Conflict-induced behavioural adjustment: a clue to the executive functions of the prefrontal cortex

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Abstract | The behavioural adjustment that follows the experience of conflict has been extensively studied in humans, leading to influential models of executive-control adjustment. Recent studies have revealed striking similarities in conflict-induced behavioural adjustment between humans and monkeys, indicating that monkeys can provide a model to study the underlying neural substrates and mechanisms of such behaviour. These studies have advanced our knowledge about the role of different prefrontal brain regions, including the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC), in executive-control adjustment and suggest a pivotal role for the DLPFC in the dynamic tuning of executive control and, consequently, in behavioural adaptation to changing environments.

In our daily life, we often rely on executive, or cognitive, control processes[1], which can be defined in general terms as the means by which our brain optimizes the flexible use of limited cognitive resources to currently prioritized tasks. Such control may become necessary when automatic or previously learned behaviours can no longer achieve a goal — for example, when we need to override habitual responses, inhibit distracting stimuli, solve new problems or shift between different tasks. This capability is crucial because in changing environments we constantly need to adapt our behaviour by detecting and focusing on the goal-relevant information and selecting the most appropriate behaviour. For example, consider the ability to drive a car while simultaneously engaging in a discussion with a passenger. If we enter a narrow mountain road and a heavy storm breaks out, we might feel the need to discontinue our conversation in order to better focus our cognitive resources on safe driving. Our brain needs to detect such changes in environmental demands and allocate more cognitive resources to prioritized tasks when necessary.

An experimentally well-studied example of behavioural adjustment in changing environments is the kind of behavioural modulation that is triggered by the presence of competition or conflict between behavioural options. Computational models[2] have succeeded in emphasizing the importance of conflict-driven feedback as a key mechanism by which the brain can adjust cognitive control. In terms of the neuronal architecture that underlies the cognitive processes involved, one of the most influential models[2] asserts that the anterior cingulate cortex (ACC) (BOX 1) detects the occurrence of conflict and signals other areas, such as the dorsolateral prefrontal cortex (DLPFC) (Supplementary information S1 (figure)), to implement cognitive control. This model assumes a conflict-monitoring role for the ACC in a broad range of situations in which conflict might occur in information processing.

In this Review we discuss evidence for and against this proposed neural architecture. In particular, we emphasize how recent studies have shown that non-human primates exhibit similar conflict-induced behavioural adjustments, which has enabled neuroscientists to directly probe the neural structures and mechanisms involved. These studies have directly challenged the importance of the ACC in these functions, indicating a crucial role for the DLPFC instead. We proceed to propose that some revisions to the computational model itself may be necessary to incorporate these latest findings in order to better explain our current understanding of the neural substrates of cognitive control.

Behavioural effects of experienced conflict

The need to resolve behavioural conflict arises in many everyday circumstances. For example, consider a person who is used to driving on the left side of the road in Japan who travels to Korea: she will face the prospect of having to drive on the right side of the road — that is, she will face conflict between a learned behaviour (driving on the left) and the currently appropriate behaviour

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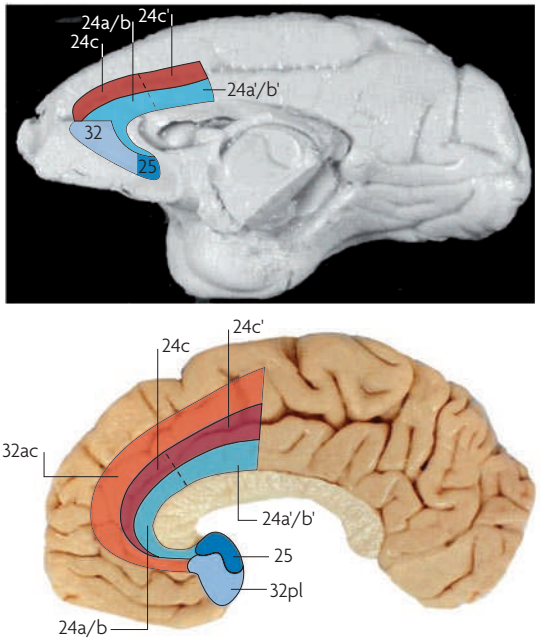
Box 1 | **Cytoarchitecture, anatomy and functions of the anterior cingulate cortex**



In humans and macaques the anterior cingulate cortex (ACC) is situated below the superior frontal gyrus in the medial frontal cortex. Clues to the function of the ACC can be derived from its connectivity patterns[70,75–78], which include dense projections to the motor cortex and spinal cord, implicating the ACC in motor control; projections to the ACC from the midline thalamus and brainstem nuclei, suggesting an important role for arousal and drive states in influencing ACC function (the ACC is also implicated in modulating bodily arousal states[69]); and strong reciprocal connections between the dorsal ACC and the lateral prefrontal cortex, pointing to an interaction between these two areas in cognition[75]. The more ventral (subgenual) ACC is well connected with the ventral striatum, the orbitofrontal cortex and the medial temporal lobe, and the idea of dorsal 'cognitive' and ventral 'emotional' ACC regions in humans has proved popular[79].

As can be seen in the figure, dorsal and ventral cytoarchitectural subdivisions of the ACC can be discerned in macaques (top) and humans (bottom), broadly corresponding to the ACC sulcus (ACCs) and ACC gyrus (ACCg) (shown in red and blue, respectively)[76]. Although some species differences exist (for example, a greater proportion of area 32 is situated supracallosally in humans than in macaques), there are many similarities; note that the rostral cingulate motor area is located in area 24c′. Recent lesion studies in macaques have determined the crucial contributions of these subregions to cognition. ACCs lesions do not impair error correction or conflict-induced behavioural adjustments, as the conflict-monitoring theory would predict[49,67], but they do impair animals' abilities to make optimal decisions about actions, as the animals become deficient in updating action values on the basis of positive and negative reinforcement histories[67]. Recent single-unit recording studies have shown that many ACC neurons encode action–reward combinations. This is consistent with a role for the ACC in goal-based action selection; the encoding can also represent the direction and amount of error in action value predictions, which is consistent with a role for the ACC in adjusting actions to better attain goals[68,80]. ACCg lesions, by contrast, impair animals' abilities to attach value to social stimuli[81]. The macaque image in the figure is modified, with permission, from REF. 78 © (2004) Elsevier Sciences. The human ACC image is modified, with permission, from REF. 82 © (2005) Macmillan Publishers Ltd. All rights reserved.

(driving on the right). Many studies in humans have shown that when such competition or conflict arises between behavioural choices in experimental tasks, performance is adversely affected in terms of speed and accuracy, and this is referred to as the 'conflict cost'.

The nature and source of the conflict depend on the structure of the task. A particularly well-studied paradigm is the Stroop test[3–5], in which subjects are presented with the name of a colour printed in coloured ink (FIG. 1a). They must identify the colour of the ink as fast and as accurately as possible. In incongruent (high-conflict) conditions, when the colour's name differs from the ink colour, the subjects are less accurate and slower than in congruent (low-conflict) conditions, in which the colour name matches the ink colour, or than in neutral conditions, in which the word is not colour-related. Reading out words is considered a more overly learned and automatic skill than the required task, which is to name the ink's colour; it is assumed that information regarding the ink colour and information regarding the word are processed separately, leading to distinct motor responses, and that conflict arises in this case owing to competition between the two processing pathways[2,3].

