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Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning

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Abstract

Convergent evidence highlights the differential contributions of various regions of the prefrontal cortex in the service of cognitive control, but little is understood about how the brain determines and communicates the need to recruit cognitive control, and how such signals instigate the implementation of appropriate performance adjustments. Here we review recent progress from cognitive neuroscience in examining some of the main constituent processes of cognitive control as involved in dynamic decision making: goal-directed action selection, response activation and inhibition, performance monitoring, and reward-based learning. Medial frontal cortex is found to be involved in performance monitoring: evaluating outcome vis-à-vis expectancy, and detecting performance errors or conflicting response tendencies. Lateral and orbitofrontal divisions of prefrontal cortex are involved in subsequently implementing appropriate adjustments.

Keywords: Cognitive control; Prefrontal cortex; Medial frontal cortex; Orbitofrontal cortex; Action selection; Response inhibition; Performance monitoring; Performance adjustment; Reward-based learning

1. Introduction

Flexible goal-directed behavior requires an adaptive cognitive control system for selecting contextually relevant information, and for organizing and optimizing processing pathways. In goal-directed behavior, decision-making (deciding which action to take) is biased by the anticipation of the action's outcome. Differences between anticipated and actual outcome can be used to optimize behavior. Evaluating the adequacy and success of performance is instrumental in determining and implementing appropriate behavioral adjustments. For instance, if anticipated reward is not delivered this can be used to learn regularities in action-reward contingencies; negative feedback can be used to shift from one set of stimulus-response translation rules to another; detection of a performance error may be used to tighten control (e.g., shift to a more conservative speed/accuracy balance). Evidence from cognitive neuroscience is beginning to converge on differential contributions of various regions of the prefrontal cortex (PFC) in the service of cognitive control, but conspicuously little is known about how the brain determines and communicates the need to recruit cognitive control, and how such signals

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instigate the implementation of appropriate performance adjustments. Here we review evidence from recent reports on some of the main constituent processes of cognitive control as involved in dynamic decision making: goal-directed action selection, response activation and inhibition, performance monitoring, and reward-based learning.

Clearly, the agent that selects, activates, inhibits, monitors, and learns is 'the individual' rather than the PFC. It is, therefore, essential to specify more precisely the way in which such decision-making operations are supported by PFC; this, in turn, requires an understanding of the functional anatomy and effective connectivity of PFC. The next section will describe in some detail the current state of affairs and advancements in this regard. This framework will provide the background for the present review.

2. Anatomy and connectivity of the PFC

The main gyri of PFC in humans roughly comprise three main anatomical divisions: the lateral gyri (superior, middle, and inferior frontal gyri), the orbitofrontal gyri (medial and lateral), and the medial wall (medial frontal gyrus and cingulate gyrus). More conventional, but along similar lines, a cytoarchitectonic partitioning of PFC yields again three main divisions: lateral PFC, orbitofrontal cortex (OFC), and medial frontal cortex (MFC). Using the dimensions medial/lateral, rostral/caudal, and ventral/dorsal to describe the relative positions of these main divisions, lateral PFC covers all lateral gyri and sulci except the most rostrally and most ventrally located regions; MFC covers most of the medial wall except the most rostrally and most ventrally located regions; and OFC covers the most rostrally and most ventrally located regions of the lateral and medial gyri and sulci. As the correspondence between gyral and sulcul landmarks and the underlying cytoarchitechtonic areas (often classified in terms of Brodmann areas, BA) is only approximate, relating functional activation patterns or lesion damage to any subregion of PFC should be performed with some caution.

Within lateral PFC (see Fig. 1A) we can further distinguish dorsolateral PFC (dlPFC: BA9/46, BA46, and BA8a in the middle frontal gyrus), ventrolateral PFC (vlPFC: BA44 and BA45, corresponding to the pars opercularis and pars triangularis of the inferior frontal gyrus, respectively), and the inferior frontal junction (IFJ: in the posterior end of the sulcus between the medial and inferior frontal gyri, at the junction of BA8a, BA6, and BA44).

Within MFC (see Fig. 1B) we can distinguish anterior cingulate cortex (ACC) and, to the dorsal end, the medial frontal gyrus. (Although the ACC is a transition zone between limbic and frontal cortex, we are focusing here on its functions in cognitive control in frontal networks.) ACC consists of ventral (BA32pl, BA25), rostral (BA32, BA24), and dorsocaudal portions (BA32′, BA24′). The medial frontal gyrus consists of, from caudal to rostral, the supplementary motor area (SMA) and pre-SMA (medial BA6), the frontal eye fields (medial BA8), and dorsomedial PFC (BA9).

