thickness was chosen to minimize signal dropout related to magnetic susceptibility variations in the orbitofrontal cortex.

The image analysis pathway and statistical analysis of the images encompassed the following steps. First, the anatomical and functional images were reconstructed using programs developed by the UCSD fMRI group. All subsequent image processing was done using the Analysis of Functional Neuroimages (AFNI)

software package (Cox, 1996). Second, the echoplanar images were coregistered using a 3-D-coregistration algorithm to the echoplanar image that resulted in the smallest amount of image translation and rotation relative to all other images. Third, a regression analysis was carried out with a 0-1 boxcar reference function to predict the fluctuation in the linearly de-trended echoplanar image intensities as measured by a voxel-wise regression or fit-coefficient. Fourth, a Gaussian filter with FWHM 3.4 mm was applied to the regression-coefficient image to account for individual variations of the anatomical landmarks. Fifth, a voxelwise *t*-test with the null-hypothesis that the regression coefficient, predicting the signal intensity fluctuations between the two-choice prediction task and the two-choice response task equals to zero was conducted across all subjects to obtain a voxel-wise *t*-score image. Sixth, to control for false-positive regions of activation in the statistical images, the activation significance threshold was adjusted based on a Monte-Carlo simulation of filtered voxels' activation patterns, which takes into account spatial correlations (Gaussian FWHM 3.4), *a priori* significance thresholds ( $P < 0.05$ ), slice characteristics (3.4 × 3.4 × 3 mm), and number of voxels in an average brain volume (44 × 51 × 36) (Forman *et al.*, 1995). Based on these simulations, it was determined that a voxel-wise *a priori* probability of 0.05 would result in an *a posteriori*, cluster-wise activation probability of 0.05 if a minimum volume of 350  $\mu$ l and a connectivity radius of 3.43 mm was considered. This statistical threshold was applied to all subsequent analyses and corresponds to an *a posteriori* voxel-wise probability of  $P < 8.83 \times 10^{-6}$ . All results are presented as volume-thresholded *t* scores of the regression coefficient between the off-task condition (two choice response task) and the on-task condition (two-choice prediction task).

*Behavioral reference function.* The image analysis pathway described above used a reference vector based on the experimental block design comparing the two-choice prediction task with the two-choice response task. In addition, a reference vector was developed based on the response characteristics of each individual subject during the two-choice prediction task. Specifically, the behavioral reference function was obtained from the sequences of left/right responses and the presentation of the car obtained during the two-choice prediction task blocks. First, each response was classified as consistent with a win-stay/lose-shift strategy (+1), i.e., the subject selected the same response if it was previously reinforced (win-stay) or shifted to the other response if it was not reinforced (lose-shift). Otherwise the response was classified as inconsistent with a win-stay/lose-shift strategy (-1), e.g., if the subject switched from one response to the other despite correctly predicting the previous re-

sponse (win–shift). Second, a cumulative behavioral record was obtained from the sequences of win–stay/lose–shift strategy consistent or inconsistent responses (see Fig. 4A, gray line with black points). Third, in order to assess the fluctuation of win–stay/lose–shift consistent responses around the general tendency of the individual subject to select responses consistent with this strategy, a linear regression analysis was performed. Specifically, the cumulative behavioral record was fitted to a linear function. The residual or detrended behavioral record, i.e., the difference between the linear function and the cumulative behavioral record, quantifies when the subject was more or less likely to select responses consistent with a win–stay/lose–shift strategy during the two-choice prediction task blocks (see Fig. 4A, thin black line). Fourth, the detrended behavioral record of win–stay/lose–shift fluctuations was convolved with a Gaussian kernel (SD 2.8 s (Frackoviak *et al.*, 1997)) to account for the hemodynamic response inherent in the fMRI signal (see Fig. 4A, thick black line). Fifth, a regression analysis analogous to the analysis with the boxcar reference function described above was performed with the detrended behavioral record as a predictor for the echoplanar image intensity fluctuations during the two-choice prediction task. Sixth, the statistical analysis of the regression coefficients was conducted analogously to that described for the boxcar reference function. To summarize, a positive volume-threshold  $t$  score derived from the behavioral reference function signifies that the increased frequency of responses consistent with a win–stay/lose–shift strategy predicted increased echoplanar image intensity. In comparison, a negative  $t$  score signifies that an increase frequency of responses inconsistent with a win–stay/lose–shift strategy predicted an increased echoplanar image intensity.

