

Functional organization of the medial frontal cortex

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The anterior cingulate cortex (ACC) and adjacent areas of the medial frontal cortex (MFC) have been implicated in monitoring behaviour and in detecting errors. Recent evidence, however, suggests that the ACC not only registers the occurrence of errors but also represents other aspects of the reinforcement history that are crucial for guiding behaviour. Other studies raise the possibility that dorsal MFC areas not only monitor behaviour but also actually control response selection, particularly when the task in hand is changing. Many decisions are made in social contexts and their chances of success depend on what other individuals are doing. Evaluation of other individuals is therefore crucial for effective action selection, and some ACC regions are implicated in this process.

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Introduction

The medial frontal cortex (MFC) is a collective term used to describe cortex dorsal and rostral to the corpus callosum (Figure 1a). In the primate brain, it is usually taken to include the anterior cingulate cortex (ACC) as well as several areas in the more dorsal superior frontal gyrus, such as the pre-supplementary motor area (pre-SMA), the supplementary motor area (SMA) and the supplementary eye fields (SEF). In this review, we focus on the studies from the past two years that have attempted to understand the role of the MFC in executive control, action selection and social cognition. Changes in activity, as indexed by the blood oxygenation-level-dependent (BOLD) signal measured using functional magnetic resonance imaging (fMRI), are prominent in the MFC when human subjects start a new cognitive task or switch between performing two different tasks [1^{••}–4^{••}]. An

influential account of such findings has emphasized the importance of the MFC in monitoring brain response systems to ascertain whether different, and therefore conflicting, responses are being prepared [5]. This might occur if the stimulus guiding behaviour is ambiguous, as is the case in the Stroop task, or because a change in context means that a different set of stimulus–response associations should be called into play, as occurs when switching from one task to another.

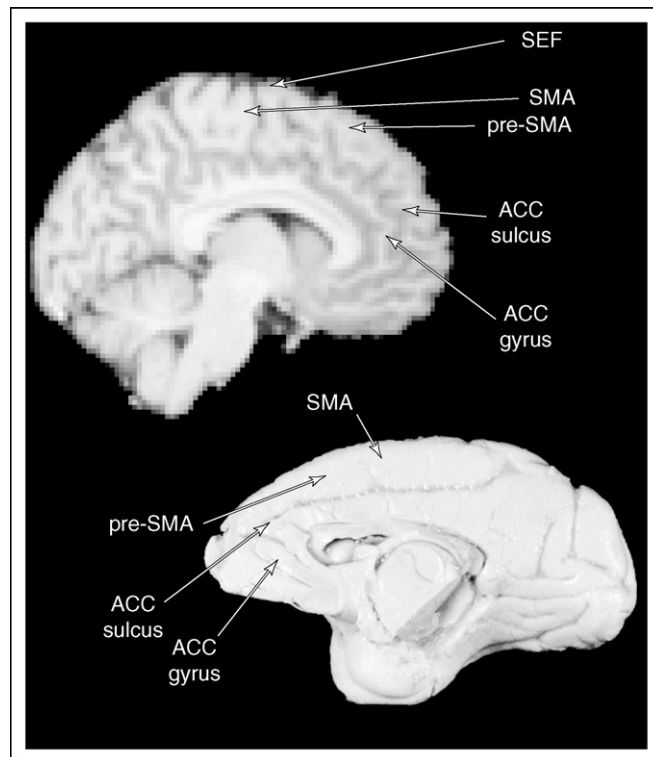
A recent fMRI study [6] reported activation of the MFC when stimuli afforded competing and conflicting responses, but found that there was no effect on MFC activity when conflict was manipulated at a perceptual level by altering the salience of irrelevant stimulus information. According to the conflict monitoring hypothesis, the increase in MFC activity leads to activation of the dorsolateral prefrontal cortex on the next trial of the task and this, in turn, ensures careful control of the process of response selection. Kerns *et al.* [7] used fMRI to scan subjects while they were performing the colour-naming Stroop task. There was increased MFC activity in trials where the ink colour (which subjects were to name) spelled out an incongruent colour word that afforded an alternative naming response (e.g. the word blue printed in red ink). MFC activity on the conflict trial was correlated both with dorsolateral prefrontal activity on the subsequent trial and with the extra control exerted over response selection, as indexed by slower response times.

