

Error Rate and Outcome Predictability Affect Neural Activation in Prefrontal Cortex and Anterior Cingulate during Decision-Making

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Decision-making in the presence of uncertainty is a complex process that involves both affective and cognitive factors. Both error rate and predictability have been implicated in the process of response selection during decision-making. This study examined the hypothesis that the rate of errors during decision-making differentially affects the activation in prefrontal and cingulate cortex. BOLD echo-planar signal intensity was obtained during a two-choice prediction task across 90-s blocks with 20, 50, or 80% error rates. This study yielded three main findings. First, at chance level error rates, activation of the right dorsolateral (BA 9, 46), inferior prefrontal (BA 44), and precuneus (BA 7) during the two-choice prediction task replicated the finding previously reported. Second, premotor (BA 6) and parahippocampal (BA 36) areas were relatively more active at high error rates, and dorsolateral (BA 9, 46) and inferior prefrontal cortex (BA 44) as well as parietal (BA 40) and cingulate cortex (BA 25, 32) were more active during low error rates. Third, the relationship between the frequency of the dominant strategy underlying decision-making (win-stay/lose-shift) and the activation in the dorsolateral prefrontal cortex and the anterior cingulate was dependent on error rate or outcome predictability. These results support the hypothesis that error rates and predictability affect the activation patterns in the neural systems underlying decision-making because these structures maintain a representation of the reinforcement history for the available response alternatives to select an “optimal strategy.” © 2002 Elsevier Science (USA)

INTRODUCTION

Decision-making when the outcome is uncertain is a complex process. This investigation examines the neural substrate activation underlying two components of this complex process. Error rate, i.e., the number of responses associated with an adverse outcome, and predictability, i.e., whether the subject can predict a successful or adverse outcome, are varied in a para-

metric design using a simple decision-making task during functional magnetic resonance imaging (fMRI). Error rate and outcome predictability are central to several psychological models that have been proposed to explain the response selection process during decision-making. When the outcome of a decision is uncertain, subjects typically select the response which is associated with the highest anticipated reinforcement, i.e., how likely the response will lead to a “correct” outcome (Calfee and Atkinson, 1966; Goulet and Barclay, 1967; Ludvigson, 1966). This behavior corresponds to the well-known matching law that has been observed in a large number of animal studies (Herrnstein *et al.*, 1997). Several psychological models have been proposed to explain how response selection depends on reinforcement history, even in the presence of random reinforcement (Rose and Vitz, 1966). However, the neural substrate underlying these processes is poorly understood.

Behaviorally, the ventromedial prefrontal cortex has been implicated in this type of decision-making, perhaps driven by unconscious hunches (Bechara *et al.*, 1998), presumably by signaling the degree to which a response predicts rewards or punishments (Damasio *et al.*, 1996). Previous neuroimaging studies using a simple two-choice decision-making paradigm have shown task-related activation in both ventromedial (Elliott *et al.*, 1999) and dorsolateral prefrontal cortex (Paulus *et al.*, 2001), as well as anterior cingulate activation (Elliott and Dolan, 1998), an area that has been implicated in the monitoring of response conflict (Carter *et al.*, 1999). Ventromedial prefrontal and subcortical areas have been associated with reward-related aspects during decision-making (O’Doherty *et al.*, 2001). Fluctuation in reward, as defined by an average value of points gained during a simple decision-making task, was associated with activation in ventral striatum, hippocampus, and parahippocampal gyrus (Elliott *et al.*, 2000). Moreover, “context-dependent” reward-related responses, as defined by gains or losses relative to overall amount of reward gained, were associated with activation in thalamus, pallidum, insula, and lateral

orbitofrontal cortex. Differential activation of both amygdala and inferior prefrontal cortex (BA 44/47) has been reported with “winning” versus “losing trials” (Zalla *et al.*, 2000). Finally, dopaminergic activation in the ventral striatum has been observed during video game playing (Koepp *et al.*, 1998). These results are consistent with extensive experimental evidence from animal studies (Robbins and Everitt, 1982) supporting the hypothesis that target areas of the dopamine system may be critically involved in modulation of response selection based on reinforcement history.

Thus, although there is some evidence that several prefrontal, limbic, subcortical, and parietal areas are involved in decision-making, their precise role as it relates to the reinforcement history is not well understood. Therefore, this study examined the influence of error rate and predictability on the neural activation patterns during a simple decision-making task. Activation of neural substrates as measured by the BOLD change of echo-planar image intensity was obtained during three different conditions of the two-choice prediction task. The number of “correct” responses was a priori determined by a computer algorithm to be 20, 50, or 80%. Thus, the error rate was either low (80% “correct” responses), at chance level (50% “correct” responses) or high (20% “correct” responses). Correspondingly, the predictability of the outcome was either low (50% “correct” responses) or high (20% “correct” responses, predictably “wrong”; 80% “correct” responses, predictably “right”). It was hypothesized that, if prefrontal cortex is critical in signaling the reward-ef ficacy of responses, increased task-related activation should be observed during decision-making with low error rates. In addition, if the anterior cingulate serves to resolve response conflict, as has been proposed by others (Carter *et al.*, 1999), and response conflict is related to the degree to which a response predicts the outcome, a task-related change in activation would be predicted when the predictability of the outcome was low (50% “correct” responses, chance level) compared to a more predictable outcome (20 or 80% “correct” responses).