*Statistical analysis.* A mixed model ANOVA was used to analyze the behavioral measures. Specifically, two within-subjects factors (block: two-choice prediction task or two-choice response task; repetition: 5 blocks) were used to determine whether the behavior differed across the two task conditions. In order to adjust the degrees of freedom for the correlations in within-subjects designs (violations of sphericity), Greenhouse–Geisser (GG) corrections were applied.

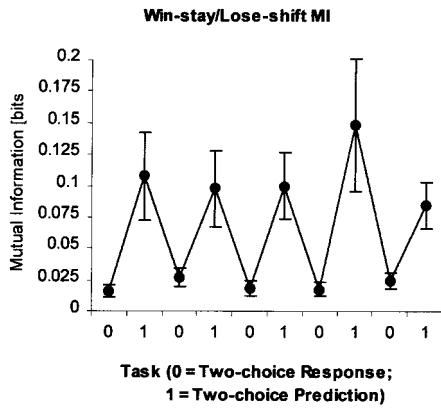
## RESULTS AND DISCUSSION

*Behavioral measures.* For each 30-s block, subjects selected on average 33.1 ( $\pm 2.3$ ) responses during the two-choice prediction task and 34.3 ( $\pm 1.2$ ) responses during the two-choice response task. The response frequency per block did not differ across task conditions ( $F_{GG}(1,11.0) = 0.48$ , NS) or repetitions ( $F_{GG}(2.1,23.8) = 2.92$ , NS), indicating that both tasks pose similar sensorimotor demands on the subject's response selection. The subjects selected the right response 47.7% ( $\pm 1.6$ )

of the time during the two-choice prediction task and 50.3% ( $\pm 0.8$ ) of the time during the two-choice response task. There was no significant difference in the number of right choices during the two-choice prediction task relative to the two-choice response task ( $F_{GG}(1,11.0) = 3.55$ , NS). However, there was an effect of repetition ( $F_{GG}(3.0,33.5) = 4.12$ ,  $P < 0.05$ ) and a repetition by task-type interaction ( $F_{GG}(3.3,36.1) = 2.93$ ,  $P < 0.05$ ), indicating the number of right versus left response fluctuated more during the two-choice response task when compared to the two-choice prediction task. The subject switched responses (from left to right or right to left) 46.9% ( $\pm 2.0$ ) during the two-choice prediction task and 49.6% ( $\pm 0.4$ ) during the two-choice response task. Response switching did not differ significantly across task conditions ( $F_{GG}(1,11.0) = 1.95$ , NS) but did differ across repetitions ( $F_{GG}(2.9,31.7) = 9.89$ ,  $P < 0.01$ ), indicating that while on the average subjects switched with similar frequency during the two-choice prediction task and the two-choice response task, different blocks during testing resulted in different rates of switching.

During the two-choice prediction task 4% of the information contained in the current response (or  $0.042 \pm 0.008$  bits per choice) was related to the selection of the previous response as determined by the mutual information measure whereas only 2% (or  $0.02 \pm 0.004$  bits per choice) of the current response was predictable by the previous response during the two-choice response task. The degree to which the previous response predicted the current response differed significantly across task-type ( $F_{GG}(1,11.0) = 9.36$ ,  $P < 0.05$ ) but did not vary significantly across repetition ( $F_{GG}(1.57,17.3) = 3.55$ , NS). Therefore, the previous response determined the current response during the two-choice prediction task but not during the two-choice response task. Ten percent (or  $0.108 \pm 0.027$  bits per choice) of the uncertainty underlying the current response selection could be accounted for by a win–stay/lose–shift strategy of during the two-choice prediction task. In comparison only 2% (or  $0.020 \pm 0.004$  bits per choice) of the uncertainty in the current response selection could be accounted for by a win–stay/lose–shift strategy during the two-choice response task. There was a significant effect of task-type ( $F_{GG}(2.9,31.7) = 9.36$ ,  $P < 0.01$ ) but not repetition ( $F_{GG}(2.2,24.6) = 0.47$ , NS), indicating that response selection was significantly influenced by a win–stay/lose–shift strategy during the two-choice prediction task but not during the two-choice response task.

