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Interactions between decision making and performance monitoring within prefrontal cortex

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Our ability to judge the consequences of our actions is central to rational decision making. A large body of evidence implicates primate prefrontal regions in the regulation of this ability. It has proven extremely difficult, however, to separate functional areas in the frontal lobes. Using functional magnetic resonance imaging, we demonstrate complementary and reciprocal roles for the human orbitofrontal (OFC) and dorsal anterior cingulate cortices (ACd) in monitoring the outcome of behavior. Activation levels in these regions were negatively correlated, with activation increasing in the ACd and decreasing in the OFC when the selected response was the result of the participant's own decision. The pattern was reversed when the selected response was guided by the experimenter rather than the participant. These results indicate that the neural mechanisms underlying the way we assess the consequences of choices differ depending on whether we are told what to do or are able to exercise our volition.

A key component to survival in a constantly changing environment is the ability to evaluate the consequences of one's actions and to adapt one's behavior accordingly. There is a large body of evidence tying primate prefrontal regions, particularly the anterior cingulate and OFC, to this ability[1–3]. Several neuroimaging studies involving reward-related behavior or outcome monitoring show activation in both the OFC and the dorsal and supracallosal parts of the anterior cingulate cortex[4–6]. The ACd has tended to be associated with monitoring for errors and conflict between competing responses[7,8], whereas several studies have shown the OFC to be involved in the tracking of current reward values[9,10]. Both regions contain neurons that respond to the anticipation and delivery of reinforcement or recognition of errors, and damage to either can impair the ability to use such information during decision-making[1,11–16]. Both have also been implicated in the pathology of common psychiatric disorders such as obsessive-compulsive disorder and schizophrenia, conditions that are frequently characterized by abnormal performance monitoring[17,18]. To date, however, it has proven extremely difficult to distinguish separate functional areas within the frontal lobe, and there have been few indications of how the functions of these two particular regions might differ[19,20].

One aspect of response evaluation that has received less attention is the fact that actions can be selected through either individual volition or by an individual's being told what to do (the former characterized by having increased degrees of freedom in choice and often referred to as 'free selection" or 'willed action selection'[21]). Here, using functional magnetic resonance imaging (fMRI), we have investigated how the opportunity to decide what action to perform affects the neural basis of outcome monitoring. We undertook a series of experiments in which participants carried out a variant of a response-switching paradigm, which was previously shown to activate prefrontal regions and ACd[22]. By varying whether subjects needed to make choices and monitor feedback (see Methods), we demonstrated a reciprocal relationship between the ACd and OFC during the evaluation of the outcome of a choice. The nature of the relationship varied according to whether the action was freely selected by the participant or guided by the experimenter, with activation increasing in the ACd and decreasing in the OFC when the action was freely selected, and the reverse occurring when the action was designated by the experimenter. In a second experiment, we showed that activation in the ACd could not be explained solely by error detection after feedback, by response conflict, or by the requirement to make a willed selection of an action from a wider range of possibilities[7,8,21,23]. Instead, activation in the ACd was driven by the combination of deciding on a choice and assessing the consequences of that choice.

RESULTS

Experiment 1

Subjects were trained on three versions of the response-switching experiment, each of which involved differential degrees of choice behavior and feedback monitoring (**Fig. 1a–c**). In the GUESS condition, after a 'switch' cue, subjects had both to decide upon an appropriate response and to monitor the resultant feedback to ascertain which set of response rules was in place. In FIXED, by contrast, subjects were told always to make a particular finger press response on the first trial after the switch cue. As before, they were unaware of which response set was subsequently in place and so had to monitor the feedback from this instructed action (which was correct on ~50% of trials) and utilize this information to work out which set to use. Finally, in INSTRUCTED, subjects were informed by the switch cue which response set was in place, meaning they could switch sets without needing to monitor their responses. Comparing blood oxygen

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level–dependent (BOLD) signal increases following switch cues with those following 'stay' cues (switch–stay: 'Sw–St') in the GUESS and FIXED conditions allowed us to examine activation related to monitoring the outcome of uncertain actions. In GUESS, this was connected with the consequences of an action freely decided upon by the subject themselves. In FIXED, the BOLD response was due to monitoring an externally instructed response.