Within OFC (see Figs. 1B and C) we can distinguish medial, ventral, lateral, and frontopolar portions. The medial part consists of BA14 in the medial wall, adjacent to rostral ACC (BA32) on the ventral side. The ventral part consists of BA13 (bordering medially to BA14) and BA11 (anterior of BA13). OFC extends laterally into BA47/12 (bordering BA13 and BA11; BA47/12 corresponds to the pars orbitalis of the inferior frontal gyrus) and rostrally into frontopolar cortex (BA10, bordering ventromedially to BA11, ventrolaterally to BA47/12, and dorsolaterally to BA46, BA9/46, and BA9).

All areas within PFC are richly interconnected. ACC projects to, or receives projections from, virtually all areas of the frontal cortex (for a review see Barbas, 1995). Rostral and dorsocaudal ACC (BA24, BA24′, and BA32′) is interconnected with dlPFC (BA46) (Koski & Paus, 2000). Ventral ACC (BA25) is interconnected with ventral OFC (mostly BA13), a connection implicated in the control of respiration, blood pressure, and other autonomic functions (Barbas & Pandya, 1989). Rostral ACC (BA32) has strong reciprocal connections with ventromedial OFC (BA14 and medial BA11) and frontopolar OFC (medial BA10) (Öngür & Price, 2000). ACC is not connected with lateral OFC (BA47/12) (Koski & Paus, 2000). dlPFC (BA9 and BA46) has reciprocal connections with extensive parts of OFC (including BA14, BA11, BA10, and BA47/12; Barbas & Pandya, 1989; Carmichael & Price, 1995). dlPFC (particularly BA46) is also well interconnected with the motor system (Koski & Paus, 2000), with reciprocal connections with SMA and pre-SMA (medial BA6) and with premotor cortex (lateral BA6), and projections to the frontal eye fields (BA8). PFC has no direct connections with primary motor cortex, but has extensive connections with premotor areas that, in turn, send projections to primary motor cortex and the spinal cord. In short, the PFC is a richly intraconnected system with widespread projections to and from almost all other parts of the brain, rendering the PFC ideally suited for the control of many aspects of behavior.

3. Functional specialization within PFC

Hardwired connections (whether or not potentiated by extensive learning and experience) between sensory stimuli and corresponding responses afford rapid performance of natural, stereotyped, or well-trained behaviors

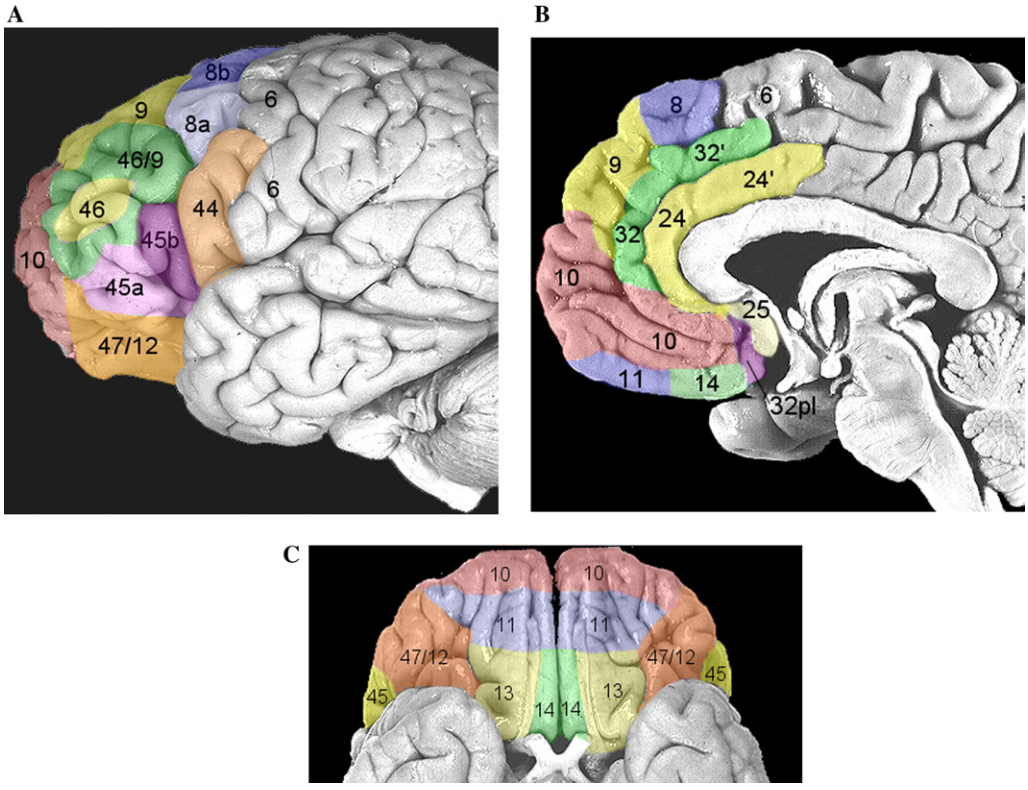

Fig. 1. Cytoarchitectonic maps rendered on the lateral PFC surface (A), on the medial wall (B; midsaggital view), and on the ventral orbital surface (C; viewed from below) of PFC. Numbers refer to Brodmann areas.

