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The gateway hypothesis of rostral prefrontal cortex (area 10) function

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Rostral prefrontal cortex (PFC) is a large brain region, and is unusually large in humans. Therefore, it seems likely that it might support functions that are central to cognition. However, until recently, almost nothing was known about what these functions might be. The 'gateway hypothesis' places these abilities at the centre of human mental processing. It maintains that rostral PFC supports mechanisms that enable us to attend, to a novel degree, either to environmental stimuli, or by contrast, to self-generated or maintained representations (i.e. the 'thoughts in our head'). In this way, investigations into the functions of rostral PFC will reveal key new insights into how human and non-human mental abilities differ.

Introduction

The study of the functions of rostral prefrontal cortex (PFC) (approximating Brodmann's area 10) presents one of the greatest scientific puzzles to cognitive neuroscience. Functional neuroimaging studies show that haemodynamic changes in area 10 can occur during virtually any kind of cognitive paradigm, from the simplest conditioning paradigms to the most complex tests involving memory, judgement, or problem-solving, via studies of, for example, language, perception, navigation and motor control (reviewed in Refs [1–3]). A natural expectation based on these results would then be that lesions to this region in humans should cause deficits on a correspondingly large range of tests. However, every human lesion study so far reported suggests that this is not the case. Lesions to this region in humans typically leave performance on tests of intellectual, memory, language, motor skills, visual perception, and many problem-solving abilities virtually intact. But they do seem to cause performance impairments in two classes of situations in particular. The first class is open-ended situations, which require self-organized behaviour (e.g. multitasking and other 'ill-structured' situations). These are, typically, where the correct way of behaving is underspecified, there are many possible courses of action, and what constitutes success has to be self-determined (Figure 1, panel 1). The second class of situation is where sustained, self-maintained attending behaviour is required, such as when maintaining response consistency [4–14].

The 'gateway hypothesis' of rostral PFC was developed as an attempt to find a solution to this apparent conundrum. In particular, it presents a putative principle for the functional organization of rostral PFC along a medial-lateral dimension. In other words, how the anatomical organization of this brain region in this dimension might relate to one simple principle at the information processing level. We maintain that lateral and medial regions of rostral PFC are differentially sensitive to changes in demands for stimulus-oriented or stimulus-independent attending, and that this provides evidence

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Glossary

Central representation: a percept; the representation of what is perceived; the point at which a sensory experience is afforded meaning, particularly in such a way as it can be related to previous or future sensory experiences.

Contention scheduling (CS): the process of routine selection between well-established action sequences or thought operations (see schema).

N-order cognition: cognition beyond first-order (e.g. second-, third-order, etc.). There are various versions of this concept in cognitive science. Here, an example of first-order cognition is given by situation 1 in Box 1: thoughts about a stimulus. By contrast, an example of N-order cognition would be situation (vii) in Box 1, where one is, for example, reflecting on one's own mental representations, or having thoughts about one's (or someone else's) thoughts about a stimulus.

Schema: a well-established action or thought routine; plural schemata. Schemata receive activation either by direct environmental triggering on the basis of previously learned associations, or in some situations (e.g. novelty, or situations that require us to overcome a well-learned but inappropriate response) via the influence of the supervisory attentional system. For further information see Refs [20,28–31].

Sensory processing: aspects of cognition that relate to sensory experiences prior to the formation of a percept.

Stimulus-oriented (SO) attending: the attending behaviour that enhances our ability to notice change in the environment.

Stimulus processing: where a stimulus is analysed for its characteristics, usually with some purpose in mind (e.g. to understand its meaning, or make a conditional response).

Stimulus-independent (SI) attending: the attending behaviour that is a pre-requisite to experience a novel degree or form of stimulus-independent cognition.

Stimulus-independent cognition: self-generated or -maintained thoughts or representations. Where the current contents of thought are not closely linked to, or determined by, current sensory input. However, not all forms of stimulus-independent thought have as a pre-requisite stimulus-independent attending. Consider for instance, solving the written arithmetic sum '2 + 2 = 4'. Here the answer, ('4') is a self-generated representation, in the sense that it is never witnessed as a stimulus. However, its production does not require a novel degree of stimulus-independent attending: the generation of the representation ('4') is the product of the operation of existing (routine, automatized) schemata (see schema).

Supervisory Attentional Gateway (SAG): collective term for those parts of the cognitive system that effect unusual degrees of either stimulus-oriented or -independent attending behaviour. This is one subsystem of the Supervisory Attentional System, and the gateway hypothesis holds that rostral PFC supports processing crucial to it.

Supervisory Attentional System (SAS): collective term for a number of processing resources whose purpose is to create new schemata or to adapt existing ones. Key aspects of these processing resources are held to be supported by frontal lobe structures. The individual processing resources (other than the rostral PFC ones described here) are described in more detail elsewhere [20,30].