MATERIALS AND METHODS

Subjects

This study was approved by the UCSD Institutional Review Board (No. 000730). Sixteen normal control, right-handed subjects (4 females and 12 males) age $38.9 \text{ years} \pm 1.8$ (range 21–50) with an average education level of 15.3 ± 0.6 years (range 12–21) participated in this study. Subjects were recruited via advertisement in local newspapers. Only subjects that did not have a lifetime history of Axis I DSM IV disorders based on a structured clinical interview for DSM IV diagnosis (Spitzer *et al.*, 1992) or did not have a

MMPI-2 clinical profile (Greene, 1991) with *t* scores >70 were asked to participate in the study. 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). Briefly, a house flanked by a person to the left and right is shown on a computer screen. The goal for the subject is to respond in such a way that a person on the computer screen can meet up with a car that is presented on the far left or right side of the screen. For the *two-choice prediction task*, the subject is told to decide on which side the car will be presented. AFTER the subject has made a response, the car is presented for 300 ms on the far left or right side. If the selected response matches the side on which the car is presented, the person on the selected side meets up with the car. Unbeknownst to the subject, the car is presented according to a predetermined schedule. Specifically, a computer program, which takes the response of the subject into account, determines whether a response will be “correct” or “incorrect.”

For the *two-choice response task*, the car is presented on the left or right side BEFORE the subject is asked to respond. The duration of each trial depends on the latency to make a decision, i.e., the time between presentation of the initial situation and the selection of the response. Therefore, the number of trials per experimental block depends on the subject’s average decision-time during the block. The key difference between these two tasks is that during the *two-choice prediction task*, the *subject does not know the correct response in advance*, has to decide in the presence of uncertainty, and can use the previous responses, stimuli, and outcomes to determine the current response. In comparison, during the *two-choice response task* the *subject knows the correct answer before selecting a response*, decides in the presence of certainty, and does not need to use the sequences of previous responses, stimuli, or outcomes. The task was presented to the subjects using an LCD projector, back-projected onto a screen at the subject’s feet, which could be seen via a mirror attached to the head coil. Subjects requiring corrective lenses were provided with a pair of plastic-framed lenses that approximated their degree of correction. Motor responses were made using a fiber-optic button box.

A block design was used for this study. The two-choice prediction task was divided into three trial blocks, each lasting 90 s. During the first trial block the computer program ensured that 50% of all responses were “correct,” during the second trial block, 20% of all responses “correctly predicted” the location of the car,

and during the third trial block, 80% of all responses were “correct” predictions. Therefore, the first trial block corresponds to “evenly right or wrong,” the second trial block to being “mostly wrong,” and the third trial block to being “mostly right.” To examine task-related activation the two-choice prediction task was contrasted with the two-choice response task, which was presented between the 50 and the 20% as well as between the 20 and the 80% trial blocks for 30 s.

Behavioral Measures

The choice selected by the subject (*left* or *right*), the computer-selected response (*left* or *right*), and the latency to select a response (time from the presentation of the current situation to the selection of the response) were obtained for both tasks. 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* followed by *left* response) versus *switch* responses (*left* followed by *right* response). (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 (Herzel and Grosse, 1995).

fMRI Protocol and Image Analysis Pathway

Magnetic resonance images were obtained using a 1.5-T whole-body system (Siemens, Erlangen). Anatomical T1-weighted images of the whole brain (MPRAGE, TR = 11.4 ms, TE = 4.4 ms, flip angle 10°, FOV 256 × 256, 1-mm³ voxels) were obtained sagittally to identify the anterior/posterior commissure, to coregister the functional image, and to transform the images into Talairach space (Talairach and Tournoux, 1988). Thirty-two slices of T2*-weighted images were obtained in the transverse plane using gradient-recalled echo-planar imaging (TE = 40 ms, flip angle 90°, 64 × 64-pixel FOV = 220 × 220 mm, 3-mm contiguous slice thickness) every 3000 ms for 112 repetitions yielding a voxel size of 3.43 × 3.43 × 3 mm in order to minimize signal dropout related to magnetic susceptibility variations in the orbitofrontal cortex. The inferior frontal slices of all echo-planar images were examined for signal intensity.

All structural and functional image processing was done using the Analysis of Functional Neuroimages (AFNI) software package (Cox, 1996). Echo-planar images were coregistered using a 3D-coregistration algorithm to the echo-planar image that resulted in the smallest amount of image translation and rotation relative to all other images. The main measure of task-related activation was the percentage signal change during the two-choice prediction task relative to the two-choice response task across three delay times. Multiple regression analysis was used to quantify the

fMRI time series data (Courtney *et al.*, 1997). First, three different reference functions were used to measure the degree of echo-planar signal change during the 50, 80, and 20% error rate conditions, respectively. Second, the AFNI program 3dDeconvolve was used to calculate the estimated impulse response function between the reference function and the echo-planar time series using a time shift of 1 to 3 TR (i.e., 3 to 9 s) at each voxel. Third, the regressor coefficients for each time shift were added and divided by the zeroth order regressor coefficient, which measures the average signal intensity for the “off” task condition (i.e., the two-choice response task trial blocks). Fourth, a Gaussian filter with FWHM 3.4 mm was applied to voxel-wise percentage signal change data to account for individual variations of the anatomical landmarks. Fifth, the data of each subject were normalized to Talairach coordinates. Sixth, the measure of relative change of signal intensity during a task of interest (two-choice prediction task during different reinforcement conditions) relative to the baseline task (two-choice response task) was entered into a mixed-model ANOVA. In order to examine the effect of error rates, the task-related activation during low error rates (80% correct) was compared to the high error rate condition (20% correct). Second, to determine the effect of predictability on neural substrate activation, the activation pattern during the 50% reinforcement condition was compared to the average activation during the 20 and 80% reinforcement condition. Seventh, a threshold adjustment method based on Monte Carlo simulations was used to guard against identifying false-positive areas of activation (Forman *et al.*, 1995). 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 350 μ l and a connectivity radius of 3.43 mm was considered. This statistical threshold was applied to all subsequent analyses and corresponds to an uncorrected voxel-wise probability of $P < 8.83 \times 10^{-6}$. All results are presented as volume-thresholded *t* maps of the planned comparisons across the different task conditions. Labels for brain activation foci were obtained in Talairach coordinates using the Talairach Demon software (Lancaster *et al.*, 2000), which provides accuracy similar to that of neuroanatomical experts.