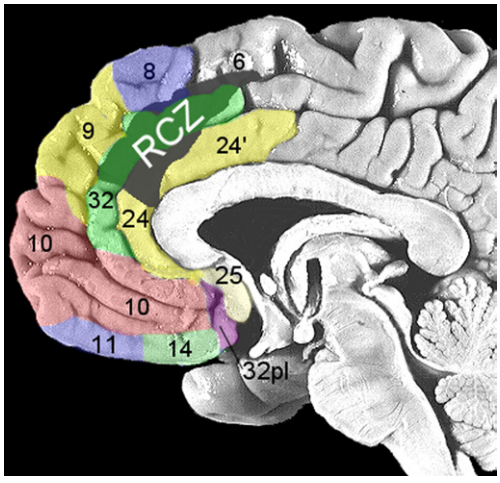

Fig. 2. The Rostral cingulate zone (RCZ) superimposed on de cytoarchitectonic maps as rendered on the medial wall (midsaggital view) of PFC. Numbers refer to Brodmann areas.

without demanding much attention. However, these behaviors are typically rigid, resisting generalization to novel situations, and thus need to be overruled when our goals and intentions require an alternative behavioral repertoire. When goal-directed action selection is needed (such as when learning new stimulus-reward contingencies, when prepotent stimulus–response mappings are inappropriate, or when environmental demands are rapidly changing), PFC comes into play. PFC sends out signals to subcortical and posterior cortical brain regions so as to configure, modulate, and direct processing in these areas in accordance with current goals and task demands; this top-down bias is especially important when the pathways leading to the desired action compete for expression in behavior with concurrent, more habitual pathways (Miller & Cohen, 2001).

The extent to which subregions of PFC are functionally differentiated, that is, the extent to which different cognitive functions can be mapped to discrete regions of PFC, remains controversial. On the one hand, situations that require cognitive control often elicit co-occurring activations in dlPFC, vlPFC, and MFC, suggesting a generic role for these areas in adaptive coding of the current task demands (Duncan & Owen, 2000). On the other hand, at the risk of engaging in neophrenology, various subdivisions of PFC can be considered essential for implementing different cognitive control functions, which interact to facilitate task performance (thus explaining their recurrent co-activation). Yet, even when we acknowledge some degree of functional specialization within PFC, it cannot be maintained that any region within PFC subserves one function only. For instance, vlPFC has been argued to be involved in response inhibition (Aron, Robbins, & Poldrack, 2004), in task switching (Braver, Reynolds, & Donaldson, 2004), in associative learning (Passingham, Toni, &

Rushworth, 2000) and category learning (Freedman, Riesenhuber, Poggio, & Miller, 2001), and in memory encoding (Bor, Duncan, Wiseman, & Owen, 2003), and memory retrieval (Fletcher, Shallice, Frith, Frackowiak, & Dolan, 1998). Thus, rather than examining which cognitive control functions are served by specific PFC areas, we will consider a number of specific functions thought to be central to dynamic decision-making, and evaluate which brain areas are effectively involved in each of these.

To preview the main outcomes, cognitive control processes in adaptive decision-making comprise both a regulative component, responsible for the activation and implementation of executive control processes to coordinate and adjust goal-directed behavior, and an evaluative component, responsible for monitoring the need for regulative control and signaling when adjustments in control are necessary. The evaluative component predominantly involves MFC, while the regulative component relies crucially on subdivisions of PFC, in particular lateral PFC and orbitofrontal cortex (OFC).

4. Goal-directed action-selection and reward-based association learning

The neurocognitive processes involved in decision making are especially relevant in choices that involve some perplexity, that is, when the alternatives are difficult to distinguish, have uncertain pay-offs or require prior knowledge to resolve them (Schall, 2001). Whereas choice refers to the final commitment to one alternative, decision refers to the preceding deliberation about the alternatives, the process that leads to a particular choice. By reinforcing the patterns of PFC activity responsible for achieving a goal, associations can be formed between environmental stimuli, actions, rules, and subsequent reward. Thus, when similar conditions recur in the future, the appropriate neural representations can readily be retrieved and put in operation so as to facilitate the decision-making process that leads to advantageous choices. Accordingly, the vlPFC has been related to the recollection of visual stimulus associations (Bunge, Burrows, & Wagner, 2004). Thus, PFC must be able to represent task rules and stimulus–response (S–R) associations in its patterns of neural activity; indeed, the activation and maintenance of task goals is central to executive function (Nieuwenhuis, Broerse, Nielen, & de Jong, 2004). Based on monkey lesion studies and human neuroimaging studies, vlPFC (BA45) has been implicated as a crucial part of the circuitry via which associations are formed between visual cues and the actions or choices that they specify (Passingham et al., 2000). Moreover, lateral PFC is responsible for maintaining such representations in an active state until the goal is achieved, often in the face of other intervening, irrelevant, and potentially interfering events (Miller & Cohen, 2001). PFC plays a key role in optimizing the decision making processes underlying goal-directed action selection.