*fMRI measures.* As shown in Fig. 3, the activation differences between the two-choice prediction task and the two-choice response task support the hypothesis that prefrontal structures are involved in decision-making and are in support of previous findings. Specifically, as shown in Table 1, in comparison to the

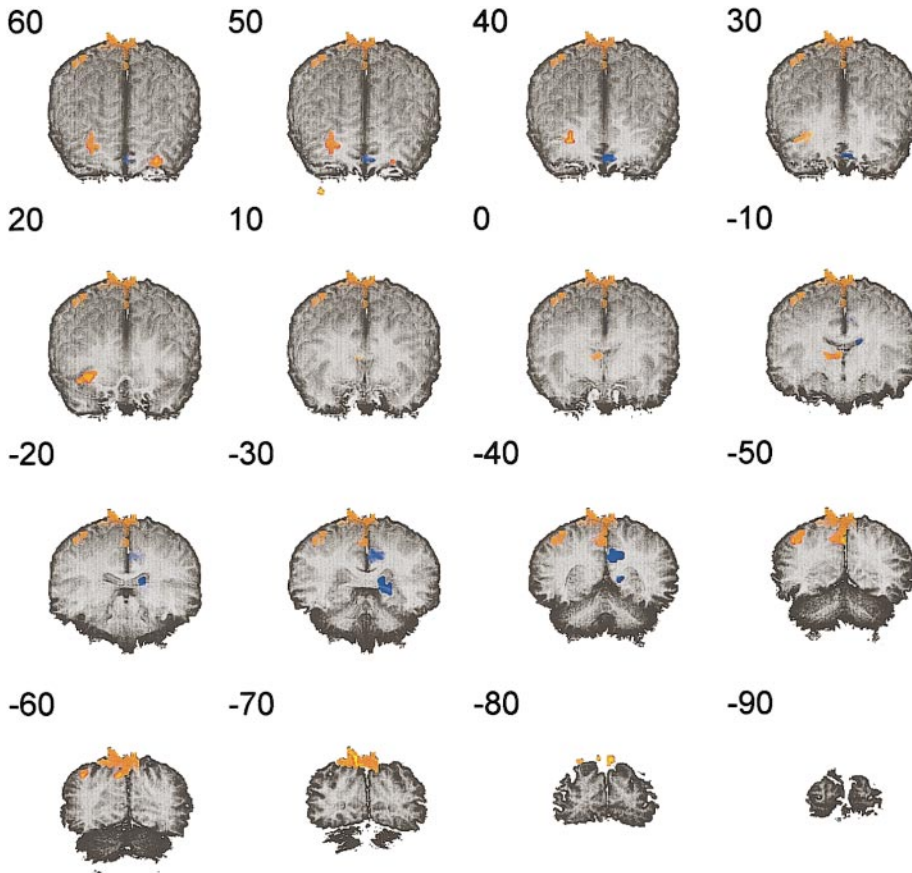


**FIG. 2.** The degree to which the previous outcome (win-stay/lose-shift MI) influences the current response during each trial block. The mutual information measures the degree to which the previous outcome predicts the selection of the current response during the on-task (two-choice prediction) and off-task (two-choice response) condition.

two-choice response task, subjects showed significant bilateral activation during the two-choice prediction task in Brodmann Area 10 (superior/middle frontal

gyrus) and Brodmann Area 7 (precuneus) (Fig. 3A). In addition the two-choice prediction task relative to the two-choice response task was associated with activation in the right insula, inferior parietal lobule, and MD thalamus nucleus. These results support the findings of a recent study using a similar experimental design, i.e., comparing a two-choice prediction task with a two choice reporting task (Elliott *et al.*, 1999). In contrast, there was significantly more activation during the two-choice response task relative to the two-choice prediction task in the corpus callosum and the posterior cingulate gyrus.

