

---

# The neural correlates of consciousness: an analysis of cognitive skill learning

---

**Marcus E. Raichle**

*Departments of Radiology, Neurology and Neurobiology, Washington University School of Medicine, St Louis, MO 63110, USA  
(marc@nbg.wustl.edu)*

This paper presents a functional brain-imaging strategy designed to isolate neural correlates of consciousness in humans. This strategy is based on skill learning. In the example presented (rapidly generating verbs for visually presented nouns), a cognitive skill is examined before and after practice. As shown, there are marked qualitative differences in the neural circuitry supporting performance of this task in the naive and practised state that include, importantly, both increases and decreases from the baseline activity of the brain.

**Keywords:** imaging; human; consciousness; resting; activation; deactivation

## 1. INTRODUCTION

Two components of human conscious behaviour are 'content' and 'arousal' (Plum & Posner 1980). One of the great challenges of modern neurobiology is to identify the brain systems responsible for these components. As Damasio (1995) has recently stated: '... knowing how [the brain engenders consciousness], to a considerable extent, requires that we first know where'.

Much work points to systems ascending from the reticular core of the brainstem via the thalamus to the cortex as responsible for arousal or alert wakefulness (Steriade 1996*a,b*). We are much less certain, once alert wakefulness has been achieved, which cortical systems are responsible for the content of our consciousness. One of the difficulties in identifying these cortical systems is distinguishing them from those concerned with the many non-conscious cognitive, attentional and emotional processes that occur in support of our conscious experiences. Several approaches have been used.

One approach is to examine patients with lesions that deprive them of some aspect of their normal conscious experience. Typical of such an approach is the study of patients with blindsight (Weiskrantz 1986, 1997). Such patients, fully awake and otherwise alert, have lost the conscious perception of visual information presented to their blind hemifield. However, information entering the blind hemifield still influences behaviour. The inference to be drawn is that the area of the brain damaged by the lesion contributes to the content of conscious experience.

A second approach is to examine normal activities in which consciousness is transiently suspended. Francis Crick and Christof Koch have provided a recent review of this approach (Crick & Koch 1998). A typical experiment might involve an analysis of the suppression of conscious visual experience during eye movements or so-called saccadic suppression (Bridgeman *et al.* 1994). During saccadic suppression, visual perception is suspended yet information presented during this period of

time influences behaviour. By identifying changes in the neural circuitry that occur when a conscious visual perception is momentarily suspended, one would hope to identify regions that contribute to conscious experience. Functional brain imaging with positron emission tomography (PET) has recently been used to identify changes during saccadic suppression in humans (Paus *et al.* 1995).

William James once aptly said, 'habit diminishes the conscious attention with which our acts are performed' (James 1890). This comment captures the essence of a third approach. In some ways analogous to the second, this approach would be to identify the brain systems supporting a task when it is novel and effortful and compare these systems with those engaged when the task is routine and reflexive. The performance demands of such a task must necessarily be sufficient to require conscious attention (or 'willed action' (Frith *et al.* 1991)) for its initial performance. The brain systems unique to the novel state, if identified by comparison with the practised state, then become candidate systems necessary for conscious experience.

Because tasks involving motor as well as cognitive skills can be transformed from reflective, effortful tasks to reflexive, seemingly effortless tasks within a short period of time (Petersen *et al.* 1998), it is feasible to employ this third approach together with modern functional imaging techniques. We already know from such functional imaging studies in normal humans that this transformation is accompanied by dramatic changes in the underlying brain circuitry concerned with the task (Raichle *et al.* 1994). These transformations provide important insights into those brain systems concerned with conscious elements of naive task performance.

It is the purpose of this paper to explore the use of this approach in the context of a simple word-reading paradigm involving cognitive skill learning in normal human subjects. As will become apparent, the results present a complex picture of widely distributed change

(both increases and decreases) in the activity of brain systems uniquely associated with naive task performance. The richness of the information provided should stimulate, as well as constrain, theories about brain systems serving consciousness.

## 2. THE PARADIGM

Studies of word reading have played a central role in functional brain-imaging studies of language over the past decade (for recent reviews, see Fiez & Petersen (1998), Posner & Pavese (1998)). This work has benefited from the large amount of information already known about this skill (for review, see Rayner & Pollatsek (1989)). These extant behavioural data on word reading have provided the basis for the design of many imaging experiments with both PET and functional magnetic resonance imaging (fMRI).

Beginning in the 1980s, the author and his colleagues Steven E. Petersen, Michael I. Posner, Peter T. Fox, Julie Fiez and Mark Mintun began their own imaging and behavioural experiments of word reading (Petersen *et al.* 1988, 1989, 1990; Raichle *et al.* 1994; Shulman *et al.* 1997b). It is from these published experiments that the data to be presented in this paper have in part been culled.

A key feature of the experiments to be discussed in this paper is their hierarchical design. In concert with most other functional imaging studies, the strategy here compares images of blood flow obtained with PET in a control state with those obtained when the brain is engaged in a task of interest (for a more detailed review of the strategy and its physiological basis see Raichle (1998)). The five behavioural states include: (1) awake, alert with eyes closed performing no task; (2) maintaining visual fixation on a television monitor containing only a fixation point; (3) maintaining visual fixation on a television monitor while common English nouns are presented just below the point of fixation; (4) reading aloud the nouns as they are presented; and (5) speaking aloud an appropriate use or verb for each noun as it is presented. In the initial experiments (Petersen *et al.* 1988, 1989) the words were presented 60 times per minute and were on the monitor for 500 ms. In the later experiments (Raichle *et al.* 1994) the words were presented 40 times per minute, again for 500 ms each. English was the native language of the subjects and they were all skilled readers. The behavioural-state subtractions to be discussed in this paper include  $2 - 1$ ,  $3 - 2$ ,  $4 - 3$ ,  $5 - 4$  and  $5_{\text{practised}} - 5_{\text{naive}}$ .

## 3. OBSERVATIONS

Figure 1 illustrates, in horizontal sections, the areas of the brain that increase their activity (i.e. blood flow) in association with incremental increases in the complexity of a simple word-reading task. Figure 2 is a sagittal representation of the information in figure 1 and more clearly depicts the changes occurring along the midline in parietal and frontal cortices.

As shown in the first row of figure 1, opening the eyes and maintaining fixation on a small crosshair on an otherwise blank television monitor results in activation of the visual cortex compared with resting quietly with eyes

closed. The images in the second row of figures 1 and 2 represent those additional areas of the brain that become active when common English nouns appear on the screen. The subjects' instructions were simply to maintain fixation. Multiple areas within visual cortices become active when words are presented even though no specific processing of these words has been requested. Much effort has been devoted to an analysis of changes such as these (Fiez & Petersen 1998; Howard *et al.* 1992; Petersen *et al.* 1990; Price *et al.* 1994, 1996), but the results have so far been inconclusive.

