AN ADAPTIVE CODING MODEL OF NEURAL FUNCTION IN PREFRONTAL CORTEX

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The prefrontal cortex has a vital role in effective, organized behaviour. Both functional neuroimaging in humans and electrophysiology in awake monkeys indicate that a fundamental principle of prefrontal function might be adaptive neural coding — in large regions of the prefrontal cortex, neurons adapt their properties to carry specifically information that is relevant to current concerns, producing a dense, distributed representation of related inputs, actions, rewards and other information. A model based on such adaptive coding integrates the role of the prefrontal cortex in working memory, attention and control. Adaptive coding points to new perspectives on several basic questions, including mapping of cognitive to neurophysiological functions, the influences of task content and difficulty, and the nature of frontal lobe specializations.

There is much evidence that the prefrontal cortex makes a vital contribution to effective, organized behaviour. Patients with prefrontal lesions can show a broad loosening in the structure of thought and action: the normal picture, a coherent sequence of actions and mental activities that allow the achievement of some selected goal, is distorted, sometimes bizarrely, by the omission of crucial components and by the intrusion of irrelevant or interfering material[1,2]. According to the circumstances, the patient might seem mentally passive or inert, or disinhibited and distracted. In formal testing, the result is quantitative impairment in a broad variety of tasks, including picture description[1], SPEEDED RESPONSE CHOICE[3], EPISODIC MEMORY[4], maze learning[5], problem solving[6] and many others. Similarly, functional imaging studies show activation of the prefrontal cortex in many different task contexts. A broad role in effective cognition is also shown by prefrontal activation in conventional tests of 'general intelligence'[7] (FIG. 1).

Although of unquestioned importance, prefrontal functions are particularly difficult to characterize and understand. On the one hand, accounts based on highly specific deficits — such as an impairment of 'delayed response' after frontal lesions in the monkey[8] — seem too restricted to apply convincingly to the broad problem of disorganization in many different forms of behaviour (BOX 1). On the other hand, more general accounts — including concepts such as EXECUTIVE FUNCTION[9], temporal structuring of behaviour[2], control by cognitive context[10] or goal–subgoal selection[11] — can be hard to apply in detail to any specific problem.

Essentially, there are two approaches to understanding broad deficits of the sort associated with prefrontal lesions. The first is to assume that damage to combinations of functionally specialized frontal regions underlies the range of deficits seen after typical lesions. Certainly, this is a plausible view, given the size of prefrontal cortex, and its diversity in terms of cytoarchitecture and patterns of connectivity with other brain structures[12]. The second approach is to assume that, in some frontal regions at least, functions are sufficiently broad to contribute to many different cognitive tasks. This view, in turn, is given plausibility by the extensive interconnections between one frontal region and another, indicating substantial sharing and exchange of information[12].

In this review, the question is considered in the light of evidence from functional neuroimaging in humans and single-unit electrophysiology in the behaving monkey. From imaging results, there is a strong indication

SPEEDED RESPONSE CHOICE
Tasks in which simple stimuli, such as lights or tones, call for speeded keypress or other responses.

EPISODIC MEMORY
The recollection of events in an autobiographical context.

EXECUTIVE FUNCTION
High-level processes that are proposed to organize and control cognitive function.

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that many different types of cognitive demand produce similar broad patterns of prefrontal recruitment. Electrophysiological data explain this result, in part, by showing substantial adaptability of function even at the level of the single neuron[13,14]. These conclusions are captured in an outline model of the role of the prefrontal cortex in working memory, attention and control — the adaptive coding model (see also REF. 15). The model has important implications for the nature of prefrontal specializations, and for the future design of imaging, single-unit and lesion studies. It also explains why it is so difficult to characterize frontal functions in terms of specific cognitive operations; essentially, prefrontal cortex adjusts its function to match the requirements of the particular task undertaken.

Evidence from functional imaging

In early positron emission tomography (PET) studies of human brain function, it seemed that distinct, focal activations of the frontal lobe were produced by such cognitive demands as word generation[16], DIVIDED VISUAL ATTENTION[17] and response suppression[18]. However, as evidence from PET and functional magnetic resonance imaging (fMRI) has accumulated, a different picture has begun to emerge. Certainly, there is some differentiation between frontal activations associated with different mental activities. Dorsomedial activity, for example, has been repeatedly and specifically associated with the processing of social materials[19,20], whereas retrieval from episodic memory is reliably associated with activations towards the frontal pole[21,22]. Accompanying these results, however, is increasing evidence of commonalities in the patterns of frontal activity associated with many quite different cognitive demands.

DIVIDED VISUAL ATTENTION
A requirement to process two or more simultaneous stimuli in a visual display.