Behavioral data. Switch costs (the difference between median reaction times on trials after switch cues compared with those after stay cues) from GUESS and INSTRUCTED were almost identical, with large switch costs on the first trial but no difference between reaction times following either the switch or stay cue by trial two (**Fig. 2**). This was confirmed by planned *t*-tests which showed a significant switch cost on trial 1 in both GUESS and INSTRUCTED (GUESS: 347 ms (switch reaction time = 1,006 ms, stay reaction time = 659 ms): $t = 3.60$, $P < 0.01$; INSTRUCTED: 256 ms (switch reaction time = 914 ms, stay reaction time = 658 ms), $t = 2.57$, $P < 0.05$), but no difference between the switch costs in the two conditions. By contrast, in FIXED, there was only a minimal switch cost on trial 1 (16 ms (switch reaction time = 508 ms, stay reaction time = 492 ms)). However, there was a small, though not significant | $P > 0.1$), switch cost on the second trial after a switch cue in this condition (75 ms (switch reaction time = 674 ms, stay reaction time = 599 ms) between reaction times on trial 2 after switch and after stay cues). This suggests that there were still reaction time costs from switching between response sets in the FIXED condition that were not present when continuing to use the same set. The error rates (excluding the first trial after a switch cue where, in GUESS and FIXED, subjects made ~50% errors) were low in all conditions (GUESS = 4.2%, FIXED = 4.8%, INSTRUCTED = 3.6%).

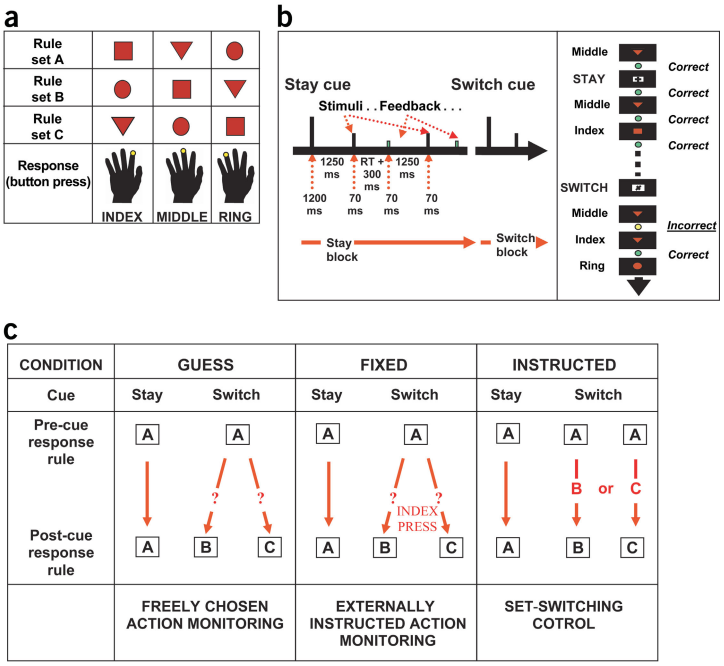

Figure 1 Experimental design. (**a**) Representation of the three response rules used during the task. (**b**) Schematic of the paradigm used in all three versions of the response switching task. Left, timing of the switch and stay cues, visual stimuli and feedback. Right, a typical set of trials. (**c**) A schematic of the three different versions of the response switching task at the presentation of either the stay cue (left of each panel) or the switch cue (right of each panel). A–C refer to the three different response sets.

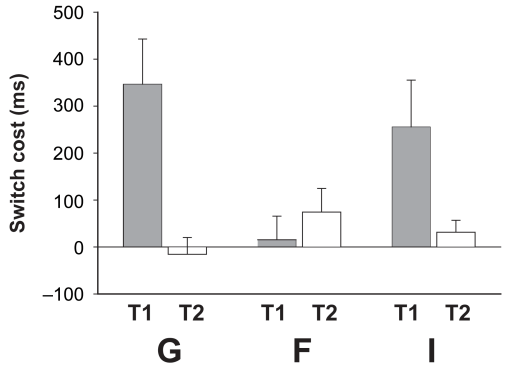

Figure 2 Mean switch costs across subjects (and their standard errors) for trials 1 and 2 (T1 and T2) after the cues in Experiment 1. Switch costs are the difference in reaction time on trials following a switch cue compared with those following a stay cue. G, GUESS; F, FIXED; I, INSTRUCTED.

Imaging data: interactions between decision making and monitoring. Our first aim was to identify regions activated when evaluating the outcome of an action that was the result of a freely chosen action, relative to an externally specified response ($GUESS_{Sw–St} - FIXED_{Sw–St}$). A random-effects analysis revealed significantly greater activation in a connected area containing two peaks, lying in the rostral cingulate sulcus (peak activations: –6, 22, 36; $z = 3.91$ and 0, 10, 40; $z = 4.89$) (**Fig. 3a**). The increase in BOLD signal in this region of ACd was nearly twice as large in the GUESS condition (that is when monitoring the outcome of the subjects' own decisions) than in either of the other two conditions (**Fig. 3b**). An ANOVA revealed a main effect of condition ($F_{2,14} = 9.17$, $P < 0.01$), caused by significantly greater signal change in GUESS than in FIXED ($t = 4.79$, $P < 0.01$) or INSTRUCTED ($t = 4.42$, $P < 0.01$) conditions.