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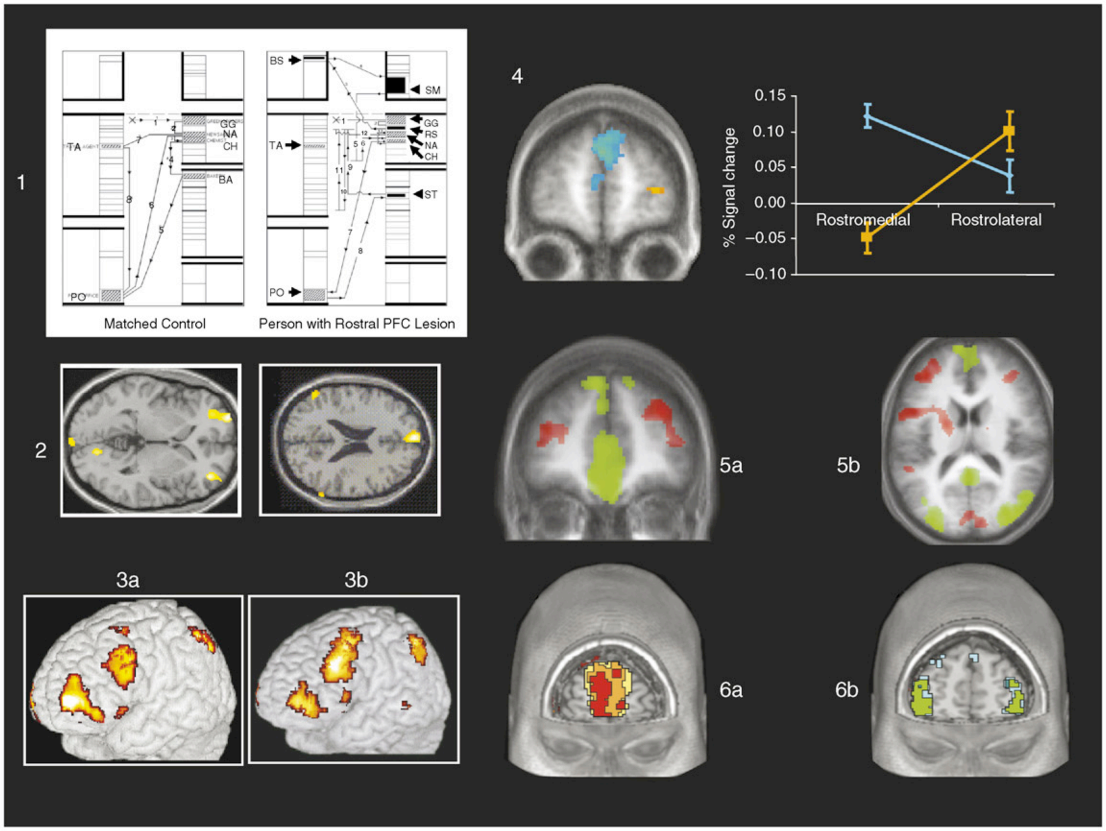

Figure 1. The puzzle that rostral PFC presents to cognitive neuroscience: findings from our laboratory that an account of the role of rostral PFC in human cognition needs to explain. **Panel 1:** Patients with rostral PFC damage can be unimpaired on tests of intellect, simple memory, language and problem-solving but can show disorganization in everyday life activities such as the Multiple Errands multitasking test shown here, which is a real-world test carried out in a shopping precinct (data from Ref. [13]; see also Refs [5,6,9]). **Panel 2:** Functional neuroimaging studies of prospective memory (PM) paradigms typically show increases in BOLD (blood oxygen level dependent) signal or rCBF increases in lateral rostral PFC and medial rostral PFC decreases during PM conditions, relative to performance of the ongoing task alone (data from Refs [36,48]; reviewed in Refs [46]). **Panel 3:** There are regions of lateral rostral PFC that show BOLD signal increases in context or source memory paradigms (relative to baseline conditions) regardless of the precise form of the stimuli or what it is that is being retrieved. Panel 3a shows results from Simons *et al.* [42] where memory for either stimuli position or which task was being performed at the time is being tested. 3b shows the results of Simons *et al.* [41] where memory for task and memory for temporal order are being tested. **Panel 4:** We contrasted performing three different tasks using stimuli presented on a screen display with performing the same task but 'in one's head' only [37]. Relative medial rostral PFC increases were found when people were attending to the displayed stimuli (blue), with lateral rostral PFC increases when people were switching to or from performing the tasks 'in their heads' (orange) only. The graph shows relative BOLD signal change across the two conditions. **Panel 5:** Regions of activation in the contrast of stimulus-oriented > stimulus-independent (green) and stimulus-independent > stimulus-oriented (red) in the study of Gilbert *et al.* [38], averaging across the two tasks. **Panel 6:** Data from Ref. [7]. We have observed similar regions of anterior rostral PFC activated across two different tasks and three conditions that stressed SO attending (6a), and similar regions of caudal lateral rostral PFC activated across two tasks and three conditions that stressed SI attending by promoting three different forms of SI cognition (rehearsal, manipulation of self-generated representation and mind-wandering) (6b).

for a brain system that serves to underpin this cognitive faculty. The history of the development of this idea is described elsewhere [7,15,16]. In this Opinion article, we outline an updated version of this theory and summarize our attempts to test the hypothesis.

The gateway hypothesis

The hypothesis rests on four interlinked propositions. The first is that some forms of cognition are provoked by perceptual experience (i.e. input through basic sensory systems), whereas other forms of cognition occur in the absence of sensory input. This distinction has precedent in cognitive neuroscience (e.g. Refs [17–19]). It also underpins many accounts of intelligent or 'human' behaviour from artificial intelligence that share a family relation with these cognitive neuroscience accounts (e.g. Refs [20,21]).

The second proposition underpinning the gateway hypothesis is that some central representations are activated both when a person witnesses an external stimulus and when they merely imagine it (e.g. Refs [22,23]).

The third proposition is that if the first and second are true, then it is plausible that there is some brain system that can determine, when required, the source of activation of the central representations. We call this system the 'supervisory attentional gateway' (SAG) (see Glossary).