Such commonalities have been shown clearly in a recent systematic review[21]. For this exercise, we chose studies in the literature that had, as far as possible, manipulated a single demand in the context of an otherwise identical task. Five demands were considered. First, a common theme in accounts of prefrontal function is the suppression of strong but inappropriate response tendencies. When subjects are asked to name the ink colour of a printed word, for example, there is a strong tendency to read the word itself if this spells the name of a different colour[23]. For our first category, we combined data from six studies that contrasted tasks with and without such strong, inappropriate response tendencies. A second common theme is the role of the prefrontal cortex in the early, subjectively attentional phase compared with the later, more automatic phase of task performance. For our second category, we combined data from five studies that compared early and later phases of a single task. A third theme in the literature is the role of the frontal lobe in working memory; for our third and fourth categories, we combined data from two studies that manipulated the number of items to be retained in a simple working memory list, and, separately, data from three studies that manipulated the length of the working memory delay. Finally, we chose to address a cognitive demand that is less conventionally associated with prefrontal function. For this final category, we selected four studies in which perceptual difficulty was manipulated; for example, object recognition with varying degrees of stimulus degradation.

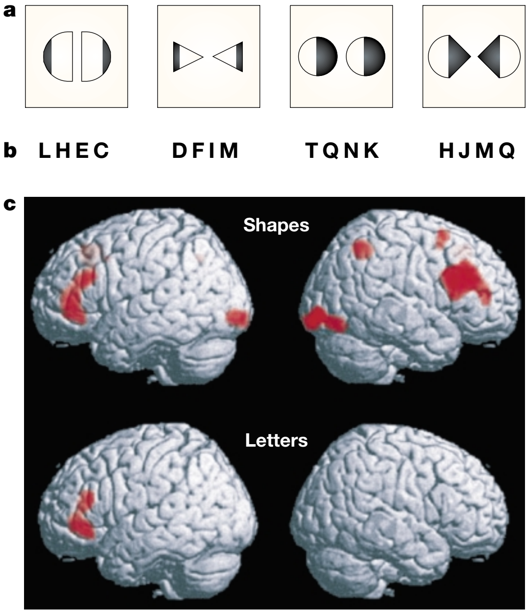

Figure 1 | **'General intelligence' reflects prefrontal function.** If any battery of cognitive tasks is administered to a large group of people, the resulting matrix of correlations is universally positive — to some extent at least, a person doing well on one task is also likely to do well on others[97]. What common factor in different tasks is reflected by this result? Using multivariate analysis, it can be found which single tasks are the best measures of a broad ability to perform well — empirically, some of the best such measures are novel problem solving tasks, which have been used as tests of 'general intelligence'. **a**,**b** | Spatial and verbal examples of problem solving tasks. Here, the task is to find the set of shapes (**a**) or the letter string (**b**) that does not belong with the others. **c** | As shown by positron emission tomography (PET), lateral prefrontal recruitment is a characteristic property of such tasks. The suggestion is that general intelligence is in large part a reflection of prefrontal function. Answers: **a** | Item 3 (asymmetrical); **b** | Item 3 (different alphabetical progression). Adapted with permission from REF. 7 © 2000 American Association for the Advancement of Science.

Combined results from all twenty selected studies appear in FIG. 2. Only activations within the prefrontal cortex are plotted, on views of the lateral (top row) and medial (middle row) surfaces of each hemisphere, and on views of the whole brain from above (bottom left) and below (bottom right). Each point is a focus of peak activation for a direct contrast between high (strong response suppression, early learning phase, long working memory list, long working memory delay, high perceptual difficulty) and low demand, with different colours distinguishing the five demand types.

In anatomical terms, the results provide striking evidence for regional specialization within the prefrontal cortex. On the medial surface, activations are almost entirely restricted to the region immediately dorsal to the corpus callosum, in and around the dorsal anterior cingulate. On the lateral surface, activations

Box 1 | **The delayed response task**

Study of prefrontal function in the monkey has been profoundly influenced by the early finding of deficits in a 'delayed response' task after prefrontal lesions[48]. In this task, a cue at the start of a trial indicates a target location; after a few seconds' delay, the monkey must reach or make an eye movement to that location to receive a reward. Because of the need to retain the target location across a brief delay, the deficit has been interpreted as one of 'working memory'[8,9]. In this context, variants of the delayed response task have been used in highly productive investigations of the neurophysiology[30,36], neuropharmacology[91], development[92] and many other aspects of prefrontal function. Delay itself, however, is not the only important factor in determining task deficits — among other influential factors are interference from distracting sensory inputs[50] and competition from the response made on the previous trial[92]. Lesions of the type that impair delayed responses also impair other complex response choices that involve no element of working memory delay[93]. Undoubtedly, deficits in delay tasks are just one example of a more general cognitive impairment after prefrontal lesions.

are more scattered, but strong clusters are again visible. A more dorsal cluster in each hemisphere lies in and around the posterior part of the inferior frontal sulcus (IFS). A more ventral cluster, plotted in the figure as a set of points just anterior to the Sylvian fissure, in fact extends into the brain along the surface of the frontal operculum, becoming continuous with further activations within the anterior insula. Although further scattered points are seen elsewhere, much of the dorsolateral surface is entirely free of demand-related activations (see brain view from above). Finally, on the whole orbital surface, only occasional points are seen, indicating little response to demands of this sort (see view from below).

