

# Risk-sensitive neurons in macaque posterior cingulate cortex

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People and animals often demonstrate strong attraction or aversion to options with uncertain or risky rewards, yet the neural substrate of subjective risk preferences has rarely been investigated. Here we show that monkeys systematically preferred the risky target in a visual gambling task in which they chose between two targets offering the same mean reward but differing in reward uncertainty. Neuronal activity in posterior cingulate cortex (CGp), a brain area linked to visual orienting and reward processing, increased when monkeys made risky choices and scaled with the degree of risk. CGp activation was better predicted by the subjective salience of a chosen target than by its actual value. These data suggest that CGp signals the subjective preferences that guide visual orienting.

To survive and thrive, animals must make choices that relate internal states to the current environment. For example, choosing to pursue food or water depends not only upon available resources but also on whether hunger or thirst is greater. The decision to make a particular action thus depends on subjective needs and desires as well as any objectively measurable gains<sup>1–3</sup>.

In addition to state-dependent variables such as hunger, thirst and even wealth, subjective biases also contribute to decision making. Since the 18<sup>th</sup> century, it has been known that people's choices reflect reward uncertainty as well as reward value<sup>4</sup>. When confronted with two options of the same mean value but differing in uncertainty, both people and animals typically avoid choosing the uncertain, or risky, option<sup>5,6</sup>. The idea that subjective preferences guide decision making has since become a core concept in the decision sciences<sup>2,7</sup>. However, the impact of subjective preferences on neural mechanisms of decision making remains largely unexplored (but see ref. 8).

The simplest economic models of decision making posit that rational choosers select the alternative with the highest expected value<sup>9,10</sup>. Recent neurophysiological studies of visual orienting decisions have demonstrated that neurons in several brain areas linking visual perception with eye movements also track target value<sup>11–15</sup>. These observations suggest that orienting decisions are computed, in part, by scaling neuronal responses by target value<sup>11,14,16</sup>. One question these observations raise, however, is whether reward modulation of neuronal activity in these brain areas reflects scaling by subjective value<sup>17</sup>, predicted reinforcement<sup>14,18</sup> or motivation<sup>19</sup>.

As people and animals often demonstrate strong attractions or aversions to options with uncertain rewards<sup>2,6,20</sup>, risk preference provides a promising behavioral framework for exploring neural mechanisms underlying decision making and offers a potential way to dissociate subjective value from objective rewards. Specifically,

neurons participating in the decision process should be sensitive to subjective risk preferences, even when available options have the same objective value.

To test this prediction, we recorded from single neurons in posterior cingulate cortex (CGp), a limbic area linking reward with spatial attention<sup>21,22</sup> and orienting<sup>23,24</sup>. Two adult male rhesus macaques performed a visual gambling task in which they chose between two visual targets offering the same mean reward but differing in reward uncertainty (Fig. 1a). We found that monkeys preferred orienting to targets offering uncertain rewards, and neuronal activity in CGp reflected these risk preferences. Our data suggest that neuronal responses in CGp signal subjective spatial biases that guide orienting.

## RESULTS

### Behavioral risk preferences in monkeys

Although numerous studies have sought to understand risk preferences in humans, birds and insects (reviewed in refs. 3,6), risk preferences in monkeys remain largely unstudied. Therefore, we first probed monkeys' behavioral sensitivity to reward uncertainty in a visual gambling task. Shifting gaze to the 'certain' target resulted in 150-ms access to fruit juice; shifting gaze to the 'risky' target resulted in the random receipt of less than 150 ms on one-half of the trials and more than 150 ms on the other half of trials (mean = 150 ms). The locations of the certain and risky targets, as well as the degree to which risky reward values deviated from the mean, were varied across blocks of 50 trials (Fig. 1a, lower panel). Here we define risk as the coefficient of variation (CV) of rewards associated with the risky target, a dimensionless measure of relative risk permitting direct comparisons with other studies<sup>3</sup>.

$$\text{Reward CV} = \sqrt{((x_1 - \text{mean})^2 + (x_2 - \text{mean})^2) / n} / \text{mean}$$

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where  $x_1$  and  $x_2$  are values for risky target and  $n$  is the number of risk values. Overall, both monkeys preferred the risky target and the frequency of choosing it increased systematically with the degree of risk (Fig. 2a).

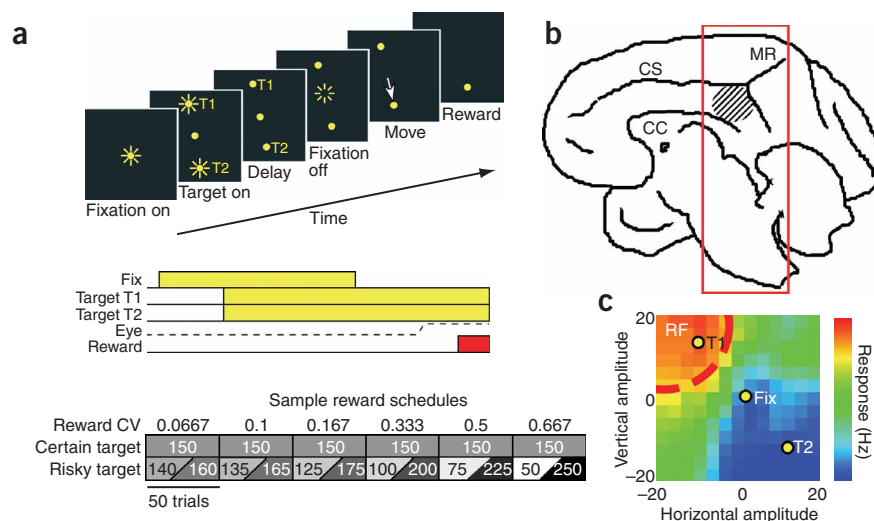
Sensitivity to reward uncertainty is not predicted by standard models of reinforcement learning. Specifically, reinforcement learning models predict that the associative strength of any stimulus for controlling behavior is determined by rewards delivered in association with that stimulus<sup>25,26</sup>. Because average reward size was the same for risky and certain targets, such models would not predict a preference for one option over the other. To explore this surprising behavioral pattern further, we therefore examined the impact of prior reward outcomes on subsequent choices. We found that receipt of smaller-than-average rewards on the previous trial blunted the likelihood of choosing the risky target on the next trial (Fig. 2b) but not nearly as much as would be expected by standard reinforcement learning<sup>25</sup>. Moreover, monkeys behaved as if they overvalued relatively large rewards. Our behavioral dataset was large enough to examine sequences of up to seven prior reward outcomes with statistical confidence. Analysis showed that monkeys significantly preferred the risky target even after a sequence of six smaller rewards that followed a large reward ( $F = 5.709$ ,  $P < 0.00001$ ). These data make plain that the choices monkeys make depend not only on expected reward value, as shown previously<sup>16</sup>, but also on reward uncertainty.