The learning process in decision making requires the ability to predict reward, and to pursue the actions that will ensure its procurement. Reward-related activity is wide-spread in the brain (Schall, Stuphorn, & Brown, 2002; Schultz, 2002). In animals, ascending dopaminergic systems are critically involved in responses to reinforcing stimuli; the ventral striatum, particularly the nucleus accumbens, is probably the structure most reliably linked to reward-related processes (Robbins & Everitt, 1992; Stern & Passingham, 1996), but other structures are also involved. Yet, little is understood about the neural encoding of response–reward relationships, a process deemed essential for purposeful behavior.

As will be discussed in more detail in a later section, performance monitoring in posterior MFC mediates this learning by selectively strengthening the neural patterns of activity that predict reward and guide the behavior needed to achieve it. In addition, studies in non-human primates have shown that cells in posterior MFC, which has direct and indirect projections to primary and supplementary motor areas, are involved more directly in goal-based action selection (i.e., selecting between competing actions in view of the anticipated reward associated with each of these actions) (Matsumoto & Tanaka, 2004a, 2004b). Studies in rats indicate that, after learning specific stimulus-reward contingencies, neurons in MFC (~BA32) show a sustained firing pattern that develops in parallel with the behavioral learning curve and is highly sensitive to a switch in reward contingencies (Mulder, Nordquist, Orgut, & Pennartz, 2003). In a study with non-human primates (Tremblay & Schultz, 2000), when two out of three stimulus types were rewarded, animals initially expected reward in every stimulus type but rapidly learnt to discriminate the rewarding stimuli. In close correspondence, in the initial learning phases activations of OFC neurons that were related to the expectation of reward occurred for each stimulus type, but adapted during the course of learning and became restricted to rewarded trials. Accordingly, activity in an area of OFC (caudolateral, bordering vlPFC) in humans was found to be related to detecting a change in reward contingencies (O'Doherty, Critchley, Deichmann, & Dolan, 2003). This type of neural plasticity in rat MFC and primate OFC may contribute to the formation of response–reinforcer associations and of behavioral strategies for guiding goal-directed action.

In an fMRI study in humans (Elliot, Friston, & Dolan, 2000), winning streaks (e.g., the fourth reward in a series of four consecutive rewards), and losing streaks (e.g., the fourth penalty in a series of four consecutive penalties) activated OFC (BA47/12, bordering BA45),

vlPFC (the insula, BA44/45), and the head of caudate nucleus in the basal ganglia. These areas were sensitive to psychological context (the emotional salience associated with a winning or losing streak) but apparently blind to the valence (i.e., goodness or badness) of the experience. By contrast, the subgenual MFC (ventral to the genu of the corpus callosum, in the rostral part of BA24, bordering BA32 and medial BA10, see Fig. 1B) was activated only by *winning* streaks. Activation of subgenual MFC may reflect an increased expectation of reward associated with 'riding on a high,' serving to strengthen the incentive motivation to maintain behavioral responses. Interestingly, the subgenual MFC is implicated in the modulation of the neurotransmitter systems targeted by antidepressant drugs as well as in the pathogenesis of clinical depression (Drevets et al., 1997), a disorder characterized by reduced experience and expectation of reward and impaired motivation (Lewinsohn, Youngren, & Grosscup, 1979).

Expectation of reward can strongly bias our decisions and actions. Exactly how the brain links signals related to reward expectation to the signals responsible for making decisions and preparing actions remains pretty much a mystery. Recent studies in non-human primates have begun to characterize the influence of reward expectation on neural circuits involved in action selection (Hikosaka & Watanabe, 2000; Leon & Shadlen, 1999; Tremblay & Schultz, 2000). The results of two recent intracranial recording studies describe neural signals in the caudate nucleus (Lauwereyns, Watanabe, Coe, & Hikosaka, 2002) and subgenual MFC (Matsumoto, Suzuki, & Tanaka, 2003) that ostensibly relate anticipation of an uncertain reward with the preparation for goal-directed eye movements or manual actions, respectively. The caudate is involved both in generating saccades and in representing anticipated reward, especially if there is the possibility of an unrewarded alternative as well (Gold, 2003). As described above, subgenual MFC is also involved in representing reward anticipation. To select a specific action based on the anticipated reward, there needs to be a neural representation of the linkage between anticipated reward and the specific motor/oculomotor actions to be selected. Cells in subgenual MFC appear to represent such specific linkages and thus seem central to the neural mechanism for decision-making. The anticipatory signals in the caudate bring about the biased behavioral responses by indirect propagation to the superior colliculus, bringing the superior colliculus closer to initiating a rewarded saccade. Thus, the subgenual MFC and the caudate may be particularly important for decision-making in motor and oculomotor behavior, respectively.