Another task designed to elicit conflict is the flanker test[6]. Here subjects have to respond to a central stimulus that indicates that one of two different spatial responses (left or right) should be made, and conflict arises if the surrounding stimuli are associated with different responses (FIG. 1a). Conflict can also be induced in asymmetrical 'go/no go' paradigms, in which subjects are required to respond (that is, 'go') to frequently presented stimuli but have to withhold responses (that is, 'no go') to infrequently presented stimuli[7,8]. Similarly, conflict can be elicited by requiring subjects to respond to a stimulus in one context but withhold a response in another[9–13], whereas in the Simon task (FIG. 1a) conflict arises from the mismatch between the spatial location of a stimulus and the required response[14].

The behavioural effects of conflict are not just limited to the current trial, they also affect performance in the subsequent trial, in which they are manifested as a behavioural improvement if the subject is faced with conflict again (FIG. 1b). For instance, response latencies (that is, reaction time (RT)) in high-conflict trials that are immediately preceded by another high-conflict trial (HH condition) are shorter than those in high-conflict trials that are immediately preceded by a low-conflict trial (LH condition). This facilitative effect of previously experienced conflict has been demonstrated in a range of different tests, including the Stroop[15–18], the Simon[19]

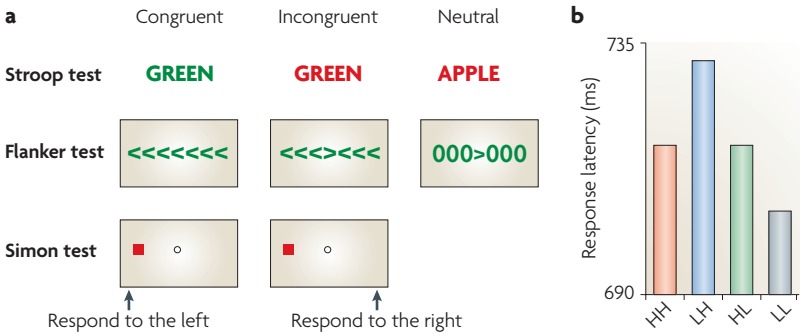


Figure 1 | **Examples of tasks that involve conflict. a** | In the Stroop test, the written word might match the ink colour (in congruent trials), be different from it (in incongruent trials) or be a non-colour item (in neutral trials). In the Flanker test, the central stimulus and the flanking stimuli might face the same (in congruent trials) or opposing (in incongruent trials) directions. In the Simon test, a cue appearing on the left or the right side instructs the subject to respond towards one of the response directions. The cue might appear on the required response side (in congruent trials) or on the opposite side (in incongruent trials). **b** | Response latencies in congruent and incongruent conditions depend on the conflict level in the previous trial. The graph shows the performance of human subjects in the face–name test[16]. In this test, subjects see photographs of famous faces on which are superimposed the names of famous people. Subjects have to discriminate between politicians and actors based on either the photograph or the name. The face and word might both belong to an actor or politician (in congruent, low-conflict (L) trials) or might differ in referring to actors and politicians (in incongruent, high-conflict (H) trials). When the face was the relevant dimension, reaction times in incongruent conditions were higher than in congruent conditions; however, the reaction times in incongruent conditions significantly decreased if the previous trial was also an incongruent condition. Part **b** is modified, with permission, from REF. 16 © (2005) Macmillan Publishers Ltd. All rights reserved.

and the flanker[20] tests, and has been referred to as the 'conflict adaptation effect' (REF. 18). Additionally, RTs in low-conflict trials that are immediately preceded by a high-conflict trial (HL condition) are longer than those in low-conflict trials preceded by a low-conflict trial (LL condition), although the magnitude of this effect is smaller than the difference between HH and LH conditions[15,16]. Recent studies[15–18] have confirmed that the effect of experienced conflict on the next trial is not due to repetition of stimuli or responses in consecutive trials[21,22].

Current models and conflicting data

Two current models of the ACC in conflict-induced behavioural adjustment. A large number of studies in humans involving event-related potential (ERP) recordings, functional MRI (fMRI) or positron emission tomography have reported activation of the ACC to be higher in high-conflict conditions than in low-conflict or neutral conditions during the performance of various tasks that were designed to elicit conflict between behavioural options[16–18,23–32]. Although such effects are most consistently observed in the ACC, modulations in other areas have also been reported, particularly in the DLPFC[7,9,16–18,29,33–35] and the posterior parietal cortex (PPC)[7,9,17,26,29,31,33–36].

Based on these observations, one highly influential theory proposed that the ACC monitors or detects the presence of conflict and then conveys this information to areas such as the DLPFC, which then adjust the level of cognitive control accordingly[2,13,30]. In this model (FIG. 2a), the adjustments in the level of cognitive control lead to better resolution of the conflict and consequently enhance performance should subjects face conflict again. The model assumes that the task-relevant and task-irrelevant stimulus features (for example, the ink colour and the colour name, respectively, in the Stroop task) are processed by separate neural pathways. These separate representations of the task-relevant and task-irrelevant information map distinctively on to their associated responses and compete in gaining control over the ensuing behaviour. A conflict-driven augmentation of cognitive control boosts the task-relevant neural pathway by enhancing the processing of task-related stimulus features and/or by facilitating the selection and execution of the task-relevant response. In parallel, the processing in the task-irrelevant pathway might be inhibited. This theory and associated computational models[2] therefore provided an answer to the long-standing question of how and when executive control is recruited to support ongoing behaviour. It could also explain the behavioural slowing that is seen following error trials by assuming that the ACC detects interference between representations of correct and incorrect responses as conflict and subsequently triggers control adjustments. This hypothesis proposes that brain regions that are more active during high-conflict trials are involved in the conflict-detection process, whereas regions that are more active in HH than LH conditions mediate the executive-control adjustment[2,13]. Further studies[15–18,31] provided empirical support for this hypothesis by showing, first, that in high-conflict trials the magnitude of ACC activity predicted the degree of behavioural adjustment and the activity level in the DLPFC on the subsequent trial; second, that ACC activity in the second trial of the HH conditions was lower than in LH conditions, which fits with the idea that adjustments in control serve to decrease the conflict detected by the ACC in the HH conditions; and third, that increases in DLPFC activity observed in HH trials tended to correlate with greater degrees of behavioural adjustment. Further support arose from observations that patients with ACC lesions have impairments in conflict-related behavioural modulations[37] and also from direct recordings of single-cell activity in the human ACC, which showed that activity was related to conflict[38].

One influential alternative to the ACC conflict-monitoring theory is the idea that the ACC is part of the neurocircuitry that actually exerts the executive control by selectively biasing processing in favour of task-relevant pathways in situations in which there is a need for executive control[39,40] (FIG. 2b). According to this ACC 'regulatory' theory, the ACC is not primarily involved in conflict monitoring but rather has a more direct response-regulatory function and is crucially involved in implementing some of the adjustments that are necessary to resolve conflict[35,39,40]. This idea is closely aligned with evidence that indicates an important role for the ACC in action selection (BOX 1). It was reported that in an arrow–word Stroop variant ACC activation was larger for neutral than for congruent stimuli — both conditions in which there is no response conflict[35]. This finding does not fit with the conflict-monitoring hypothesis,

Event-related potential (ERP). An electrophysiological response of the brain to an internal or external stimulus, which can be measured through electrodes on the scalp.