Statistical Analysis

All analyses for the behavioral data were carried out with SPSS 10.0 (Norusis, 1990). A mixed-model ANOVA was used to analyze the behavioral measures. Specifically, one within-subjects factor (error rate 20, 50, or 80%) was used to determine whether the behavior differed across the two task conditions. The planned comparisons were evaluated using the least significant difference (LSD) post hoc analysis. 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

Subjects made 78 ± 7 , 85 ± 6 , and 86 ± 6 responses during the 90-s 50, 80, and 20% error rate trial blocks, respectively. The response rate did not differ significantly across the three error rate conditions ($F_{GG}(1.4, 21.6) = 1.74$, $P = 0.21$). The response frequency measured as responses per second was calculated to determine whether the number of motor responses differed between the two-choice prediction and the two-choice response task. The response frequency for the two-choice prediction task was 0.86 ± 0.07 , 0.92 ± 0.07 , and 0.96 ± 0.06 for the 50, 20, and 80% reinforcement condition. In comparison, the response frequency for the two-choice response task was 0.98 ± 0.07 . The response frequency did not differ significantly across all trial blocks ($F_{GG}(1.8, 27.2) = 1.52$, $P = 0.23$). Moreover, pair-wise comparison across different trial blocks did not yield significant differences in response frequency between the two-choice prediction task and the two-choice response task.

Subjects chose the RIGHT response $51\% \pm 2$, $46\% \pm 2$, and $48\% \pm 1$ of the time during the 20, 50, and 80% error rate trial blocks, respectively. The rate of choosing RIGHT versus LEFT differed significantly across error rate conditions ($F_{GG}(1.9, 29.1) = 4.70$, $P < 0.01$). Specifically, subjects chose the RIGHT response significantly more often during low error rates than during high error rates (LSD, $P < 0.05$). Subjects switched from RIGHT to LEFT or LEFT to RIGHT $37\% \pm 3$, $47\% \pm 2$, and $55\% \pm 2$ of the time during the 20, 50, and 80% error rate trial blocks, respectively. The rate of response switching differed significantly across error rate conditions ($F_{GG}(1.7, 25.8) = 12.76$, $P < 0.01$). Specifically, subjects switched more frequently during high error rates relative to chance level error rates (LSD, $P < 0.01$) and low error rates (LSD, $P < 0.01$). Correspondingly, subjects switched significantly less frequently during the low error rates relative to chance level error rates (LSD, $P < 0.05$). The degree of win-stay/lose-shift strategy as measured by the win-stay/lose-shift mutual information function accounted for approximately 9% of the predictability of the current response and did not differ significantly across error rate conditions ($F_{GG}(1.6, 24.7) = 1.32$, $P = 0.28$). Subjects responded consistently with win-stay $66\% \pm 5$, $59\% \pm 4$, and $66\% \pm 6$ and with lose-shift $48\% \pm 6$, $54\% \pm 6$, and $59\% \pm 3$ of the time during the 20, 50, and 80% error rate trial blocks, respectively.

fMRI Measures

Task-related activation (percentage signal change two-choice prediction task–two-choice response task) was observed in bilateral premotor and prefrontal cortex (BA 6, 44, and 46), superior temporal gyrus (BA 39), and precuneus (BA 7) during the 50% reinforcement condition (Figs. 1A–1C, 2A, and 2B and Table 1). These areas include those reported earlier in a separate experiment (Paulus *et al.*, 2001). During high error rates (80% versus 50% errors), subjects showed more task-related activation in the left superior frontal gyrus (BA 6) and the right parahippocampal gyrus (BA 36). In comparison, during low error rates (20% versus 50%), subjects showed more task-related activation in bilateral prefrontal cortex (BA 9, 10, 44, 46, and 47) and the parietal cortex (BA 40) (Figs. 1D–1F, 2C, and 2D and Table 1). Finally, higher outcome predictability (80 and 20% versus 50% error rate) was associated with more task-related activation in prefrontal (BA 9, 44, and 47), parietal (BA 18 and 40), and different areas of the anterior as well as the posterior cingulate (BA 25, 31, and 32) (Figs. 1G–1I, 2E, and 2F and Table 1). Specifically, there was less task-related activation in both subgenual and dorsal anterior cingulate (Fig. 4B) when the outcome was most uncertain (Fig. 4A).