Recent fMRI studies have emphasized the role of dlPFC (BA46, BA9/46) in choosing among the most task-relevant internal representations (Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000; Rowe & Passingham, 2001). rTMS over dlPFC interferes with free selection of finger responses (Hadland, Rushworth, Passingham, Jahanshahi, & Rothwell, 2001). dlPFC is highly sensitive to factors that make response selection more difficult (Schumacher & D'Esposito, 2002; Schumacher, Elston, & D'Esposito, 2003), suggesting that dlPFC is involved in the rule-based selection of responses (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Jiang & Kanwisher, 2003). Taken together, these findings point at an integrative role for dlPFC in linking short-term memory representations to goal-directed motor behavior. In addition, neurons in dlPFC encode past choices and their payoffs (Barraclough, Conroy, & Lee, 2004; Paulus, Hozack, Frank, & Brown, 2002), thus providing signals for updating the expectation of reward, as is necessary in dynamic learning. dlPFC may thus contribute to successful decision making by using payoff expectation to guide the conscious and deliberate goal-directed selection of task rules and appropriate actions.

However, more ventromedial divisions of PFC (vmPFC) may mediate less-deliberate, emotion-driven influences on action selection (Bechara, Damasio, & Damasio, 2000; Rolls, 2000). Patients with damage in this sector (which includes large portions of BA10, BA11, BA13, and BA47/12 in OFC, as well as the inferior parts of BA25 and BA32 in MFC) fail to make advantageous choices despite their intact ability to update expected reward values (Bechara et al., 2000). While normal individuals experience a state of arousal during the time of deliberation prior to making risky and disadvantageous choices, the insensitivity to future consequences ('myopia for the future') seen in vmPFC patients is presumed to derive from their failure to experience this affective state. This affective experience is normally accompanied by bodily signals and somatic states that have come to be associated with risky decisions, presumably derived from prior experiences with reward and punishment. Through this association these somatic signals constitute a preconscious bias against bad choices. In vmPFC patients, however, such a bias signal fails to elicit the affect that should keep them from pursuing a course of action that is disadvantageous in the future (Bechara et al., 2000).

Thus, while various brain structures are involved in processing reward in general (including the basal ganglia, Gold, 2003; parietal cortex, Platt & Glimcher, 1999; dlPFC, Tsujimoto & Sawaguchi, 2004; and MFC, Shidara & Richmond, 2002), a few areas (dlPFC, vmPFC, and several MFC regions, as well as the caudate nucleus, all reviewed above) are dedicated more specifically to representing the hedonic properties of reward, focusing on learning appropriate action-reward contingencies and selecting those actions that potentially lead to reward.

5. Response activation and response inhibition

Especially when the selected action has to compete for activation with strong alternatives, cognitive control may be needed to resist interference from these alternatives and ensure the timely and uninterrupted activation of the selected response (cf. Miller & Cohen, 2001). Inhibitory control is postulated as one of the mechanisms by which PFC exerts its coordinating effects on subsidiary processes implemented by posterior cortical and subcortical regions to optimize behavior. Inhibition can be defined descriptively as the "suppression of inappropriate responses, S–R mappings or task-sets when the context changes, and suppression of interfering memories during retrieval" (Aron et al., 2004), or as the "mechanism or set of processes that result in the containment of prepotent behavioral responses when such actions are reflex-like, premature, inappropriate, or incorrect" (Burle, Vidal, Tandonnet, & Hasbroucq, 2004). Inhibitory control has for a long time been associated with dlPFC (Mishkin, 1964) and vlPFC (Iversen & Mishkin, 1970) based on classic monkey-lesion work, a picture strengthened by more recent fMRI studies. Attention-deficit/hyperactivity disorder, thought to exhibit response-inhibition deficiencies (Aron, Dowson, Sahakian, & Robbins, 2003; Nigg, 2001; Ridderinkhof, Scheres, Oosterlaan, & Sergeant, in press), has been associated with abnormalities in PFC (especially in vlPFC; Casey et al., 1997; Castellanos et al., 1996; Sowell et al., 2003; Vaidya et al., 1998).

Various experimental paradigms have been designed such as to allow the investigation of response inhibition. For instance, response inhibition is often thought to be invoked in conflict tasks (such as the Stroop, Simon, and Eriksen tasks), in which responses are typically slowed when some irrelevant feature of the stimulus is associated with the response opposite to that associated with the relevant stimulus feature. While response inhibition has often been invoked implicitly as a mechanism to overcome interference from distractor elements, only recently have analyses of reaction time distributions provided explicit evidence for the role of selective response suppression in resolving or preventing conflict (Burle, Possamai, Vidal, Bonnet, & Hasbroucq, 2002; Ridderinkhof, van den Wildenberg, Wijnen, & Burle, 2004). In neuroimaging studies, comparison of incongruent trials (eliciting two conflicting responses) with congruent trials (affording only one response) has revealed specific activations in vlPFC (Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Hazeltine, Poldrack, & Gabrieli, 2000; Hazeltine, Bunge, Scanlon, & Gabrieli, 2003).