Arrow–word Stroop variant
A test in which subjects are presented with a left- or right-pointing arrow above a word (for example, 'left' or 'right') and have to indicate by button press the direction denoted by the word or arrow. The arrow and word might instruct the same direction (congruent condition) or opposite directions (incongruent condition) or only one of them might denote a direction (neutral condition).

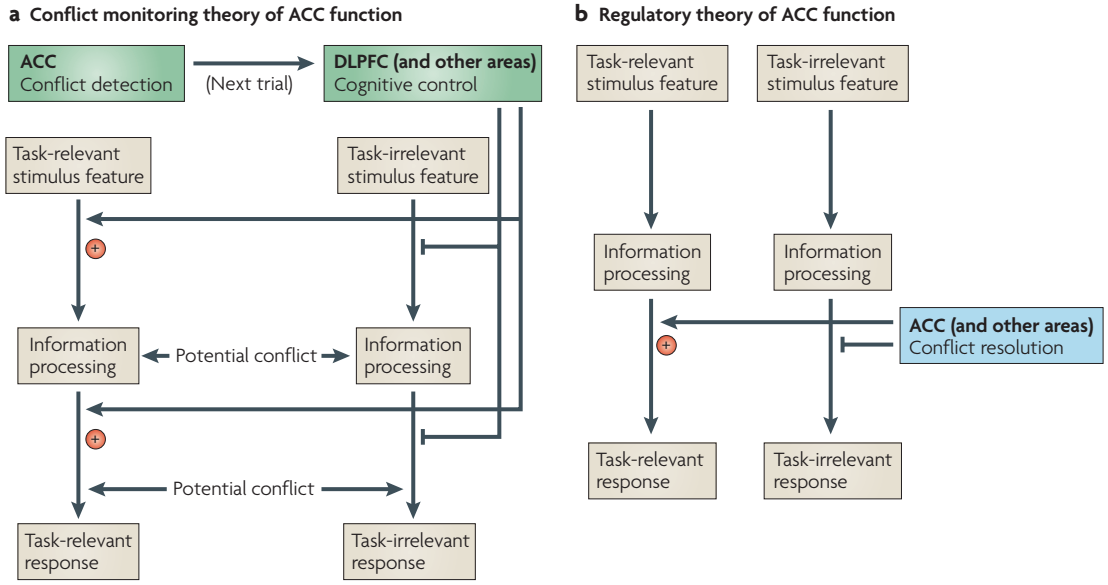


Figure 2 | **Two main theories regarding the role of the anterior cingulate cortex in conflict-induced behavioural adjustment. a** | According to the 'conflict-monitoring' theory[2,13], the anterior cingulate cortex (ACC) monitors or detects the presence of conflict by receiving task-relevant and task-irrelevant information (from separate neural pathways) and then conveys conflict-related information to areas such as the dorsolateral prefrontal cortex (DLPFC), which then adjust the level of cognitive control accordingly. The conflict might arise at two levels of processing: the stimulus or sensory level, when two sensory features (task-relevant or task-irrelevant) of the stimulus are processed; or the response level, when two behavioural responses (task-relevant and task-irrelevant) compete to gain control over the ensuing behaviour. The DLPFC in turn could stimulate the task-relevant neural pathway by enhancing the processing of task-related stimulus features and/or by facilitating the selection and execution of the task-relevant response. In parallel, the processing in the task-irrelevant pathway and task-irrelevant responses might be inhibited. **b** | According to the ACC 'regulatory' theory[39,40], the ACC is part of the neurocircuitry that exerts executive control by selectively biasing processing in favour of task-relevant information in situations in which there is a need for executive control. The red lines with the + sign and the lines with blunt ends indicate facilitation and inhibition, respectively.

which predicts that ACC activity should increase only when conflicting response alternatives are presented. It was suggested instead that greater activity in neutral than in congruent conditions reflects the greater amount of top-down regulatory control that is necessary to selectively enhance correct responses in neutral conditions (in which, unlike in congruent conditions, the correct response is not activated by the distractor).

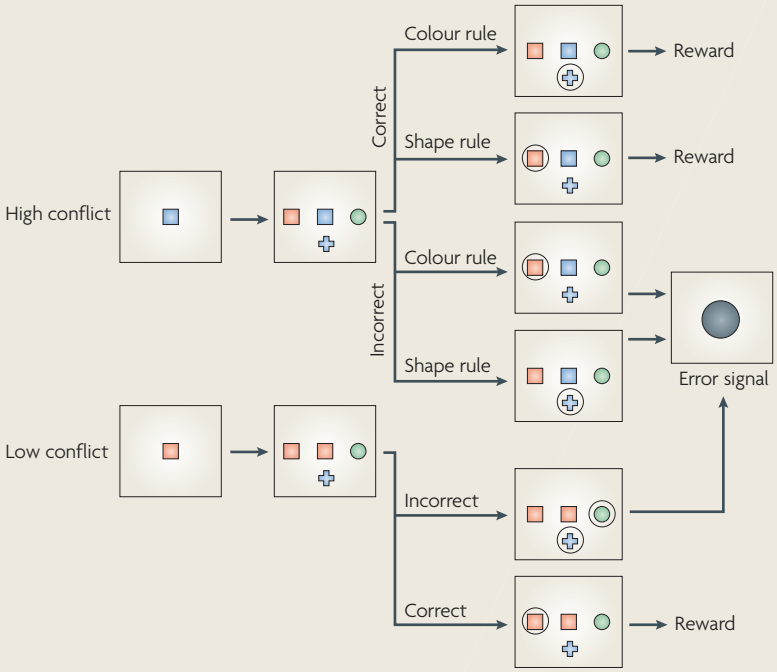
Conflicting data in humans. Despite the popularity of both conflict-monitoring theories and regulatory theories, some human studies have provided evidence that the ACC might not be crucial for conflict-induced behavioural adjustment, neither in a monitoring nor in a regulatory regard.

Emerging findings show that in some cases there is no strong relationship between behavioural measurements of conflict and ACC activity; these findings are not easily explained by the ACC conflict-monitoring theory. For example, in a colour–word-matching Stroop variant[41] two rows of letters appear on the screen and subjects are instructed to indicate by means of a button press whether the ink colour of the top row of letters matches the colour name written on the bottom row. In this task the conflict arises when the subjects compare the ink colour and the written word before they express their decision (match or non-match) by a button press. This non-verbal response separates the modality of the subjects' response from the modality of the perceptual processing in which conflict could arise. Therefore, unlike in the standard Stroop test, the interference occurs at the perceptual level, which is not confounded with interference at the response level (FIG. 2). With this variant, conflict costs were observed but they occurred in the absence of activity increases in the ACC[41]. This raises the possibility that the ACC may not be as ubiquitous a conflict detector as was previously supposed[42]. Other fMRI studies[33,43] that used variants of the Stroop test have also questioned the association between ACC activation and the behavioural effect of conflict (the conflict cost) by showing that although the behavioural effect of conflict itself persisted throughout a recording session, the ACC activation diminished and even disappeared in the later parts of the session.