Proposition four is that rostral PFC plays a part in this mechanism. We assume that there is, normally, continuous competition for activation of central representations between (i) input from sensory systems, (ii) reciprocal or associative activation from within the system, and (iii) 'top-down' influence from other supervisory systems (Figure 2). Thus many well-specified and/or familiar situations will require minimal operation of the SAG system, even those that require operation of other supervisory attentional system (SAS) subsystems. We suggest that the SAG system effects (through influence of attending behaviour) the coordination of stimulus-independent and stimulus-oriented cognition, specifically in situations where selection by this competition fails or is producing maladaptive behaviour.

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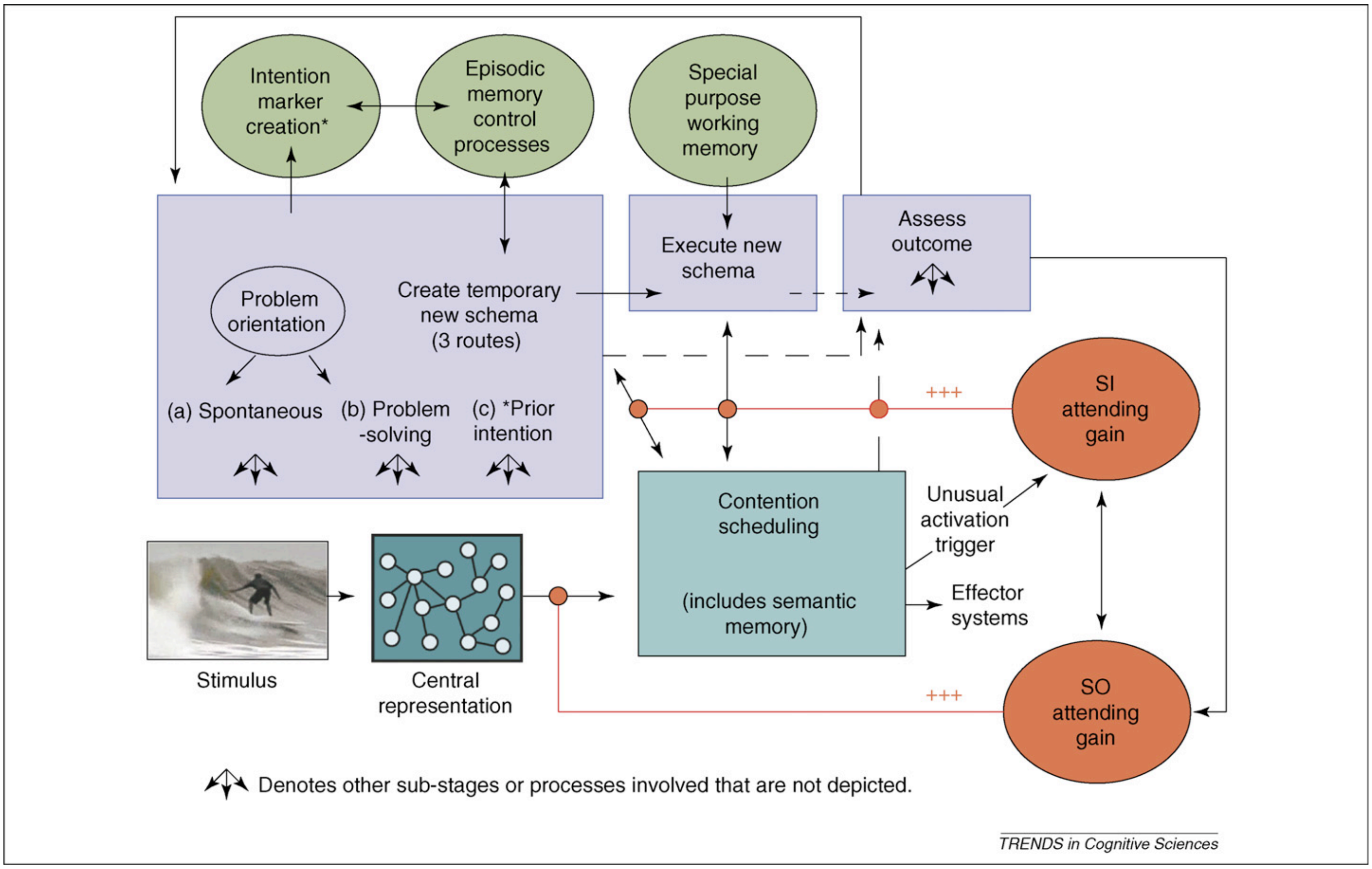

Figure 2. The 'gateway hypothesis' version 2, expressed within the framework of Shallice and Burgess (e.g. Refs [20,28–32]). Temporally distinct processing stages effected by the supervisory attentional system (SAS) are shown in light purple, with a sample of the specialized control resources these stages draw upon shown in green. Selection of established behavioural routines ('schemata') is effected at the 'contention scheduling' level. Processing stages between sensory input and the formation of a central representation or schema are not shown (for details of these see e.g. Ref. [32]). N-order cognition (e.g. Ref. [21]) is instantiated in this model as iterations of interactions between SAS and contention-scheduling. The influence of the 'supervisory attentional gateway' processing system is represented by the red ellipses. The gateway hypothesis supposes that anterior aspects of medial rostral PFC support processing relating to SO attending gain, and lateral aspects of rostral PFC support processes related to SI attending gain.