In terms of differing demands, however, there is no evidence for regional distinctions. Instead, all five demands show much the same picture of co-recruitment in the dorsal anterior cingulate, the dorsolateral region around the IFS, and the ventral region extending into the frontal operculum. Indeed, this overall pattern can be seen even in individual studies, although it is clearer when data from multiple studies are combined.

Of the two possibilities distinguished earlier, these data support broad functions in selected frontal regions. Although this pattern of activation is especially clear in the above analysis, activations within the same three frontal regions — dorsal anterior cingulate, peri-IFS, and ventral/opercular — appear repeatedly in the imaging literature, in studies of perception, response choice, memory retrieval, language processing, problem solving and many other cognitive domains[21]. So, imaging data lead to a first important discovery — a specific set of frontal regions that are commonly co-recruited in response to a diverse range of cognitive challenges.

Evidence from single-unit physiology

Of course, the imaging method has several restrictions. Might different cognitive demands, for example, be associated with distinct patterns of frontal recruitment on a scale that is too fine for imaging to resolve? Assuming that different primate species are comparable, more detailed information comes from single-unit physiology in the behaving monkey.

Many monkey studies have examined the properties of single prefrontal neurons during a wide range of simple and complex tasks, including perceptual categorization, working memory for objects and spatial locations, rule learning and switching, CROSS-MODAL INTEGRATION and many other forms of decision making. Commonly, recordings are made in a large region of the lateral surface, spanning the principal sulcus and much of the cortex above and below (FIG. 3a). In detail, each of these studies is valuable in analysing the prefrontal response to a specific task demand. Taken as a whole, the work casts light on questions of functional specialization and adaptation.

A first remarkable fact is that, whatever arbitrary task a monkey has been trained to carry out, a substantial proportion of lateral prefrontal neurons will be found to show selective responses to some aspect of that task's events. In early studies, this result was obscured by an unknown degree of sampling bias; neurons that seemed to be task related were investigated in detail, whereas neurons that did not were abandoned without thorough testing. However, even with random sampling, the same result has been found in a number of tasks, including object–saccade association[24], rule switching[25], spatial delayed responses[26], sound–colour matching[27] and visual same–different comparisons[28]. If task-related activity is defined simply as a significant

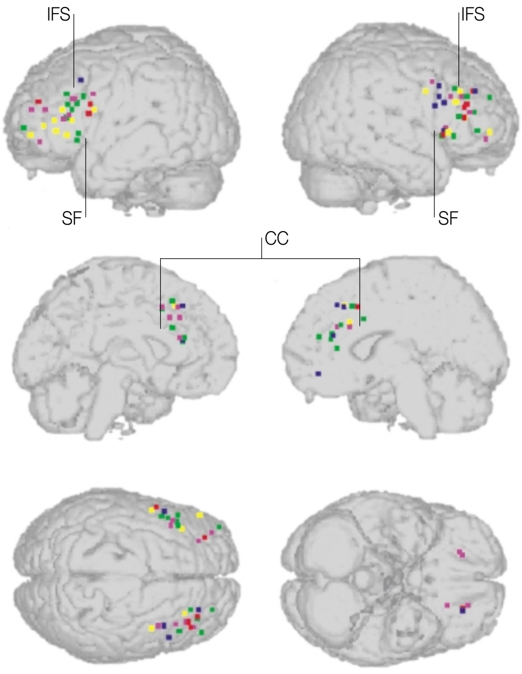

Figure 2 | **Prefrontal activations associated with five different cognitive demands.** Green, response conflict; pink, task novelty; yellow, number of elements in working memory; red, working memory delay; blue, perceptual difficulty. Lateral (top) and medial (middle) views of each hemisphere, together with whole brain views from above (bottom left) and below (bottom right). CC, corpus callosum; IFS, inferior frontal sulcus; SF, Sylvian fissure. Adapted with permission from REF. 21 © 2000 Elsevier Science.

CROSS-MODAL INTEGRATION
A requirement to combine information from different sensory modalities.