fMRI–Behavior Relationships

Given that more than half of the responses were consistent with either win-stay or lose-shift, the relationship between task-related activation and individual differences in the frequency of win-stay or lose-shift consistent responses was examined to determine the computational role of the areas involved in decision-making (Table 2). Task-related activation in the left dorsolateral prefrontal cortex (BA 9, 45) at low error rates (20%) was reduced when subjects generated more win-stay consistent responses (Fig. 3). In contrast, when the outcome was most unpredictable, task-related activation in left dorsolateral prefrontal cortex (BA 9) increased when subjects generated more win-stay consistent responses (Table 2, Fig. 3). The increased activation in the parahippocampal gyrus during high error rates was associated with an increase in lose-shift consistent responses (Table 2). Subjects that generated a higher frequency of win-stay consistent responses during low error rates showed less activation in both dorsal and rostral ventral anterior cingulate (Figs. 4C and 4D). Finally, rostral-ventral anterior cingulate activation (BA 24/32) was related in opposite directions to lose-shift consistent responses at low and high error rates. Subjects that generated many lose-shift consistent responses at low error rates showed less activation (Fig. 4C), whereas subjects that generated more lose-shift consistent responses at high error rates showed more activation in this structure (Table 2). In combination these findings support the hypoth-

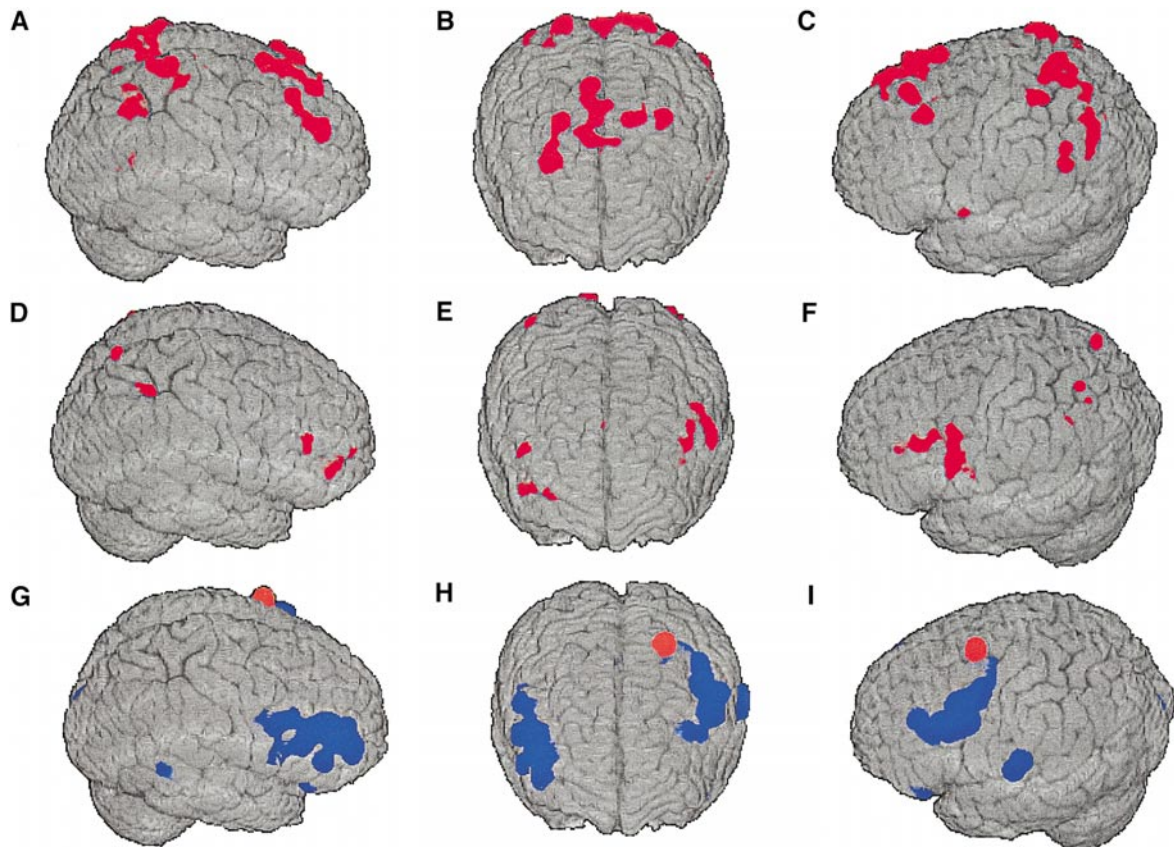


FIG. 1. Rendering of volume-thresholded task-related activation (red, increased echo-planar signal intensity; blue, reduced echo-planar signal intensity) for 50% reinforcement (A–C) and 80% reinforcement (D–F) and contrast between 50% and 20 or 80% reinforcement (G–I).

esis that the frequency variations of the predominant response selection strategies underlying decision-making are associated with task-related activation in the prefrontal cortex and anterior cingulate in a context-dependent manner. That is, error rate and predictability modulate whether adherence to a strategy is associated with an increase or decrease in activation.

This investigation yielded three main findings. First, at chance level error rates activation of the right dorsolateral (BA 9, 46), inferior prefrontal (BA 44), and precuneus (BA 7) during the two-choice prediction task replicated the finding previously reported (Paulus *et al.*, 2001) and is consistent with other reports of simple two-choice decision-making tasks (Elliott *et al.*, 1999). Second, relative to chance level error rate decision-making, premotor (BA 6) and parahippocampal (BA 36) areas were relatively more active at high error rates and dorsolateral (BA 9, 46) and inferior prefrontal cortex (BA 44) as well as parietal (BA 40) and cingulate cortex (BA 25, 32) were more active during low error rates. Third, the relationship between the frequency of the dominant strategy underlying decision-making (win–stay/lose–shift) and activation in the dorsolateral prefrontal cortex and the anterior cingu-

late was dependent on error rate or outcome predictability.