Go/NoGo tasks (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956) and stop-signal tasks (Logan & Cowan, 1984; Ollman, 1973) require subjects to perform speeded responses on Go trials (such as pressing a button in response to a target stimulus) and to inhibit responding on incidental NoGo trials (containing non-target stimuli) or stop trials (when the target stimulus is followed by a stop signal). Behavioral indices of inhibitory control are the percentage of commission errors (failures to refrain from responding) on NoGo or stop trials, and (in stop-signal tasks) the duration of the stopping process, mathematically approximated as the stop-signal reaction time (SSRT). Just like speeded responding, response inhibition processes can be examined experimentally using SSRT as the prime dependent measure (van den Wildenberg & van der Molen, 2004). For instance, presenting stop signals less frequently results in a reduced efficiency and thus a lower probability of successful response inhibition (Ramautar, Kok, & Ridderinkhof, 2004). Neuroimaging studies demonstrate the engagement of dorsomedial PFC (Garavan, Ross, & Stein, 1999; Garavan, Ross, Murphy, Roche, & Stein, 2002), caudal dlPFC (de Zubicaray, Andrew, Zelaya, Williams, & Dumanoir, 2000), and vlPFC (Bunge, Dudukovic et al., 2002; Konishi et al., 1999; Rubia et al., 2003) in response inhibition in these tasks, and the greater the damage to vlPFC in lesion-patients, the more impaired is SSRT (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003).

Animal work has provided further evidence for the role of lateral PFC in response inhibition. Lesions to a monkey homologue of vlPFC (the inferior prefrontal convexity; BA45) impaired NoGo performance (Iversen & Mishkin, 1970). Depth-electrode recordings from non-human primates showed that NoGo stimuli were followed by firing of cells in the principal sulcus (the monkey homologue of dlPFC, BA46; Sakagami et al., 2001; Sasaki, Gemba, & Tsujimoto, 1989; Watanabe, 1986). Excitation of the latter cells during regular responses yielded a decrease of activity in primary motor cortex and either a delay or the complete suppression of responses (Sasaki et al., 1989).

The saccade-countermanding task, a variety of the stop-signal paradigm often used in monkeys, manipulates monkeys' ability to withhold planned saccades. The efficacy of saccade countermanding depends on the balance of activation between gaze-shifting and gaze-holding neural processes in the frontal eye field (FEF) and superior colliculus (SC). Presentation of a stop-signal yields a rapid increase in activity in FEF gaze-holding neurons and a rapid decrease in activity in gaze-shifting neurons (Schall et al., 2002). The initiation of saccades is suppressed by electrical stimulation of neurons deep in FEF (BA8, bordering vlPFC; Burman & Bruce, 1997), which have direct inhibitory projections to oculomotor nuclei in the superior colliculi. Another study found that neurons in the pre-FEF (the caudal PFC area surrounding the FEF anteriorly, BA8a and BA46) are active specifically when suppressing eye movements to particular locations (Hasegawa, Paterson,

& Goldberg, 2004). A decreased ability to suppress reflexive saccades as a consequence of lateral PFC damage has been demonstrated in antisaccade tasks in both monkeys and humans (Guitton, Buchtel, & Douglas, 1985), most notably in patients with focal lesion damage specifically affecting dlPFC (BA46; Pierrot-Deseilligny et al., 2003), although such effects might be explained in part in terms of differential sensitivities to working-memory demands (Eenshuistra, Ridderinkhof, & van der Molen, 2004).

Compared to oculomotor inhibition, the neural circuitry involved in implementing motor inhibition is more complex and less well understood (for a recent fMRI overview see Kelly et al., 2004). Various areas in lateral PFC project to SMA (BA6) via the basal ganglia and reticular and motor nuclei of the thalamus (e.g., Strick, Dum, & Picard, 1995). For instance, lateral PFC can modulate thalamic transfer through an excitatory influence on the subthalamic nucleus (STN) in the basal ganglia (yielding an attenuation of output to the motor cortex) (Band & van Boxtel, 1999). The output of the feed-forward loop, which serves the selection of appropriate responses (Crutcher & Alexander, 1990), is modulated by projections from somatosensory and posterior association areas to primary motor cortex via the cerebellum and thalamic motor nuclei. This feedback-dependent loop serves the context-dependent adjustment of the parameters of the first loop by translating sensory information into immediate adjustments of motor activity to improve the timing and smoothness of actions (e.g., Goldberg, 1985). The involvement of the basal ganglia in response inhibition has been evidenced by van den Wildenberg et al. (2004), who showed that deep brain stimulation of the STN in Parkinson's disease improved response inhibition in the stop-signal paradigm.