Other observations from neuroimaging studies seem to oppose the 'ACC-regulative' account; for instance, ACC activation has been seen to decrease in the second trial of HH conditions, when performance improves and the control level is presumed to be higher than in the LH condition[15].

Neuropsychological examinations of patients with brain damage also do not support a causative or indispensable role for the ACC. One study with 32 patients with frontal lesions found that the region that was most related to the Stroop error rate was not the ACC but

Box 2 | **Wisconsin Card-Sorting Test in monkeys**



The clinical Wisconsin Card-Sorting Test (WCST) assesses the ability of the participant to shift between different rules. The participant has to match test cards with a sample card by applying one of a number of possible rules, but the 'correct' rule changes without notice during the test. An analogue of this test has been developed for monkeys. In each trial of the WCST analogue, the sample appeared first and then three test items were added (see the figure)[49]. In a limited period, the monkey was required to touch the test item that matched the sample in the relevant dimension (either colour or shape). The relevant dimension was not cued and changed without notice whenever performance reached 85% correct in 20 consecutive trials. Trials with two different levels of conflict, high and low, were randomly mixed. In the high-conflict condition, the sample matched one test item only in colour and another only in shape. Therefore, the monkey had to resolve the competition between two potential responses. In the low-conflict condition, the sample matched one test item in both colour and shape, and it did not match the other two test items in either colour or shape; thus there was no conflict between matching rules. In the figure, the circle indicates the test item selected by the monkey. The monkeys rarely selected the item that did not match the sample in either colour or shape[49].

In the low-conflict condition one of the test items was identical to the sample, and it may be assumed that making the correct response was based on the identity of the object, rather than on implementing colour- or shape-matching rules. However, the overall structure of the WCST analogue did not allow this strategy: there was no cue for the currently relevant rule, and therefore the monkeys had to maintain the relevant rule across trials in working memory to respond correctly in high-conflict trials. The essential role of keeping a rule in working memory was further supported by the monkeys' quick recovery of performance after a rule change, with only a few errors. This working memory is very sensitive to interruption: for example, inserting a face-discrimination trial between consecutive WCST trials reduced the monkeys' performance from 85% correct down to chance level (F.A.M., K.T. & M.J.B., unpublished observations). Thus, if the monkey had used object identity rather than a rule-based strategy in a low-conflict trial, then working memory of the relevant rule would be compromised and performance would drop in the next high-conflict trial. The high performance in high-conflict trials that were preceded by low-conflict trials suggests that the monkeys used the colour- or shape-matching rule in low-conflict trials. Furthermore, the rule-dependent activities of dorsolateral prefrontal cortex cells were maintained in low-conflict trials and were as strong as those in high-conflict trials, suggesting that the monkeys used the colour- or shape-matching strategy in both low-conflict and high-conflict conditions. Figure is modified, with permission, from REF.49 © (2007) American Association for the Advancement of Science.

the right lateral PFC[44]. Another lesion study found that 15 out of 21 individuals with ACC lesions performed within normal limits on all aspects of the Stroop task, and an exaggerated Stroop effect was found only in patients with medial frontal lesions that were located more superiorly than the ACC[45]. More recently, four patients with ACC damage showed normal adjustments in performance following response conflict manipulations in both Stroop and go/no go tasks, and post-error behavioural adjustments were also intact[46].

Emerging evidence from ERP-recording studies is also troubling for the hypotheses outlined above. For instance, the conflict-monitoring hypothesis predicts that monitoring-related activation should occur in the ACC before control-related activation appears in the DLPFC, whereas the reverse was found to be the case in one ERP study[47].

Conflicting data in animals: recording studies. Recent studies have shown that animals respond to conflict in similar ways to humans — for example, studies in macaque monkeys on analogues of the Stroop test[48], the Wisconsin Card-Sorting Test (WCST)[49] and other paradigms[50–52], and in rodents on related paradigms[53,54]. Such animal models are important in that they provide an opportunity to address many unresolved issues regarding the neurobiology of conflict-induced behavioural adjustments.

Recording studies in monkeys to date have failed to find any evidence for conflict-related signals in the ACC. One study[55] in which monkeys performed a saccade-countermanding task showed a behavioural effect of conflict but no conflict-related activity in ACC neurons. In another study[50], single-cell activity was recorded from the ACC and the supplementary eye field (SEF) while monkeys performed tasks in which the colour of cues instructed them to make left or right saccades. In high-conflict conditions the location of the cue was incompatible with the instructed saccade, whereas in low-conflict conditions the cue's location matched the required saccade direction. Although the presence of conflict was evident from behavioural measures (a higher error rate and increased RT in high-conflict conditions), there was a complete absence of a conflict-related increase in ACC neuronal activity. Rather, neurons situated more dorsally in the SEF fired more strongly in tasks involving conflict, but even this effect seemed to be related to the modulation of task-related activity among direction-selective neurons rather than to a pure conflict-monitoring signal[56,57].

In monkeys performing another task-switching paradigm[51,52] the behavioural responses to incongruent stimuli were significantly slower than those to congruent stimuli, which again shows that the conflict influenced the monkeys' behaviour. Simultaneous recording, in this case from the PPC, showed that — similar to the activity pattern that was observed in the SEF — the conflict-related activity of PPC cells did not appear as a distinct signal and only modulated the directional selectivity of neuronal activity[51,52].

We trained monkeys to perform a close analogue of the WCST[49] (BOX 2). In the WCST, the relevant rule and

Saccade-countermanding task
A task in which subjects fixating their eyes on a spot at the centre of a display should change their gaze direction (saccade) towards a peripherally cued location when the fixation point goes off. In some trials the fixation spot reappears at an unpredictable time and the subjects should cancel the saccade.

its frequent changes are uncued — that is, subjects have to deduce by trial and error what the rule is and whether it has changed, and they therefore face conflict or competition between potential matching rules. Patients with prefrontal cortex damage typically show impaired performance on the WCST, as well as on other tasks in which they have to resolve conflict between potential rules and responses[3,58,59]. In the WCST analogue, monkeys were required to select, either under low-conflict or high-conflict conditions, which of three different test items matched a sample item in any given trial (BOX 2). A marked similarity in conflict-induced behavioural adjustment was observed between monkeys and humans on this specific task: the monkeys' RTs in high-conflict trials were longer than in low-conflict trials, indicating that they experienced conflict. Monkeys' RTs in the HH condition were shorter than in the LH condition, indicating that conflict experienced in the preceding trial enhanced performance in the next trial (FIG. 3a,b). The neuronal activity of a group of DLPFC neurons represented the conflict level in the current trial independently of the relevant rule, the direction of upcoming response or the identity of the sample stimulus[49] (FIG. 3d). This indicates that the currently experienced conflict is encoded