Two prominent recent theories of ACd function are that this region is primarily involved with detecting errors or in monitoring for response conflict[7,8]. Therefore, to determine whether ACd activity was being principally driven by incorrect responses on the first trial after a switch cue, we compared the ACd signal in GUESS when people chose correctly to when they chose erroneously on the first trial after a switch cue. This demonstrated there was no difference in ACd signal regardless of whether positive or negative feedback was received (**Fig. 3c**). Moreover, further analyses demonstrated that there was no relationship between activation in ACd and response conflict, as indexed by increased reaction times (**Fig. 3d**). These data are therefore consistent with ACd activation arising from monitoring the outcome of freely chosen responses where there are increased degrees of freedom in choice.

The second main objective was to discover in which areas there was activation specific to monitoring the outcome of an externally

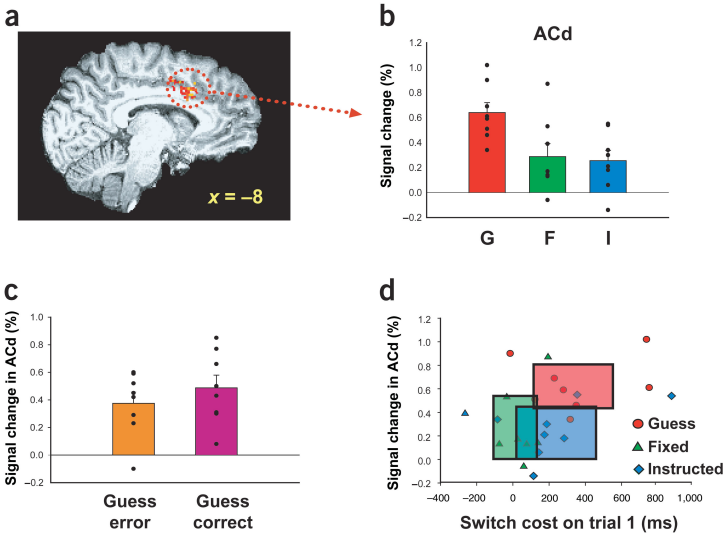

Figure 3 Monitoring the outcome of freely chosen actions. (**a**) ACd activation in $GUESS_{Sw–St}$ – $FIXED_{Sw–St}$ (peaks: –6, 22, 36; 0, 10, 40). (**b**) Graph of the signal change in this activated region. G, GUESS; F, FIXED; I, INSTRUCTED. (**c**) Plot of the effect size in ACd in the GUESS condition (switch – stay) divided up by whether subjects chose correctly or erroneously on the first trial after a switch cue. (**d**) Plot of the switch cost against the signal change in ACd for each individual subject. Rectangles represent 95% confidence limits for each variable (the left and right sides of each representing confidence limits for the switch cost, top and bottom, confidence limits for the signal change). Red rectangle, GUESS condition; blue rectangle, INSTRUCTED; green rectangle, FIXED.

instructed action ($FIXED_{Sw–St}$ – $GUESS_{Sw–St}$). By contrast with the previous comparison, this analysis revealed two regions with significant responses located in anterior medial OFC (peak: 12, 54, –22; z = 3.26) and right lateral OFC (peak: 40, 32, –12; z = 3.44) (**Fig. 4**). Plots of the effect size in these areas demonstrated that activity was only present when switching between response sets in the FIXED condition and was absent from this contrast in GUESS and INSTRUCTED. A main effect of condition (medial OFC: $F_{2,14}$ = 11.58, P < 0.01; lateral OFC: $F_{2,14}$ = 9.56, P < 0.01) was demonstrated to be the result of significantly greater responses in the FIXED condition than in either GUESS (medial OFC: t = 6.22, P < 0.01; lateral OFC: t = 4.38, P < 0.01) or INSTRUCTED (medial OFC: t = 2.84, P < 0.05; lateral OFC: t = 4.03, P < 0.01).

These results show a double dissociation between activations in ACd and OFC when evaluating the consequences of actions. However, it was not initially evident to what degree these regions have distinct roles in feedback monitoring depending on the task being performed and the strategy subjects use. There is anatomical data showing that parts of ACd and OFC are interconnected in monkeys[24], yet a study examining functional connectivity with human anterior cingulate cortex showed that the lateral orbitofrontal gyri were the one area in frontal cortex likely not to be coactivated with this region[20]. To investigate this issue, we plotted the signal change in ACd against that in lateral and medial OFC in both the GUESS and FIXED conditions separately for each subject, assuming independence in the data. This demonstrated a significant negative correlation between the effect size in ACd and the lateral OFC cluster (R = –0.582, P < 0.05) (**Fig. 5**). Even if no assumption about independence is made and GUESS and FIXED data points for each subject are paired, we still find a significant mean negative gradient between the two (t = –2.83, P < 0.05), indicating that within each subject there was an inverse relation between activation in ACd and lateral OFC for the GUESS and FIXED conditions. Notably, the reciprocal coupling only appears present when contrasting conditions in which subjects are required to monitor feedback; there was no significant relationship between the signal change in ACd and lateral OFC when comparing INSTRUCTED with either GUESS or FIXED, and the mean gradients for these were not significantly different from zero.