We do not suppose that the SAG system effects complex cognitive calculations. We assume that these are the largely the domain of processes supported by other sub-regions of PFC and elsewhere (for ideas about how these might operate see Refs [24–27]). Instead, we see the role of SAG processes as altering the flow of information between these other parts of the cognitive system. In this way, the SAG system operates as a 'gateway' between the internal mental life that occurs independently of environmental stimuli, and the mental life that is associated with interaction with the outside world.

Figure 2 presents this hypothesis, newly framed within the well-known information processing framework of frontal lobe function outlined by Shallice and colleagues (e.g. Refs [20,28–31]). We propose that the information processing mechanism, supported at least in part by rostral PFC (i.e. the SAG system), effects 'gain' (in the sense of amplification) at two different stages of the organizational hierarchy of the cognitive system.

The first point of influence [the stimulus-oriented (SO) attending system] affords amplification of input at a level between basic sensory processing and contention scheduling. One might describe the effect as being to strengthen the relationship between perceptual triggering and schema control units (see Ref. [32] for details of 'schema control units'). This view does not hold that the relative valence of schemata are altered (i.e. there is no change in the associations between any one percept and its associates at a contention scheduling level). We assume that this occurs through, for example, the influence of other SAS structures and as part of the normal learning process. Instead, the influence exerted by this first system will have the effect that behaviour and thoughts will be relatively more triggered by sensory input than by being determined by self-generated thoughts emerging from SAS-level systems. We assume that this is, at least in part, the instantiation of a 'fast route' of attending (e.g. Ref. [33]). The 'gain' effected by the proposed system is the model's analogy of the construct 'attention', and the behavioural correlate would be increased attending to the environment either in the presence or absence of stimuli. We propose that the most anterior aspects of medial rostral PFC (area 10) play a crucial part in this aspect of the SAG.

The second, inter-related, influence exerted by the SAG system effects gain at a stage between the contention scheduling process and other supervisory system processes (the stimulus-independent (SI) attending system). The effect is to ensure that activation of representations (i.e. thought) is less determined by sensory input and more closely aligned to the products of the interaction between

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SAS and contention scheduling. The gateway hypothesis supposes that this second influence is triggered by unusual degrees of activation at the contention scheduling (CS) level (Figure 2). This occurs principally in four situations: (i) where no particular schema is sufficiently triggered by incoming stimuli. This can happen in several situations. For instance, where there is no established way of behaving, the stimulus is entirely novel, or where several schemata are triggered by the same stimulus and the correct one is underspecified by the context or instruction; (ii) schema-trigger relations have become specialized through practice, meaning that only a closed set of schemata are now triggered, in other words, the task has become 'easy'. In this situation, mind-wandering will be encouraged because of an increase in influence from free associates (i.e. within the CS level) or SAS structures; (iii) where too many schemata are being simultaneously activated (e.g. in a difficult, complex or exploratory situation, or one where there are many possible established behaviours that might be adopted, without an obvious advantage to one of them); (iv) where triggering of the contention scheduling process is unusually high because of, for example, danger. We propose that lateral aspects of rostral PFC support processing that is crucial to this second (SI attending) capacity.

In this way, the SAG system, considered in its totality, operates under unusual conditions to ensure (i) optimal use of cognitive resources (we assume that mind-wandering, dreaming, and other forms of stimulus-independent cognition serve some psychological purpose in the same way as goal-directed stimulus-independent thought might), and (ii) overcome a potential impasse that would otherwise be experienced by the system. A mechanism of this kind would be involved in optimizing performance in many situations, from ones requiring exploration [34] to those involving task- or attentional-switching [35] or behavioural organization, particularly over long periods of time [36].

Evidence in support of the gateway hypothesis

If rostral PFC does support the kind of SAG described above, a series of predictions about the patterns of empirical findings might follow. We will now outline the most obvious of these, and briefly describe the data that relates to them (see Refs [15,16] for further explanation).

Prediction 1: Lesion effects

Lesions to rostral PFC should cause relatively isolated deficits on tasks that make unusual demands for either SO or SI attending. Furthermore, there is likely to be: (i) mild attenuation of performance across a wide range of tasks because we assume that many tasks might infrequently make unusual attentional demands, plus (ii) more marked impairment across classes of situation regardless of the precise characteristics of stimuli or the individual processing operations that are being performed on them (see Ref. [19] for definition of 'operations').

Evidence

As we have noted above, rostral PFC lesions typically do not cause widespread cognitive decline, at least as assessed by most of the standard neuropsychological tests currently in use, even traditional tests of 'frontal lobe function' such as the Wisconsin Card Sorting Test, cognitive estimation, proverb interpretation, verbal fluency, or Tower of London test (reviewed in Ref. [5]). We presume that the reason for this is that although they might involve other supervisory attentional system processes, they present situations to the participant that are well-specified (i.e. there are well-established links between central representations and contention scheduling (CS), and/or between CS and SAS structures). However, rostral PFC lesions do seem to cause impairments in self-initiated multitasking and other 'ill-structured' situations (e.g. Refs [6–9]; Figure 1, panel 1). These situations have two characteristics in particular that mean that they would stress the SAG: (i) they require one to 'bear in mind' or 'reflect upon' (i.e. involve SI attending) self-generated and maintained goals and constraints while interacting with the world (SO attending); (ii) the correct way of behaving is underspecified, which would be expected to trigger SI attending in healthy individuals, for example, a 'what do I do now?' feeling [see situations (i) and (iii) in which the SI attending system is involved, outlined above]. In addition, there is also some evidence that medial rostral lesions can affect performance on simple tasks that stress the maintenance of attending (i.e. require unusual levels of SO attending) [11]. This is also consistent with prediction 1.