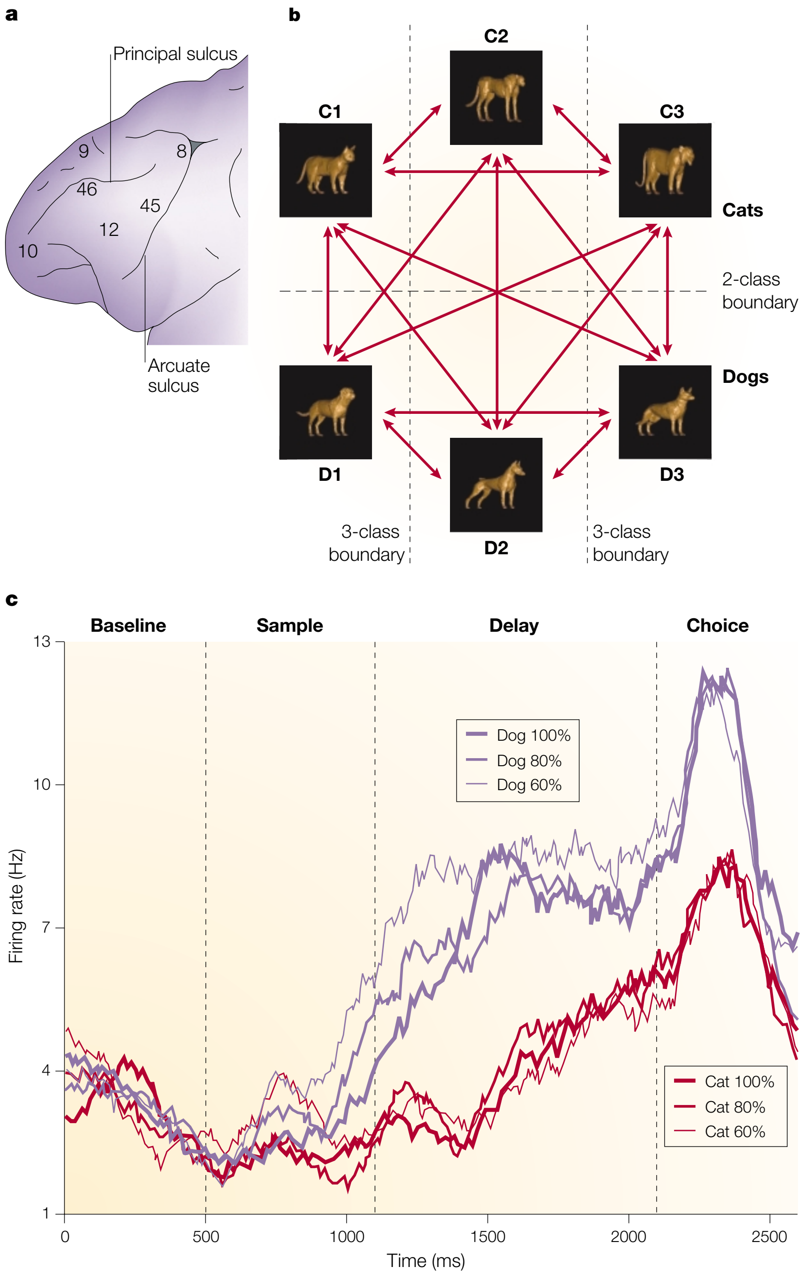

Figure 3 | **Neural responses in macaque prefrontal cortex. a** | Lateral view of macaque prefrontal cortex, with numbers indicating approximate cytoarchitectonic subdivisions (Brodmann areas). **b** | Cat–dog stimuli from REF. 42. Morphing software created blends between all prototype pairs (double-headed arrows), including within-category (for example, C1–C2) and between-category (for example, C1–D1) cases. **c** | Mean response of one neuron to six blends. Vertical lines indicate (left to right) sample onset, sample offset, choice onset. This neuron responded well to all dogs but poorly to all cats, irrespective of proximity to the category boundary. Adapted with permission from REF. 42 © 2001 American Association for the Advancement of Science.

change from baseline in any trial epoch, the proportion of task-related cells in such studies can be close to 100% (REFS 24,25), and even more specific forms of selectivity are frequent. In a two-choice object–saccade association task, for example, Asaad *et al.*[24] found 80% of all cells to be selective for object identity, saccade direction or both; similarly, in a sound–colour matching task, Fuster *et al.*[27] found 29% of all cells to be tone selective.

Second, these selective responses are of many different kinds, capturing different aspects of task events. Some responses reflect the occurrence, identity or location of stimuli in visual[24,29–32] or other[27,33] modalities. Some are motor related, occurring at the time of manual[34,35] or saccadic[24] responses. Many carry information across delays, indicating a role in working memory[30,36]. There is information concerning higher-level aspects of task rules, such as whether a response should be made to matching or mismatching stimuli[28], or whether the task is to match the identity of successive stimuli, associate a visual shape with a specific saccade, or simply remember where a previous stimulus was presented[25]. Cells of the lateral frontal cortex can also carry information on reward state — for example, which reward is available in the current trial block[37] — or respond at the time rewards are given[38].

Third, a given type of neural selectivity — such as a response to a given stimulus or delay event — is typically widely distributed across the lateral frontal surface, with neurons of different types within any given task closely intermingled. To a first approximation (see below), the usual result is that neurons of all types examined in any given study are distributed throughout the recording zone, on dorsolateral, ventrolateral and sometimes even orbital surfaces[28,31,38–41].

A recent experiment by Freedman *et al.*[42] is worth considering in detail. For this experiment, morphing software was used to create stimuli that fell into two general categories: 'cats' and 'dogs' (FIG. 3b). Three species of cat and three breeds of dog were used as prototypes; the software produced linear blends between all possible prototype pairs (FIG. 3b, double-headed arrows), allowing stimuli to vary continuously, either between 'cat' and 'dog' (for example, blends between prototypes C1 and D1), or between two prototypes within the same category (for example, C1 and C2, or D1 and D2). For the main experiment, these stimuli were used to train monkeys in a successive cat–dog categorization task. On each trial, two stimuli — 'sample' and 'choice' — were presented for 600 ms each, separated by an empty interval of 1,000 ms. Monkeys responded to indicate whether the sample and choice came from the same or different categories, ignoring within-category differences.