The images in the third row of figures 1 and 2 reflect those areas of the brain associated with the motor aspects of reading words aloud. Not surprisingly, these include the primary motor cortices bilaterally, the supplementary motor cortex (best seen along the anterior midline in figure 2) and the paramedian cerebellum. There was also prominent activity over Sylvian-insular cortices bilaterally (figure 1, row 3,  $z=20$ ).

Finally, the images in the fourth row of figures 1 and 2 reflect those additional areas of the brain active during verb generation. These include the anterior cingulate cortex (best seen in figure 2), the left prefrontal cortex, the left temporal cortex and the right hemisphere of the cerebellum. The latter finding was a particular surprise because the subtraction producing this image had eliminated all of the motor aspects of speech production.

Reviewing all of the changes in figures 1 and 2 it is possible to appreciate those associated with the perfected skill of word reading (i.e. the first three rows) and those changes associated with the much more difficult and novel task of verb generation. It should be noted that all subjects performing verb generation initially found it difficult. This was reflected in a much slower voice onset latency and a failure to supply a verb for all nouns in order to keep pace with the task (Raichle *et al.* 1994).

The data presented in figures 1 and 2 illustrate nicely a hierarchical dissection of word reading in terms of regions of the brain increasing their activity in support of the component processes involved. In keeping with the thesis of this paper it would be attractive to assume that areas of the brain added in support of the verb-generation task (i.e. fourth row, figures 1 and 2) become candidates for those concerned with task-associated consciousness. However, before making such an assumption it is important to appreciate, rather more fully, additional changes taking place in brain organization not revealed in these two figures. To set the stage for a presentation of these changes, we should first examine one of the major criticisms of the subtractive logic leading to the images in figures 1 and 2.

The strategy employed in the experiments depicted in figures 1 and 2 was first introduced by the Dutch physiologist Franciscus C. Donders in 1868 (reprinted in Donders (1969)). Donders proposed a general method to measure thought processes based on a simple logic. He subtracted the time needed to respond to a light (say, by pressing a key) from the time needed to respond to a particular colour of light. He found that identifying the colour of the light required about 50 ms. In this way, Donders isolated and measured a mental process for the first time by subtracting a control state (i.e. responding to a light regardless of its colour) from a task state (i.e.

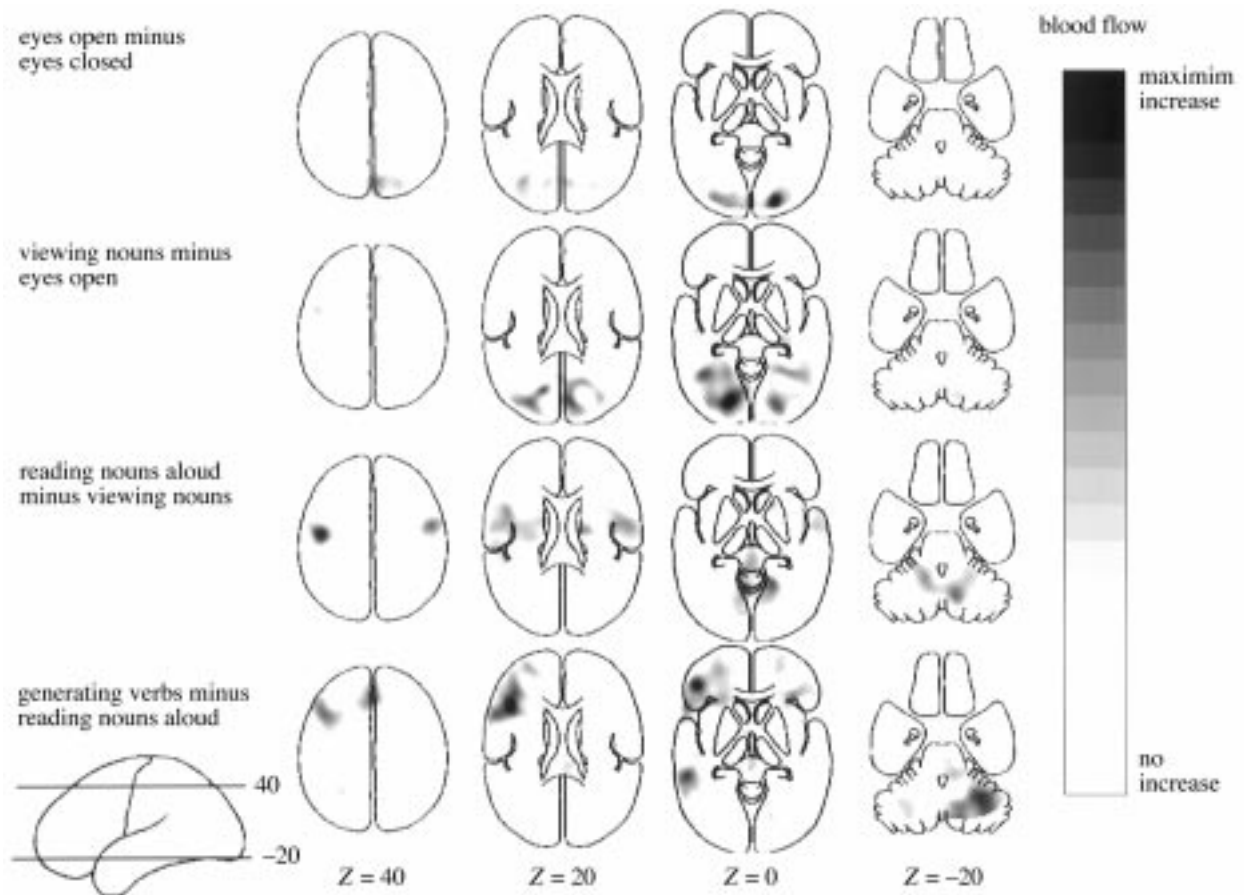


Figure 1. Four different hierarchically organized conditions are represented in these mean blood flow difference images obtained with PET. All of the changes shown in these images represent increases over the control state for each task. A group of normal subjects performed these tasks involving common English nouns (Petersen *et al.* 1988, 1989; Raichle *et al.* 1994). These horizontal images are oriented with the front of the brain on top and the left side to the reader's left.  $Z=40$  indicates millimetres above and below a horizontal plane through the brain marked  $Z=0$  (Fox *et al.* 1985).

discriminating the colour of the light). It is this logic that is now applied in the experiments presented in figures 1 and 2.