Prediction 2

In neuroimaging experiments, bespoke tasks that test a participant's ability to concentrate on external stimuli, when contrasted with tasks that require concentrating 'on the thoughts in one's head' should activate anterior medial rostral PFC. The opposite contrast (i.e. tasks requiring SI attending versus those requiring SO attending) should activate lateral aspects of rostral PFC.

Evidence

Gilbert *et al.* [37] invented three tasks that could be performed either using stimuli that were presented by visual display (i.e. requiring stimulus-oriented attending), or by performing the same tasks 'in one's head' only (i.e. stimulus-independent attending). Consistently, across all three tasks, medial rostral PFC exhibited sustained increased activity when participants attended to externally presented information (for paradigm details see Figure 3a; for results see Figure 1 panel 4). By contrast, right lateral rostral PFC exhibited transient activity when subjects switched between these phases, regardless of the direction of the switch. A second fMRI study [38] then demonstrated that this anterior medial rostral PFC region could also be activated in simple reaction time (RT) situations. Moreover, this activation was performance-related (i.e. increased activation was associated with faster reaction times), ruling out an account of this finding in terms of task-unrelated processes such as 'mind-wandering' (for paradigm see Figure 3b; for results see Figure 1, panel 5a,b). This second experiment also showed that lateral rostral PFC was activated bilaterally during periods of extended stimulus-independent cognition (i.e. not only at SI/SO attending switch-points) [7]. Burgess *et al.* then showed that some regions of rostral PFC, while sensitive to SI versus SO attending demands, are insensitive to what

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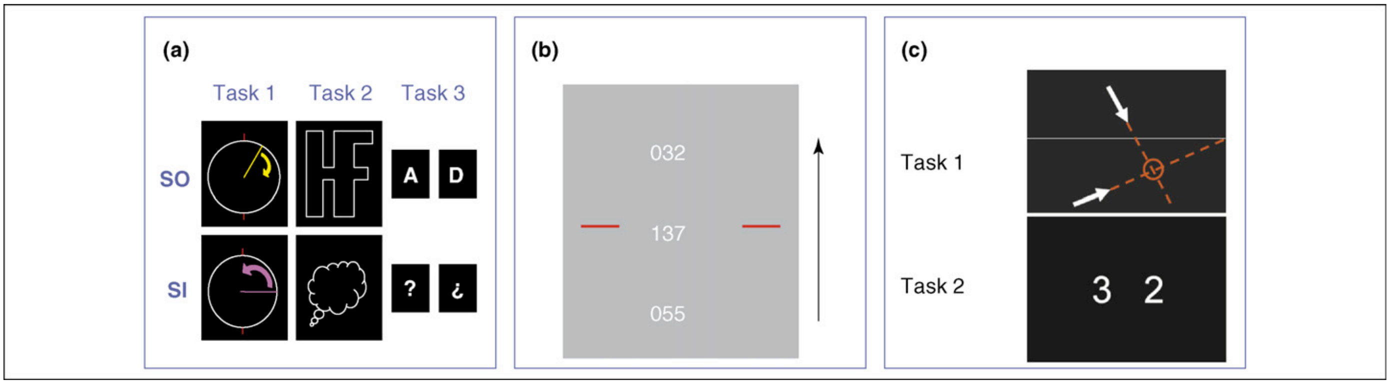

Figure 3. Methods of direct testing of the gateway hypothesis. **(a)** Example stimuli used by Gilbert *et al.* [37]. Three tasks were administered under two conditions [stimulus-oriented (SO); stimulus-independent (SI)] in a conjunction design. In the SO conditions, stimuli were presented to subjects (Ss); in the SI conditions the participants had to continue the task 'in their heads'. For instance in the SO condition of task 3, participants were presented with letters of the alphabet that skipped through the sequence +2 at a time, and they were asked to judge if the letters were composed only of straight lines (as is 'A'). In the SI condition they were required to carry on doing this task 'in their heads', and the stimuli were replaced with question marks. **(b)** Example stimuli used by Gilbert *et al.* [38]. Numbers scrolled steadily up the screen during four conditions: (i) simple reaction time (press a key when the screen flashes); stimulus processing (SP) (are the subsequent two numbers the same?); stimulus-Independent attending (SI) (count increments of 7 in head and report the total at the end of the trial block); SI + SP = combined condition (is the presented value the last digit +7?). **(c)** Example stimuli used by Burgess *et al.* [7]. Two tasks were administered under four conditions in a conjunction design. Task one required participants to make judgments about the relative position of arrows on a screen (e.g. would the intersection of the two arrows be below or above the horizontal line?). Task two involved number processing. The four conditions were (with examples for the number task): (i) Basic attention: alternatively press left or right button when any stimulus appears; (ii) SP: 'press the key that is on the same side as the larger number'; (iii) SI + SO, for example, 'is the sum of the numbers smaller or larger than the previous sum?' (iv) Rehearsal: 'Is the number on the left smaller or larger than the previous number on the left?' Please note that for experiments 2 and 3, the stimuli witnessed in all conditions are identical, and the methods of responses (finger key presses) are similar or identical within all studies. It is only the instruction that changes (see also Refs [36,45]).

it is that is being attended to (in tasks stressing SO attending) or the precise form of the SI mental experience [7]; for results see panel 6 in Figure 1, paradigm details in Figure 3c.