The increased activity of the bilateral dorsolateral (9, 46) and inferior prefrontal cortex (BA 44, 47) as well as the inferior parietal lobule (BA 40) and both dorsal and rostral-ventral cingulate cortex during low error rates (20%) is consistent with the first main hypothesis. Previous behavioral studies have shown that subjects adjust their response strategies according to the reinforcement history (Calfee and Atkinson, 1966). At low error rates, subjects switch relatively less frequently from one response to another, which is consistent with establishing a predominant response pattern. An infrequent error may signal to the subject that the established pattern is incorrect. Consequently, the subject may have to inhibit the currently ongoing strategy and shift to an alternative strategy. Thus, it is not surprising that the areas activated during low error rates have also been reported to mediate “cognitive inhibition” (Liddle *et al.*, 2001; Rubia *et al.*, 2001). The response requirements for the two-choice prediction task are sequences of left and right button pushes. If these sequences are generated by underlying strategies then changes in strategies require the inhibition of ongoing

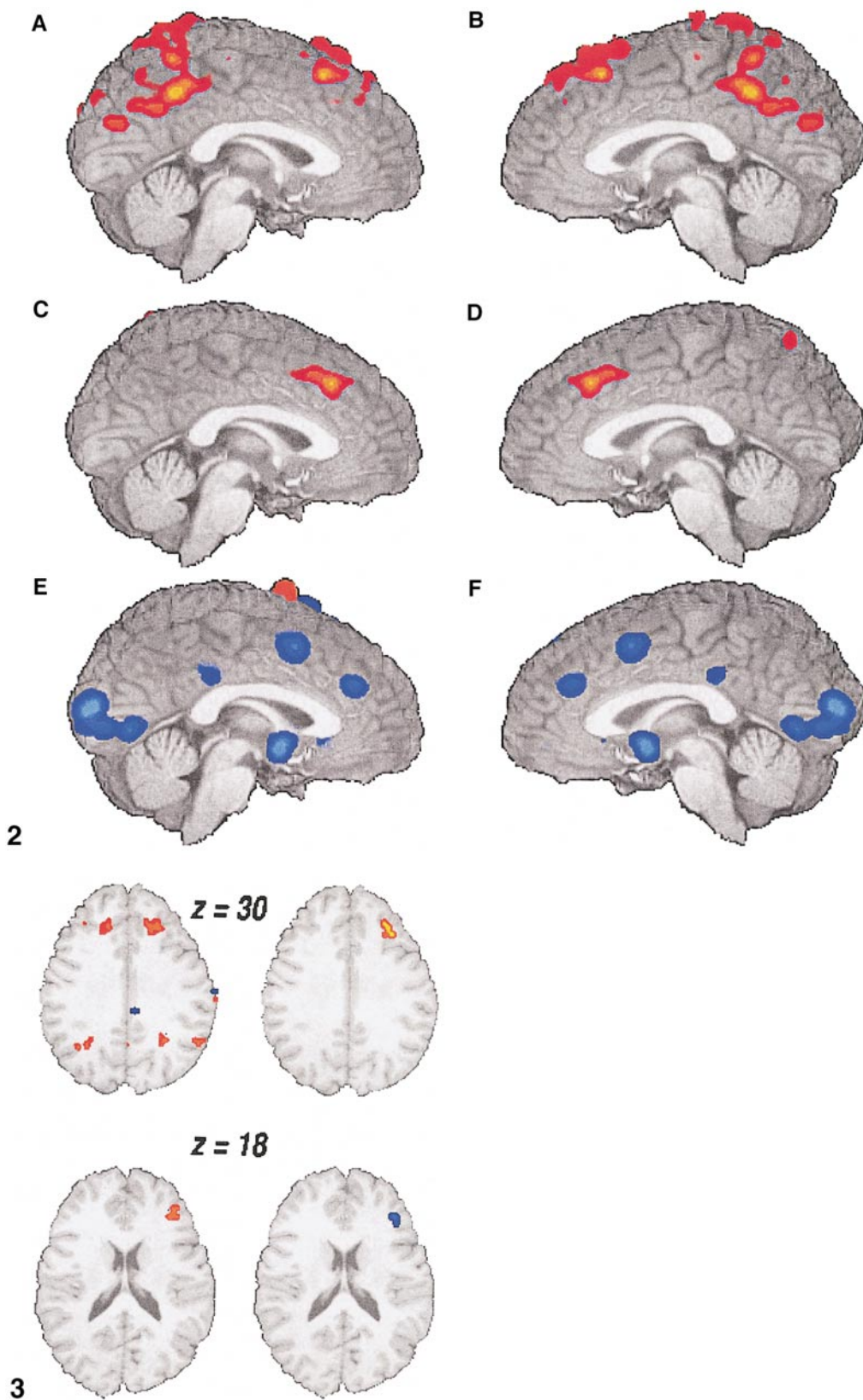


FIG. 2. Midsagittal sections of volume-thresholded task-related activation for 50% reinforcement (A, B) and 80% reinforcement (C, D) and contrast between 50% and 20 or 80% reinforcement (E, F).