One criticism of this approach has been that the time necessary to press a key after a decision to do so has been made is affected by the nature of the decision process itself. By implication, the nature of the processes underlying key pressing, in this example, may have been altered. Although this issue (known in cognitive science jargon as the assumption of pure insertion) has been the subject of continuing discussion in cognitive science, it finds a resolution in functional brain imaging, where changes in any process are directly signalled by changes in observable brain states.

Careful analysis of the changes in the functional images reveals whether processes (e.g. specific cognitive operations) can be added or removed without affecting ongoing processes (e.g. motor processes). This is accomplished by examining the data not only for areas activated during the course of a particular cognitive paradigm but also for those that become deactivated. An analysis of regional deactivations is presented in figures 3 and 4. Figure 4 is a sagittal representation of the information in figure 3 and more clearly presents changes occurring along the midline of the brain in the parietal and orbital frontal cortices. By examining

the images in figures 1–4, together, a much more complete picture emerges of the dramatic changes taking place in the word-reading paradigm under analysis here.

Finally, to exploit fully the paradigm depicted in figures 1–4 for the purpose of identifying candidate regions of the brain concerned with task-related consciousness, it is important to assess the effect of practice on the regions uniquely recruited in the verb-generation task (row 4, figure 1). As we have previously demonstrated (Raichle *et al.* 1994), a brief period of practice on the verb-generation task results in a significant reduction in voice onset latency (i.e. subjects are able to respond more quickly when they see the same noun on multiple occasions). In addition, responses become stereotyped, with the same verb being chosen each time a particular noun is presented. These changes in performance are associated with dramatic changes in the brain regions supporting task performance. The brain changes associated with practice are illustrated in figures 5 and 6. In these two figures it can be seen that the anterior cingulate cortex (and associated medial frontal cortices), the left prefrontal cortex (including the left as well as the right frontal operculum), the left temporal cortex and the right cerebellum (not as well shown; see Raichle *et al.* (1994) for more details), which are all active

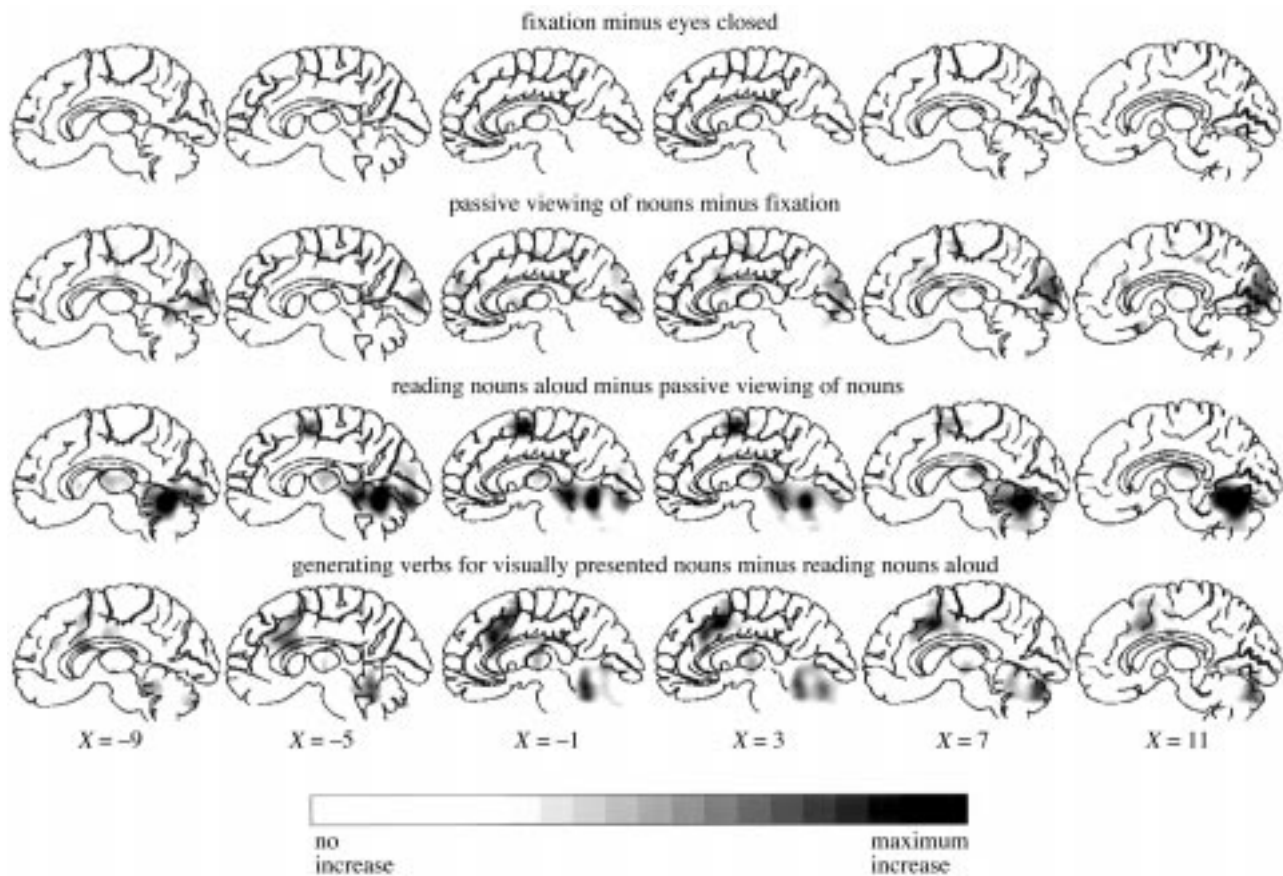


Figure 2. Data identical to those shown in figure 1, except that they are presented in the sagittal plane. These images begin 9 mm to the left of the midline ( $X = -9$ ) and end 11 mm to the right of the midline ( $X = 11$ ).

during naive verb generation, return to their baseline level of activity.

Activity in the ventral medial frontal cortex, reduced in the naive condition (see figure 3, rows 3 and 4) is reduced even further after practice. Regional activity within Sylvian-insular cortices, active during word reading (figure 1, row 3,  $Z = 20$ ) yet inactivated during naive verb generation (figure 3, row 4,  $Z = 20$ ), are now reactivated, especially on the right side. Finally, midline activity within the region of the precuneus and posterior cingulate cortex, reduced from baseline during naive word reading and verb generation (figure 4), increases in association with increased activity in visual cortices as the result of practice on the verb generation task (figure 6, row 2).