We next examined the impact of both received rewards and risk experienced for prior choices on the probability of choosing the risky target using logistic regression<sup>27</sup>. We found that both the degree of risk and normalized reward value associated with the target chosen on the previous trial biased the probability of choosing the risky target on the following trial (logistic regression coefficients: target risk = 2.768; target reward value = 4.16 (risky), 3.378 (certain); all  $P$ -values  $\ll 0.001$ ); moreover, including both risk and rewards received for prior choices significantly improved the explanatory power of the model over any other single variable or combination of variables (Akaike's Information Criterion (AIC)<sub>combined</sub> = 14,629.66; AIC<sub>target risk</sub> = 15,476.45; AIC<sub>risky target reward</sub> = 14,847.19; AIC<sub>certain target reward</sub> = 18,079.97; all other combinations, AICs  $>$  (AIC)<sub>combined</sub>).

Next, we developed a simple model of monkeys' subjective preference for the risky target—which we refer to here as subjective target utility—on the basis of the difference in the experienced value of the risky and certain targets. Since the logistic regression analysis showed that both experienced risk and rewards received influenced the probability of choosing the risky target on subsequent trials, we denoted the experienced value of the risky target  $V_{\text{risky}}$  on each trial as the sum of the risk and reward associated with that target when the monkey chose it:

$$V_{\text{risky}} = \text{Reward received}_{\text{risky target}} + \text{Risk}_{\text{risky target}} \quad (1)$$

Similarly, we denoted the experienced value of the certain target  $V_{\text{certain}}$  on each trial as the sum of the reward and risk associated with that



**Figure 1** Method for investigating risk sensitivity in macaque posterior cingulate cortex. (a) Visual gambling trials were used to investigate risk sensitivity. On each trial, subjects initially fixated ( $\pm 1$ – $2^\circ$ ) a central yellow LED (200–800 ms). Two peripheral yellow LEDs were then illuminated diametrically opposite the fixation LED (200–800 ms). The fixation LED was extinguished, cueing the monkey to shift gaze to either target ( $\pm 3$ – $5^\circ$ ) within 350 ms. Correct trials were rewarded with a 300-ms noise burst and juice. Lower panel: example of reward schedule. Mean reward size for each target was 150 ms; the range of reward differences for the risky target was 20–250 ms across blocks of trials. (b) Recording sites in posterior cingulate cortex (CGp), estimated by digital ultrasound imaging. Diagonal hatches indicate approximate neuron locations within areas 31 and 23. Recording chamber projection (red box) and major landmarks in the ultrasounds are indicated (CS: cingulate sulcus, horizontal limb; MR: marginal ramus; CC: corpus callosum). (c) Example of target geometry. One target was inside the response field (RF) while the other was diametrically opposite the fixation point. Neuronal response is plotted as a function of target location using an arbitrary color scale from blue to red (low to high firing rate).

target when the monkey chose it:

$$V_{\text{certain}} = \text{Reward received}_{\text{certain target}} + \text{Risk}_{\text{certain target}} \quad (2)$$

where the risk of the certain target was always 0.

We next estimated the subjective utility of the risky target  $U_{\text{risky}}$  on a given trial ( $t$ ) according to the following algorithm:

$$U_{\text{risky}}(t) = \sum_{n=1}^i [V_{\text{risky}}(t-n) - V_{\text{certain}}(t-n)] \times \alpha_n \quad (3)$$

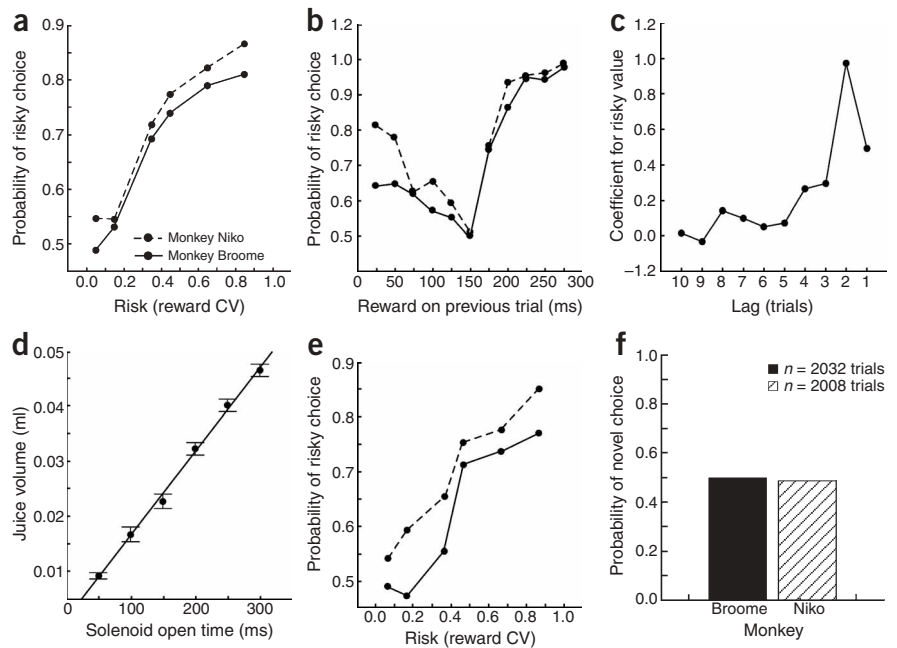
where  $\alpha_n$  is the logistic coefficient for the difference in the experienced value of the risky and certain targets lagged  $n$  trials. Multiple logistic regression analysis of the probability of a risky choice as a function of the difference in experienced value for the two targets ( $V_{\text{risky}} - V_{\text{certain}}$ ) on each of up to ten prior trials was used to derive the weighting factor  $\alpha_n$ . This analysis showed that the value function difference ( $V_{\text{risky}} - V_{\text{certain}}$ ) significantly influenced the probability of choosing the risky target at all lags up to five trials (AIC<sub>lags1–5</sub>  $<$  AICs for all other combinations) but declined rapidly thereafter (Fig. 2c). As the addition of further lags did not significantly improve the model,  $i$  was set to 5 trials. Using the weighting factor  $\alpha_n$ , our estimate of subjective target utility, derived from prior choices and their associated rewards and risk, provided a good prediction of the probability of choosing the risky target (logistic regression coefficient = 5.2222, Wald statistic = 2,560.93,  $P < 0.00001$ ).