FIG. 3. Left: Task-related activation during 50% error rate (top) and 20% error rate (bottom). Right: Correlation clusters between win-stay consistent responses and task-related activation, 50% error rate (top) and 20% error rate (bottom).

TABLE 1

Center of Mass for Volume-Thresholded Mixed ANOVA Clusters of Task-Related (Two-Choice Prediction–Two-Choice Response Task) Activation for the 50% Reinforcement Condition and the Differences in Task-Related Activation Comparing 50% Reinforcement Condition with Both 20 and 80% Reinforcement, Respectively.

Condition	Volume (μ l)	% Signal change	Talairach coordinates and anatomical description					BA	
			<i>x</i>	<i>y</i>	<i>z</i>	L/R	Structure		
50% error	2,619	0.28	23	8	68	R	Superior frontal gyrus	6	
	1,134	0.52	54	46	1	R	Inferior frontal gyrus	44	
	14,391	0.26	-44	39	28	L	Middle frontal gyrus	46	
	3,726	0.34	-22	-40	67	L	Postcentral gyrus	5	
	22,599	0.87	6	-53	46	R	Precuneus	7	
	1,998	0.84	-48	-55	24	L	Superior temporal gyrus	39	
		% Signal difference							
80–50%	405	1.2	-6	8	48	L	Superior frontal gyrus	6	
	351	0.33	37	-29	-20	R	Parahippocampal gyrus	36	
20–50%	1,755	1	44	4	29	R	Inferior frontal gyrus	9	
	1,269	1.14	-47	12	32	L	Middle frontal gyrus	9	
	2,214	1.16	40	43	18	R	Middle frontal gyrus	10	
	1,512	1.13	44	16	13	R	Inferior frontal gyrus	44	
	864	1.25	-37	35	14	L	Inferior frontal gyrus	46	
	810	1.32	40	29	-11	R	Inferior frontal gyrus	47	
	675	1.67	-3	4	-6	L	Anterior cingulate	25	
	648	1.17	-6	21	-8	L	Anterior cingulate	32	
	2,025	1.26	-4	-68	9	L	Cuneus	30	
	783	1.07	-33	-33	39	L	Inferior parietal lobule	40	
	Contrast	702	-0.58	-6	8	49	L	Superior frontal gyrus	6
		972	-0.45	-49	13	31	L	Middle frontal gyrus	9
		594	-0.4	48	8	31	R	Inferior frontal gyrus	9
		486	-0.53	40	51	13	R	Middle frontal gyrus	10
729		-0.4	6	52	-12	R	Medial frontal gyrus	11	
648		-0.48	48	12	14	R	Inferior frontal gyrus	44	
1,539		-0.39	43	40	18	R	Middle frontal gyrus	46	
648		-0.49	41	30	-11	R	Inferior frontal gyrus	47	
513		-0.55	-45	30	-15	L	Inferior frontal gyrus	47	
567		-0.81	-3	4	-6	L	Anterior cingulate	25	
459		-0.44	-8	-33	35	L	Cingulate gyrus	31	
459		-0.61	-7	24	-7	L	Anterior cingulate	32	
837		-0.62	-2	-88	10	L	Cuneus	18	
621		-0.45	-35	-32	38	L	Inferior parietal lobule	40	

Note. Labels are based on Talairach Demon software (Lancaster *et al.*, 2000).

motor programs. The inferior prefrontal cortex has been found to activate when subjects are required to “stop” prepotent motor responses (Jonides *et al.*, 1998; Garavan *et al.*, 1999).

Alternatively, to shift from a previously correct response to the alternative response or to repeat a response that was previously incorrect when the error rate is low may represent a strategy shift away from the predominant strategy that requires more processing resources. The increased activation in insula, inferior prefrontal cortex (BA 13, 45), and dorsal and rostral-ventral anterior cingulate (BA 24/32) in subjects that show fewer win–stay consistent responses and the increased activation in the dorsal and rostral-ventral anterior cingulate (BA 24/32) in subjects that show

fewer lose–shift consistent responses are consistent with this interpretation. The anterior cingulate is a diverse structure and has been divided functionally into areas that process cognitive and emotional information (for review see Bush *et al.*, 2000). According to the competition-monitoring hypothesis, the dorsal anterior cingulate serves to monitor conflict between brain areas (Cohen *et al.*, 2000), which may be elevated when prepotent responses (Carter *et al.*, 1999), i.e., win–stay or lose–shift, are not selected. The involvement of both the dorsal and the rostral-ventral anterior cingulate, which belong to the cognitive and affective subdivision of the cingulate gyrus, respectively (Bush *et al.*, 2000), supports the view that both cognitive strategies and affective resources may differentially

TABLE 2

Center of Mass for Correlation Clusters between Subject's Variation of Win–Stay or Lose–Shift Consistent Responses and Task-Related Activation for the Different Error-Rate Conditions