6. Performance monitoring

Flexible adjustments of behavior and reward-based association learning require the continuous assessment of ongoing actions and the outcomes of these actions. The ability to monitor and compare ongoing actions and performance outcomes with internal goals and standards is critical for optimizing decision making. According to a recent review of primate and human studies, largely overlapping brain areas, clustering in the rostral cingulate zone (RCZ, the posterior MFC border zone between the medial areas BA8, BA6, and BA32′ with some extension into BA24′, see Fig. 2), are involved in monitoring for unfavorable outcomes, response errors, response conflict, and decision uncertainty (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). These conditions have in common that they signal that goals may not be achieved or rewards may not be obtained unless the level of cognitive control is subsequently increased.

The implication of RCZ in the monitoring of unfavorable outcomes derives from electrophysiological recordings in non-human primates as well as human neuroimaging studies. Distinct neuron populations in the monkey homologue of the RCZ are sensitive to reward expectancy and reward delivery (Ito, Stuphorn, Brown, & Schall, 2003; Shidara & Richmond, 2002; Stuphorn, Taylor, & Schall, 2000). In addition, RCZ neurons exhibit sensitivity to unexpected reductions in and omissions of reward (Shima & Tanji, 1998). These findings are consistent with a role for these neuronal populations in comparing expected and actual outcomes. fMRI studies in humans, using monetary rewards and punishments (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001) or abstract performance feedback (Ullsperger & von Cramon, 2003), also implicate the RCZ in differential processing of unfavorable outcomes (Fig. 2). Similar parts of RCZ are activated by primary reinforcers such as pain affect (Rainville, Duncan, Price, Carrier, & Bushnell, 1997) and pleasantness of taste (Rolls, Kringelbach, & de Araujo, 2003), suggesting that this zone plays a general role in coding the motivational value of external events.

Primate studies show that, in addition to feedback-sensitive cells, the RCZ also contains error-sensitive cells (Gemba, Sasaki, & Brooks, 1986; Ito et al., 2003). Corroborating these results, subsequent human functional neuroimaging studies have reported increased RCZ activation to errors compared to correct responses in various two-alternative forced-choice tasks (Ullsperger & von Cramon, 2004). Consistent with these single-cell recordings and brain imaging studies, electrophysiological scalp recordings have found an error-sensitive event-related brain potential localized to RCZ, which is attenuated in patients with damage to the dorsal ACC (Holroyd, Nieuwenhuis, Mars, & Coles, 2004).

The role of the RCZ in coding outcome- and error-related information may be understood in terms of a common functional and neurobiological mechanism (Holroyd & Coles, 2002). Errors in reward prediction are coded by phasic changes in activity of the midbrain dopamine system: a phasic increase or decrease when ongoing events are suddenly better or worse (respectively) than expected (Schultz, 2002; Waelti et al., 2001). These phasic dopamine signals are communicated to the RCZ, where basic reinforcement-learning principles are applied to use the dopamine signals for improving task performance (Holroyd & Coles, 2002). Furthermore, the phasic dopamine signals modulate the activity of motor neurons in the RCZ, and the same region of RCZ is activated by response errors and unexpected negative feedback, as shown using neuroimaging, electrophysiological measurements, and computational modeling (Holroyd & Coles, 2002; Holroyd et al.,

2004; but see van Veen, Holroyd, Cohen, & Carter, 2004, for some critical notes). In addition, several studies have shown that event-related brain expressions of error monitoring are intensified after administration of dopamine agonists (de Bruijn, Hulstijn, Verkes, Ruigt, & Sabbe, in press; Tieges, Ridderinkhof, Snel, & Kok, 2004; Zirnheld et al., 2004) and impaired after administration of dopamine antagonists (de Bruijn et al., in press; Ridderinkhof et al., 2002).

RCZ may also be involved in the monitoring of response conflict (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Response conflict occurs when a task concurrently activates more than one response tendency, for example, when the stimulus primes a prepotent but incorrect response. When the correct response is underdetermined, that is under conditions requiring choosing from a set of responses, none of which is more compelling than the others, decision uncertainty occurs, similar to response conflict. The conflict monitoring theory is consistent with the neuroimaging evidence for RCZ activation in response to errors, reviewed above, and with evidence that RCZ is active on correct trials characterized by high pre-response conflict (Carter et al., 1998; Donkers & van Boxtel, 2004; Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003; Yeung, Botvinick, & Cohen, in press). Importantly, it may be that the detection of high post-response conflict is a reliable basis for internal error detection, thereby obviating the need for an explicit error detection mechanism (Yeung et al., in press).

As a potential link between the conflict and reinforcement-learning theories, Ridderinkhof, Ullsperger et al. (2004) suggested that the RCZ is engaged when the need for adjustments to achieve action goals becomes evident: pre-response conflict and decision uncertainty signal a reduced probability of obtaining reward, whereas errors and unexpected negative feedback signal the loss of anticipated reward.