Conflict detection or context-dependent control of action

There has been uncertainty about which MFC region is the key region concerned with conflict. A meta-analysis of fMRI studies emphasized the variable location of conflict-related activity within the MFC [8]. Single-neuron recording studies in macaques, in which the location of activity can be precisely determined, have failed to find evidence for conflict-related activity in the ACC (Figure 2) [9]. Such findings are consistent with demonstrations that ACC lesions do not impair task switching or performance on more direct tests of conflict monitoring [10,11,12^{••}].

It is equally difficult to identify pure conflict-detecting neurons in more dorsal MFC areas such as the SEF. Nevertheless, it is clear that the activity of saccade-selective SEF neurons is modulated by the context — conflict or non-conflict — in which an action is selected (Figure 2) [9]. Even if the SEF does not detect conflict, it

Figure 1



Medial view of the human (top) and macaque (bottom) brain. The medial frontal cortex (MFC) is usually taken to include the anterior cingulate cortex (ACC) and the more dorsal superior frontal gyrus, which contains areas such as the pre-supplementary motor area (pre-SMA), the supplementary motor area (SMA) and the supplementary eye field (SEF). In macaques, the SEF is usually just lateral to the SMA so that it extends over the crown and onto the lateral surface. Identifying homologies in brain structures across divergent species is difficult but some medial frontal areas of the rat brain, particularly ACC areas, resemble primate brain areas [53].

might be part of a system that changes the way in which actions are selected or inhibited depending on the current task and context. Such a possibility is consistent with the finding that intracortical microstimulation of the SEF region affects the control of saccades in a context-dependent manner [13^{••}].

The SEF is most important when the response that must be altered or inhibited is a saccade response rather than a manual one. fMRI studies suggest that other adjacent parts of the superior frontal gyrus, such as the pre-SMA, are active when subjects switch between rules for making manual or saccadic responses, or when they inhibit manual or saccadic responses [2^{••}, 3^{••}, 14^{••}, 15[•], 16^{••}]. Transcranial magnetic stimulation of the pre-SMA affects task performance on the same trials [17].

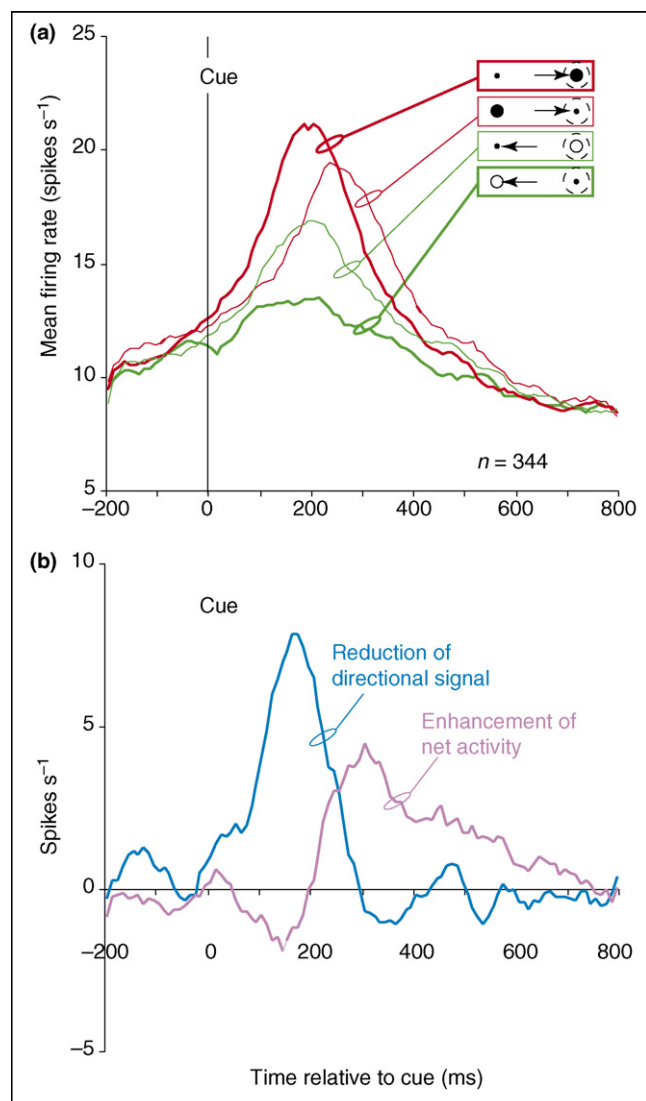
Monitoring performance for errors: the role of the ACC

There has been considerable interest in the neural mechanisms that monitor behaviour for errors. It is argued that the detection of errors is important because errors are highly informative of how best to adjust future behaviour

[8, 18[•], 19]. An event-related potential called the event-related negativity (ERN) can be recorded from the scalp when human subjects make mistakes or when their gambles lead to an undesired outcome [20]. The ERN is present not just when subjects made mistakes themselves but even when they witness others making mistakes [19]. It is now clear that trial by trial, fluctuations in the strength of the ERN can be correlated with simultaneously recorded trial by trial variations in the BOLD signal in the ACC [18[•]]. Despite the clear identification of the ERN with the ACC, it is evident that the presence of the ERN is also contingent on the integrity of the striatum, prefrontal cortex and interconnecting white matter [21^{••}, 22^{••}].