In order to link the win-stay/lose-shift strategy specifically to the activation pattern of a neural substrate, a behavioral reference function was generated for each subject based on the choice sequences during the two-choice prediction task. As shown in Fig. 4B, the degree to which an individual utilizes this strategy fluctuates substantially during the trial blocks, which is consistent with the notion that subjects use varying strategies during this task. In contrast to the hypothesis, there was no significant activation of the prefrontal cortex with fluctuations of win-stay/lose-shift. In-



**FIG. 3.** Volume-thresholded *t* map rendering of 12 controls. Anterior-posterior (*x*) cutpoints of the rendering are shown in Talairach coordinates. The two-choice prediction task relative to the two-choice response task activates bilateral prefrontal cortex, right middle frontal gyrus, bilateral precuneus, and deactivates posterior cingulate (Cluster coordinates are shown in Table 1).

TABLE 1

Clusters Activated during the Two-Choice Prediction Task Compared to the Two-Choice Response Task

Volume	Cluster location			Coordinates			T statistics		
	Location	BA	L/R	x	y	z	Mean	SEM	T <sub>Max</sub>
1134	Precuneus	BA 7	R	9	-73.3	49.6	3.8648	0.1666	6.3194
378	Middle frontal gyrus	BA 10	L	-28.1	55.5	6.5	3.4088	0.2612	5.6757
405	Precuneus	BA 7	L	-7.6	-77.4	45.3	3.8315	0.2331	5.3493
567	Superior frontal gyrus	BA 10	R	28.2	43.8	18	3.0018	0.1656	5.1332
486	Inferior parietal lobule	BA 40	R	40.5	-53.6	43.5	3.0768	0.2009	5.0252
756	Precuneus	BA 7	R	3.3	-57	43.3	2.8741	0.1291	4.5723
378	Insula		R	33.1	18.5	8.1	3.2603	0.1782	4.3976
378	MD thalamus		R	8.1	-13.1	10.8	2.2221	0.1307	3.0022
675	Cropus callosum		L	-17	-37.5	6.7	-2.5466	0.1215	-3.8735
432	Cingulate gyrus	BA 31	L	-10.1	-41.5	34	-2.768	0.1582	-3.7148

Note. Each voxel was thresholded at  $t > 2.06$  (voxel-wise  $P < 0.05$ ) and a minimum volume of 350  $\mu\text{l}$  ( $>10$  contiguous voxels) with a cluster connectivity radius of 3.43 mm. The  $T_{\text{max}}$  indicates the largest  $t$  value within the cluster. A  $t$  score greater than zero signifies that the area is more activated during the two-choice prediction task relative to the two-choice response task,  $t$  less than zero corresponds to an area with increased activation during the two-choice response task relative to the two-choice prediction task.

stead, as shown in Fig. 5 and Table 2, two areas posterior to the activation associated with the two-choice prediction task relative to the two-choice response task are involved in generating the win-stay/lose-shift strategy.

First, increased right superior temporal gyrus (BA 22) activation is associated with an increased response selection consistent with a win-stay/lose-shift strategy. Second, increased bilateral precuneus activation (BA 7) was associated with decreased response selection that consistent with a win-stay/lose-shift strategy. These results support the hypothesis that changes in frequency of win-stay/lose-shift is associated with temporal and parietal cortex and not with prefrontal areas.

Decision-making in the presence of uncertainty involves a network of structures including prefrontal (BA 10) and parietal cortex (BA 7, 40). The relative frequency with which a subject selects a response that is consistent or inconsistent with a win-stay/lose-shift strategy was associated with fluctuating activation in the temporal (BA 22) and parietal (BA 7) cortex but not in the prefrontal cortex. The response frequency and decision times were similar for both tasks, which supports the notion that similar efforts are exerted during

both tasks. Finally, the main difference between the two tasks is the utilization of information about past responses and past outcomes when generating the current response. Therefore, the activation differences between the two tasks are primarily related to the dynamical aspects of decision-making, i.e., how the current response is part of a sequence of responses that are generated according to a plan of action.