Prediction 3
Tasks in the literature that, putatively, should require the operation of the SAG should show a predominance of rostral PFC involvement (when compared with tasks that do not). Such tasks would typically include, for example, multitasking paradigms, prospective memory ones, and those kinds of episodic memory tasks that make a high demand upon memory control processes (Figures 1 and 2).

Evidence
The relationship between episodic memory retrieval and rostral PFC activation in neuroimaging experiments is well established (e.g. Refs [1,39,40]), and this relationship seems particularly strong for tasks that involve complex control processing, such as context memory (e.g. Refs [41–43]; Figure 1, panel 3) and prospective memory (e.g. Refs [36,44–46]). Indeed, virtually all neuroimaging studies of prospective memory have implicated rostral PFC, particularly in the maintenance of intentions (e.g. Figure 1, panel 2). As might be predicted by the gateway hypothesis, at least some of these activations are remarkably insensitive to the precise demands of the paradigm (e.g. within prospective memory tasks, either stimuli, cues, or to-be-performed actions [45,46]; within context/source memory, whether one is recalling the temporal order or spatial position of stimuli ([41], see Ref. [7] for review).

There are few neuroimaging studies that use multitasking paradigms that are similar to those used with patients with rostral PFC damage (e.g. Ref. [6]). However, some procedures that bear a family resemblance do show rostral PFC activations (e.g. Refs [36,47,48]).

Prediction 4
Across a wide range of individual types of test that activate area 10, there should be a relation between operation of the SAG and differences in RT to stimuli. If anterior medial rostral PFC activation indexes the operation of a 'fast route' at the central representation to contention scheduling level (i.e. automatic processing), then in imaging experiments where activation of this region is found (relative to a comparison task), it is likely to be accompanied by relatively fast RTs. By contrast, if lateral rostral PFC activation indexes a demand for the kind of iterative processing that the model assumes is required for N-order processing (i.e. beyond simple zero- or first-order algorithms; see Glossary, and Box 1 for examples), then reaction times to stimuli in the tasks that have provoked the activation are likely to be longer, relatively, than whatever comparison task was used in the experimental design (i.e. because it is likely that there will have been less SI attending required by the comparison task).

Evidence
Gilbert *et al.* [49] have shown, using meta-analysis, that RTs during tasks that provoke lateral area 10 activations tend to be slower than RTs during whatever control task is used. Furthermore, RTs during tasks that provoke medial area 10 activations tend to be as fast, or faster, than during the comparison task (Figure 4a). This pattern occurs regardless of the type of task under study and, thus, seems to be a general principle of area 10 neuroimaging findings. Moreover, the effect is so strong that it can even be seen within the context of a single experiment (Figure 4b,c).

Summary of aims
We have sought to find a principle for the organization of rostral PFC that cuts across domains of cognition (e.g. memory and perception) and behaviourally defined

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Box 1. The stimulus-independent versus stimulus-oriented distinction: definition of constructs

The gateway hypothesis makes a distinction between attending and cognition. Attending refers to the allocation of processing resources that are required to effect cognition, which is the transformation of information. Thus, stimulus-independent (SI) attending refers to the attending behaviour that is required, in certain situations, as a prerequisite to stimulus-independent cognition. SI attending is when our attention is 'directed towards' the thoughts in our head rather than the environment, as when we are, for example, 'mind-wandering', 'actively thinking something over' or 'thinking up something new'. Stimulus-oriented (SO) attending by contrast is where one's attention is turned towards stimuli being experienced through the senses and external to the body. This can occur in the presence of stimuli (e.g. reading a book, watching the television, listening to a conversation), or in the absence of it (e.g. when one is waiting in anticipation for something to occur). All mental experiences could, in theory, be classed as composed of varying amounts of SO or SI cognition, so the distinction is best made in relative terms, and experimentally one might consider, for instance, as a metric varying the proportions of time that a participant is engaged in SO or SI attending over a given time period. We have listed below a series of situations that vary in these demands, with increments of increase in proportional demand from SO to SI attending. These are for illustrative purposes only: (i) Studying, closely, the physical details in the picture of a surfer in Figure 2. (ii) Thinking about that picture once you have turned the page, but have not yet looked at anything else. (iii) Recollecting the picture after you have considered some other stimulus, or thought about something else (i.e. free recall, not e.g. recognition or cued recall). (iv) Imagining a (different) image of a surfer, but one that you have previously witnessed, when asked to think of 'Hawaii'. (v) Imagining an image of a surfer that one has previously seen, independently of any cue (e.g. mind-wandering). (vi) Spontaneously imagining an image of a surfer when one has never before seen an image of a surfer. (vii) Ruminating on the psychological significance of imagining an image of a surfer when one has never before seen an image of a surfer. Only in situation (i) is the relative demand for SO attending likely to be higher than for SI attending. Note: none of these situations require a meaningful response, which usually necessitates some momentary SO attending through engagement with the external world.

function (e.g. task-switching). At the outset of our studies it was not clear that this would be possible. Indeed, one plausible model for the organization of rostral PFC (area 10) was that sub-regions of area 10 might be so highly specialized for different functions that no higher-level principle could be found that linked anatomical structure to cognitive process. However, our studies have shown that this seems not to be the case. Instead, our findings suggest that at least some regions of rostral PFC are specialized, along a medial-lateral dimension, for differences in requirements for stimulus-oriented or stimulus-independent attending. On the basis of these results, we suggest that rostral PFC might play a crucial role in a processing system that effects gain between these attending modes, when routinized determination of the relative values would be inadequate for optimal behaviour. We maintain that many neuroimaging findings of area 10 activation can be explained by the differences in demand the experimental and control tasks have made for SO or SI attending. Moreover, the cognitive deficits in humans seem to be consistent with such a view (i.e. it is those situations that require particularly substantial involvement of the SAG that are impaired).