Although the ERN does not correlate with the response times recorded on the same trial, it is correlated with longer response times on the subsequent trial [18[•]]. This suggests that detection of an error by the ACC does indeed lead to subsequent behavioural adjustment. Most paradigms provide subjects with no opportunity to adjust their performance more rapidly than on the next trial. However, Magno *et al.* [23] recently designed a visual

Figure 2



SEF neuron activity during a conflict task. (a) Nakamura and colleagues [9] taught macaques to perform tasks that involved response conflict. In the 'spatial incompatibility task', the macaques learned to make a saccadic eye movement to the left or to the right when shown a red or a green cue. Because the cue itself could appear on either the left or the right, it drew attention to the same location and predisposed each animal to make a saccade in that direction. Conflict, indexed by increased response time, occurred when the cue colour was associated with a different response to the cue position. From the average response of 344 neurons, it is clear that many responded more when saccades were made in a preferred direction (red lines) than in the opposite direction (green lines). There was little evidence for neurons in the SEF that responded only to conflict but many had activity that also reflected whether it was a conflict or non-conflict trial (thin or thick lines, respectively). (b) The population as a whole was more active on conflict trials than non-conflict trials (pink line) and the same effect was evident in the activity of individual SEF neurons. The direction signal decreased on conflict trials (blue line). In the ACC, however, conflict had no effect on the net firing rate of the population and there was little evidence for a net increase in firing rates on conflict trials in the activity of individual neurons. Adapted, with permission, from [9].

search task in which subjects were given the option of not actually trying to respond, even after the trial had begun, if they thought that the response might be incorrect. The ACC BOLD signal was high on the trials in which subjects opted not to respond to avoid an error.

The need for behavioural adjustment is obviously particularly acute when subjects are learning the rules of a new task. During the early stages of learning, the ACC BOLD signal can be recorded when feedback cues are presented to inform subjects that they have made the wrong response. Gradually during the course of learning, however, the ACC signal on error trials becomes more closely time-locked to the execution of the response itself, rather than the feedback [24]. The ACC BOLD signal occurs in response to both internal and external indicators of errors [25].

It is also possible that the ACC responds not only to errors per se but also to conditions associated with a high likelihood of error [26**]. Such a hypothesis might begin to explain why the ACC is active in many contexts, such as task-switches or other difficult situations, even when no overt errors actually occur.

Errors and other important outcomes

Despite the emphasis on errors, there is also evidence that single neurons in the ACC are active when positive reinforcement is delivered [27]. Although errors are indeed often useful sources of information about how to improve performance, so are correct outcomes. This is especially true when the correct way to perform the task is unclear. Walton *et al.* [28] asked subjects to perform a task-switching paradigm in which the switch cues did not tell subjects which of two alternative task sets was the correct one. In such a situation, positive feedback after a decision carries equivalent information to negative feedback in the sense that, after either type of feedback, subjects should know which is now the correct way to perform the task.

Procyk *et al.* [29] used a similar approach while recording from neurons in the ACC of macaques. For the macaques, the response set was not a particular set of visuomotor rules but one of different possible movement sequences. The macaques discovered by trial and error which way of ordering the component movements was correct. ACC neurons were active when an action was followed by error feedback and when, for the first time, it was followed by positive feedback (positive feedback is no longer informative once the animals have worked out which sequence to perform). The ACC neurons then became relatively unresponsive on correctly performed trials. What is important for driving ACC activity, therefore, might not be the valence of the outcome (positive or negative) but its saliency for guiding behaviour.