After training in this task, many prefrontal neurons gave responses that were themselves categorical. For such neurons, activity differentiated between cats and dogs, even those close together across the category boundary, but much less between morphs within a category. An example is shown in FIG. 3c; for this neuron, strong responses were given to all dogs, even those made up of only 60% dog and 40% cat, whereas weak responses were given to all cats, even those made up of only 60% cat and 40% dog. Overall, significantly different responses to cats and dogs were seen in more than 20% of all neurons encountered throughout a broad, largely ventrolateral area of prefrontal cortex.

It is hardly likely that, outside the context of this particular task, more than 20% of prefrontal units act as cat–dog categorizers. Already, therefore, the results point to an important conclusion: in all probability, the

Box 2 | Integrated competition in visual attention

Physiological models of visual selective attention provide a concrete example of the problem of processing coherence. Representations of an object's different properties — its colour, shape, motion, location in the environment and so on — are distributed across multiple, partially specialized regions of extrastriate cortex[94]. But cognitive experiments show that visual objects are attended as wholes: directing attention to an object makes its multiple properties concurrently available to awareness[95]. According to the integrated competition hypothesis[54–56], objects compete simultaneously for representation in multiple extrastriate systems. As an object gains dominance in any one system, its representation elsewhere is supported. The net result is a tendency for multiple systems to converge, giving dominance to the same selected object with all of its properties and implications for action. In part, the prefrontal cortex might have a guiding role in this process[56], giving initial prominence or support to objects of current behavioural significance.

properties of prefrontal neurons are strongly tuned by the particular task that the monkey has learned. To confirm this directly, Freedman *et al.*[42] went on to train one monkey in a new task that was based on the same stimulus set. Now the cat–dog distinction (FIG. 3b, 2-class boundary) was irrelevant; instead the animal had to sort stimuli into three new categories, each based on one cat–dog pair (FIG. 3b, 3-class boundaries). After training on this new task, cat–dog information was now lost from neural responses. Instead, these respected the new category distinctions relevant to the new task that the monkey had learned.

Other experiments show a similar focus on information of specific relevance to current behaviour. In a study by Rao *et al.*[39], monkeys performed a combined 'what–where' working memory task. In different phases of each trial, monkeys retained either target identity or target location. Over a wide region of lateral prefrontal cortex, many single neurons carried both identity and location information. Importantly, when the task required a switch from identity to location, this switch was reflected in the responses of individual neurons, identity information being discarded and location information taken up. Studies of visual selective attention also indicate selective prefrontal representation of attended or task-relevant objects[43–45] and object properties[32] in a visual display.

It is worth emphasizing that most recording studies in the monkey have focused on the middle and posterior parts of the dorsolateral and ventrolateral surfaces. Less is known, for example, about neural properties in the anterior cingulate, although the picture that is beginning to emerge is again one of multiple, intermingled response types, with activity related to stimuli, responses, delays, rewards and other aspects of task events[38,46,47]. Indeed, when lateral prefrontal and anterior cingulate responses have been directly compared, the data have indicated highly similar response properties in these regions[38].

At least for the lateral surface, the electrophysiological results lead to much the same conclusions as does functional neuroimaging. Throughout this region, there is conspicuous neural activity in many different tasks. Such activity produces a dense, distributed description of inputs, outputs, rewards and other relevant events. Importantly, individual neurons are strongly influenced by task context, with a selective focus on information of relevance to current behaviour.

The adaptive coding model

An outline model makes the above conclusions more concrete. This adaptive coding model relates closely to three ideas that are prominent in accounts of prefrontal function. The first is a concern with working memory, in large part based on the deficits in delayed response tasks that follow prefrontal ablations in the monkey[8,48]. The second is a concern with selective attention, reflecting distractibility and the processing of irrelevant inputs in frontal patients[49,50]. The third is a concern with cognitive control, which derives from the disorganization and fragmentation of behaviour in patients with frontal lesions[1]. The adaptive coding model owes much to previous accounts based on each of these ideas (REFS 10,51,52 and, in particular, REFS 14,53). In this model, working memory, selective attention and control are simply three different perspectives on the same underlying processing function.

The central idea is that, throughout much of prefrontal cortex — certainly including much of the lateral surface — the response properties of single neurons are highly adaptable. Any given cell has the potential to be driven by many different kinds of input — perhaps through the dense interconnections that exist within the prefrontal cortex[12]. In a particular task context, many cells become tuned to code information that is specifically relevant to this task. In this sense, the prefrontal cortex acts as a global workspace or working memory[53] onto which can be written those facts that are needed in a current mental program. It is exactly this adaptability that is reflected in the large proportions of frontal neurons that are found to code events in whatever arbitrary task a monkey carries out. The same adaptability is reflected in the imaging finding that the same overall patterns of prefrontal recruitment are associated with widely different cognitive demands.