In animals and humans, preference for risky options has been associated with impoverished physiological<sup>6,28</sup> or financial<sup>2,29</sup> status. We therefore asked how the risk sensitivity of our monkeys was affected by their hydration status. In our experiments, access to fluids was limited during the week but freely available on weekends. Risk sensitivity was therefore examined as a function of the day of the

week, as well as time during an experimental session, under the assumption that fluid balance would decrease over the course of the week and increase as juice was consumed during each daily session. We found no effect of day of the week (logistic regression coefficients, day of the week = 0.005,  $P > 0.97$ ; subject = 0.23,  $P < 0.000001$ ; risk = 0.281,  $P < 0.000001$ ) or number of trials performed in each session (logistic regression coefficients: trial = -0.00004,  $P > 0.42$ ; subject = 0.22,  $P < 0.000001$ ; risk = 2.44,  $P < 0.000001$ ). Thus, monkeys showed consistent preferences for uncertain fluid rewards, and these preferences were apparently independent of fluid balance.

One important question is whether any nonlinearity in the computer-driven solenoid controlling fluid delivery might explain why monkeys preferred the risky option. In fact, fluid reward size was a linear function of solenoid open time (volume =  $0.0026 + 0.001 \times (\text{open time in ms})$ ; Fig. 2d). Thus, the risk preferences of our monkeys could not be explained by an asymmetry in the size of rewards delivered across the range of values tested. We also performed a control experiment in which choosing the risky target was followed by delivery of larger-than-average rewards on one-third of trials and smaller-than-average rewards on two-thirds of trials (as compared with one-half larger-than-average and one-half smaller-than-average rewards in standard visual gambling trials). The certain target, as before, offered 150-ms access to juice on all trials, and the specific values of high and low rewards were unchanged from standard gambling trials. Choosing the risky target thus resulted in a net loss of juice compared with choosing the certain option, and this loss increased with increasing risk. Despite the fact that the expected value of the risky target now declined with increasing risk, monkeys continued to prefer it (Fig. 2e).

Another question these data raise is whether the observed risk preferences might simply reflect a preference for the novelty, or variability, of rewards associated with the risky target. In other words, perhaps a changing target or reward is simply more interesting for monkeys. This is an important potential confound which we sought to address in a control experiment. Reward size was held constant at 150 ms access to juice for both targets while novelty was introduced by systematically changing the color of one of the targets during reward delivery. For the 'monotonous' target, the color of the target remained yellow throughout the trial. For the 'novel' target, target color changed from yellow to green on half of the trials and from yellow to red on the other half of the trials. Notably, both targets were yellow until the delivery of reward such that any difference in luminance by color would not affect the monkeys' choices. The locations of the novel and monotonous targets were reversed across blocks of trials to mitigate any spatial bias in the monkeys' choices. Neither monkey showed any preference for the novel colored target (Fig. 2f). Thus, monkeys' preference for risky targets is unlikely to be explained by novelty alone.

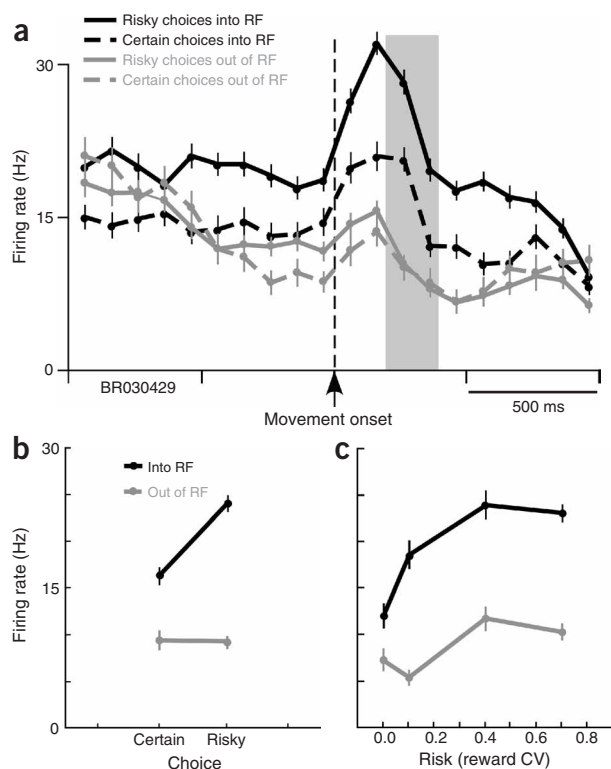


**Figure 2** Monkeys prefer targets offering uncertain rewards. (a) Probability of choosing the risky target as a function of risk for each monkey. Risk preference increased with increasing risk (logistic regression coefficients: Broome, 2.442,  $P < 0.0000001$ ; Niko, 2.426,  $P < 0.0000001$ ). (b) Monkeys discount low payoffs at the risky target. Probability of choosing the risky target is plotted as a function of reward received on the previous trial for both monkeys. Both monkeys were indifferent to the average reward size (150 ms) but systematically preferred the risky target after either small or large payoffs. (c) Influence of rewards received and risk on current choice declines with time. Logistic regression coefficient for the experienced value of the risky target, estimated as the sum of the reward and risk received for choosing that target, plotted as a function of trial lag. (d) Juice volume varies linearly with solenoid open-time. (e) Monkeys preferred the risky target despite receiving a net loss of juice. Probability of choosing the risky target as a function of risk for control experiment in which choosing the risky target resulted in a two-thirds chance of a lower-than-average reward and a one-third chance of a higher-than-average reward. (f) Monkeys were indifferent to targets that changed color. Probability of choosing novel colored target when reward size was equal is plotted for both monkeys. Broome,  $n = 2,032$  trials; Niko,  $n = 2,008$  trials.