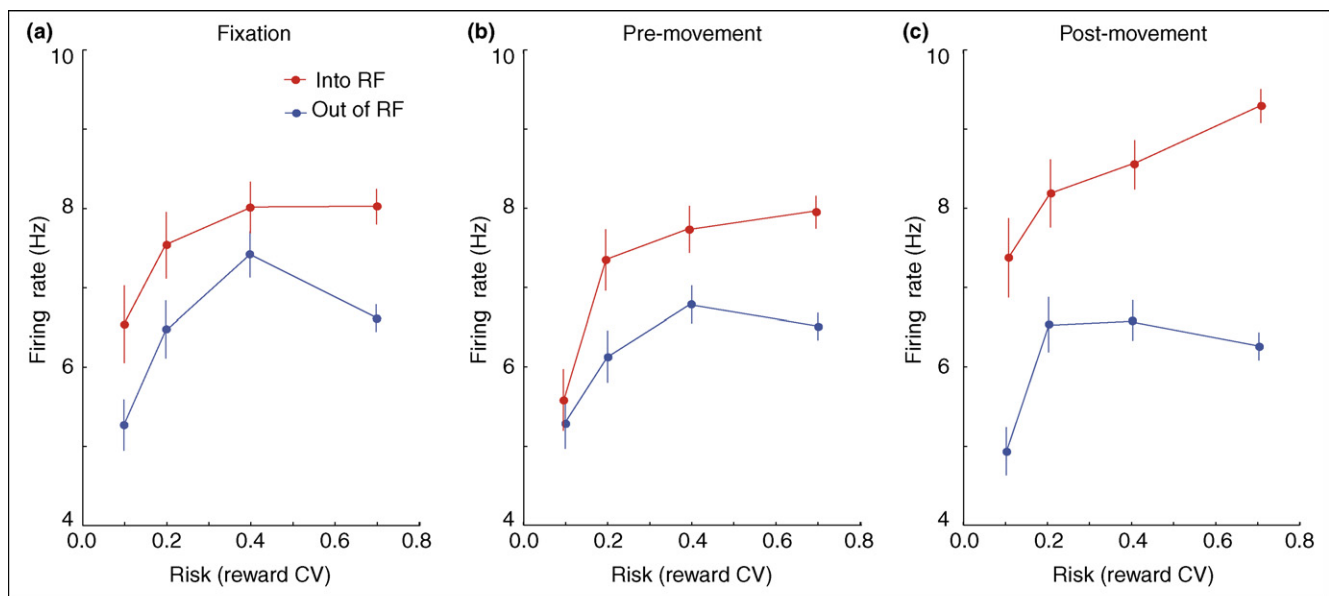
Detecting errors or representing the reinforcement history

For an animal foraging in an uncertain environment, the outcomes of actions are unlikely to be either categorically correct or erroneous, and both positive and negative outcomes are important sources of information about the potential value of actions. Although the ACC can register when an error occurs, its function might not be error detection per se and instead it might represent aspects of a more extended choice–outcome history, based on both positive and negative feedback, that can be used to guide future decisions. Evidence for this comes from a study by Kennerley *et al.* [30], who trained macaques to make one of two movements using a joystick. In one version of the task, only one of the actions delivered reward. Which action was the correct one was changed periodically, and the only information that told animals which action was correct was the presence or absence of a food reward after each movement. It was noticeable that control animals did not immediately switch to the alternative response every time an action was not followed by a reward; instead, they became gradually more and more likely to switch to the alternative action as they gathered experience that the first action was no longer rewarding and that the alternative

action was rewarding. In other words, behaviour was determined not only by the occurrence of a single error but also by the history of reinforcement over the course of several previous trials. Animals with lesions of the ACC sulcus responded in a similar way to controls on error trials but, noticeably, the longer-term reinforcement history did not have the same influence over their behaviour. The outcomes of actions that had been made several trials ago normally influenced the next actions that the macaques made, but this was no longer true after an ACC sulcus lesion. Such a pattern of impairment suggests that the ACC is not so much concerned with detecting or correcting errors but in guiding decisions on the basis of the history of previous actions and their outcomes.

The activity of single neurons in the ACC reflects the reinforcement history of the options that are available to the macaque. Amiez *et al.* [31] taught their animals to choose between two options that were associated with different rates of differently sized rewards. For example, one option was associated with 1.2 ml of juice with a probability of 0.7 and with 0.4 ml juice with a probability of 0.3, so that its average value was 0.96 ml. Other options were consistently associated with either 1.2 ml or 0.4 ml