#### 4. DISCUSSION

The purpose of this exercise was to identify brain activity changes associated with task-related conscious behaviour. The strategy involved comparing PET images of blood flow change obtained in a novel reading task (verb generation) with those obtained during a well-practised task with identical perceptual and motor requirements (word reading). Additionally, comparisons were made between the naive and practised performance of the verb-generation task itself. On these comparisons, it was hypothesized that regions of the brain concerned with conscious task performance could be isolated and identified. Consistent with this hypothesis, regional changes in brain activity associated with conscious,

effortful performance of the verb-generation task were identified. These included widely distributed regions of both increases and decreases in brain activity.

##### (a) *Regions of increased activity*

When naive performance of the verb-generation task was compared with word reading, regions in the anterior cingulate cortex, left prefrontal cortex, left temporal cortex and right cerebellar hemisphere were found to exhibit increased activity. Consistent with our hypothesis that these regions were uniquely associated with the conscious performance of this task, their activity ceased with practice that both produced significant improvement in performance and elicited stereotyped responses (Raichle *et al.* 1994). Further support for the unique role of these regions in conscious task performance was given by changes in the opposite direction in Sylvian-insular cortices bilaterally (Raichle *et al.* 1994). Thus, regions active during naive task performance disappeared with practice whereas regions within Sylvian-insular cortices bilaterally, inactive during naive task performance, become active with practice. The reciprocal nature of these changes make it unlikely that practice simply results in a more efficient use of regions always devoted to task performance.

Thus, reading aloud familiar words uses a pathway from word-perception regions to speech-production regions via regions in Sylvian-insular cortices bilaterally. Before practice, a completely different pathway connects word-perception regions to speech-production regions.

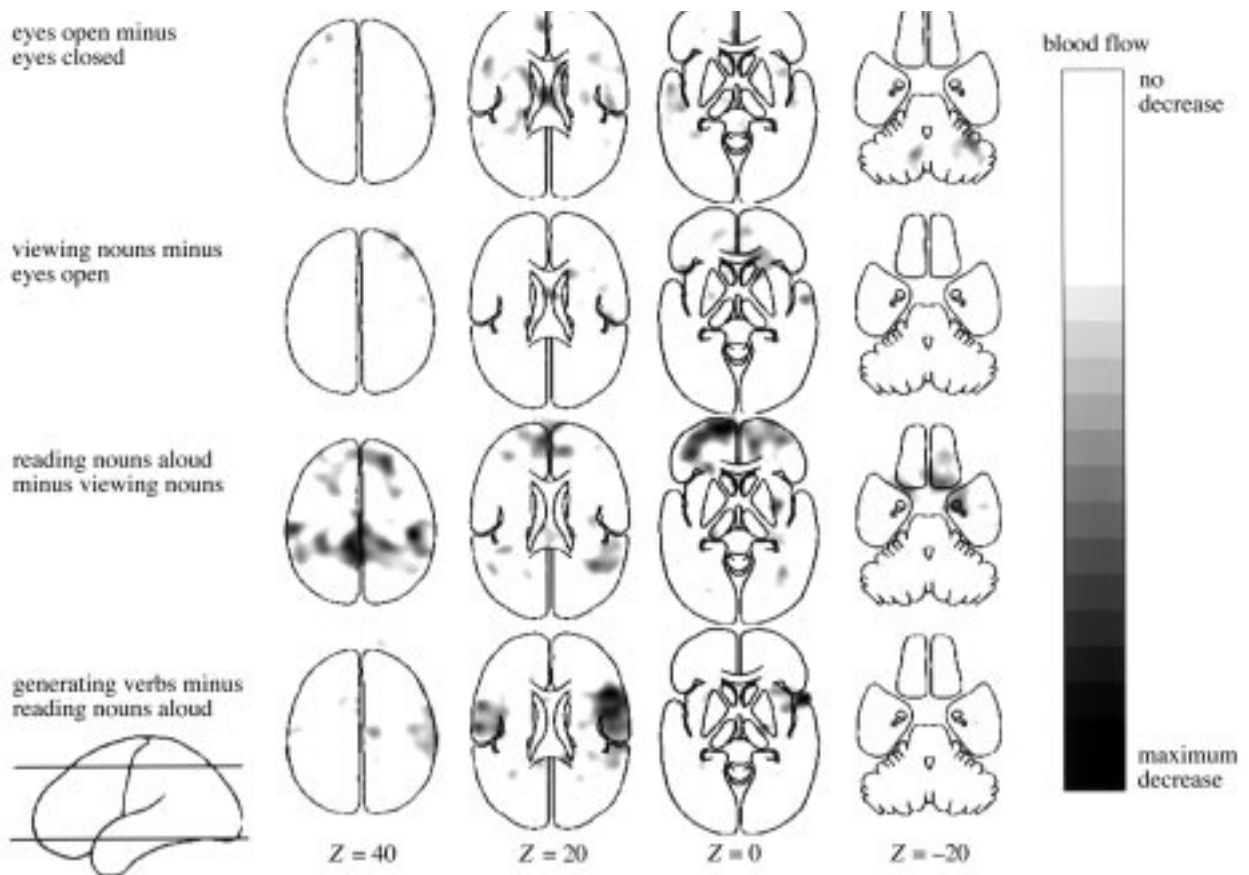


Figure 3. Hierarchically organized subtractions involving the same task conditions as shown in figure 1, the difference being that these images represent areas of decreased activity in the task condition compared with the control condition.

How are we to think about these two pathways and the circumstances under which they are used? What is their relationship, if any, to the several instances of dual route ideas in speech production? What, if anything, does this have to say about conscious versus non-conscious behaviours?

To begin, the two routes revealed by our studies of the verb-generation task (Petersen *et al.* 1988, 1989; Raichle *et al.* 1994) would qualify for the two routes envisioned in Lichtheim's original theoretical formulation (Lichtheim 1885; McCarthy & Warrington 1984). Although probably first suggested by John Hughlings Jackson (Jackson 1874), the idea of two pathways was first advanced most clearly by Lichtheim, a Swiss neurologist. In an attempt to provide a conceptual framework for the various forms of aphasia reported by Broca, Wernicke and others, he devised a scheme centred around three brain systems: an auditory word-form area concerned with the perceptual aspects of language; a centre for the motor representations of words, or a motor centre of speech; and a very distributed system 'for the elaboration of concepts'. As he envisioned it, information coming from the auditory word-form system could advance to the motor centre for speech either directly, or via the concept system. The latter route via the concept system he characterized as more 'conscious' and less fluent than the former (see Lichtheim 1885, p. 474). One pathway used a direct route from perception to production whereas the other used a more indirect route involving a distributed system of widely separated areas of the cerebral cortex.