### Neural correlates of reward uncertainty in CGp

Having established the risk preferences of two monkeys performing a visual gambling task, we next examined the activity of single neurons in posterior cingulate cortex (Fig. 1b) for evidence of similar risk sensitivity. Neurons in this area respond to the illumination of contralateral visual stimuli<sup>30</sup>, after contraversive gaze shifts<sup>16,24,30</sup> and after reward delivery<sup>16</sup>, and the strength of these responses is modulated by reward size and expectancy<sup>16</sup>. Because most CGp neurons respond selectively for a broad range of contralateral saccades, experiments were conducted such that one target was placed inside the response field of the neuron under study while the other target was diametrically opposite the fixation point (Fig. 1c). The response field was determined during 100–400 standard mapping trials in which monkeys were asked to shift gaze to targets throughout the visual field.

The activity of a single CGp neuron recorded during visual gambling trials is shown in Figure 3. Neuronal activity increased after movement onset, and this activity was modulated both by whether the movement was into or out of the response field as well as whether those choices were for risky or certain rewards (Fig. 3a). During the epoch 200–400 ms after movement onset, firing rate was modulated by both movement direction and risk (Fig. 3b). Neuronal activity increased systematically with increasing risk, and this risk-related modulation was stronger for movements in the neuron's preferred direction (Fig. 3c).



**Figure 3** Posterior cingulate neurons are risk-sensitive. **(a)** Post-stimulus time histogram for a single CGp neuron aligned on movement onset. Points indicate average ( $\pm$  s.e.m.) firing rate measured in 100-ms bins. Firing rate was greater for choices into RF than out of RF, as well as for risky choices than for certain choices. Gray shaded box indicates 200-ms epoch analyzed in **b,c**. **(b,c)** Average firing rate of the same CGp neuron plotted as a function of choice (risky or certain) and reward CV for choices in the neuron's preferred (black) and non-preferred (gray) directions. Firing rate systematically increased for risky choices as well as with increasing reward CV for movements in the preferred direction (**b**: *t*-test,  $t = 5.55$ ,  $df = 375$ ,  $P < 0.000001$ ; **c**: multiple regression,  $r = 0.230$ ,  $df = 375$ ,  $P < 0.00003$ ).

here as a larger separation between black and gray lines (**Fig. 4**; post-hoc Tukey's honestly significant difference tests for saccade direction; fixation epoch: low-risk, not significant (n.s.); high-risk,  $P < 0.000001$ ; pre-movement epoch: low-risk, n.s.; high-risk,  $P < 0.000001$ ; post-movement: low-risk,  $P < 0.01$ ; high-risk,  $P < 0.00000001$ ). Thus, increasing risk did not seem to be associated with global or uniform changes in neuronal activity, but rather with selective enhancement of task-related neuronal activity.

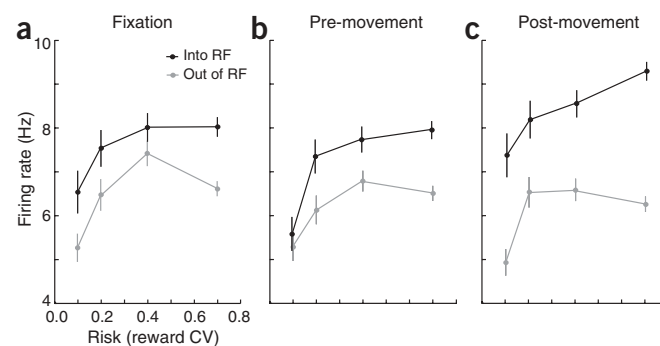
The enhancement of spatial sensitivity by risk is difficult to explain by global changes in arousal. Nevertheless, we sought to examine whether changes in neuronal activity associated with risky choices reflected changes in autonomic arousal. Correlates of autonomic arousal such as heart rate, galvanic skin response, and cortisol levels are elevated during gambling in humans<sup>31–33</sup> and are attenuated in medial prefrontal lesion patients with poor impulse control in gambling tasks<sup>34</sup>. We therefore recorded the heart rates of both monkeys while they performed visual gambling trials in a separate set of experiments (monkey Niko: 4,471 trials; monkey Broome: 3,780 trials). Although there were fluctuations in heart rate over the course of behavioral sessions as well as upon block changes, we found no systematic effect of risk on heart rate (**Fig. 5**).

We examined other potential behavioral correlates of arousal or motivation that might vary with reward uncertainty<sup>35</sup>. Reaction times were not significantly faster when monkeys made risky choices ( $F = 2.7$ ,  $P > 0.1$ ) but were significantly slower on trials after delivery of either unusually large or small rewards ( $F = 13.8$ ,  $P < 0.000001$ ). Similarly, risky choices had no influence on peak saccade velocity scaled by saccade amplitude ( $r_{\text{amplitude}} = 0.519$ ,  $P < 0.000001$ ;  $r_{\text{risky choice}} = -0.00850$ ,  $P > 0.322$ ), but peak saccade velocity was significantly higher after delivery of both the smallest and largest rewards

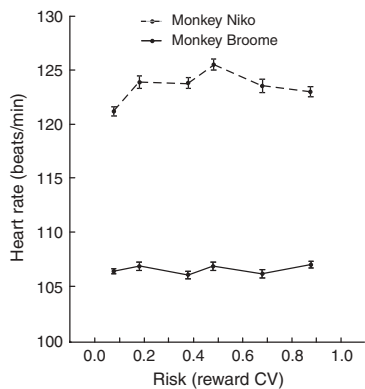
Neuronal activity was modulated both by which target was chosen and whether that target was associated with uncertain rewards. Overall, the activity of 22/41 (53.7%) studied neurons was significantly modulated by whether the risky target was chosen (14/25 neurons in monkey Broome and 8/16 neurons in monkey Niko). Across the population, average neuronal activity was greater for risky target choices than for certain target choices (ANCOVA: fixation epoch,  $F = 3.957$ ,  $P < 0.05$ ; pre-movement,  $F = 11.321$ ,  $P < 0.001$ ; post-movement,  $F = 2.346$ ,  $P > 0.10$ ), even when the effects of movement amplitude, latency, peak velocity and direction were removed statistically.