Figure 3



McCoy and Platt [32] showed that the saccadic choices of macaques are best accounted for by both the size of rewards that were previously associated with each option and the variation in reward size (i.e. the degree to which the reward sizes deviated from the mean value). Both macaques that they studied preferred the riskier of two options. Recordings were made in the posterior cingulate cortex, in an area that is connected to the ACC and has receptive fields that are allocentrically organized [33,54]. Neurons were more active when the target of the saccade in the receptive field (RF) was associated with greater variation in reward size. The neurons were less active when a saccade was made into the receptive field if the saccade was directed to the target associated with less reward variance. On such trials, the target associated with greater reward variance was outside the receptive field of the neuron from which recordings were being made (out of RF). The three panels show the average neuronal firing rate on the ordinate as a function of increasing risk, which is indexed by the coefficient of variation in reward (reward CV) on the abscissa: (a) at the beginning of a trial (fixation), (b) immediately before movement and (c) immediately after movement. Adapted, with permission, from [32].

rewards. Many ACC neurons had activity that reflected the average value of the probabilistic option. This average, 0.96 ml, was 70% of the difference in value between the certain 0.4 ml option and the certain 1.2 ml options. Correspondingly, the activity increase of ACC neurons on presentation of the probabilistic option was 70% of the activity increase recorded when animals were presented with the certain 1.2 ml option as opposed to the certain 0.4 ml option.

Preferences do not depend only on an estimate of the average reward value based on the recent reward history. They also reflect variation in the level of reward, and the activity of neurons in a posterior cingulate region interconnected with ACC reflects preferences based on such information (Figure 3) [32,33*]. In addition to several parameters of the reinforcement history, ACC activity might even reflect the subject's knowledge of the inter-relationships between the value of choice options and other decision-making biases [34*,35**].

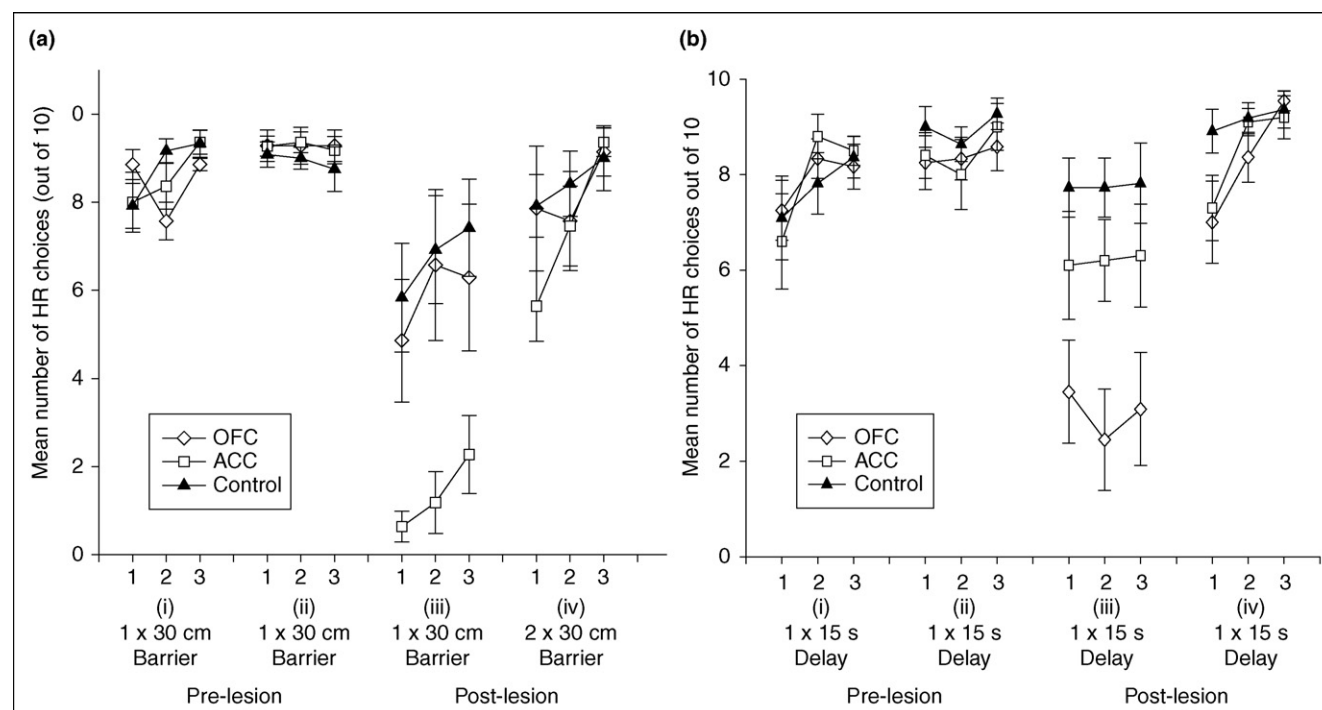
Making decisions about the costs and benefits of actions

It is important to know the reinforcement history of an action before a choice can be made. However, in addition to the potential benefits that the action might entail, it is also important to know what costs the action might entail. Optimal foraging theories have, for some time, emphasized that costs, as well as rewards, are important determinants of which options animals will pursue outside the laboratory. When animals are foraging, their choices are influenced not only by their reinforcement expectations for each action but also by the metabolic costs associated with each action [36]. Recent investigations of the rat ACC [37,38] suggest that this region is crucial for making decisions about how much effort it is worth investing to obtain reinforcement (Figure 4).