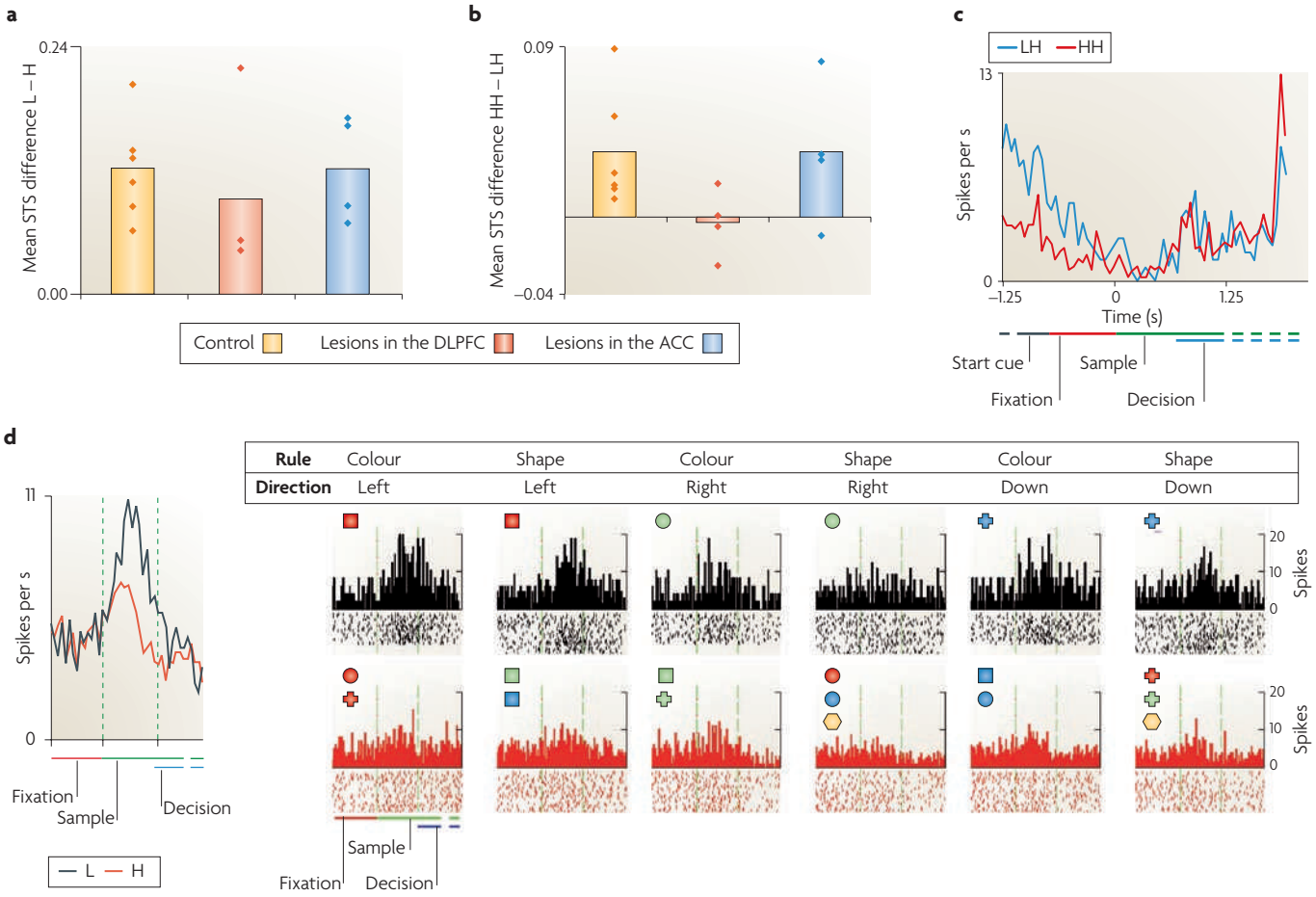


Figure 3 | **Conflict-induced behavioural adjustment and prefrontal cell activity in monkeys.** The monkeys performed an analogue of the Wisconsin Card-Sorting Test, in which they had to match a sample with one of three test items by colour or shape. The trials were either high (H) or low conflict (L) (see BOX 2). **a** | The mean difference in normalized speed of target selection (STS) in L and H trials in monkeys with lesions in the dorsolateral prefrontal cortex (DLPFC) or anterior cingulate cortex (ACC) and in monkeys without a brain lesion (controls). In all three groups the STS was lower in H conditions, indicating an adverse effect of conflict on the monkeys' behaviour. **b** | The mean difference in STS with respect to the second trial of HH versus LH trial sequences. In control and ACC lesion groups, but not in the DLPFC lesion group, the STS was higher in the second trial of HH pairing, indicating that the monkeys were faster in resolving the conflict if they had experienced a high level of conflict in the preceding trial. **c** | The activity of a DLPFC cell represents the level of conflict experienced in the previous trial. The graph shows activity during an H trial that occurred after an L trial (LH) and activity during an H trial that occurred after another H trial (HH). **d** | The activity of a DLPFC cell represents currently experienced conflict. The left-most histogram shows mean activities in L and H trials. In this cell, the activity was significantly higher in the L condition; however, cells with higher activity in H conditions were also found in the DLPFC. Each column shows activities in L (black) and H (red) trials in which the same matching rule had to be applied and which had the same correct response direction. The stimuli that were presented in each conflict condition are shown above the individual histograms. In parts **c** and **d**, mean activities are aligned at the time of sample onset. Figure is reproduced, with permission, from REF. 49 © (2007) American Association for the Advancement of Science.

Box 3 | **Malfunction of executive control in mental diseases**

Neuropsychological examinations have suggested that deficiencies in executive-control adjustment might underlie the disorganized and inflexible behaviour that is seen in patients with psychiatric diseases that afflict the prefrontal cortex. Several psychiatric disorders are associated with abnormal conflict costs and/or post-conflict behavioural adjustments and with concomitant alterations in activation patterns in the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC), offering insight into the nature of executive malfunction in these conditions.

Patients with schizophrenia exhibit normal conflict costs but their post-conflict and post-error adaptations are reduced or absent[83]. Moreover, neuroimaging studies have shown hypoactivity in the ACC, the parietal cortex and the DLPFC in these patients[3,83–88]. In addition, morphometric and histological studies have reported reduced volume and neuronal density in the ACC and DLPFC in patients with schizophrenia[89]. These findings suggest that some symptoms of schizophrenia might be related to deficiencies in adjustment of executive control.

By contrast, patients with mood disorders, such as depression or mania, tend to show higher than average conflict costs and a general increase in reaction time in Stroop tests, particularly when they are symptomatic[83,90]. Such patients show concomitant hypoactivation in the caudal ACC but overactivation of the rostral ACC (BOX 2) and the DLPFC[90,91]. Reduced volume and decreased cell densities in the ACC and the DLPFC have also been reported in such patients[89,92]. It has been assumed that functional interactions between the ACC and the DLPFC are disturbed in these patients, resulting in deficient executive control — particularly when distracting events must be ignored and task-relevant information must be focused on[83].

Patients with obsessive–compulsive disorder (OCD) typically exhibit an 'obsessional slowness' in many cognitive tasks, and although some studies have reported normal conflict costs in these patients, others have found greater interference effects in their reaction time[83,93]. Patients with OCD have been found to have heightened ACC-associated error-related negativity in event-related potential studies[94] and ACC hyperactivity in neuroimaging studies[95]. However, a failure of patients with OCD to accomplish task switching has also been associated with hypoactivation of the ACC, the PFC, the parietal cortex and the striatum[96]. The cognitive inflexibility that is exhibited by patients with OCD could be due to a general impairment in inhibitory functioning as well as to an abnormal monitoring system[83,93,96,97].