Some support for a functional–anatomical dissociation between on the one hand regions subserving pre-response conflict monitoring and on the other hand structures sensitive to errors and omission of reward has been provided by recent research in non-human primates (Ito et al., 2003; Shidara & Richmond, 2002). No consensus exists as to such a dissociation in humans (Hester, Fassbender, & Garavan, 2004; Holroyd et al., 2004; Ullsperger & von Cramon, 2004). In a meta-analysis of the human neuroimaging literature (Ridderinkhof, Ullsperger et al., 2004), focusing on RCZ activations in response to these types of events, the most pronounced cluster of activations was in BA32′ for all types of monitored events, suggesting the importance of this area for a unified performance monitoring function. Thus, although initial studies arrived at the conclusion that error monitoring and conflict monitoring are performed by different areas, the meta-analysis provided some support against this dissociation inference. However, the dissociation hypothesis could not be abandoned altogether, since activations related to pre-response conflict and uncertainty were found to occur more often in the more dorsal BA8 and less often in the more ventral BA24 than activations associated with errors and negative feedback. Thus, depending on whether one prefers the forest or the trees, once could either emphasize the considerable overlap or the apparent differences. Activation foci associated with reduced probabilities of obtaining reward clustered in the same RCZ region, albeit slightly more dorsally than foci associated with errors and failures to obtain anticipated reward.

The RCZ has extensive connections with brain areas involved in the control of cognitive and motor processes, and has been implicated in the regulation of autonomic arousal (Critchley et al., 2003; Paus, 2001). This presumably places the RCZ in a strategically located position for signaling the need for performance adjustments and for interacting with brain areas involved in motor, cognitive, as well as autonomic and motivational functions. Indeed, deviant ACC-related activity has been observed in individuals scoring high on negative affective experience (Hajcak, McDonald, & Simons, 2004) and under conditions of uncertainty regarding task performance (Pailing & Segalowitz, 2004).

7. The relation between performance monitoring and performance adjustment

Response errors have been reported to be consistently foreshadowed by modulation of RCZ activity during the immediately preceding (correct) response (Allain, Carbonnell, Falkenstein, Burle, & Vidal, in press; Ridderinkhof, Nieuwenhuis, & Bashore, 2003). This modulation, as expressed in event-related brain potentials, may reflect a transient disengagement of the monitoring system, resulting in occasional failures to implement appropriate control adjustments, and hence errors. Consistent with the monitor-disengagement notion, the behavioral adjustments normally seen after subjects have committed an error are eliminated after alcohol-induced impaired error monitoring (Ridderinkhof, de Vlugt, Bramlage, Spaan, & Elton, 2002). Recent neuroimaging studies revealed that greater RCZ activity during error trials was associated with greater post-error behavioral adjustment and with greater activity in lateral PFC on the next trial (Garavan et al., 2002; Kerns et al., 2004). In the latter studies, those erroneous responses that were followed, on the next trial, by the strongest behavioral adjustments were associated with increased activity in lateral PFC. These and other findings suggest a tight link between modulations of activity in RCZ and subsequent changes in performance, with

the monitor (RCZ) and the controller (lateral PFC) interacting to regulate goal-directed behavior (cf. Botvinick et al., 2001).

Evidence from monkey and human research is also beginning to delineate a link between RCZ activity and reward-based association learning. In the monkey homologue of RCZ (the rostral cingulate motor area, rCMA), cells have been identified that fired when reward was less than anticipated, but only when the reduction in reward was followed by changes in the monkeys' action selection (Shima & Tanji, 1998). fMRI studies in humans have corroborated that activity in RCZ, as observed when reward was less than anticipated, was most pronounced when the reduction in reward was followed by subsequent behavioral adjustments (that is, different choices; Bush et al., 2002; O'Doherty et al., 2003). Reversal learning studies like these typically also show activation of lateral PFC and other structures in association with changes in decision-making behavior (Cools, Clark, Owen, & Robbins, 2002).

Thus, the generic performance monitoring function endows RCZ with the capacity to signal the need for performance adjustment. The monitored signals may index the failure (errors, negative feedback) or reduced probability (conflicts, decision uncertainty) of obtaining anticipated rewards (Ridderinkhof, Ullsperger et al., 2004). The evidence for a tight link between activity in this area and subsequent adjustments in performance suggests that monitoring-related RCZ activity serves as a signal that engages control processes in lateral PFC that are needed to regulate task performance in an adaptive fashion.

8. A special edition

This review paper sets the stage for a special issue of *Brain and Cognition* dedicated to neurocognitive mechanisms of performance monitoring and inhibitory control. The special issue was inspired by a symposium organized by the present guest editors in Amsterdam, April 2003, with financial support from the EPOS graduate school and the Netherlands Organization for Scientific Research. The articles in this special issue are all invited, but fully peer-reviewed to meet the high standards of *Brain and Cognition*. We hope and trust that the reader will find these papers to make novel state-of-the-art contributions to the cognitive-neuroscience literature on performance monitoring and inhibitory control.

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