Social information and the ACC

In many situations, the best decision to make will depend both on the reward histories associated with each possible

Figure 4



ACC lesions impair effort-based decision making whereas lesions of the orbitofrontal cortex impair delay-based decision making. **(a)** Rats were trained to choose one of two arms of a T-maze, each of which was baited with food pellets. Choosing one arm of the maze, the high-reward arm (HR responses plotted on the ordinate) was consistently associated with more food rewards. In addition to the larger reward, however, the same arm of the maze was also associated with a greater cost: the animal had to climb a barrier before it could consume the food reward. Although rats normally chose the high-reward but high-cost option (i,ii) they stopped doing so after a lesion was made in the Cg1 and Cg2 fields of the ACC (iii). When a second barrier was also placed into what had been the low-cost arm, there was no longer a need to integrate both the costs and benefits associated with each option before a choice was made: because the costs associated with each T-maze option were equated, the choice could simply be based on the difference in expected reward. Under such conditions, the choices of the ACC lesion group returned to normal (iv). **(b)** The ACC appears to be specifically concerned with effort costs. The Cg1 and Cg2 ACC lesion did not alter the way that rats made choices in which the cost was the delay before food was delivered. The opposite pattern of impairment was seen after lesions of the orbitofrontal cortex (OFC); again, pre-operative data are shown in (i,ii), post-operative data are shown in (iii), and data from an equal delay condition are shown in (iv). OFC lesions did not change effort-based decision making but they did affect delay-based decision making. Adapted, with permission, from [38].

course of action and on what choices other individuals are taking [39]. Some parts of the ACC, particularly more ventral and rostral parts, seem to be particularly active when subjects are acquiring or using information about other individuals [40,41].

When the acquisition and encoding of social information is emphasized, there is activity in ACC and adjacent MFC areas [42,43^{••}]. Lesions of the ACC in the macaque lead to a reduced interest in acquiring information about other individuals [44]. Again, as in humans, the crucial region seems to be a ventral gyral part of the ACC. Memory retrieval success for information encoded in a social context is correlated with the level of MFC activity that was measured during encoding [42,45^{••}].

Amodio and Frith [46] have reported increased activation in the ACC when human subjects make decisions while thinking that they are interacting with another person as opposed to an inanimate computer. Recent event-related fMRI experiments [40,47,48^{••}] suggest that distinct cingulate regions are active when decisions are taken or observed in a social context. A particularly clear example of the involvement of the ACC in understanding other individuals is provided by the case of empathy. It is well known that the experience of pain is associated with cingulate activity [49] but it is now also clear that empathy for the pain of another individual is associated with activity in overlapping and adjacent regions [50–52].

Conclusions

The dorsal MFC has a central role in decision making and action selection. The ACC is important when decisions are guided by the history of reinforcement and when consideration is given to the costs associated with the action. More dorsal regions, such as the pre-SMA, become more important when subjects are changing or initiating a new task that entails distinct ways of selecting actions. Importantly, many decisions are made by individuals that are within a social context, not in isolation. The ACC is needed for the acquisition and use of the social information that will guide such decisions.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

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Activation in the MFC, including the ACC, was consistently related to the initiation and maintenance of a new task set across ten very different tasks.

2. Yeung N, Nystrom LE, Aronson JA, Cohen JD: **Between-task competition and cognitive control in task switching.** *J Neurosci* 2006, **26**:1429–1438.

The pre-SMA, together with a network of other areas, was active when subjects switched between tasks that required them to attend to faces or

to words. Distinct regions of the ventral occipitotemporal cortex were identified with face and word processing. Activity in the area specialized for the irrelevant task was positively correlated with the behavioural costs of switching task set.

3. Crone EA, Wendelken C, Donohue SE, Bunge SA: **Neural evidence for dissociable components of task-switching.** *Cereb Cortex* 2006, **16**:475–486.