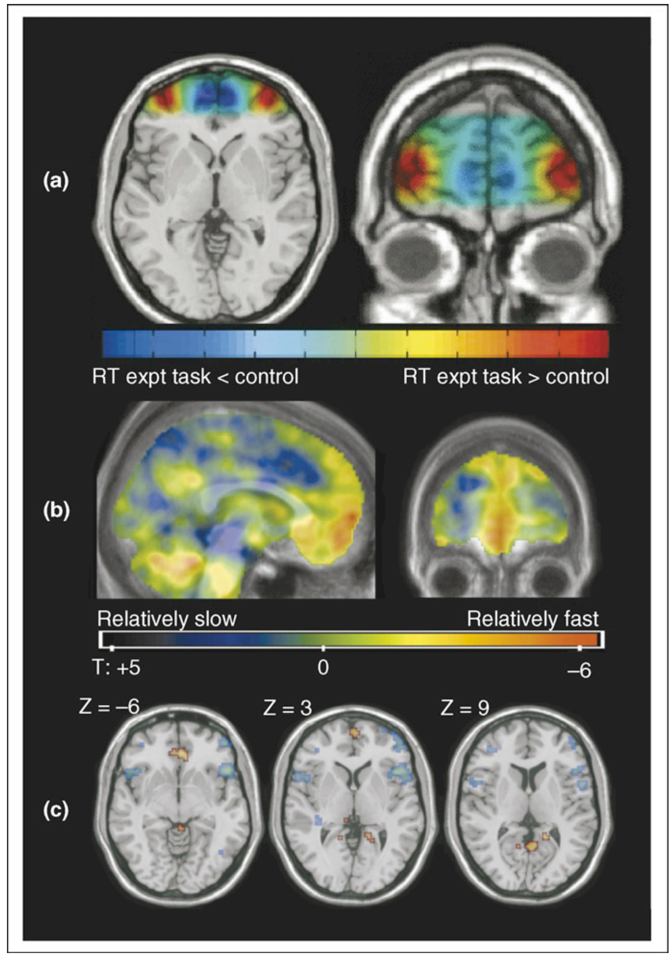

Figure 4. Medial anterior rostral PFC activation is associated with relatively fast reaction times, and lateral rostral PFC activations with relatively slow ones. **(a)** Results from the neuroimaging meta-analysis by Gilbert *et al.* [49]. Across a wide range of different types of paradigm that had provoked area 10 activations, we found that reaction times (RTs) during those conditions that were associated with lateral rostral activations tended to be longer than whatever comparison task had been used. However, for tasks that had provoked medial rostral PFC activations, RTs tended to be the same or shorter than whatever comparison task had been used. **(b)** Data from Ref. [38]. Unthresholded statistical parametric map illustrating correlations between trial-by-trial variation in RT in a simple RT task and BOLD signal. Yellow or red indicates negative correlations (i.e. greater signal on those trials with relatively fast RT). Blue indicates positive correlations. Results are plotted on sagittal ($x = 0$) and coronal ($y = 54$) slices of the mean normalized structural scan. Variation can be seen both along a rostral–caudal axis within medial frontal cortex, and along a medial–lateral axis within rostral frontal cortex. **(c)** Data from Ref. [7]. These transverse slices demonstrate correlations between reaction times and neural activation within conditions and regardless of task. Regions showing activation increases related to fast RTs are shown in yellow or red, and those related to slow RTs are shown in blue or green.

The gateway hypothesis and other accounts of rostral PFC function

We have outlined some of the evidence that is consistent with the gateway hypothesis. However, how do other accounts fare in explaining the same set of data?

Most existing accounts of rostral PFC function are challenged by (i) the human lesion data and (ii) findings of similar regions of activation within rostral PFC across a wide range of tasks. For instance, some have maintained that rostral PFC is specialized for memory retrieval (e.g. Ref. [50]). However, rostral PFC lesions need not cause impairments on traditional clinical tests of episodic retrieval (reviewed in Ref. [46]). Moreover, rostral PFC activations are also not found more frequently during

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performance of episodic retrieval tasks that during performance of other types of task [15,16]. Similarly, Koechlin and colleagues (e.g. Ref. [47]) maintain that a principle function of rostral PFC is 'branching', and Ramnani and Owen [2] have suggested a 'specific role for this region in integrating the outcomes of two or more separate cognitive operations in the pursuit of a higher behavioural goal'. However, it is not clear how these accounts explain either the fairly specific pattern of deficits in humans with rostral PFC lesions, or why tasks that do not obviously require these processing components appear to activate similar regions of rostral PFC. Similar criticisms can be made about other theories relevant to rostral PFC function (reviewed in Ref. [2]).

But we are not suggesting that these other accounts are wrong. Indeed, the gateway hypothesis is in many ways a synthesis of them. Our view instead is that the situations that these authors describe as requiring processes supported by rostral PFC accounts are, largely, single examples of broader classes of situations that will stress the SAG system. For instance, memory retrieval is one situation where stimulus-independent attending is likely. Similarly, 'branching' tasks share similarities with prospective memory ones, requiring 'bearing something in mind while doing something else'. And 'integrating the outcomes of two or more separate cognitive operations in the pursuit of a higher behavioural goal' also seems likely to be an operation that would require considerable SI attending. Similar cases can be made for other situations where rostral PFC activations have been found, such as those requiring attentional control (e.g. Refs [12,35,51]) or exploratory behaviour [34]): at first sight there often appears to be a high level of similarity between the situations these present to the participant and the characteristics of situations likely to require the SAG system outlined in the theoretical sections above.