We collected data from 39/41 CGp neurons in the same four conditions of risk. Population neuronal activity increased systematically with increases in risk throughout trials (**Fig. 4**; multiple regression: fixation epoch,  $r_{\text{risk}} = 0.030$ ,  $n = 9,153$ ,  $P < 0.005$ ; pre-movement epoch,  $r_{\text{risk}} = 0.048$ ,  $n = 9,153$ ,  $P < 0.00001$ ; post-movement epoch,  $r_{\text{risk}} = 0.047$ ,  $n = 9,153$ ,  $P < 0.00001$ ), roughly paralleling the frequency of risky choices made by monkeys in these experiments (compare to **Fig. 2a**). Notably, the effect of risk on neuronal firing rates persisted as a tonic change throughout trials but was maximal when superimposed upon phasic, movement-related responses (**Fig. 4c**). Consistent with previous reports, the CGp population was also sensitive to whether the chosen target was in the neuronal response field, even while monkeys maintained central fixation before target onset (**Fig. 4**; fixation epoch:  $r_{\text{direction}} = 0.056$ ,  $n = 9,153$ ,  $P < 0.000001$ ; pre-movement epoch:  $r_{\text{direction}} = 0.067$ ,  $n = 9,153$ ,  $P < 0.000001$ ; post-movement epoch:  $r_{\text{direction}} = 0.125$ ,  $n = 9,153$ ,  $P < 0.000001$ ). These data indicate that CGp neuronal activity is sensitive to reward uncertainty as well as to target choice. For any particular choice, either into or out of the response field, CGp neuronal activity varied with risk.

Our data also indicate that the spatial selectivity of CGp neurons was enhanced by increasing risk: in high-risk blocks, the neuronal population more accurately discriminated movement direction, visualized



**Figure 4** Target risk enhances neuronal activity in CGp as well as sensitivity to movement direction. Plots of average ( $\pm$  s.e.m.) neuronal firing rate as a function of risk (reward CV) for the epochs after fixation **(a)**, before movement onset **(b)** and after movement onset **(c)**. Activity was greater for movements made into the RF and scaled with the degree of risk.



**Figure 5** Average heart rate does not increase with increasing risk. Average heart rate ( $\pm$  s.e.m.) measured at 12 Hz by means of pulse oximetry is plotted as a function of risk (reward CV) for both monkeys.

( $F = 23.858$ ,  $P < 0.000001$ ). Thus, while the saccade metrics and choices of monkeys suggested that monkeys were, in fact, sensitive to risk, the effects of risk on firing rate are not readily explained by global changes in arousal.

### CGp neurons track subjective target preferences

Despite the fact that the amount of reward received from choosing each target was equivalent over time, monkeys systematically preferred the risky target. Moreover, neuronal activity in CGp increased with the selection of risky targets. These data suggest that, under these conditions, the activation of CGp neurons reflects subjective biases for targets associated with uncertain rewards. If this is true, then firing rate on any particular trial should be more closely associated with subjective preferences for a particular target than with the actual rewards harvested by choosing it. We tested this hypothesis by first examining neuronal activity as a function of prior rewards received and, second, by computing an estimate of subjective target utility on the basis of the influence of both risk and reward received for previous choices<sup>27</sup> and asking whether neuronal activity was related to this measure.

First, we examined neuronal activity in the CGp population on each trial as a function of the size of the rewards delivered on the previous trial to ask whether neuronal activity reflected in any simple way the actual rewards received (Fig. 6). In all three measured epochs, firing rate discriminated between target choices into and out of the response field (fixation:  $F = 29.951$ ,  $P < 0.000001$ ; pre-movement:  $F = 42.226$ ,  $P < 0.0000001$ ; post-movement:  $F = 148.152$ ,  $P < 0.0000001$ ). Moreover, firing rate was elevated when monkeys received rewards that deviated from the average, certain value (fixation:  $F = 5.358$ ,  $P < 0.0000001$ ; pre-movement:  $F = 7.022$ ,  $P < 0.0000001$ ; post-movement:  $F = 5.649$ ,  $P < 0.0000001$ ). However, CGp neuronal activity did not distinguish between the lowest and highest rewards received on previous trials (post-hoc Tukey honestly significant difference tests,  $P > 0.15$  in all epochs). Thus, neuronal responses in CGp did not monotonically reflect the actual value of rewards received. We suspected that, instead, CGp responses for a particular target choice reflected monkeys' subjective valuation of the target on the basis of their own internal preferences (compare with Fig. 2b).

As a second test of this hypothesis, we computed a local estimate of subjective target preference, which we refer to as subjective target utility. Analysis of behavioral data, described above, showed that both the risk and reward value associated with prior choices roughly equally biased the probability of choosing the risky target on subsequent trials.