Obsessive–compulsive disorder
A behavioural disorder that makes people repeatedly and unnecessarily express a behaviour.

Schizophrenia
A mental disorder that makes it difficult to have normal emotional responses, social interaction and organized thoughts and that is accompanied by unreal experiences, such as delusions or hallucinations.

Mood disorder
A mood disorder is a mental disorder characterized by periods of depression that sometimes alternate with periods of elevated mood.

Error-related negativity
A negative deflection in a response-locked ERP that reaches its peak ~100 ms after the response initiation in error trials.

in DLPFC cell activity as a distinct entity. The activity of another group of DLPFC cells was modulated by the conflict that had been experienced in the previous trial. This modulation was seen in the inter-trial interval before the start of the next trial (FIG. 3c), suggesting that the level of conflict experienced in the previous trial is another type of task-relevant information that can be encoded and maintained across trials in DLPFC cell activity.

Neuronal recording and neuroimaging are correlational techniques and do not show that a brain region is necessary for the cognitive function. A conclusive way to demonstrate that a brain region is crucial for supporting a cognitive function is to show impairment of that function after damage to the brain region. Lesion studies in patients are inherently limited by the variability in the extent of lesions between subjects, whereas it is possible to experimentally target anatomical regions of interest with a far greater degree of consistency and precision in animal lesion studies. Important findings from these studies are reviewed next.

Conflicting data in animals: lesion studies. We determined whether the ACC and/or the DLPFC were necessary for conflict-related behavioural adjustments in the WCST analogue, by comparing the behaviour of monkeys with circumscribed bilateral lesions in these regions to that of intact monkeys[49]. The behavioural effect of conflict (conflict cost as expressed by higher RT) in the current trial was unaffected by ACC or DLPFC lesions. In addition, the behavioural adjustment related to the conflict experienced in the previous trial remained intact after lesions in the ACC, but it disappeared entirely following lesions in the DLPFC[49] (FIG. 3a,b). This study therefore provides direct evidence that the DLPFC, but not the ACC, has an indispensable role in conflict-induced behavioural adjustment in monkeys.

To investigate the importance of the ACC in conflict resolution in rodents, Haddon and colleagues used a biconditional discrimination task, in which rats learned to differentially respond to two auditory cues in one context and two visual cues in a different context[53]. The context differed in terms of the pattern of wall paper covering the training chamber and also in the type of reward given. They then exposed these rats to compound stimuli that comprised an auditory and a visual cue from one of the experienced contexts. The auditory and visual cues could indicate the same (congruent condition) or a different (incongruent condition) response direction. The rats had to use contextual cues to disambiguate the conflicting response information provided by the incongruent compound stimuli. The rats with frontal lesions that included the ACC, the prelimbic cortex and the infralimbic cortex failed to resolve the conflict in the incongruent condition; however, rats with lesions that were restricted to the ACC resolved the conflict if they were exposed to the compound stimulus for long enough[53]. Subsequent studies confirmed that the prelimbic area has a crucial role in the context-based resolving of conflict[54].

In spite of the contradictory findings reviewed above, the conflict-monitoring hypothesis[2,13] remains an influential theory that has stimulated many experiments and computational modelling. However, it seems necessary to update the hypothesis in order to reconcile the recent findings in humans and non-human primates. In the following sections, we re-evaluate the cognitive/computational processes that are involved in conflict-induced behavioural adjustment and discuss their likely neuroanatomical substrates.

Cognitive processes in behavioural adjustment

Conflict monitoring. A general-purpose conflict-monitoring system needs to extract and encode the conflict information as a distinct variable, because in order to modulate the control level in the following trial, information regarding conflict must be maintained in memory across periods of time in which the conflict is no longer present. Although imaging studies have shown activation of a range of different cortical areas when subjects face conflict, the mechanisms that are involved in conflict detection remain unclear.

Only one study in humans has shown conflict-related activity modulation in single cells in the ACC[38], and in this study the sampling of cells was not extensive and the patients had severe obsessive–compulsive disorder (OCD), which has been linked with atypical ACC function (BOX 3). Such conflict-related activity has not been observed in the monkey ACC[50,55]. Neurons in the SEF and neurons in the PPC did show conflict-related activity, but this effect took the

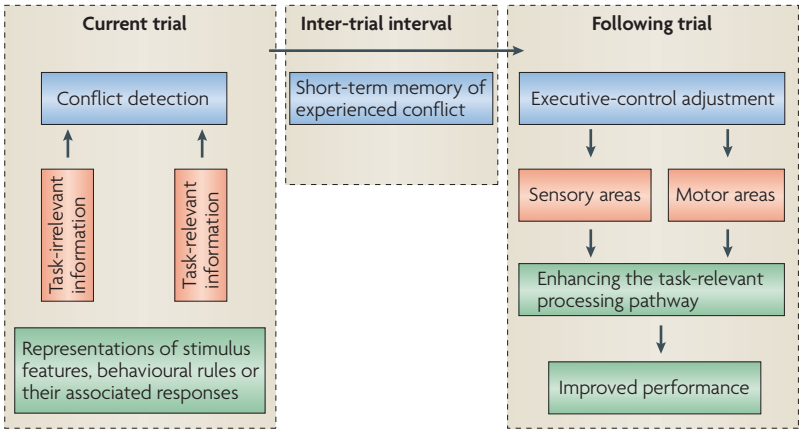


Figure 4 | **A model of the conflict detection–resolution process in goal-directed behaviour.** This model is an extension of the conflict-monitoring model[2,13] with the addition of a mnemonic compartment (for short-term memory of experienced conflict) in which information regarding conflict may be held during inter-trial intervals. The blue boxes show the three main stages in conflict-induced behavioural adjustment. This model proposes that when conflict is detected it is encoded as a task-relevant variable and maintained in short-term memory within and across trials. This information about the level of recently experienced conflict is then used in the subsequent trial to adjust the amount of control that is needed to enhance processing in task-relevant pathways to better resolve conflict and consequently improve performance when the subject confronts similar conflicting circumstances again. The original conflict-monitoring model assumes a crucial role for the anterior cingulate cortex and the dorsolateral prefrontal cortex in conflict-detection and executive-control adjustment, respectively. However, in light of recent findings, we suggest that the anterior cingulate cortex does not have a causal or indispensable role in conflict detection, but that the dorsolateral prefrontal cortex encodes the current level of conflict, maintains conflict information within and across trials and implements executive control.

form of modulation of other task-related activities and was not a pure conflict-monitoring signal[50,52]. To date, only one study in monkeys[49] has found cell activities in the DLPFC that represented conflict independently from the other aspects of the task, suggesting that these cellular activities were a neuronal signature of conflict (FIG. 3d).