Such adaptability in itself implies selective attention, or a selective emphasis on relevant inputs and the filtering out of irrelevant inputs. If a given neuron can code different information in different task contexts, it follows that, in any particular context, there is a selective removal of inputs that might drive the cell, but are currently unnecessary. Again, the loss of currently irrelevant stimulus distinctions is seen directly in the single-unit data[39,42,44,45].

Although more speculative, a further idea relates to the familiar view that frontal systems in some sense control or shape task-relevant processing elsewhere in the brain[10,52,53]. The proposal is that, to achieve processing coherence, multiple brain systems share a strong tendency to converge to represent similar or related information[54,55] (BOX 2). Because of this, a highly selective focus on task-relevant information in the prefrontal cortex supports the processing of related information in other systems, including those concerned with the description of sensory inputs, the generation of motor commands, the representation of long-term or semantic

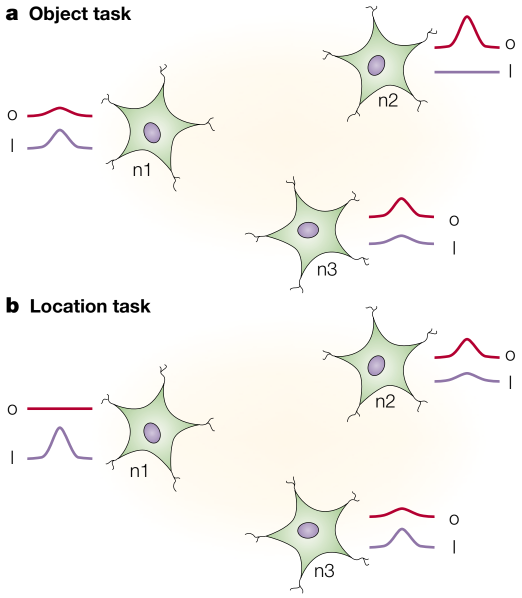

Figure 4 | **The adaptive coding model. a**,**b** | Selectivity of three model neurons (n1–n3) for object (o) and location (l) is indicated by schematic tuning curves; a sharper curve reflects greater selectivity for the indicated dimension. Although neurons vary in relative selectivity for object and location, this variation is also modulated by task context; object selectivity becomes sharper in an object task (**a**) and location selectivity becomes sharper in a location task (**b**).

knowledge, and the assessment of motivational significance. A good example is the suggested role of the prefrontal cortex in the control of visual attention[56] (BOX 2): in multiple extrastriate systems, objects in the visual input compete for representation, and the proposal is that frontal emphasis on a task-relevant object supports dominance of that object throughout the processing network. Subjectively, a selective prefrontal focus on task-relevant information, with its accompanying dominant representation in sensory, motor, memory, motivational and other systems, would correspond to the state of controlled, active attention to this information, or, equivalently, to controlled, active maintenance in working memory. In this way, the prefrontal cortex carries out a central function in configuring a flexible cognitive system to address specific, current concerns.

In FIG. 4, this general view of prefrontal representation is illustrated for the case of working memory for location and object information[30,39,57]. Throughout much of the lateral prefrontal cortex, cells with variable potential for coding location and object information are closely intermingled[39,40]. When object information must be retained in working memory (upper panel), object tuning across the population is enhanced, whereas location tuning is weakened. When location information must be retained, this situation is reversed. As a whole, the population produces a distributed representation, which selectively favours information of current task relevance. As described earlier, exactly this picture of adaptable location–object representation has been shown experimentally across a large region of dorsolateral and ventrolateral frontal cortex[39].

Of course, many central questions are left open by this outline scheme. One of these is how task relevance itself is determined as the prefrontal cortex chooses which information to represent. In simple situations, this process can be thought of in terms of rewards and their use[58]; more broadly, however, detailed world knowledge must be used to establish how facts do or do not bear on the pursuit of particular goals — the central conceptual problem that is addressed in artificial intelligence systems for effective action planning in complex, real-world domains[59] (BOX 3). A second unresolved question concerns the mechanism for achieving processing coherence; in particular, the mechanism underlying frontal control of the processing focus in sensory and other systems[60].

However, for some questions, the implications of the model are already fairly strong. In the next section, this point is illustrated with a discussion of regional prefrontal specializations.

Adaptation and specialization

Much attention has been given in both human and monkey studies to the question of prefrontal regional specialization. In imaging work, certainly, the common aim is to attach specific cognitive interpretations — control of retrieval from episodic or working memory, context setting, error monitoring and so on — to the function of specific frontal regions. On the one hand, the adaptive coding model suggests clear limits to this endeavour. As we have seen (FIG. 4), neurons carrying very different types of information are closely intermingled in the prefrontal cortex, and, even at the level of the single neuron, adaptability is the converse of specialization. On the other hand, adaptability does not imply equipotentiality: neurons undoubtedly differ in their relative potential for coding the many different types of information that the prefrontal cortex can represent (FIG. 4, compare n1 with n2). One obvious possibility is that regional specializations within the prefrontal cortex might be statistical rather than absolute (REF. 61; for a more general proposal concerning statistical specializations in brain function, see REF. 62). Across the prefrontal cortex, there might be a broad distribution of cells with the potential to carry any specific type of information; for example, location information in working memory. For different kinds of information, such as location and object, these distributions will overlap, even down to the level of the single neuron (FIG. 4); but these overlapping distributions might have different shapes and, in particular, different peaks or regions of maximal sensitivity.