In a very telling discussion Lichtheim (1885, p. 474) said '[I]t would appear as if, in naming objects, the auditory representations once found had to react in consciousness. This variety of language is a much more "conscious" one than fluent speaking, in which *we are aware of the sense of what we are saying, rather than of every word we say* [italics added]. Under certain circumstances conversational language is carried on in a similar way to naming, as, for instance, when we use an idiom not quite familiar to us. Here we must seek the words by the complicated process just mentioned; the direct communication between concept and motor center without cooperation of sound-representation does not exist; the subconscious act of speaking is not yet possible. A greater psychical exertion is obviously required, and consequently more fatigue is entailed'.

Lichtheim also envisioned, presciently, that acquisition of language occurred by imitation, 'as observed in the child, and upon the reflex arc which this process presupposes'. He went on to say 'when intelligence of the imitated sounds is superimposed, a connection is established between the auditory center (for word-representations) and the part (of the brain) where concepts are elaborated'.

Shallice and Norman (see Shallice 1988) formulate such issues more generally in terms of what they call contention scheduling and a supervisory attention system. Contention scheduling is the process by which selection is made of routine actions or thought processes. It is considered to be a decentralized process involving a very

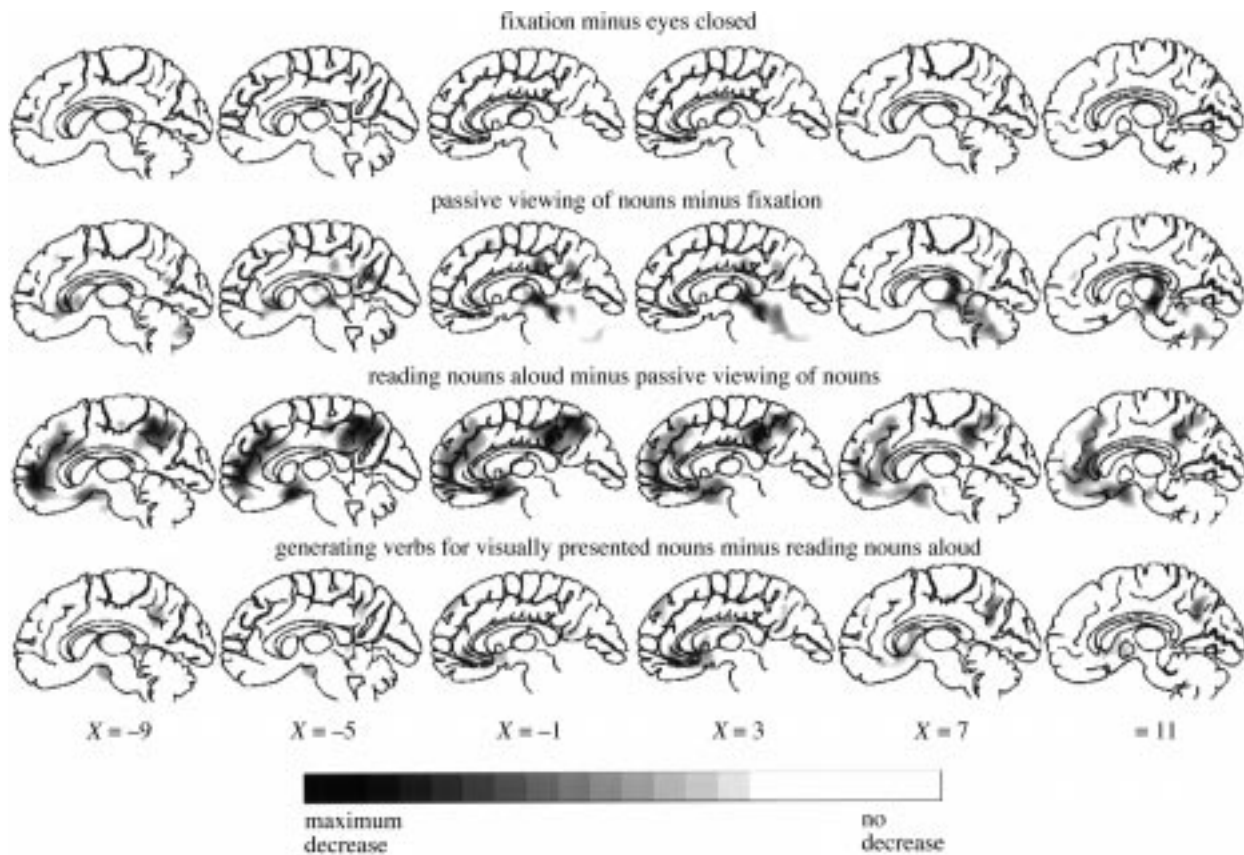


Figure 4. Data identical to those shown in figure 3 except that they are presented in the sagittal plane. The slices are positioned as noted in figure 2.

large but finite set of discrete programmes, hierarchically organized. Routine activities of our daily lives, such as driving a car back and forth to work, are managed in a non-conscious manner through contention scheduling (Lichtheim, I am sure, would have used spontaneous speech as an example). A particular set of programmes or schema has a level of activation dependent upon the triggering inputs it receives. Summarized nicely in the model of Norman and Shallice (Shallice 1988), this general idea has much support in the psychological literature (see summary discussion in Shallice (1988, p. 333)). We would suggest that, in the verb-generation paradigm (Raichle *et al.* 1994), regions within Sylvian-insular cortices represent some of the regions involved in the process of contention scheduling as formulated by Norman and Shallice (Shallice 1988).

The above formulation of the functional organization of our mental lives is obviously incomplete. A moment's reflection suggests that, useful as they may be under a majority of circumstances, routine actions and thought processes are sometimes inappropriate, occasionally embarrassing and, even, potentially dangerous (Reason & Mycielska 1982). Therefore, there has to exist a means by which routine, reflexive behaviours and thoughts can be inhibited and replaced, either transiently or permanently, by more appropriate behaviours and thoughts (Reason & Mycielska 1982). Norman and Shallice (Shallice 1988) postulate the existence of a second system to accomplish this, which they call the supervisory attention system.

The supervisory attention system of Norman and Shallice (Shallice 1988) provides a mechanism whereby

elements or schemas within the lower-level contention-scheduling system for routine, reflexive behaviours and thoughts can be temporarily modified by activating or inhibiting particular elements within it. This facilitates coping with novel situations in which the routine selections are unsatisfactory. As Shallice (1988, p. 345) states: 'the primary function of the Supervisory System is that of producing a response to novelty that is planned rather than one that is routine or impulsive'. In a general sense this fits nicely with Lichtheim's concept of a centre for the elaboration of concepts.