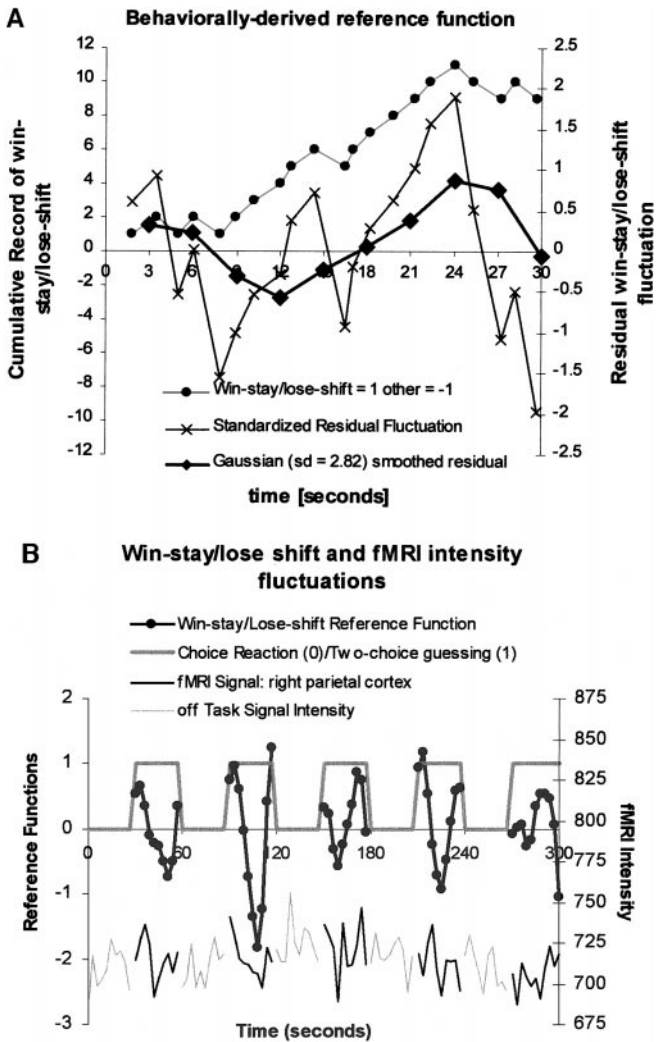
The Talairach coordinates of activation clusters in this study match several areas reported in a previous investigation comparing a two-choice guessing task with a choice reporting task reported activation (Elliott *et al.*, 1999). Specifically, the areas that activated during a two-choice prediction task relative to a choice reporting task were labeled BA 9/46 but the center of mass of the activated areas are in proximity to BA 10, which correspond to the area activated in this study. Moreover, in the previous study, the right precuneus was activated during the two-choice prediction task relative to the choice reporting task. Finally, in the previous study activation of MD thalamus was found in the two-choice prediction task relative to the choice reporting or two-choice response task. More recently, using PET technique and a two-choice gambling task, Rogers *et al.* (1999) reported that resolving conflicting

TABLE 2

Cluster Activated with the Behaviorally Defined Wins-Stay/Lose-Shift Reference Function

Volume	Cluster location			Coordinates			T statistics		
	Location	BA	L/R	x	y	z	Mean	SEM	T <sub>Max</sub>
351	Superior temporal gyrus	BA 22	R	46.9	-25.2	15.1	2.6455	0.1081	3.533
459	Precuneus	BA 7	L	-4.3	-59.9	56.5	-3.185	0.2196	-5.229

Note. Labels and statistics are analogous to those described in Table 1.



**FIG. 4.** (A) The derivation of the behavioral reference function (for details see text). The y-axis for the cumulative record is plotted on the left, the y-axis for the residual fluctuation following linear detrending and convolution with a Gaussian function is shown on the right. (B) The choice response (off) and two-choice prediction (on) boxcar reference function and the behaviorally derived win-stay/lose-shift reference function for a representative subject. The echoplanar image intensity fluctuation of a voxel in the right STG, which correlated with the behavioral reference function  $r = 0.47$ , is shown below.