This view is highly consistent with single-unit data. In one important study, Ó Scalaidhe *et al.*[63] measured face and object selectivity throughout a large region of the monkey's lateral and orbital frontal cortex. If analysis was restricted only to the most highly selective cells, a strong concentration was found on the ventrolateral surface, the region that receives direct afferents from inferotemporal cortex. However, as selection criteria were relaxed, increasing numbers of face- and object-selective cells were found to be distributed elsewhere throughout the recording region. These data directly show a broad

Box 3 | Coherence and relevance in complex behaviour

The problem of determining task relevance is well illustrated by Luria's[1] insightful analyses of impairment in frontal patients.

"These patients are unable to systematically analyse the conditions of a problem and to select the important connections within it … The selective system of operations that normally successively leads to the solution of the problem disintegrates and is replaced by a series of isolated, fragmentary connections, not subservient to the general plan and without a clearly defined hierarchical structure."

Good examples come in the solution of arithmetic problems: "Complex problems, such as 'A son is 5 years old; in 15 years his father will be twice as old as he. How old is his father now?' are completely beyond the grasp of such patients. Without listening to the conditions, they at once begin to make such calculations as 15 × 5 = 75 or 3 × 15 = 45". Such cases illustrate the potential for irrelevant operations in constructing a sequence of behaviour. The problem is to focus on just those aspects of the situation that, when adequately recognized, have a bearing on the intended goal and allow it to be reached.

Much work in symbolic artificial intelligence has been devoted to complex action planning of this sort (for example, REF. 59). As this work makes clear, the problem is one of effective use of semantic memory — it is knowledge of the world that dictates how multiple facts and actions bear on the intended goal, and so which paths to pursue and which to avoid. According to current conceptions, semantic memory is in large part a temporal lobe function[96]. The implication is that frontal–temporal interaction must have a basic role in the process of selecting relevant facts and actions for inclusion in a current task representation.

distribution of neurons carrying some face and object information, but with a focused, ventrolateral peak. In a study that compared location and object information in working memory, Rainer *et al.*[40] directly confirmed the presence of overlapping regions of selectivity for these two types of information, but found a higher frequency of location-selective cells in the posterior part of the recording area, approaching the arcuate sulcus. In a successive same–different matching task, with trial-by-trial cues indicating whether the monkey should respond to matches or mismatches, Wallis *et al.*[28] showed similar rule (match versus mismatch) and object selectivity across dorsolateral, ventrolateral and orbital surfaces, but again with statistical differences (including higher incidence of object selectivity on the ventrolateral surface) from one region to another.

Relative rather than absolute specialization between frontal regions is also the conclusion most consistent with lesion data. In human lesion studies, evidence for different patterns of deficit associated with different prefrontal regions is actually remarkably scant, being all but restricted to a few cases of hemispheric differences[64], and differential deficits after orbital and lateral lesions[65,66]. Potentially, monkey studies should be clearer, as lesion locations are better controlled; but here too, full-scale double dissociations are the exception rather than the rule. For example, despite some evidence of stronger spatial deficits after dorsolateral lesions, and stronger object deficits after ventrolateral lesions[67,68], the broad picture is of some deficit on both types of task after either type of lesion[67–69].

The view that regional specializations are statistical rather than absolute has strong implications for the interpretation of imaging data. According to this view, results will depend jointly on the level of demand imposed by the task — and so the strength of neural recruitment — and on the statistical power of the experiment. With low demand or low statistical power, the active region observed might be restricted only to the peak of the underlying neuronal distribution. Here, the conclusion will favour strong regional specialization. However, with greater demand or power, the full distribution might be made visible. In this case, the conclusion will favour overlapping frontal recruitment for different types of demand.

This pattern is clearly evident in imaging studies of working memory. There is some evidence that prefrontal recruitment is stronger in the left hemisphere if materials are verbal[70]. However, such specialization is far from absolute; although weaker, activation is also seen in homologous right hemisphere regions, themselves strongly activated when materials are non-verbal[70]. Results such as these are strongly consistent with a statistical view of hemispheric specialization, cells that code verbal information being most common on the left, but also present to some extent on the right. More generally, activation in several regions of frontal and posterior cortex becomes stronger with increased working memory demand, leading to increasing overlap of activation associated with different memory materials[71]. Along related lines, it has been proposed that episodic memory retrieval is associated specifically with right frontal recruitment when demands are low; however, with higher demands, a fuller pattern of bilateral recruitment might emerge[72].