Imaging data: monitoring independent of choice behavior. As well as activity specific to monitoring the outcome of freely chosen and externally instructed actions, we also identified regions that were commonly activated when evaluating feedback regardless of the nature of the response. Activation in $GUESS_{Sw–St}$ – $INSTRUCTED_{Sw–St}$ was masked with $FIXED_{Sw–St}$ – $INSTRUCTED_{Sw–St}$, thus providing an indication of the common areas of activation across the two contrasts. These included bilateral activations in the inferior frontal sulci (peak activation: –44, 30, 24 and 44, 18, 24) and a small cluster in the ventral striatum around the level of the nucleus accumbens (8, 12, –2) (**Fig. 6a,b**).

Experiment 2

Although the first experiment demonstrated that activation in ACd was greatest when subjects had both to decide what response to make and to monitor its outcome, it was possible that this was caused solely by the requirement to make a willed action selection from a greater range of possibilities in GUESS than in the other conditions[21,23]. As the design of the first experiment made it difficult to disentangle decision making and feedback monitoring processes, we therefore undertook a second

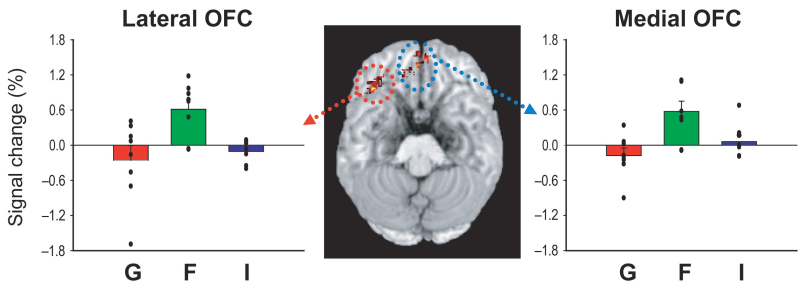

Figure 4 Monitoring the outcome of externally guided actions. Lateral and medial OFC activations in $FIXED_{Sw–St}$ – $GUESS_{Sw–St}$ comparison (peaks: lateral OFC, 40, 32, –12; medial OFC, 12, 54, –22) and plots of the signal change in these activated regions (left, lateral OFC; right, medial OFC). G, GUESS; F, FIXED; I, INSTRUCTED.

response switching experiment to investigate this issue, again including GUESS and FIXED, but with INSTRUCTED replaced by two novel conditions. In GENERATE, subjects could choose which set to switch to but were informed that whatever response they selected would be correct. This condition involves identical willed action selection and conflict components as the GUESS condition, but differs in that subjects need not monitor the feedback as they already know the outcome of their choices in advance. In CONTROL, the first response after the switch cue was also always correct, but, as in FIXED, this response was instructed by the experimenter.

Behavioral data. The pattern of reaction times in GUESS in Experiment 2 mirrored those recorded in the first experiment, with a large switch cost being present on trial 1 (416 ms (switch reaction time = 1,077 ms, stay reaction time = 661 ms), $t = 4.11$, $P < 0.01$; **Fig. 7**). Similarly, as in Experiment 1, although there was no switch cost in the FIXED condition on trial 1 (28 ms (switch reaction time = 555 ms, stay reaction time = 527 ms)), it was present on trial 2 (140 ms (switch reaction time = 731 ms, stay reaction time = 591 ms), $t = 3.07$, $P < 0.05$). Reaction times in the GENERATE and CONTROL conditions were comparable to those in GUESS and FIXED, respectively, with a large switch cost on trial 1 in GENERATE (333 ms (switch reaction time = 996 ms, stay reaction time = 663 ms), $t = 3.88$, $P < 0.01$) but not in CONTROL (–34 ms (switch reaction time = 434 ms, stay reaction time = 469 ms)). There was also a significant switch cost in GENERATE (115 ms (switch reaction time = 701 ms, stay reaction time = 586 ms), $t = 2.31$, $P < 0.05$) and a near-significant one in CONTROL on trial 2 (79 ms (switch reaction time = 657 ms, stay reaction time = 579ms), $t = 2.13$, $P = 0.07$). There was no difference between the magnitude of the switch cost on trial 1 between the GUESS and GENERATE conditions, or between that on trial 2 between FIXED and CONTROL. The error rates, excluding the first trial after the switch cue, were low in all conditions (GUESS = 4.7%, GENERATE = 4.2%, FIXED = 5.0%, CONTROL = 3.7%).