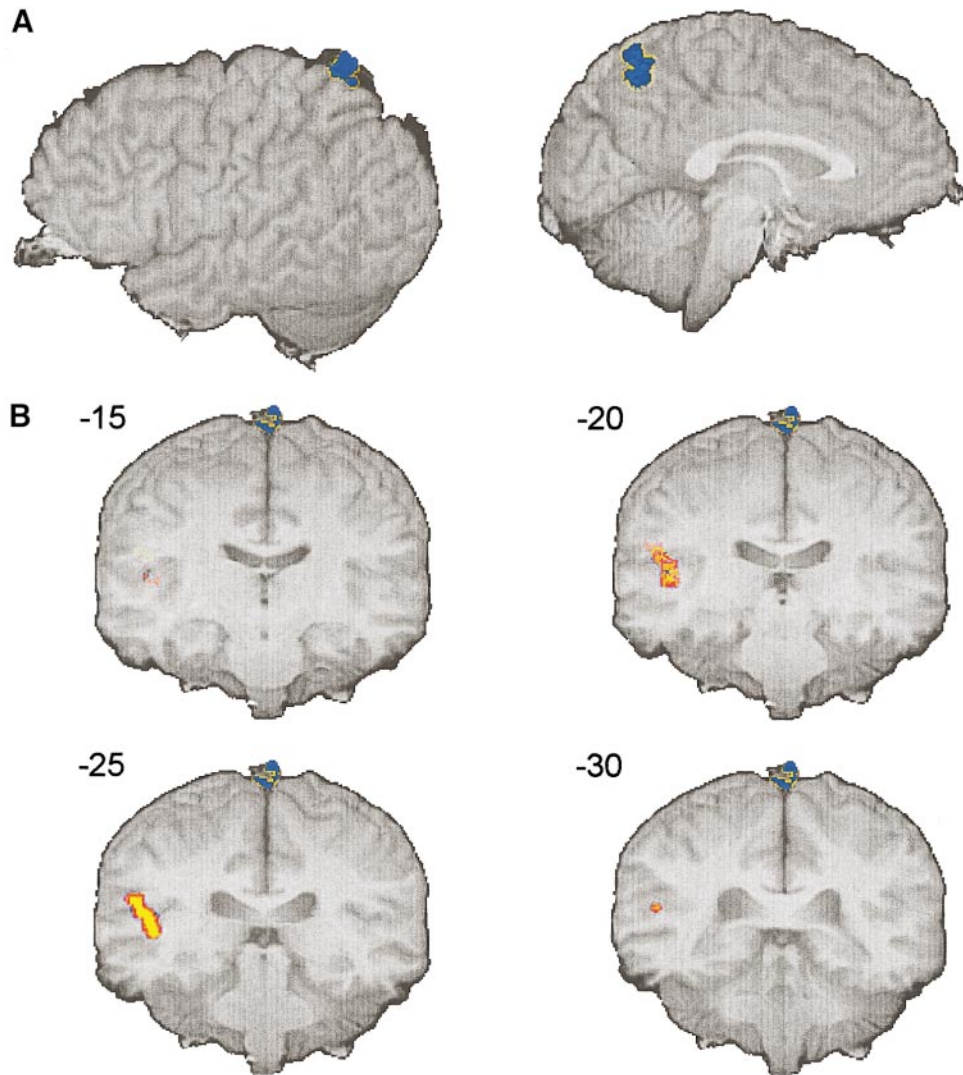
decisions was associated with activation in BA 10, BA 11, and BA 47. These results support the current finding that in the presence of equally conflicting response alternatives, i.e., choosing the left or right response with equally uncertain outcome, the prefrontal cortex provides important modulatory information that guides the selection of the responses. The modest overall degree to which win-stay/lose-shift predicted the current response (Fig. 2) and the significant fluctuations of the win-stay/lose-shift consistent responses throughout the task (Fig. 4) support the notion that

subjects switch among different strategies, which is consistent with the maintenance of prefrontal activation throughout the two-choice prediction task. Therefore, subjects do not select one strategy exclusively and select response according to one rule only, instead, the sequences of choices result from the combination of different rules.

In contrast to the proposed hypothesis, fluctuation of the win-stay/lose-shift strategy during the two-choice prediction task was not associated with fluctuation of prefrontal activation. Instead, fMRI signal intensity fluctuations in the superior temporal gyrus and the precuneus correlated with response selection consistent or inconsistent with this strategy, respectively. According to posttest reports from subjects, this task involves two complementary cognitive processes. First, subjects generate a strategy that is based on the response and/or stimulus history to “predict” the current presentation of the stimulus. Second, subjects modify their strategy based on their prediction “success.” Accordingly, subjects may alternate between initiation of a new strategy and maintaining the current strategy and assessing its success. The behavioral reference functions constructed here are able to quantify the latter but not the former. Both STG and precuneus have been associated with subprocesses that are consistent with the maintenance of strategies in the presence of uncertainty. For example, the left superior temporal gyrus activation has been associated with higher semantic associations (Jessen *et al.*, 1999), context-dependent processing (Opitz *et al.*, 1999), and with detecting the degree of predictability in a variably random sequence of stimulus presentations (Bischoff-Grethe *et al.*, 2000). Therefore, the activation in this area may relate to assessing the success of the win-stay/lose-shift strategy during the two-choice prediction task.