Such ideas might also help to explain evidence for frontal adaptability after damage. As early as three days after a stroke affecting the left inferior frontal gyrus, a verbal task that usually recruits this region can instead produce homologous activation on the right[73,74]. Such adaptability is easily comprehensible if the full distribution of relevant cells extends to both hemispheres, but with a particular focus on the left. When the left hemisphere is intact, it might be the main focus seen in an imaging study. However, when it is damaged, task demands will not be satisfied without stronger recruitment of further relevant cells on the right. Consistent with this interpretation, some control subjects show weak right-sided recruitment in addition to dominant activity on the left[74].

Of course, this general view permits some cases of relatively strong dissociation. In the monkey lesion literature, some of the clearest double dissociations come from comparisons between large lesions of the orbital and lateral surfaces[75,76]. In the imaging literature, as we have seen, simple cognitive demands produce a pattern of strong lateral but only occasional orbital recruitment (FIG. 2); instead, orbital activations might be associated with the processing of emotional[77] and motivational[78,79] materials. Single-unit data are less clear: although reward-related activity is certainly one prominent property of orbitofrontal neurons[80–82], some direct comparisons between orbital and lateral recordings have shown similar kinds of reward-related and other responses[28,82]. Further direct comparisons of this sort are needed; meanwhile, the data as a whole support relatively strong differentiation between lateral and orbital functions.

One particularly significant question raised by the imaging data concerns comparative function in lateral, opercular and anterior cingulate regions. Do all three of these show similar adaptive coding properties or, despite their common co-recruitment, do they make essentially different contributions to cognitive function? Hints of such differences already exist in the imaging literature[83,84], and are likely to be developed in future work.

Future directions

The lack of specificity in many models of prefrontal function reflects the breadth of cognitive deficits associated with frontal lesions. Adaptability helps to explain this; in different contexts, the prefrontal cortex might assist in many different cognitive operations. The adaptive coding model, for example, cannot generate detailed predictions about exact error types to be expected after prefrontal damage. At the physiological level, however, it is more specific, with fairly direct implications for how future questions can be formulated and addressed.

As we have seen, imaging studies show much the same patterns of prefrontal recruitment in association with many different kinds of cognitive demand. When this pattern is seen in any individual study, it would seem to be inappropriate to interpret this in terms of that particular study's demand. Instead, the results probably reflect an adaptation of general prefrontal mechanisms to the specific task context. Similarly, any single-unit study is likely to find large proportions of lateral prefrontal units showing task-related responses. Again, the interpretation should not be in terms of specific frontal involvement in these particular cognitive operations; rather, these data should be viewed as an adaptation of neural properties to this particular task's requirements. On the whole, the adaptive coding model argues against simply extending these common findings to an ever-expanding list of further task domains.

Instead, the model emphasizes other research questions. One, as we have seen, is the nature of adaptability itself. In monkey experiments, for example, we need to know the relative roles of long-term learning versus short-term task context in determining neural properties. Do experiments show high proportions of task-related neurons because the same task has been learned over many months, or because the monkey is carrying out this particular task at the moment the recordings are made? To answer such questions, studies need to be made of how prefrontal responses develop through successive stages of training[85], and how they alter with a switch between tasks[25] or attentional sets[44,45]. Certainly, more data are needed to support the most basic prediction of the adaptive coding model — that single frontal neurons will vary widely in the information that they code from one task context to another.

The statistical view of prefrontal regional specialization has strong implications for how such specializations should be studied. In imaging, comparisons between tasks might profitably be made at various levels of demand; as we have seen, the strong possibility is of focused peak activities at low demand, evolving into a pattern of largely overlapping activity at higher demand. In electrophysiology, statistical specializations can best be seen by a direct quantitative comparison of population properties in different prefrontal regions[28,63].

More broadly, quantitative comparisons might also be crucial in comparing prefrontal and other regions[86,87]. Although this review emphasizes adaptability in prefrontal responses, such adaptability is also, to some extent, a property of many — perhaps most — other brain representations. Selective emphasis of task-relevant information, for example, is seen in attentional modulations of neural response throughout the visual system[56], at least as early as the primary visual cortex[88]. What then is the special contribution of the prefrontal representation, leading to such a key role in overall behavioural coherence? Several possibilities immediately come to mind. In early visual areas, for example, suppression of irrelevant information is predominantly local[89], being strongest when relevant and irrelevant inputs fall within one cell's receptive field. In the prefrontal cortex, such suppression could be more global, extending to inputs in different hemifields, or perhaps even in different sensory modalities. Other possibilities are that the prefrontal representation of relevant information is particularly stable in the face of irrelevant, distracting inputs[90]; or that it can adapt more quickly as task context changes. Formulating and testing such hypotheses will be a particularly important step in developing the adaptive coding idea.

Interestingly, such approaches point to a view of the prefrontal cortex not so much as the seat of particular cognitive operations, but as a resource that gives such operations greater focus, power or flexibility. In any given experiment, the challenge is then to separate the general from the specific — to deduce general principles of prefrontal function from its contribution to one particular sample of effective behaviour.

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