Subjects selected responses that were associated with univalent and bivalent stimuli. Whereas the responses instructed by univalent stimuli were always the same, bivalent stimuli instructed different responses in different contexts. Greater activation in response to bivalent stimuli indicated that the ventral prefrontal cortex had a role in representing response selection rules, whereas greater activation in response to bivalent stimuli on rule-change trials suggested that the pre-SMA had a role in reconfiguring response selection rules.

4. Hon N, Epstein RA, Owen AM, Duncan J: **Frontoparietal activity with minimal decision and control.** *J Neurosci* 2006, **26**:9805–9809.

BOLD signal increases were recorded in the pre-SMA and ACC when stimuli — streams of words or objects — were changed. The signal increased as long as subjects were attending to the stimuli, even if the stimuli required no response and were irrelevant to the subjects' decisions and choices. Such intriguing findings challenge most current theories of MFC function.

5. Botvinick MM, Cohen JD, Carter CS: **Conflict monitoring and anterior cingulate cortex: an update.** *Trends Cogn Sci* 2004, **8**:539–546.
6. Liston C, Matalon S, Hare TA, Davidson MC, Casey BJ: **Anterior cingulate and posterior parietal cortices are sensitive to dissociable forms of conflict in a task-switching paradigm.** *Neuron* 2006, **50**:643–653.
7. Kerns JG, Cohen JD, MacDonald AW III, Cho RY, Stenger VA, Carter CS: **Anterior cingulate conflict monitoring and adjustments in control.** *Science* 2004, **303**:1023–1026.
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11. Fellows LK, Farah MJ: **Is anterior cingulate cortex necessary for cognitive control?** *Brain* 2005, **128**:788–796.
12. de Wit S, Kosaki Y, Balleine BW, Dickinson A: **Dorsomedial prefrontal cortex resolves response conflict in rats.** *J Neurosci* 2006, **26**:5224–5229.

Although other studies have failed to find impairments on conflict tasks after ACC lesion, the authors of this study identified one situation in which there is an impairment. de Wit and colleagues taught rats two different response-selection tasks. In each task, the cue that instructed which of two responses to make was one of two food rewards. A second food reward was given after correct responses. In the congruent reward condition, the initial reward and the final reward associated with a given response were the same, but in the incongruent condition they were different. ACC inactivation impaired performance only in the incongruent condition. The reward-guided nature of the action-selection process in this task might have been crucial in determining the nature of the deficit.

13. Stuphorn V, Schall JD: **Executive control of countermanding saccades by the supplementary eye field.** *Nat Neurosci* 2006, **9**:925–931.

Rather than just recording activity in MFC, this study used microstimulation to alter MFC activity while macaques were performing a saccadic stop-signal reaction-time task. In many locations within the SEF, microstimulation led to an increased probability of saccadic countermanding. The effect of microstimulation was context specific: it did not alter the way that saccades were made on trials in which the stop signal was not presented.

14. Nachev P, Rees G, Parton A, Kennard C, Husain M: **Volition and conflict in human medial frontal cortex.** *Curr Biol* 2005, **15**:122–128.

fMRI was used to contrast activity when subjects were instructed to make a saccade in a particular direction or when subjects made saccades in a freely chosen direction. On some trials, a countermmanding signal instructed subjects to change and saccade in the opposite direction. The task thus contrasted voluntary and instructed decision making in addition to conflict monitoring. Anterior pre-SMA activity was related to conflict, whereas posterior pre-SMA activity was related to the making of a voluntary response. SEF activity was greatest on successfully performed high-conflict trials, suggesting a role in resolving conflict.

15. Crone EA, Donohue SE, Honomichl R, Wendelken C, Bunge SA: **Brain regions mediating flexible rule use during development.** *J Neurosci* 2006, **26**:11239-11247.

The authors showed that, in infants, MFC activity patterns that relate to task-set reconfiguration mature more quickly than do ventrolateral prefrontal activity patterns that relate to rule representation.

16. Li CS, Huang C, Constable RT, Sinha R: **Imaging response inhibition in a stop-signal task: neural correlates independent of signal monitoring and post-response processing.** *J Neurosci* 2006, **26**:186-192.

Using a stop-signal task, this study carried out a between-subject comparison and contrasted activity in subjects who had either short or long inhibition times. The authors tried to remove any confounding effects related to attention to stimuli and found that pre-SMA activity was higher in the subjects who had shorter stop-signal reaction times.

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18. Debener S, Ullsperger M, Siegel M, Fiehler K, von Cramon DY, Engel AK: **Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring.** *J Neurosci* 2005, **25**:11730-11737.