The extensive activation of the precuneus is consistent with previous reports that have implicated this structure in temporal order retrieval (Cabeza *et al.*, 1997), attentive tracking (Culham *et al.*, 1998), category shifting (Nagahama *et al.*, 1998), generation of response sequences (de Zubicaray *et al.*, 1998), sequence learning (Sakai *et al.*, 1998), hypothesis testing (Elliott and Dolan, 1998), episodic memory retrieval (Fletcher *et al.*, 1995; Krause *et al.*, 1999; Shallice *et al.*, 1994), and temporal context recognition (Zorrilla *et al.*, 1996). Therefore, the inverse correlation between the win-stay/lose-shift behavioral reference function and the activation in the precuneus may signify that this structure is critical in supplying alternative strategies, that take into account stored contingencies between the generated responses and their outcome.

This role of the precuneus is consistent with a model that has been put forth recently, which combines sensory-motor processing, attentional modulation of sensory and motor signals with reward contingent infor-



**FIG. 5.** Volume thresholded  $t$  map rendering of the behaviorally derived reference function in 11 controls shows deactivation in left precuneus (A) and activation in right temporal cortex (B). Anterior–posterior ( $x$ ) cutpoints of the rendering are shown in Talairach coordinates.

mation (Platt and Glimcher, 1999). The contingencies represent the subject's cognitive rule set. Accordingly, the decision-making process involves attentional and postattentional processes that enable the subject to form response strategies that are based on the previous responses and stimuli as well as their associated outcome. The current data support the hypothesis that there is a close connection between brain areas that have been associated with executive functioning (prefrontal cortex) and areas that show activation to varying contingencies with stimulus presentation (parietal cortex).

Decision-making is a complex process and may involve different neural networks based on the task demands. As opposed to other decision-making tasks, e.g., the Bechara and Rogers Gamble Task, there is no advantageous or disadvantageous strategy during the

two-choice prediction task. The feedback, i.e., whether the prediction was correct or incorrect, does not assist the subject to find a "best" strategy. There is converging evidence from imaging studies (Rogers *et al.*, 1999) and studies with ventromedial prefrontal cortex lesion subjects (Bechara *et al.*, 1998) that the ventromedial prefrontal cortex is a critical neural substrate to help guide selecting advantageous strategies via noncognitive hunches. The current finding supports the hypothesis that areas more dorsal than the ventromedial prefrontal cortex are involved in initiating decision-strategies in a completely random environment. Thus, there may be a continuum of decision-making situations in the presence of uncertainty between searching for a "best" strategy in absence of an a-priori optimum rule and finding rules that result in advantageous decision-making. This hypothesis can be examined using

the two-choice prediction task by assigning differential "success" rates to *a priori* defined sequences of responses.

Alternatively, the decision-making process may parallel attentive processes during a visuospatial task. It has been proposed that attention draws upon the functional neuroanatomy of more basic sensory and motor processes for its instantiation (Nobre *et al.*, 2000). It appears that transmodal centers of higher association areas are critical computational centers for large-scale neurocognitive networks and may provide the key substrate for attentional, motivational, and emotional modulations of sensorimotor data (Mesulam, 1998). Thus, it is not surprising that the key areas reported here also correspond to neural substrates that have been reported with spatial processing and neglect (Mesulam, 1999). Therefore decision-making may correspond to the computational activity of transmodal centers of visuospatial processing areas with volitional components. Future studies can examine this hypothesis by systematically varying the visuospatial, attentional, and volitional processing demands of the two-choice prediction task. In conclusion, decision-making in the presence of uncertainty involves a network of structures including parietal, prefrontal, and cingulate cortex, which support attentional, working memory, evaluative processes, respectively. Moreover, these processes are highly dynamic and fluctuate significantly across the test session.

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