We therefore first computed the experienced values of the target in the response field (RF) and the target outside the response field (ORF) using the risk and reward outcomes associated with prior choices, as above. The experienced value of the RF target  $V_{RF}$  and the experienced value of the ORF target  $V_{ORF}$  on a trial were computed as

$$V_{RF} = \text{Reward received}_{RF} + \text{Risk}_{RF} \quad (4)$$

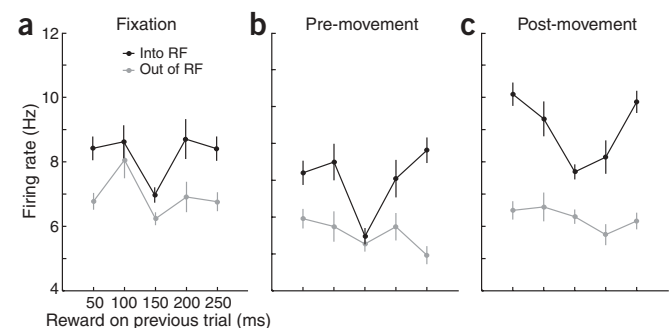
$$V_{ORF} = \text{Reward received}_{ORF} + \text{Risk}_{ORF} \quad (5)$$

The subjective utility of the target in the response field  $U_{RF}$  on a given trial  $t$  was then estimated according to the following algorithm:

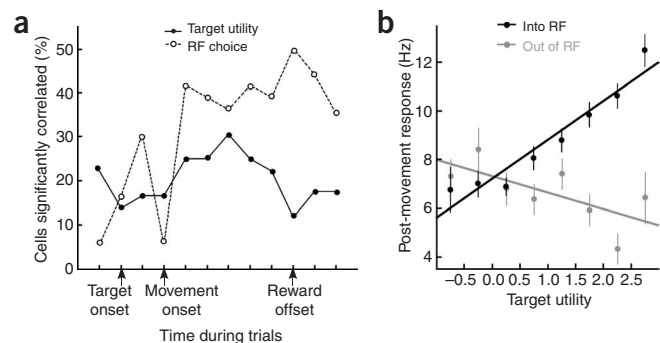
$$U_{RF}(t) = \sum_{n=1}^{10} \alpha_n [V_{RF}(t-n) - V_{ORF}(t-n)] \times \alpha_n \quad (6)$$

where  $\alpha_n$  is the logistic coefficient for the difference in the experienced value of the RF and ORF targets lagged  $n$  trials. Multiple logistic regression analysis of the probability of an RF target choice as a function of the difference in experienced value for the two targets ( $V_{RF} - V_{ORF}$ ) on each of up to ten prior trials was used to derive the weighting factor  $\alpha_n$ . We found that differences in the experienced value of the two targets significantly influenced the probability of choosing the RF target at all lags up to ten trials ( $AIC_{lags1-10} < AICs$  for all other combinations), so the weighting term  $\alpha_n$  was therefore weighted on the basis of the logistic regression coefficients for each trial lag with  $i$  set at 10 trials. The utility of the target outside the response field was computed as the sign-reversed utility of the response field target. High target utility implied that the monkey frequently chose, and therefore preferred, a particular target in the past ten trials. These computations were performed across the entire dataset.

We examined the percentage of cells in the population that were significantly correlated with the subjective utility of the response field target and whether the response field target was chosen, using a multiple linear regression analysis with movement latency, amplitude and peak velocity as co-regressors. The firing rates of 64% of cells were significantly modulated by target utility as well as target choice in any of twelve epochs examined (see Methods; Fig. 7). Modulations of firing rate by target utility and target choice, however, varied over time as well. Over 20% of the studied population of neurons showed a significant correlation between firing rate and subjective target utility during initial fixation before target onset (Fig. 7a), and the percentage of neurons with a significant correlation between firing rate and target utility gradually increased and peaked at around one-third of the



**Figure 6** Population neuronal activity reflects monkeys' preference for risky targets but not prior reward outcomes. Firing rate is plotted as a function of reward on previous trial for epochs after fixation (a), before movement onset (b) and after movement onset (c). Activity was greater for movements made into the RF as well as when relatively small or large rewards were delivered on previous trial.

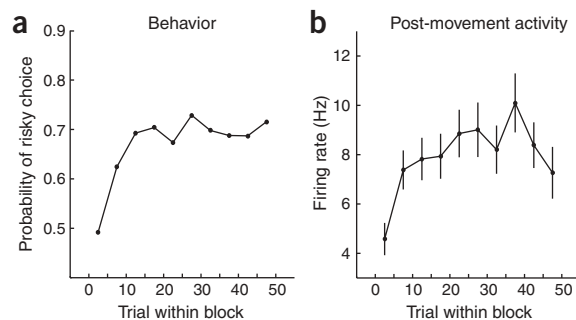


**Figure 7** CGp neurons carry information about both target choice and subjective target utility. Multiple linear regression analysis was performed with utility, RF choice and saccade kinematic parameters as co-factors. (a) Percentage of cells with a significant correlation are plotted as a function of time during trials. (b) Population activity is correlated with subjective target utility. Firing rate measured after saccade onset is plotted as a function of target utility, estimated from the influence of risk and rewards received on target choices over the previous ten trials.

population in the epochs after movement onset. In contrast, fewer than 5% of neurons showed a correlation between eventual target choice and firing rate during fixation before target onset, and the percentage of cells with a significant correlation peaked just after target choice and persisted through the end of the trial. These trends suggest a gradual temporal shift in the information carried by CGp neurons, initially favoring the subjective utility of available targets and later reflecting target choice and, to a lesser degree, target utility.

Across the studied population of neurons, firing rate was positively correlated with target utility for all trials in which monkeys chose the target in the neuronal response field (Fig. 7b, black lines; post-movement epoch:  $r = 0.146$ ,  $P < 0.0000001$ ) and negatively correlated with target utility when monkeys chose the target out of the response field (Fig. 7b, gray lines; post-movement epoch:  $r = -0.0893$ ,  $P < 0.005$ ). Activity in the CGp population was therefore well correlated with a measure of target utility, estimated from the monkeys' history of choices, rewards received and associated risk. Note that black and gray lines overlap at low measures of target utility and diverge with increasing values, indicating that the ability of CGp neurons to discriminate target choice depended on the utility of those targets.