Imaging data: performance monitoring or willed action selection? A second random-effects analysis replicated the previous finding of significantly greater activation in a region of ACd for GUESS relative to FIXED ($GUESS_{Sw–St}$ – $FIXED_{Sw–St}$: peak: 0, 18, 36; $z = 4.08$; **Fig. 8a**). However, there was no significant response in this region when GENERATE was compared with FIXED ($GENERATE_{Sw–St}$ – $FIXED_{Sw–St}$). To investigate this further, the mean percentage signal change in the region activated by $GUESS_{Sw–St}$ – $FIXED_{Sw–St}$ was obtained for each subject in each condition. The effect size was greatest in the GUESS condition, when subjects had to decide what response to make and monitor its feedback (**Fig. 8b**). By contrast, when only one of these two factors was required, such as in the GENERATE or FIXED conditions, the effect size was reduced. When these data were subjected to a two-way ANOVA, it was found that there were main effects of both decision-making ($F_{1,7} = 12.22$, $P < 0.05$) and feedback monitoring ($F_{1,7} = 5.52$, $P = 0.05$), caused by there being a significantly larger ACd signal in GUESS than in any of the other three conditions (GUESS versus GENERATE: $t = 3.62$, $P < 0.01$; GUESS versus FIXED: $t = 8.18$, $P < 0.01$; GUESS versus CONTROL: $t = 3.47$, $P = 0.01$). To verify that this result was not biased by constructing a region of interest (ROI) mask around a region maximally active during the GUESS condition, the effect size in each condition was recalculated using the ACd ROI mask from Experiment 1. All aspects of the previous analysis were replicated.

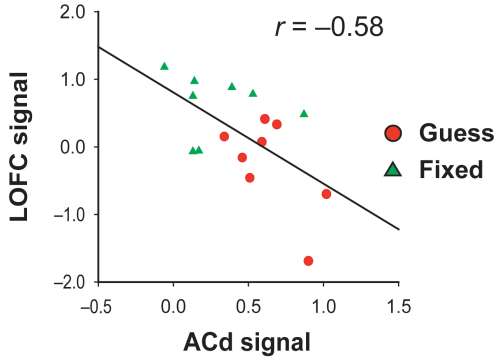

Figure 5 Correlation of the signal change in ACd (*x*-axis) against lateral OFC (*y*-axis) plotted for both the GUESS and FIXED conditions.

DISCUSSION

These findings suggest that the neural mechanisms underlying performance monitoring are strongly influenced by the process of choosing a response. When subjects were themselves able to decide what action to make and had increased degrees of freedom in choice, ACd was preferentially activated whereas activation levels in OFC were negligible. By contrast, the reverse was found when subjects were told what to do by the experimenter. Moreover, the negative correlation between the BOLD signal in the two regions suggests that these areas play complementary roles during performance monitoring, with the balance of activation dependent on the degree to which an action was internally generated or guided by an external source.

Such a division can be partly understood in relation to the anatomy of the two regions. The part of ACd activated in the present study has been designated the rostral cingulate zone[25], which has been shown to be activated in many neuroimaging studies of executive tasks[19]. This region is a possible homolog of the rostral cingulate motor area (CMAr) in monkeys. As well as having access to information regarding goals and internal state of the animal via projections from prefrontal regions and the limbic system[26,27], parts of primate ACd—including CMAr—also send efferents both to primary motor cortex and to the spinal cord, allowing it to have direct influence over motor behavior[28]. ACd activation is often present in neuroimaging studies in the absence of an OFC response during tasks where subjects have to evaluate the outcome of their chosen action and use this informa-

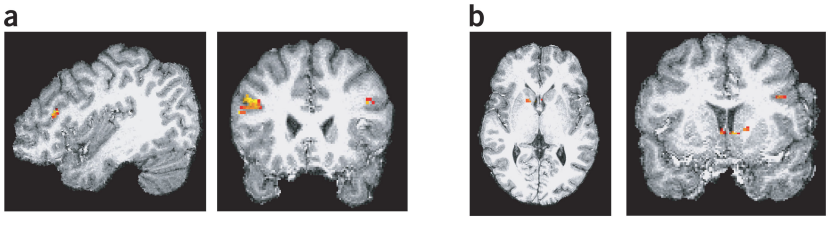

Figure 6 Representation of the activation common to both of the feedback monitoring conditions: $GUESS_{Sw–St}$ – $INSTRUCTED_{Sw–St}$ and $FIXED_{Sw–St}$ – $INSTRUCTED_{Sw–St}$ comparisons. (**a**) Bilateral inferior frontal sulcus (peak activation at –44, 30, 24 and 44, 18, 24). (**b**) Ventral striatum / nucleus accumbens (8, 12, –2).

tion to guide future behavior[23,29–32]. Moreover, several electrophysiological studies have reported cells around CMAr that respond to the receipt or omission of reward after completion of a behavioral trial, particularly in situations when the animal is monitoring the contingency between its action and the outcome[11,14,15,33]. There is also compelling evidence from both single unit and lesion studies in primate that although CMAr is vital for acquiring instrumental response-reward associations and using this information to guide behavior, this area might not be so important for learning and applying stimulus-response rules[16,33].