Whereas Lichtheim (1885) and Norman & Shallice (1985) envisioned a superimposition of higher centres for the conscious guidance of behaviour over more routine, reflexive responses, our data would suggest a substitution of regions. In our example, regions guiding non-automatic or conscious speech acts are preferentially selected, by a process yet to be defined, over those areas concerned with automatic or non-conscious speech acts when a well-learned, reflexive response such as word reading is not appropriate. As a corollary, one must also envision circumstances in which the reverse is true: automatic responses are preferred and, hence, selected. As Sutherland (1996) has pointed out, '[w]hen confronted by a predator, it is surely better to climb a non-optimal tree than to be eaten while weighing the respective merits of different trees'. The manner in which the brain is biased either way (i.e. towards or away from automatic behaviours) remains a most important and challenging question.

Lichtheim (1885) did not specify the neural correlates of his higher centres but he was quite clear that he did

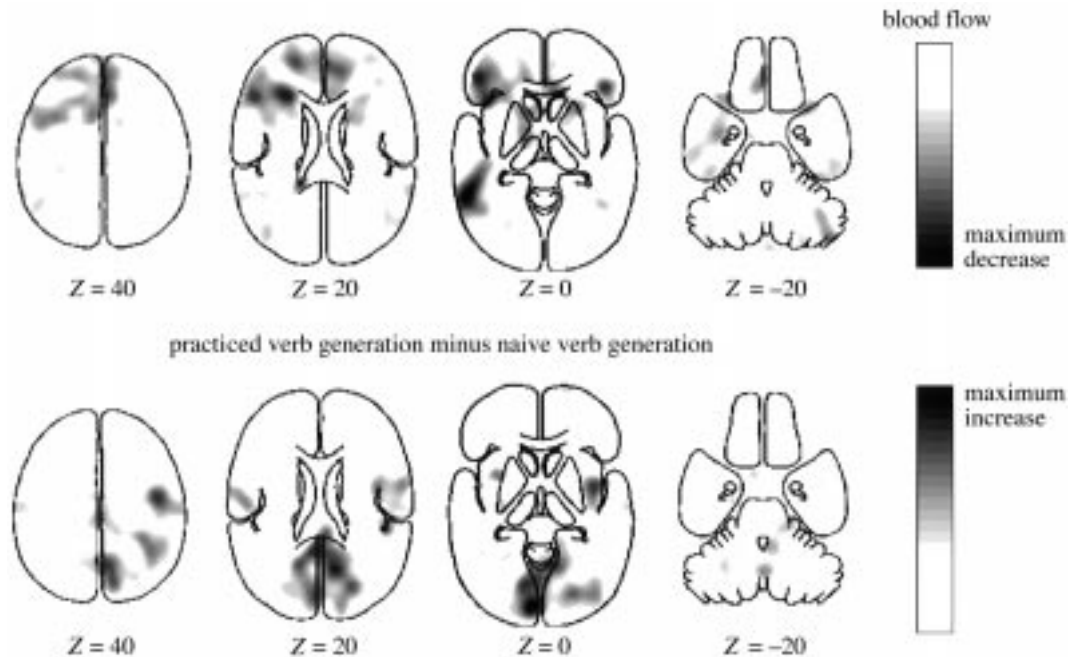


Figure 5. Changes in activity resulting from practice on the verb-generation task include decreases (top row) and increases (bottom row) in brain activity.

not believe them to be housed in a single area. 'Though in the diagram point B [see Lichtheim (1885), diagram 1, p. 436] is represented as a sort of center for the elaboration of concepts, this has been done for simplicities sake; with most writers, I do not consider the function to be localized in one spot of the brain, but rather to result from the combined action of the whole sensorial sphere. Hence, the point B should be distributed over many spots' (Lichtheim 1885, p. 477).

Shallice and Norman (Shallice 1988) were much more specific in drawing attention to the role of the frontal lobe in their supervisory attention system. They reviewed extensive evidence, primarily from neuropsychology, showing that patients with frontal-lobe injury often act in an impulsive and reflexive manner as if they lacked a supervisory attention system.

Reviewing the evidence that has now been gained from functional imaging studies in normal subjects, one would have to conclude that both Lichtheim, and Norman and Shallice, were correct in anticipating brain regions uniquely involved in conscious, reflective behaviour as distinct from regions concerned with reflexive, habitual performance. It is clear from the data presented in this paper that multiple, widely distributed areas of the normal human brain, including the cerebellum, are involved in the performance of a novel speech-production act, as Lichtheim (1885) would have predicted. Likewise, it is also clear that the frontal lobe plays a role, although not an exclusive one, as Norman and Shallice (Shallice 1988) implied.

The experiments used for illustrative purposes in this paper and the work of Lichtheim (1885) focus specifically on language. The work of Norman and Shallice (Shallice 1988), as well as others (see, for example, Passingham 1993; Shiffrin & Schneider 1977), suggest that the issues involved transcend any single domain of human performance. What other evidence do we have? Are the general principles of neural organization emerging from

imaging studies of language in normal subjects applicable to other domains of human performance, as others would suggest? Several examples are illustrative.

The data most directly comparable to the data reviewed in this paper are those from a PET functional imaging study of maze learning in strongly right-handed subjects by van Mier and colleagues (for a recent summary, see Petersen *et al.* (1998)). In the maze-learning study, subjects, with their eyes closed, used a stylus to trace a complex maze etched on the surface of a bit pad. Two groups of subjects were studied: those who used their right hand and those who used their left hand to perform the maze task. Performance was recorded in the naive state, after a period of practice and then with a novel maze. The tasks were designed to parallel directly the design of the word-reading and verb-generation studies reviewed in this paper (Raichle *et al.* 1994). The objective of the maze-tracing study was to determine whether the differences in brain organization distinguishing naive and practised verb generation applied also to naive and practised maze tracing.

The results of the maze-tracing study clearly support the hypothesis that naive and practised performance of a task are distinguished by qualitative differences in brain organization. Independent of the hand used, some brain regions (right premotor cortex, right parietal cortex and left cerebellum) were only active during a novel maze-tracing task. Other brain regions, in particular the supplementary motor cortex, were only active after practice. These are not the same areas that alternate activity when one compares naive and practised verb generation as illustrated in figures 5 and 6. Thus, when one thinks of a supervisory attention system (Shallice 1988) it must be envisioned as many regions (i.e. a distributed system) that are, importantly, task-specific.