Short-term memory of experienced conflict. Modulation of ongoing behaviour according to the history of recently experienced conflict requires a mnemonic system that can maintain information about experienced conflict across trials. In the conflict hypothesis[2,13] it is unclear how the conflict information is maintained across trials in order to modify the control level the next time conflict arises. We therefore propose that a separate processing module, namely short-term memory of experienced conflict, needs to be incorporated into the original conflict model (FIG. 4) to maintain information about the conflict within and across trials. In daily life, the time between two conflict-resolving decisions might vary; this mnemonic system can bridge the temporal gap between the two decisions so that the level of cognitive control can be adjusted according to the previous experience of conflict. Previous studies[7,9,16–18,29,33–35] have reported activation in the DLPFC in tasks that elicited conflict, which led to the assumption that the DLPFC was involved in the control-adjustment process. However, it is possible that some of these observed activations were actually related to the mnemonic role of the DLPFC in conflict processing. Indeed, one study[49] reported that, in monkeys, information about conflict experienced in the previous trial is encoded and conveyed in the activity of single neurons in the DLPFC (FIG. 3c), and that DLPFC lesions impaired the conflict-induced behavioural modulation on the next trial (FIG. 3b). Nevertheless, additional studies are needed to address the characteristics of the mnemonic processes that maintain the conflict information in terms of the neuroanatomical mapping and vulnerability to duration or distracting events.

Executive-control adjustment. The conflict-monitoring hypothesis[2,13] proposes that information about conflict recruits executive-control systems in order to bias neural processing in favour of the task-relevant information. This may be achieved either by enhancing processing in task-relevant pathways or by inhibiting processing in task-irrelevant pathways. It is also consistent with the biased-competition model of selective attention[60], in which the competition or inhibition between two representations of sensory stimuli and their associated responses in processing is biased, through top-down signals, in favour of task-relevant information. Areas such as the DLPFC, the parietal cortex and the insular cortex might be involved in this top-down control[16–18,61].

There might even be several different kinds of control that come into action depending on the specific context and task requirements[62]. In a version of the Stroop test in which subjects were instructed before the trial to read the word or to name the colour of the ink used, activation was observed in the DLPFC but not in the ACC after the subjects received the instruction to name the colour (a high-demand task). This activation correlated with the upcoming behavioural performance[28]. These findings suggest that the DLPFC is involved in implementing control by representing and maintaining the attentional demands of the task. Kerns *et al.* also reported increased activation of the DLPFC when cognitive control was at higher levels[15]. Using versions of the Stroop and Simon tasks, Egner *et al.*[16–18] reported increased activation in the left middle frontal and superior frontal gyri as well as in parietal and premotor cortices in the second trial of HH conditions (which are associated with a higher cognitive-control level) in comparison to the LH condition. Further, using the face–name Stroop task (FIG. 1a,b), high levels of control in the HH condition were accompanied by increases in activity both in the right DLPFC and in posterior cortical areas that are implicated in processing task-relevant information (in this case, the fusiform face area) when the face was the relevant attribute (FIG. 5). However, activity in these posterior cortical areas did not decrease when the face was the irrelevant attribute, leading to the proposal that cognitive control was exerted through a selective amplification of task-relevant information processing but not through inhibition of task-irrelevant features of stimuli.

In a complex and changing environment, cognitive control needs to be recruited when appropriate, but it also needs to be disengaged when it is no longer necessary

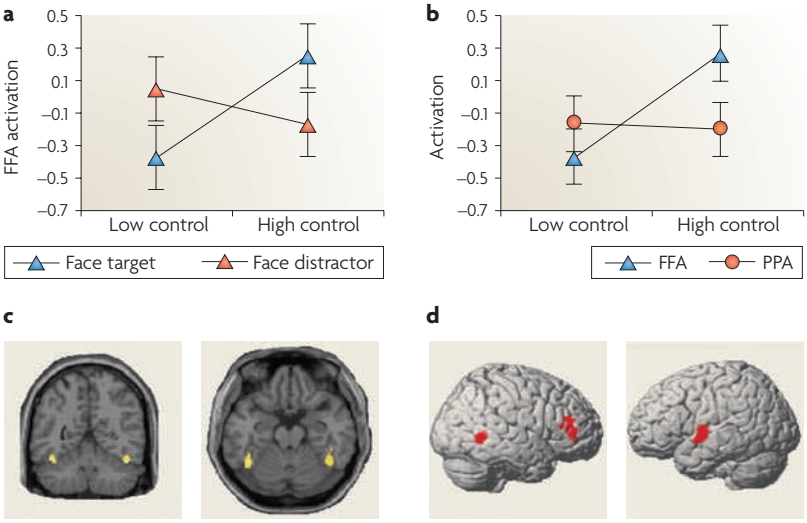


Figure 5 | **Regions associated with conflict-induced behavioural adjustment in humans. a** | Activity in the fusiform face area (FFA) in a face–word test in low-control conditions (LH) and in high-control conditions (HH). In the HH condition the subjects were faster and more accurate than in the LH condition, indicating that their performance was improved owing to a heightened control level. When 'face' was the relevant dimension (face target), the activity signal in the FFA was higher in HH conditions than in LH conditions, but no significant activity change was seen when 'face' was the irrelevant dimension (face distractor). This suggests that when control was heightened the neural processing of the task-relevant stimulus (the face) was amplified, but that when face was not the relevant dimension there was no control-dependent change in the activation. **b** | Activation in the FFA and in the parahippocampal place area (PPA) in LH and HH conditions when 'face' was the relevant dimension. The control-dependent activation change was specific to the area that is involved in the processing of the stimulus. **c** | The functional MRI signal in the FFA during the face–word test. **d** | Regions that are associated with control adjustment. The functional MRI signals in the right dorsolateral prefrontal cortex, the right middle temporal gyrus and the left anterior insula were stronger in the HH conditions than in the LH conditions. Figure is reproduced, with permission, from REF. 16 © (2005) Macmillan Publishers Ltd. All rights reserved.

or advantageous. Consider an animal engaged in a socially important task such as grooming a conspecific — it would be maladaptive to devote all of the cognitive resources to the current task at the expense of missing cues to more important events, such as the approach of a predator. Therefore, the control that is allocated to the current task should be continually regulated (in terms of amount) and should remain amenable to disengagement. One study reported that the activity of a group of DLPFC cells was modulated depending on the conflict level in the previous trial[49] (FIG. 3c). Whereas some of these DLPFC cells showed higher activity if the previous trial was a high-conflict condition than if it was a low-conflict condition, others showed the reverse[49]. One potential use of this information might be to signal the need for engagement/enhancement or disengagement/relaxation of cognitive control in the upcoming trial.

These findings suggest that the DLPFC plays a crucial part in executive-control adjustment, but the mechanisms by which executive control is engaged, disengaged and regulated (in terms of amount) remain unclear.

Neural basis of conflict processing

ACC. In their seminal review, Botvinick and colleagues[2] expounded the important principle that a key way in which the brain might regulate performance is by monitoring conflict in stimulus or response representations, and that such a conflict signal could be used as feedback in a system for adjusting top-down selection of currently task-relevant information. Although the computational aspects of this theory do not come in for any criticism in this Review, we have suggested an additional short-term memory module in light of emerging empirical evidence. In addition, we think that the other key aspect of the theory, namely that the primate ACC is an essential neural substrate for conflict monitoring, deserves significant reconsideration. As reviewed above, this aspect of conflict-monitoring theory has gained most of its support from human neuroimaging studies that found ACC activations associated with conflict monitoring. However, there seems to be little if any support for the notion that the ACC houses a general-purpose conflict-monitoring system from lesion and neuronal recording studies.