Unlike ACd, no part of OFC has any direct connection with the motor system. However, in contrast to the relative paucity of input to ACd from the sensory cortices, OFC is a rich recipient of afferents from these regions. The right lateral OFC activation observed in this study is located around the lateral orbital sulcus (area 47/12, ref. 34), which is believed to be homologous with the same sulcus in the monkey lying adjacent to Walker's area 12 (ref. 35). Among the projections to this area in monkeys is a substantial input from visual area TE[36]. Neuroimaging studies where subjects were not required to make any overt behavioral response, such as those involving appetitive classical conditioning, often report a significant response confined to OFC[5,37]. Similarly, OFC has been shown to be selectively activated when stimuli differ from expectation, either in terms of their identity or location, even in conditions where no decision is required[38,39].

Although there is consistency between the data reported here and the findings of monkey behavioral and electrophysiological studies discussed above, our results argue against strict versions of the three pervasive theories of ACd function to emerge from the neuroimaging literature, that it is involved either in willed action selection, in monitoring for conflict between competing responses or in error detection[2,7,8,21]. Although the willed selection of a response is clearly important component of ACd function, the results from Experiment 2, in which the ACd signal was significantly greater when subject were both choosing an action and monitoring its consequences (GUESS) than when they were just selecting what response to make (GENERATE), indicate that ACd is coding for the combination of deciding what to do and then assessing the consequences of this choice rather than merely for the willed selection of actions. This is comparable to the findings of a study that showed greater activity in this part of ACd when learning a motor sequence than during a free selection task in which subjects had to decide randomly which finger to move on each trial[23].

Similarly, although assessing the outcome of actions is clearly central to the conflict monitoring hypothesis, the same data from Experiment 2 are also incompatible with a strict version of this theory. In both GUESS and GENERATE, at the time of switching, subjects were faced with an identical number of possible options and showed similar reaction time costs, implying that there were equivalent levels of conflict during switching between response sets in these conditions. Finally, in Experiment 1, it was demonstrated that the effect size in ACd was identical regardless of whether the selected response after a switch was correct or erroneous, suggesting that it was the informative nature of the feedback (which always allowed subjects to work out which set of response rules were in place) rather than the error signal itself that was driving activity. These data add support to the findings from single-unit recordings which show that both rewards and errors can drive ACd activity[15,33]. However, taken together, the findings from the experiments reported here suggest that it is not performance monitoring or reward-guided action selection *per se* that caused increased ACd activity, but the process of assessing the consequences of a choice freely made by the subject themselves. Such a conclusion might help reconcile findings from neuroimaging, experimental lesion and stimulation studies of a prominent, volitional role for ACd in willed response selection[21,40,41] with the evaluative conflict monitoring and error detection theories[7,8]. It has been shown in single-unit recording studies, for instance, that neurons in and around CMAr are active before and during a response, and before and during feedback[15]. However, whether ACd itself uses this outcome information to guide subsequent behavior, or whether response selection choices are subserved by other interconnected structures, remains a question for future studies.

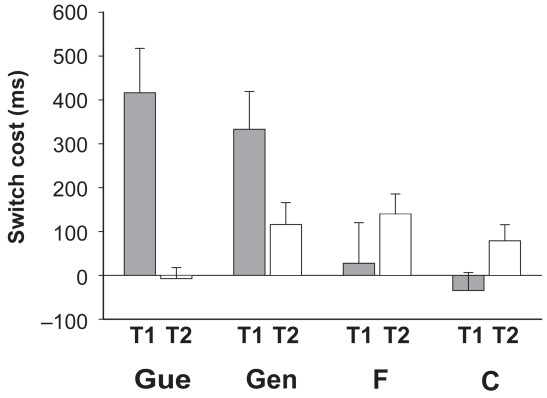

Figure 7 Mean switch costs across subjects (and their standard errors) for trials 1 and 2 (T1 and T2) after the cues in Experiment 2. GUE, GUESS; GEN, GENERATE; F, FIXED; C, CONTROL.