Using sophisticated analysis techniques, the authors identified ERN activity on single trials while subjects were in an MRI scanner. It was therefore possible, first, to relate the ERN to activity recorded simultaneously from the ACC and, second, to examine the relationship between the ERN and behaviour on a trial-by-trial basis.

19. Van Schie HT, Mars RB, Coles MG, Bekkering H: **Modulation of activity in medial frontal and motor cortices during error observation.** *Nat Neurosci* 2004, **7**:549-554.

20. Nieuwenhuis S, Yeung N, Holroyd CB, Schurger A, Cohen JD: **Sensitivity of electrophysiological activity from medial frontal cortex to utilitarian and performance feedback.** *Cereb Cortex* 2004, **14**:741-747.

21. Ullsperger M, von Cramon DY: **The role of intact frontostriatal circuits in error processing.** *J Cogn Neurosci* 2006, **18**:651-664.

The ERN was measured in subjects who had either prefrontal cortex or striatal damage. The ERN was significantly diminished in most of the patients but, intriguingly, the same patients were still able to correct errors. A subgroup of patients who had deep white matter lesions, that the authors argue disconnected the striatum from the ACC, failed to correct errors.

22. Hogan AM, Vargha-Khadem F, Saunders DE, Kirkham FJ, Baldeweg T: **Impact of frontal white matter lesions on performance monitoring: ERP evidence for cortical disconnection.** *Brain* 2006, **129**:2177-2188.

Sickle cell disease is associated with white matter infarction in the dorsal frontal horn that might disconnect frontal and ACC areas. Such lesions are also associated with reduced ERN and poor performance on neuropsychological tests of executive function.

23. Magno E, Foxe JJ, Molholm S, Robertson IH, Garavan H: **The anterior cingulate and error avoidance.** *J Neurosci* 2006, **26**:4769-4773.

24. Mars RB, Coles MG, Grol MJ, Holroyd CB, Nieuwenhuis S, Hulstijn W, Toni I: **Neural dynamics of error processing in medial frontal cortex.** *Neuroimage* 2005, **28**:1007-1013.

25. Holroyd CB, Nieuwenhuis S, Yeung N, Nystrom L, Mars RB, Coles MG, Cohen JD: **Dorsal anterior cingulate cortex shows fMRI response to internal and external error signals.** *Nat Neurosci* 2004, **7**:497-498.

26. Brown JW, Braver TS: **Learned predictions of error likelihood in the anterior cingulate cortex.** *Science* 2005, **307**:1118-1121.

This computational model of the ACC incorporates its interactions with an error signal that is similar to the one known to be carried by the dopaminergic system. The coincident arrival of the error signal and a sensory input signal into the ACC enabled the ACC layer in the model to learn the association between a particular stimulus or context and the likelihood of error. The model predicted that the ACC should be more active not only on error trials but also in a context that was associated with a high likelihood of error. ACC activity, measured using fMRI, was consistent with these predictions.

27. Matsumoto K, Suzuki W, Tanaka K: **Neuronal correlates of goal-based motor selection in the prefrontal cortex.** *Science* 2003, **301**:229-232.

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32. McCoy AN, Platt ML: **Risk-sensitive neurons in macaque posterior cingulate cortex.** *Nat Neurosci* 2005, **8**:1220-1227.

33. Parvizi J, Van Hoesen GW, Buckwalter J, Damasio A: **Neural connections of the posteromedial cortex in the macaque.** *Proc Natl Acad Sci USA* 2006, **103**:1563-1568.

Neuroimaging studies often show that the ACC and posterior cingulate regions are co-activated. In the macaque, the two regions are anatomically interconnected, confirming that the functions of the ACC can be understood only in relation to the posterior cingulate cortex.

34. Hampton AN, Bossaerts P, O'Doherty JP: **The role of the ventromedial prefrontal cortex in abstract state-based inference during decision making in humans.** *J Neurosci* 2006, **26**:8360-8367.

Reinforcement learning enables the value of an option to be estimated on the basis of previous experience of choosing that option. In many situations, however, experience is not necessary to estimate the value of choices, as long as the organism has knowledge, or a model, of the interrelationship between different options. In many of the reversal tasks of interest to psychologists, subjects come to know that when option A is low in value option B is high in value. It is only necessary to have experienced the low value associated with A to know that B is probably now a better option to choose. Hampton *et al.* demonstrated that the encoding of reinforcement predictions in a ventral MFC region is consistent with model-based knowledge of the interrelationships between different options.

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