If, as these data suggest, CGp neurons carry information about both the direction and subjective utility of movements monkeys make, an important question remaining is whether such activity causes—or reflects—the animals' choices. To address this issue, we examined the time course of neuronal activity and the pattern of behavioral choices after a switch in the location of risky and certain targets. We found that the proportion of risky choices rose steeply from indifference (0.5) and reached a plateau within 15–20 trials (averaged across multiple values of risk; Fig. 8a). Similarly, neuronal activity in the 200–400 ms epoch after movement onset increased by approximately 50% and began to plateau within 15–20 trials from a block change (Fig. 8b). Piecewise linear regression analysis for the probability of a risky choice and neuronal activity as a function of time after a switch in the location of the risky target showed break points, respectively, of 19.4 ( $r = 0.889$ ,  $r^2 = 79.1\%$ ) and 24.6 ( $r = 0.868$ ,  $r^2 = 75.4\%$ ) trials, suggesting that neuronal activity in CGp closely followed changes in monkeys' choices. This interpretation should be viewed with caution, however, as piecewise linear regression break points can be sensitive to the range of data included in the model.



**Figure 8** Both the frequency of risky target choices and neuronal activity gradually increase after block changes. Probability of risky choice (a) and neuronal activity (b) are plotted as a function of trial after a change in the location of the risky target. Behavioral preference for risky target and neuronal firing rate increased at a similar rate and reached asymptote within 15–20 trials.

Taken together, our results indicate that a subset of neurons in posterior cingulate cortex carries information about the subjective utility of targets in the visual world. Indeed, neuronal activity in CGp mirrors the behavioral sensitivity of monkeys to risk. These data are consistent with a role for CGp in signaling the subjective salience of locations in the visual scene.

## DISCUSSION

Economists, experimental psychologists and behavioral ecologists have long argued that decision making depends on the conversion of external variables into a common internal currency of value. Without such a common currency, neither animals nor people would be able to choose adaptively between apples and oranges, much less activities as disparate as eating and mating. While it is readily accepted that internal representations of value lie at the very core of decision making, most neurobiological studies of the decision process have manipulated objective value, typically by changing reward size or probability, because these factors are easily controlled and quantified. On the other hand, subjective value can be measured only indirectly, and attempts to correlate it with neuronal activity are, not surprisingly, rare<sup>14,17</sup>.

The visual gambling task used in the current study affords a unique opportunity to examine neural activity under conditions in which subjective value, but not objective value, varied, as indicated by subjects' choices. Although there was no apparent reason for monkeys to prefer one option or the other, they showed systematic preferences for targets offering uncertain rewards, much like hungry birds<sup>6,20,28,36</sup>, typical adolescents<sup>37–39</sup> and people addicted to drugs<sup>40</sup> or pathological gambling<sup>32</sup>. Moreover, preference for the uncertain reward increased parametrically with the coefficient of variation of reward or risk, in accord with some recent findings in humans<sup>3</sup>.

Similarly, neurons in posterior cingulate cortex were also risk-sensitive, carrying information about both the direction of impending movement, as shown previously<sup>24,30</sup>, and the uncertainty of rewards associated with this movement. These findings both corroborate and extend the findings of a previous study<sup>16</sup>, in which posterior cingulate neurons were reported to be sensitive to reward size and predictability, manipulations that also presumably influenced subjective value. However, the previous study could not discern whether such modulations in neuronal activity reflected subjective preferences for larger or more surprising rewards. In the present study, the average reward value of each target was held constant, yet monkeys demonstrated clear

preferences for one option over the other, thus permitting dissociation of subjective and objective value. Under these conditions, CGp neurons were sensitive to subjective target utility, consistent with recent findings in posterior parietal cortex, a premotor area that has been implicated in oculomotor decision making<sup>14,17</sup>.

Recent studies have suggested that orienting decisions are computed, in part, by scaling neuronal responses by target value and then comparing them with a threshold<sup>41,42</sup>. Our data indicate that CGp neurons signal subjective biases for uncertain rewards (or, perhaps, the potential to receive a large reward) rather than objective target value. Thus, CGp appears to carry spatial information that is scaled by subjective preferences for particular patterns of reward outcome. Other investigators have shown recently that the responses of a population of midbrain dopamine neurons are selectively enhanced by reward uncertainty<sup>43</sup>. Such dopamine responses may indirectly facilitate neuronal activity in CGp through projections to anterior cingulate cortex, a major input to posterior cingulate cortex<sup>44</sup>. Several neuroimaging studies have also shown hemodynamic responses to outcome uncertainty in midline cortical areas such as anterior cingulate cortex, orbitofrontal cortex and precuneus<sup>45,46</sup>. Our data extend those findings, demonstrating a direct relationship between subjective preferences for uncertain rewards, or the opportunity to harvest a relatively large reward, and the activity of neurons thought to participate in the allocation of attention<sup>21,22</sup>.

Neuronal activity in CGp reflects subjective preferences for risky target locations during fixation as well as before and after saccade onset, suggesting that this area contributes to visuospatial biases guiding orienting<sup>22,30,47</sup>. Our data are in sharp contrast with findings in posterior parietal cortex, where modulations by local fractional income<sup>14</sup> or subjective desirability<sup>17</sup> are found to emerge around the time of target onset and end after the eye movement. Therefore, posterior parietal cortex has been proposed to signal the relative value of potential eye movements<sup>17</sup> but is unlikely to actually compute this value, as the signals seem to be 'reset' at the start of each trial<sup>14</sup>. In contrast, modulations in neuronal activity in CGp seem to persist across trials, and the timing of these modulations is consistent with a role in predicting and/or evaluating subjective value<sup>16,41</sup>. Thus, CGp may convey information about subjective target value that scales neuronal signals in parietal cortex.

Our data also indicate that the spatial sensitivity of neurons in CGp is enhanced under conditions of risk or uncertainty. This result echoes a recent finding that the spatial selectivity of parietal neurons is greatest when target value is high<sup>14</sup>. Because both parietal and cingulate cortices have been implicated in the allocation of spatial attention, such enhancement may reflect heightened attention to regions of space with high subjective value<sup>48</sup>. We speculate that enhanced neuronal activity associated with risky rewards biases attention spatially, marking large payoffs as salient for guiding behavior<sup>48</sup> and thereby favoring behavioral responses to risky targets. Such a link between risk preference, salience, attention and action has profound implications not only for oculomotor decision making, but also for why people and animals sometimes demonstrate irrational and even harmful preferences for risky behaviors.