Condition		Volume (μ l)	Talairach coordinates and anatomical description					BA
			x	y	z	L/R	Structure	
20% error								
Win–stay	–	999	–36	29	10	L	Inferior frontal gyrus	13/45
	–	945	–2	22	32	L	Cingulate gyrus	24/32
Lose–shift	–	567	8	44	3	L/R	Anterior cingulate	32
	–	513	–5	–61	7	L	Posterior cingulate	31
	–	729	26	23	45	R	Middle frontal gyrus	8
	–	972	19	42	38	R	Middle frontal gyrus	9
	–	756	–44	21	35	L	Precentral gyrus	9
	+	513	–5	52	8	L	Medial frontal gyrus	10
	–	648	–10	2	42	L	Cingulate gyrus	24
	–	1647	1	27	31	L/R	Cingulate gyrus	32
50% error	–	513	10	42	1	R	Anterior cingulate	32
	–	513	10	42	1	R	Anterior cingulate	32
Win–stay	+	567	–26	27	25	L	Middle frontal gyrus	9
Lose–shift	+	405	–40	15	–19	L	Superior temporal gyrus	38
80% error								
Win–stay	–	2214	27	13	51	R	Middle frontal gyrus	6
Lose–shift	–	702	–6	2	65	L	Superior frontal gyrus	6
	–	1242	36	23	41	R	Middle frontal gyrus	8
	–	756	–46	17	40	L	Middle frontal gyrus	8
	–	513	–26	43	34	L	Middle frontal gyrus	9
	+	783	–20	–11	–19	L	Parahippocampal gyrus	28
	+	945	6	39	10	R	Anterior cingulate	32
	+	7911	31	–4	–15	R	Parahippocampal gyrus	
	+	540	–28	–62	–5	L	Fusiform gyrus	19
	–	1269	14	–70	52	R	Precuneus	7
	–	702	4	–9	11	R	Thalamus	
	+	1539	–40	9	–21	L	Superior temporal gyrus	38

Note. The direction of the correlation is indicated by (–) or (+).

affect the decision-making process. For example, while the rostral-ventral anterior cingulate is more active with fewer lose–shift responses at low error rates, this area is more active with more lose–shift responses at high error rates, which is directly related to “success”- or “failure”-driven response switching.

The current investigation does not support the second main hypothesis, i.e., low outcome predictability is associated with increased task-related activation in the anterior cingulate. In contrast, task-related anterior cingulate activation was higher during low and high error rates. Some investigators have suggested that anterior cingulate activation is particularly involved in situations with high levels of conflict and weak “selection-for-action” pressure (Botvinick *et al.*, 1999); however, others have not been able to confirm this finding (Zysset *et al.*, 2001). The role of the anterior cingulate in response conflict has been based primarily on the competition between different perceptual dimensions in the presence of a strong prepotent response using the Stroop task (Carter *et al.*, 1999). In the current task, however, the subject establishes a response-generating strategy as a consequence of suc-

cess or failure to predict the stimulus. Therefore, low error rates may enable the subject to establish a prepotent response, which, if the outcome prediction fails, results in a relatively larger error signal. If this speculation were correct, one would hypothesize a larger task-related activation in the anterior cingulate associated with “incorrect” response the longer the sequence of preceding “correct” responses.

Theoretically, several psychological models have been proposed for the influence of error rate and outcome predictability on response selection during decision-making. These models are based on the notion that the subject maintains a representation of the history of “correct” versus “incorrect” decisions and adjusts his/her strategies accordingly (Rose and Vitz, 1966). More recently, a computational model was developed to explain reward-related changes in response-selection biases in a simple decision-making task (Egelman *et al.*, 1998). This model is based on recent findings that the dopamine signal provides a general indicator of how well a response outcome is correlated with an expected prediction of reward (Schultz *et al.*, 1997). The error rate-dependent activation differences