It is difficult to formulate a unified theory that explains all the findings of the human and animal studies. Further research is clearly necessary to establish whether any other cognitive function(s) may better characterize the role of the ACC. For example, the ACC has often been linked to response selection (BOX 1). Deciding on the most appropriate actions necessitates the ability to evaluate the outcome of previous responses; however, in stochastic and changing natural environments, animals' estimates of reward expectation and the value of their actions will be uncertain. A recent study suggested that the ACC might be important for tracking uncertainty and environmental volatility in order to influence action selection[63]. Indeed, environmental volatility and associated uncertainty correlate with activity in the human ACC sulcus at the time that new outcomes are observed[64], and single-neuron activity in the macaque ACC that is related to the prediction errors of action values is strongest when the animals are least certain of the value of their actions[65]. ACC cells encode reward expectancy, which changes as the proximity of reward changes in successive trials[66], and ACC lesions have shown that the region is necessary for animals to base decisions on the recent history of obtained reward[67]. The ACC might be involved in extracting an estimate of the likelihood of a reward based on the context of the task.

In this article we have reviewed many studies that examined how task-induced conflict influences brain and behaviour, but could a role of the ACC framed in terms of context-driven estimation of reward uncertainty provide a more parsimonious account of the ACC activations that have been observed during the performance of various tasks? For example, is the ACC more active in high-conflict than in low-conflict conditions because of the greater uncertainty in goal achievement that is detected in the former? Could the greater ACC activation that is observed in neutral compared with congruent conditions[35] (which conflict theory cannot explain as neither condition exhibits conflict) reflect the fact that there is less uncertainty in congruent conditions in which both stimulus elements indicate the same response? Is the lower activation of the

ACC in HH than in LH conditions[15–20] a consequence of less uncertainty in the likelihood of obtaining rewards given the higher levels of control in HH conditions? Might the reason that the ACC is more active in earlier than in later epochs of fMRI sessions with the Stroop task and other tasks[33,43], despite the constant conflict costs, be due to the fact that subjects are unfamiliar with the task in the earlier periods and that this novelty[68] increases the uncertainty of goal achievement? And might the explanation for ACC activation following DLPFC activation in ERP studies[47] be that the DLPFC represents the task context and the ACC extracts the context-driven uncertainty signal? A signal such as this might be used to adjust the emotional aspect of the task performance. The ACC has strong connections with brain areas that control the autonomic nervous system (BOX 1) and can influence emotion-induced changes in autonomic functions[69,70]. These and other related questions deserve to be addressed by future research.

DLPFC. We have reviewed evidence that is consistent with the notion that the DLPFC represents currently experienced, incompatible or conflicting stimuli or rules or their associated responses; encodes a neural representation of conflict as a distinct task-relevant variable; maintains conflict information within and across trials; and implements executive control (FIG. 4). Indeed, recordings of single-cell activity from the DLPFC have shown that the DLPFC cell activities represented conflict independently of the other aspects of the task[49], and that task-relevant rules and stimulus features are maintained and updated in the DLPFC neurocircuitry[1,61,71]; by maintaining a rich representation of the task context (for example, relevant rules or stimulus-response mappings), the DLPFC might support the kind of top-down control that mediates cognitive control. However, in monkeys the conflict cost remained intact in the WCST analogue after lesioning of the DLPFC[49], which suggests that the behavioural effects of conflict in the current trial might be independent of the process of conflict representation in the DLPFC and be mediated by other brain structures.

PPC. Although many studies have registered activity changes in the PPC in conflict tasks[7,9,17,26,29,31,33–36], the potential importance of the PPC in conflict detection–resolution processes has not received as much attention as that of the ACC and the DLPFC. One study found that activity in the ACC but not in the DLPFC or the dorsal PPC was sensitive to conflict at the level of the behavioural response, whereas activity in the DLPFC and the dorsal PPC but not the ACC was sensitive to conflict at the level of the stimulus representation[31]. The authors suggested that the ACC and the PPC act in concert to detect conflict at different stages of information processing (FIG. 2), with both structures signalling the need for increased control to the DLPFC. A study recently observed that patients with left-hemispatial neglect due to right-PPC damage do not demonstrate the normal conflict costs associated with incongruent (left-directed) flankers when they are cued to make right-directed movements; in fact, they showed facilitated right-directed responses[72]. The authors concluded that the PPC might be involved in selecting for action when there is conflict between stimulus-evoked responses. Further evidence that control processes probably operate in parallel in different brain regions, including the PPC, was provided in a study that showed control-related activation specific to the resolution of stimulus-level conflict in the Stroop test in the superior parietal cortex, and control-related activation specific to the resolution of response-level conflict in the Simon test in the ventral premotor cortex[18]. The PPC has likewise been implicated in conflict processes in monkeys: in one study, monkeys were slower and committed more errors in high-conflict conditions, indicating that their behaviour was influenced by the experienced conflict[52]. Moreover, PPC cell activity was modulated by the conflict; however, cellular activity did not represent the conflict as a separate variable and only modulated the onset of directional selectivity in neuronal activity[52].

Other brain regions. Recent neuroimaging evidence suggests that a network of prefrontal, parietal and subcortical regions contributes to cognitive control in various tasks that demand such control, including variants of the Stroop test. This network includes frontolateral regions that are considerably more posterior than the DLPFC, around the junction of the inferior frontal sulcus and the inferior precentral sulcus[73]. The importance of this inferior frontal junction area deserves more research, as does that of the cerebellum, in which activation in the presence of conflict has also been reported[7,17]. Patients with cerebellar lesions exhibit higher conflict costs in the absence of task-switching costs, suggesting that the cerebellum has a crucial role in conflict processing[74]. Whether either of these regions provides a neural substrate of the conflict detection–resolution process remains to be seen.

Conclusions and future directions

Studying the neural substrate and mechanisms of conflict-induced behavioural adjustment has opened an important window to the neural basis of executive control. These studies indicate a crucial role for the DLPFC in adaptive and dynamic modulation of executive control and also suggest involvement of the PPC, the inferior frontal junction area and the cerebellum in conflict-induced behavioural adjustment. Contrary to prominent theories, our review of the literature leads to the conclusion that the ACC does not seem to have a causal or indispensable role in conflict-induced behavioural adjustment. This need not rule out a selective role for the ACC in detecting conflict in the context of specific tasks, and perhaps in cases in which there is conflict in the selection of competing motor responses rather than at the stimulus or perceptual level. However, the role of the ACC might be better understood more generally in terms of response selection and/or in context-driven estimations of reward uncertainty. Understanding the precise role of all of these areas awaits further investigation. A multidisciplinary approach that involves testing different species with the same tasks would help to

bridge the gaps between the results from human and animal studies and reveal the neural substrate and mechanisms that underlie context-dependent adjustment in executive control.

The context-dependent tuning of executive control optimizes the use of our limited cognitive resources to perform prioritized tasks while allowing continued exploration of other possibilities in changing environments. Deficiencies in these processes might underlie some of the behavioural manifestations of patients with brain damage or mental diseases (BOX 3). Elucidating the neurobiology of executive control remains a key challenge for researchers, not only because it addresses one of the most advanced functions of the brain, which underlies our behavioural complexity and flexibility, but also for its possible clinical applications in the diagnosis and treatment of mental diseases that afflict millions of people.

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FURTHER INFORMATION

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SUPPLEMENTARY INFORMATION

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