In conclusion, two monkeys were systematically risk prone when offered choices of targets associated with certain and uncertain fluid rewards. Posterior cingulate neurons were similarly risk sensitive, and their firing rates conveyed information about the direction of impending movements as well as the subjective utility of those movements. Moreover, the spatial sensitivity of CGp neurons was enhanced under conditions of high risk. Neurophysiological studies of risk preferences, as reported here, may serve as an important model for probing the

neural processes that underlie pathological risk taking in individuals with addictions to drugs, sex, food or gambling.

## METHODS

**Surgical and training procedures.** All procedures were approved by the Duke University Institutional Animal Care and Use Committee and were designed and conducted in compliance with the Public Health Service's Guide for the Care and Use of Animals. Initially, a head restraint prosthesis and scleral search coil<sup>49</sup> were implanted using standard surgical techniques<sup>50</sup>. Six weeks later, animals were habituated to head restraint and trained to perform oculomotor tasks for liquid rewards. A second surgical procedure was then performed to implant a stainless steel recording chamber (Crist Instruments) over posterior cingulate cortex at the intersection of the interaural and midsagittal planes. The chamber was kept sterile with regular antibiotic washes and sealed with sterile caps. Animals received analgesics and antibiotics after all surgeries.

**Behavioral techniques.** Horizontal and vertical eye positions were sampled at 500 Hz (Riverbend Instruments) and recorded by computer (ryklinssoftware.com). Visual stimuli were LEDs (LEDtronics), which were illuminated to appear yellow, red or green to normal human observers, fixed on a tangent screen 144.78 cm (57 inches) from the animals' eyes and forming a grid of points separated by 1°, spanning 49° horizontally and 41° vertically.

Behavioral datasets were collected for 12 sessions from both monkeys before physiological recording. A 300-ms broadband noise before juice delivery served as a secondary reinforcer on all correct trials. During visual gambling trials, one target was placed in the response field of the neuron under study, while the other target was placed diametrically opposite the fixation point. One target was associated with a 'certain' reward outcome of 150 ms access to juice on every trial, while the other 'risky' target was randomly rewarded with less than 150 ms on half of trials and greater than 150 ms on the other half of trials (mean = 150 ms across trials). The locations of the certain and risky targets, as well as the coefficient of variation in reward for the risky target, were varied every 50 trials. Heart rate was measured at 12 Hz by pulse-oximetry (SurgiVet) on eight sessions for both monkeys.

Two control experiments were performed for risk and novelty. First, for the risk control, visual gambling trials were as above with the following important difference: the risky target was associated with larger-than-average rewards on one-third of trials and smaller-than-average rewards on two-thirds of trials (as compared with one-half larger-than-average and one-half smaller-than-average rewards in standard visual gambling trials). Second, for the novelty control, reward size was held constant at 150-ms access to juice for both targets while novelty was introduced by systematically changing the color of one of the targets during reward delivery. The color of the 'monotonous' target remained yellow throughout trials, while the color of the 'novel' target randomly changed color from yellow to green on half of trials, and from yellow to red on the other half of trials.

**Microelectrode recording techniques.** Single electrodes (Frederick Haer) were lowered under physiological guidance until the waveform of a single neuron was isolated. Individual action potentials were identified in hardware by time and amplitude criteria (BAK Electronics) and recorded by computer at 25 KHz. Neurons were selected for recording experiments on the basis of the quality of isolation and apparent task-sensitivity. Neuronal activity was first monitored during 100–400 single-target trials to identify the neuron's response field and select appropriate target locations for subsequent visual gambling trials. Data were collected for 4 to 14 blocks of gambling trials for each neuron, depending on the duration and quality of isolation.

Following some recording sessions, we confirmed the location of the electrode using a hand-held digital ultrasound device (Sonosite 180) placed against the recording chamber<sup>50</sup>. Ultrasound images taken in the sagittal plane showed that recordings were made in areas 23 and 31 in the cingulate gyrus and ventral bank of the cingulate sulcus, anterior to the intersection of the marginal and horizontal rami<sup>30</sup>.

**Analysis.** Data were analyzed off-line using custom software (Eyemove, supported by K. Pearson, D. Sparks Laboratory, Baylor College of Medicine), which computed saccade direction, amplitude, latency, peak velocity and times

of spike occurrence. For behavioral data, logistic regression was used to estimate the effects of experienced rewards and risk associated with prior choices on the probability of choosing the risky target. Statistics were computed using Statistica 6 or Matlab.

Firing rates were measured for each trial during 12 200-ms intervals aligned with the time of an event during the trial: (i) 0–200 ms after the onset of fixation; (ii) 0–200 ms after the illumination of the eccentric target; (iii) 200–0 ms before target offset; (iv) 200–0 ms before movement onset; (v) 0–200 ms after movement onset; (vi) 200–400 ms after movement onset; (vii) 0–200 ms after the reinforcing noise burst; (viii) 200–0 ms before juice onset and (ix–xii) 0–200 ms, 200–400 ms, 400–600 ms and 600–800 ms after juice delivery. Analysis of firing rates focused on three 200 ms intervals in particular: 0–200 ms after the onset of fixation (fixation epoch), 200–0 ms before target offset (pre-movement epoch) and 200–400 ms after movement onset (post-movement epoch). Multiple regression was used to quantify the relationship between neuronal firing rate and target risk, independent of the effects of latency, amplitude and peak velocity of eye movements.

In addition, neuronal activity was also analyzed as a function of subjective target utility, which was estimated by assuming that the experienced value of each target was the sum of both the received rewards and risk associated with prior choices. Experienced value for each target was incorporated into the model of subjective target utility by first multiplying this value by a weighting factor and then summing across up to ten previous trials. Weighting factors for the influence of experienced value at each trial lag were estimated by logistic regression of the effects of experienced target value on the probability of choosing the response field target. Aikake's Information Criterion (AIC) was used to evaluate the inclusion of experienced target value for trials at different lags in the model.

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#### COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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