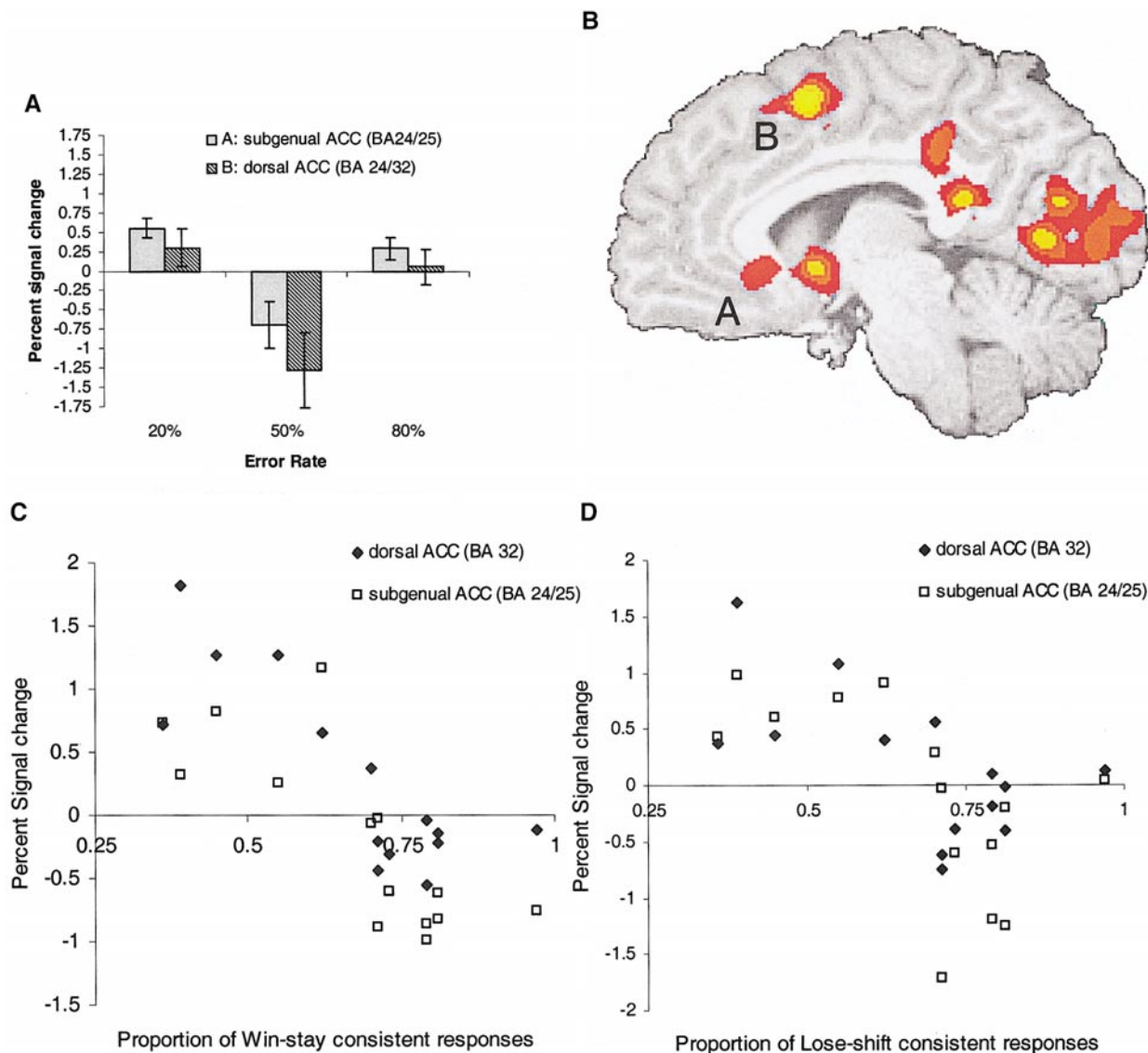


FIG. 4. (A) Task-related activation in subgenual (A) and dorsal (B) anterior cingulate for the three error rate conditions. (B) Volume thresholded clusters of signal difference between low or high and chance level error rate. (C and D) Correlation between proportion of win-stay (C) or lose-shift (D) consistent responses in different subjects and the task-related activation in subgenual and dorsal anterior cingulate.

in the prefrontal cortex are consistent with those of cortical dopaminergic target areas. Increased activation of inferior prefrontal, parietal, and cingulate areas during low error rates and during higher outcome predictability is consistent with the view that the prefrontal cortex maintains a representation of response sequences in relation to their outcome success.

The correlations between win-stay/lose-shift consistent responses in the prefrontal cortex and the anterior cingulate varied as a function of error rate (Fig. 3). At low error rates, an increase in task-related activation in the left inferior prefrontal cortex (BA 13/45) was associated with a decrease in win-stay consistent responses. In comparison, when the response outcome

was most unpredictable, i.e., during the 50% reinforcement condition, increased task-related activation in the middle frontal gyrus (BA 46) was associated with an increase in win-stay consistent responses. The opposite sign of these correlations is consistent with the notion of a context-dependent task-related activation in the prefrontal cortex. During low error rates the average number of win-stay responses (26.9) was more than twice that of the win-stay responses during the chance level error rate condition (12.9). Thus, when the base rate of win-stay consistent responses is low, activity in the more dorsal part of the prefrontal cortex may signal to maintain responses that “correctly” predicted the outcome. In comparison, when the base rate

of win-stay consistent responses is high, activity in the more ventral part of the prefrontal cortex may signal a switch to alternative behavioral strategies. The latter observation is consistent with correlations between the task-related activation of the anterior cingulate and win-stay behavior. In combination, these changes support the hypothesis that inferior prefrontal cortex (BA 45) and anterior cingulate (BA 24/32) are activated together in situations that result in "risky" decision-making, i.e., selecting an alternative response even though the previous response "correctly" predicted the stimulus.

This study has several limitations. First, the number of responses was not controlled a priori. The two-choice prediction task and the two-choice response task require subject-initiated responses to examine the effect of self-generated actions as opposed to stimulus- or cue-contingent responses. Consequently, response frequency may significantly affect the activation of the different neural systems that are hypothesized to be involved in decision-making. Two analyses were carried out to examine the possibility of response frequency affecting the areas of activation. First, behaviorally, response frequencies did not differ across task type (two-choice prediction versus two-choice response task) or across the different error rate conditions. Second, between-subjects differences in response frequency did not correlate significantly with the areas that showed significant differences in activation across reinforcement conditions. Nevertheless, future studies will need to examine the influence of self-generated versus cued decision-making on the activation of the frontal-parietal network. Second, the volume thresholding procedure used to guard against false-positive activations is not well suited to the analysis of subcortical structures, which may exhibit small volumes of task-related activation. However, region-of-interest analysis did not yield significant task-by-condition interactions for average percentage signal intensity changes in caudate, putamen, or amygdala (data not shown).

In summary, error rates and predictability affect the activation of the neural systems underlying decision-making that is consistent with the view that these structures maintain a representation of the reinforcement history to select for an "optimal strategy." Specifically, at low error rates, increased frontoparietal-cingulate activation may signal the error-related switch from a predominant response strategy to alternative strategies. The increased inferior prefrontal cortex activation when the outcome was predictably "right" or predictably "wrong" supports its critical role in evaluative processes so as to supply information to generate autonomic responses (Tranel and Damasio, 1994), which are critical components of decision-making (Damasio *et al.*, 1996). Moreover, the error-rate-dependent relationship between the activation of the

prefrontal cortex and the win-stay consistent responses support the general hypothesis that the prefrontal cortex is involved in both maintenance and switching of strategies underlying the decision-making process.

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