Do we have other instances of this type of neural organization that distinguishes naive from practised

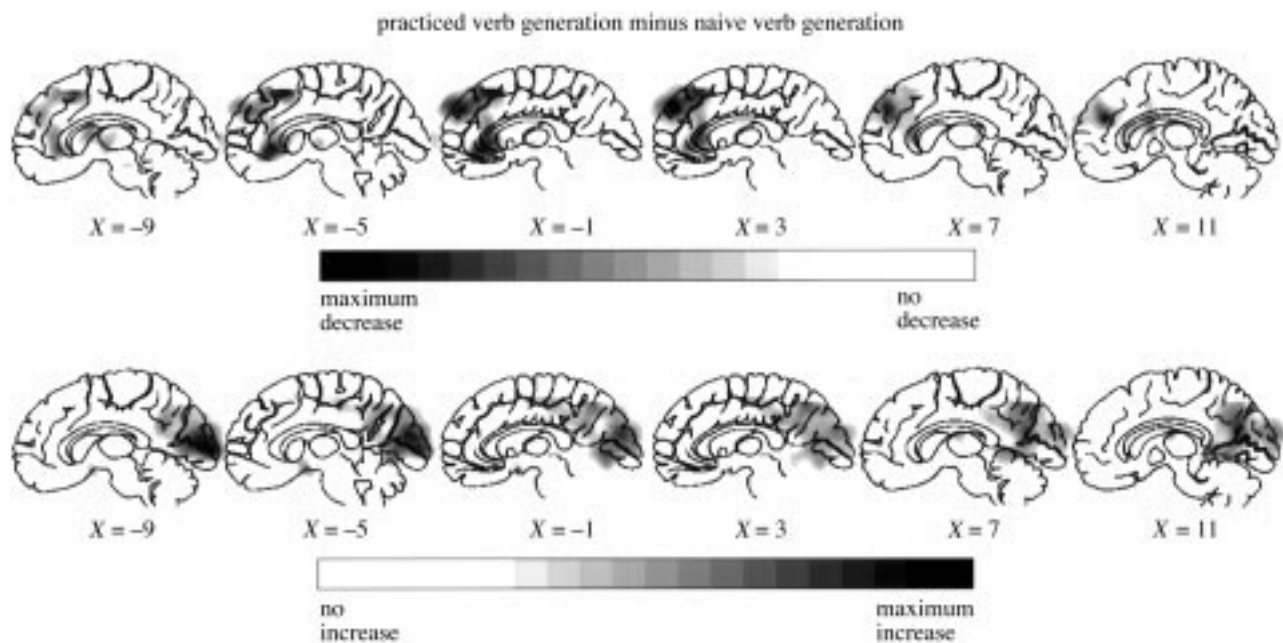


Figure 6. Data identical to those shown in figure 5 except that they are presented in the sagittal plane. The slices are positioned as noted in figure 2.

performance? Two illustrative examples come to mind: acquisition of conditional motor associations in the monkey (Chen & Wise 1995*a,b*; Mitz *et al.* 1991) and song learning in birds (for review see Nottebohm (1991)).

In a series of innovative experiments Wise and his colleagues (Chen & Wise 1995*a,b*; Mitz *et al.* 1991) studied conditional motor responses in the monkey, correlating unit activity in the cerebral cortex with performance. In these studies monkeys learned to saccade to specific targets in their visual field based on an association between the appearance of a visual cue and a particular target location. In the naive state the monkeys had to guess which locus in their visual field was indicated by a particular stimulus. Correct guesses were rewarded with juice. Performance was measured as the number of correct responses. As expected, performance improved with practice as the monkeys learned the correct association between target location and a particular stimulus. Unit recording of neuronal activity was performed in two cortical locations, the supplementary eye field (SEF) and the frontal eye field (FEF).

The results of these studies in monkeys show a remarkable parallel to the studies of word reading reviewed in this paper (Petersen *et al.* 1988, 1989; Raichle *et al.* 1994) and the maze-learning experiments discussed above (Petersen *et al.* 1998). In the SEF of the monkey, Chen & Wise (1995*a*) identified two populations of neurons that they termed, respectively, learning-selective and learning-dependent. The learning-selective neurons were only active in the presence of a novel cue. As the monkey learned the relationship between novel cue and its associated saccade location, activity in the learning-selective neurons ceased. The converse was true for the learning-dependent cells, which only became active as the monkey learned the correct association between target and cue. Similar classes of neurons were also found in the FEF but their proportions were much less (Chen & Wise 1995*b*).

This difference suggested that the roles of the SEF and the FEF in conditional motor responses differed significantly.

Another illustrative example of alternative neural organizations underlying the performance of the same task is singing in birds such as canaries and zebra finches. Work by a variety of groups (Nottebohm 1991) has provided a detailed description of the areas within the songbird brain responsible for the acquisition and production of song. Central to this organization is an area known as the higher vocal centre (HVC). This area plays an important role in the acquisition and production of song. Two pathways emerge from the HVC. One pathway projects directly from the HVC to the robust nucleus of the archistriatum (RA). It is known as the 'direct pathway'. From the RA, fibres pass through a series of areas and lead to brainstem nuclei that control the vocal apparatus responsible for the actual production of song. The second pathway also leaves the HVC on its way to the RA but only arrives at the latter location after passing through a number of intermediate areas in the songbird brain. This is known as the 'recursive loop'. Thus, there are two pathways from the HVC to the RA: a short, direct one and the long, recursive one. The recursive loop is of particular interest because it is critical for song learning but not for the production of learned song. Alternatively, the direct loop is quite capable of supporting a song after the skill has been mastered but is not capable of supporting the learning process.

The similarities in neural organization supporting these very different tasks (verb generation and maze tracing in humans, conditional oculomotor responses in monkeys and singing in birds) are striking. Brain regions as well as local populations of neurons active in naive task performance, especially where it competes with a more reflexive or habitual response to the same stimulus or instruction, are replaced by other brain regions and populations of neurons in the practised (i.e. routine, habitual or reflexive) performance of the same task. From



these data it seems possible to make a distinction between brain systems supporting conscious, reflective performance and brain systems supporting the non-conscious, reflexive performance of the same task. The general organizational principles underlying such a distinction appear to transcend species, levels of organization (general systems as well as local neuronal networks seem similarly organized) and tasks. The detailed organization surrounding individual tasks, however, appears to be unique to each task.

Many analyses might conclude at this point with comments about the potential role of brain regions that increase their activity during reflective or novel task performance. However, the data presented in this paper suggest that there is more to the story. While some regions of the brain increase their activity during novel task performance, others, just as dramatically, decrease their activity.