There are also more direct consistencies between the gateway hypothesis and other accounts. For instance, Christoff and colleagues variously implicate activation of rostral PFC during 'spontaneous thought processes' and 'evaluating self-generated information'; the gateway hypothesis suggests a way in which both these observations could be simultaneously true (i.e. 'mind-wandering' and evaluating self-generated information are both situations where there are high demands for SI attending). The link we make between medial rostral PFC activation and perceptual attending (particularly accompanied by performance increases) is also consistent with other findings (e.g. Ref. [52]). However, here lies the largest apparent contradiction between this account and some others. There are several studies that have found regions of medial PFC function that show greatest activation during 'mentalizing', and similar tasks (reviewed in Ref. [53]). Because tasks such as mentalizing could be expected to require consideration of internally generated representations, this might seem at first sight contradictory to the position maintained here. However, it now seems most likely that a simple resolution is possible. We have conducted a meta-analysis of functional imaging studies [3] that reported rostral PFC activations, and have found that the medial region associated with mentalizing typically lies more caudal within medial PFC than the very anterior, polar, aspect of medial rostral PFC that we have identified as supporting SO attending. Furthermore, we investigated this possibility directly by experimentation [54]. We designed an experiment where two SO/SI attending tasks of the kind illustrated in Figure 3 were administered under either mentalizing or non-mentalizing conditions in a 2×2 factorial design. As with our previous studies [7], during the SO attending conditions of both tasks, very anterior aspects of medial rostral PFC showed activation increases (in comparison with the SI attending conditions). The mentalizing versus non-mentalizing manipulation also provoked activations in medial PFC, stretching into rostral PFC. However, although the regions activated by

Box 2. Questions for future research

Despite a remarkably fast advance in our understanding of rostral PFC over the past 5–10 years, little is known about this area (approximately, area 10 in humans). Some of the current questions, which if answered, would constitute a considerable advance are:

- What is the developmental course of those functions that are thought to be supported by rostral PFC brain structures, and how does this relate to structural changes?
- Large regions of area 10 appear to be supra-modal. However, are there also sub-regions that are more specifically linked to manipulations involving particular classes of material or sensory input?
- To what extent are the rostral PFC activations found in a wide variety of paradigms indicative of the requirement of those paradigms for the rostral PFC 'attentional gateway'?
- Abnormalities of area 10 have recently been implicated in a wide range of psychiatric, developmental and psychological disorders. Does this relate in some way to dysfunction of the 'supervisory attentional gateway'?
- What is the processing relation between the anterior medial area 10 (SO attending) system and the lateral area 10 (SI attending) system? In many situations, it would seem that they work in concert, with decrease of activity in one system accompanied by increase in the other (e.g. Ref. [36]). But is this necessarily the case?
- Virtually nothing is known about the cognitive characteristics of switching between 'the thoughts in your head' and attending to the outside world. How does this relate to other forms of switching (e.g. task-switching, concept-shifting)? What is the time course of these switches? Are there task-, sense- or material-specific effects?
- The gateway hypothesis suggests a principle for the medial-lateral functional organization of rostral PFC. However, both meta-analysis and direct experimentation from this group and others (e.g. Refs [3,7]) suggest that there might be an additional principle for the functional organization of rostral PFC that runs along a rostral–caudal dimension. For instance, the medial rostral PFC region identified as important for attending to the external environment in our studies is probably anterior to that which is involved in, for example, mentalizing (e.g. Refs [53,54]). What is the principle underlying this organization, are there others, and how might these relate to principles discovered for other regions of PFC (e.g. Ref. [55])?
- The association between SO attending and medial rostral PFC function proposed by the gateway hypothesis appears to run directly contrary to some other views of the functions of this region (e.g. Ref. [56]). Moreover, there are other potentially relevant findings where a synthesis might be possible (e.g. Refs [51,57]). In particular, there is growing evidence for functional specialization within area 10 [3]. However, it is also possible that the use of consistent methodologies, and close examination of assumptions will solve several apparent conundrums (see Ref. [58] for debate). Resolutions of this kind are probably a necessary precursor to further theoretical advance.

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the SO attending and mentalizing manipulations were anatomically close, there was virtually no spatial overlap between them. The region most active during the 'mentalizing' condition was caudal to that most active during the 'SO attending' condition, as suggested by the meta-analysis.

Limitations of the gateway hypothesis

We think that we have discovered an important information processing capacity that is supported, at least in part, by rostral PFC (i.e. the SAG). Moreover, we suggest that the SO/SI distinction might provide one principle for understanding the functional organization of rostral PFC along a lateral-medial dimension. However, we do not suggest that SAG processing resources are the only capacities supported by rostral PFC. Neither do we maintain that our hypothesis provides a processing principle that relates to other anatomical dimensions (e.g. rostral-caudal or ventral-dorsal) within area 10. We have so much still to learn about the functions of rostral PFC (Box 2). However, the considerable body of evidence that has emerged over the past few years suggests that we are entering a period of extremely rapid scientific advance in this area of research. It now seems almost inevitable that these advances will provide such fundamental insights into the highest levels of human cognition and its disorders, and that they will transform the way we think about how information processing is effected in the brain.

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