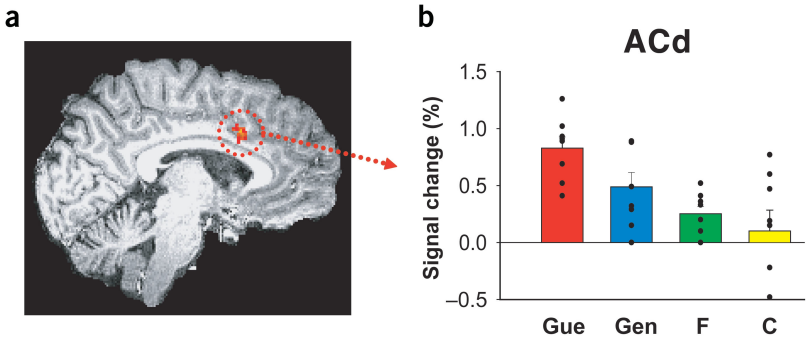

Figure 8 Activations and effect sizes in Experiment 2, investigating the contributions of decision making and performance monitoring to ACd activation. (**a**) ACd activation in the second experiment from $GUESS_{Sw–St}$ – $FIXED_{Sw–St}$ (peak: 0, 18, 36). (**b**) Graph of the signal change for this activated region. GUE, GUESS; GEN, GENERATE; F, FIXED; C, CONTROL.

As well as demonstrating a dissociation between the regions involved with evaluating the outcome of actions chosen by the subject themselves or instructed by the experimenter, we also found that a bilateral region of the inferior frontal sulcus and part of the right ventral striatum were both activated when subjects had to monitor feedback, regardless of who had chosen the response. This part of the inferior frontal sulcus has previously been shown to be recruited during tasks involving response selection relying on

arbitrary visuomotor mapping or when reversing such associations[42,43]. The ventral striatum receives projections from parts of both ACd and OFC[44] and is also considered to be part of a system involved in predicting the contingency between stimuli, actions and reinforcement. Notably, a number of recent studies have also shown that activity in this region corresponds to a temporal difference learning signal that has been suggested to allow flexible representation of likely future reward and an up-to-date valuation system for stimuli in the environment[5,37].

In summary, we have demonstrated that ACd and OFC have complementary and reciprocal roles in the assessment of the consequences of actions, dependent on whether subjects are told what to do or were themselves able voluntarily to chose between the possible responses. ACd, through its intimate relationship with both the limbic and motor systems, appears to be vital for learning about the consequences of internally generated decisions, assessing the value of chosen responses and guiding subsequent choices accordingly. By contrast, OFC, with its extensive connections from sensory cortex, seems to have an important role in monitoring the outcome of externally guided actions and in altering stimulus-reward associations. These results may help resolve several of the outstanding questions as to how ACd and OFC interact to work out what is worth doing.

METHODS

Subjects. Eighteen right-handed subjects (12 male, 6 female; aged 21–35) took part in this experiment, with 8 participating in Experiment 1 and 10 in Experiment 2. Two subjects from Experiment 2 were discarded because they did not show any behavioral effect of response switching. Each subject gave informed consent and all experiments were approved by the Oxford Ethics Research Committee.

Behavioral task. On each trial, subjects were presented with one of three visual stimuli (subtending a 1.2° visual angle) in the center of a screen, and were required to register one of three possible responses on a button box by pressing down their index, middle or ring finger. Their responses were governed by three sets of response rules (**Fig. 1a**). After each response, the subjects received feedback in the form of a small, centrally displayed yellow circle for a correct response, or a blue circle for an error. After 8–12 such trials, a cue appeared on the screen either instructing the subject to continue responding using the same set of rules ('stay' cue) or to switch to a different set ('switch' cue).

Experiment 1 involved three versions of this task, which differed only in the instructions that followed the switch cue (**Fig. 1c**). In the GUESS condition, the switch cue indicated that subjects should switch to one of the other two sets of response rules, but did not specify which. To ascertain which set was in place, the subjects had to monitor the feedback after each response.

In the FIXED condition, the switch cue, as before, did not indicate which rule set was currently in place. Instead of deciding on a response themselves, however, the subjects were instructed by the experimenter, before performing the next block of trials in the MRI scanner, to register a pre-determined finger-press response on the first trial after the switch cue, irrespective of the visual stimulus. This stimulus could always be mapped onto the designated finger-press response under one of the two other rule sets, and would never correspond to the designated finger under the previous rule set. As before, they had to monitor the on-screen feedback from this choice ("correct" on ~50% of trials) and use this information to work out which of the other two sets of response rules to use from trial 2 until the next cue.

In the INSTRUCTED condition, the subjects were informed onscreen which response set was in place: a single black bar on a white background for set A, two black bars for set B or three black bars for set C. The subjects could therefore switch sets without having to monitor the response feedback. This condition acted as a control, because the subjects, as in the other two conditions, had to inhibit the previous stimulus-response association when switching between rule sets, but did not have to monitor the outcome of their actions.

Experiment 2 consisted of the GUESS and FIXED conditions as well as two additional conditions. In the GENERATE condition, subjects were instructed to switch to one of the other two rule sets but were informed that whichever response they chose on the first trial after the switch cue would be correct. In the CONTROL condition, the first response after the switch cue was also always made to be correct. However, as in the FIXED condition, subjects were required each time to make the same finger press response (instructed prior to the commencement of the block of trials) on the first trial after the switch cue.

Subjects were trained outside of the MRI scanner on the task in the week before the fMRI experiment. Scanning was carried out using blocks of 200 trials of one condition, lasting ~7 min and containing approximately ten 'switch' and ten stay cues. Each condition was performed twice, the order counterbalanced across subjects, with a 2-min pause between blocks during which no images were acquired.

Data acquisition. A 3T MRI scanner was used to acquire 28 functional T2*-weighted echoplanar images (EPI) (4- × 2.5-mm coronal slices, TR = 3 s, TE = 30 ms, flip angle = 90°, matrix 64 × 64, field of view 256 × 160), scanning the front of the brain rostral to a point level with the central sulcus. The timing of all stimuli and response events, along with the onset of each volume acquisition, was recorded using Spike4 software (Cambridge Electronic Design, Ltd., Cambridge, UK). A single whole-brain volume of EPI (48 coronal slices, TR = 5 s) was obtained after subjects had completed behavioral testing in order to assist in the registration of the partial brain functional images to a high-resolution T1 structural scan (acquired either at the end of scanning or in a separate session).

To minimize susceptibility and distortion artifacts, we used a shim weighted towards ventromedial parts of prefrontal cortex[45], took coronal slices, and used a relatively small voxel size. Owing to a computer error, local shimming was not performed in Experiment 2. This greatly reduced our ability to record a reliable signal from OFC in this experiment.

Data analysis. Analysis was carried out using tools from the FMRIB software library (http://www.fmrib.ox.ac.uk/fsl). The first four volumes were discarded to allow for T1 equilibrium effects. The remaining images were then realigned to compensate for small head movements[46] and were spatially smoothed using a 5-mm full-width-half-maximum (FWHM) Gaussian kernel. The data were filtered in the temporal domain using a non-linear high-pass filter with a 75-s cut-off. Registration of the EPI images with high resolution structural images and into standard (MNI) space was carried out using affine transformations[47].

Random effects statistical analysis was carried out using a general linear model approach with local autocorrelation correction[48]. All the task components in each data block (stay cues, switch cues, visual stimuli, correct feedback, and incorrect feedback) were modeled separately after convolution with a canonical hemodynamic response. Temporal derivatives and individual subjects' motion parameters were included as covariates of no interest to improve statistical sensitivity. Individuals' contrast images for the two blocks of each condition were averaged to give a single image, and these were used in subsequent levels of analysis to derive statistical maps. All images were thresholded using cluster detection statistics, with a height threshold of $z > 2.3$ and a cluster probability of $P < 0.01$, corrected for multiple comparisons[49,50]. A second analysis, identical to that described above, was also performed on the data in Experiment 1 except that the 'switch' cue events were divided into two categories: (i) switch cues followed by a correct response, and (ii) switch cues followed by an erroneous response.

Statistical contrasts. In each condition, a comparison was made to identify regions showing greater BOLD signal increase following switch cues than following stay cues (switch–stay). There was approximately a 15- to 30-s interval between cue stimuli, depending on the number of intervening trials and subjects' speed of response. The processes of interest—choosing a response and monitoring its outcome—all began with the switch cue and terminated with the feedback from the first stimulus. As we were concerned with the relationship between these two factors, they were captured by a single explanatory variable corresponding to the cue onset with a brief (0.5 s) duration.

The focus of the experiment, however, was to compare how the activation recorded in the switch–stay comparison differed across conditions. In Experiment 1, we were specifically interested in the regions that showed greater activation when subjects had to monitor the outcome of a freely cho-

sen response compared to when they were monitoring the outcome of an externally instructed action ($GUESS_{Sw–St}$ – $FIXED_{Sw–St}$), and vice versa ($FIXED_{Sw–St}$ – $GUESS_{Sw–St}$). The areas of activation in the above contrasts were used as ROIs to investigate the effect sizes in our regions of interest—ACd and OFC—in the three conditions. To investigate whether any activation observed in ACd was being driven by error feedback, effect sizes were also calculated from the second analysis, using the same ACd ROI, to compare activation following correct or erroneous responses after a switch cue in the GUESS condition.

The second experiment addressed the question of whether ACd activation observed in Experiment 1 could be explained solely by the fact that subjects had to decide for themselves which response to make or whether it was the combined effect of freely choosing a response and monitoring its feedback. We therefore concentrated on an ACd ROI defined by the activated cluster in the ($GUESS_{Sw–St}$ – $FIXED_{Sw–St}$) contrast in a whole brain analysis and calculated effect sizes in the four separate task conditions within this region.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interest.

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