### (b) *Regions of decreased activity*

When subjects become actively involved in word reading, both reading aloud and verb generation, multiple regions across both cerebral hemispheres show a significant decrease in activity (figures 3–6). These include regions along the midline in the orbitofrontal cortex, posterior cingulate cortex and precuneus that have been noted to decrease in a wide variety of tasks (for details of a large meta-analysis of such changes, see Shulman *et al.* (1997b)). Characteristic of the experiments in which these particular decreases are regularly seen are ones in which subjects must actively process a visual stimulus. The control state is one in which the same stimulus is passively viewed. Additionally, decreases should also be noted in Sylvian-insular cortices bilaterally. These appear only in naive verb generation and not in word reading, where increases are observed (figure 1, row 3,  $\zeta=20$ ).

What are we to make of these reductions? Physiologists have long recognized that individual neurons in the cerebral cortex can both increase or decrease their activities from a resting, baseline firing pattern depending on task conditions. Decreases, however, seem to have received somewhat less attention. Nevertheless, examples of decreases abound in the neurophysiological literature (see, for example, Georgopoulos *et al.* 1982). A parsimonious view of these decreases in neuronal activity is that they reflect the activity of inhibitory interneurons acting within local neuronal circuits of the cerebral cortex. Because inhibition is energy-requiring (Ackerman *et al.* 1984; Batini *et al.* 1984; Biral *et al.* 1984), it should be impossible to distinguish inhibitory from excitatory cellular activity on the basis of changes in either blood flow or metabolism. Thus, on this view, a local increase in inhibitory activity is just as likely to increase blood flow and the fMRI BOLD signal (see below) as a local increase in excitatory activity. How, then, might decreases in blood flow as seen with PET (figures 3–6) or the fMRI BOLD signal arise?

To understand the significance of the decreases in blood flow in a functional imaging experiment it is important to distinguish two separate conditions in which they might arise. The usual circumstance accounting for reductions in activity arises when two images are compared, one containing a regional increase in blood

flow caused by some type of task-induced activity and the other not.

Let us consider, for example, the increase in activity over the Sylvian-insular cortices that occur when individuals read aloud a word compared with viewing the same word passively. This is seen bilaterally in figure 1, row 3 at  $\zeta=20$ . Turning to figure 2, row 4, note that we now observe a reduction in activity in almost the same region as subjects perform, naively, verb generation compared with reading aloud. What has occurred is that images in which the region is activated (i.e. word reading) are subtracted from images in which the region is not activated (i.e. verb generation). These results suggest that this region is used in automatic speech production such as word reading, not for a novel reading task such as verb generation. However, as verb generation becomes more automatic this region is reactivated (figure 4, row 2,  $\zeta=20$  and  $\zeta=0$ ).

The second circumstance in which decreases in blood flow and the fMRI BOLD signal are observed are not due to data manipulations of the type just described. Rather, blood flow and the fMRI BOLD signal decrease regionally from a baseline state for that region. The immediate question that arises in the mind of most is how such a baseline state is defined. How, for instance, is it to be distinguished from just another activation state? The definition arises from a consideration of the metabolic and circulatory events surrounding the activation of a typical cortical region (for a recent review, see Raichle (1998)) and how these differ from the metabolism and circulation of the baseline state of the awake human brain.

Measurements in the normal, adult, awake human reveal a brain that consumes approximately  $0.27 \mu\text{m}$  of glucose and  $1.54 \mu\text{m}$  of oxygen per gram of tissue per min (Siesjo 1978). This is supplied by a blood flow of approximately  $0.55 \text{ ml}$  of blood per gram of tissue per min (Siesjo 1978). Although these values vary from one region of the brain to another (for example, the average value in white matter is typically one-quarter that of grey matter) the relation among them remains remarkably constant. As a consequence, the fraction of available oxygen removed by the cerebral cortex of the resting brain from circulating blood (i.e. the so-called oxygen extraction fraction (OEF)) is quite uniform.

What is so distinctive about areas of increased activity are the deviations from these baseline relations. One might have assumed that when there is an increase in local cellular activity in the cerebral cortex it would be accompanied by a proportionate increase in blood flow and oxygen consumption. This would be reflected in an unchanged OEF. However, this is not observed (Fox & Raichle 1986; Fox *et al.* 1988). Blood flow actually increases substantially in excess of any increase in oxygen consumption, leading to a significant decrease in the OEF. The direct correlate of this is a local increase in the ratio of oxyhaemoglobin to deoxyhaemoglobin as oxygen supply exceeds demand. It is the local increase in the oxyhaemoglobin : deoxyhaemoglobin ratio that forms the basis for the fMRI signal. This fMRI signal usually is referred to as the BOLD or blood oxygen level-dependent contrast (Kwong *et al.* 1992; Ogawa *et al.* 1990, 1992).

Positive BOLD contrast is now routinely seen by investigators worldwide doing functional brain imaging

studies with fMRI. There is a remarkable correspondence between the location of BOLD contrast and changes in blood flow measured with PET when the same tasks are studied (for recent review, see Raichle (1998)). This correspondence has become routine confirmation of the fact that blood flow changes in excess of any change in oxygen consumption during changes in the functional activity of the cerebral cortex.

Given the above information, we are now in a position to ask a rather obvious question. What is the baseline-state metabolic and circulatory status of brain regions that exhibit a reduction in blood flow and a negative BOLD contrast when subjects actively engage in task performance? The regions of particular interest are those seen along the midline in figures 3–6 and previously noted to behave similarly across a wide variety of visual attention tasks (Shulman *et al.* 1997*b*). For these medial regions of orbital–frontal and posterior cingulate or parietal cortex, the OEF does not differ significantly from the overall brain average in the baseline state (data from 20 normal adult controls; M. E. Raichle, A.-M. MacLeod, W. Drevets and W. J. Powers, unpublished observations), whereas the blood flow, oxygen consumption and glucose use significantly exceed the brain average. Remarkably, the region of the posterior cingulate cortex and adjacent precuneus is actually the metabolically most active region of the cerebral cortex in the resting brain (data from 20 normal adult controls; M. E. Raichle, A.-M. MacLeod, W. Drevets and W. J. Powers, unpublished observations).

The above analysis leads to the inescapable conclusion that anterior as well as posterior regions of the cerebral hemispheres, particularly prominent but not exclusively along the midline, are intensely active during the baseline state of the awake brain (such as when the eyes are closed or during passive viewing of a television monitor and its contents). With focused attention on a variety of tasks (see, for example, Shulman *et al.* (1997*b*), as well as figures 3–6), these regions exhibit a conspicuous reduction in activity. What makes the active state of these regions so distinctive is that it is characterized by metabolic and circulatory relationships that typify baseline, not functionally activated, cerebral cortex. It is as though these areas of the brain are uniquely active as a default baseline state of the conscious resting brain.

Several additional general comments about these decreases from a baseline state should be made. First, they are not, as some have informally suggested, merely the haemodynamic consequence of increases elsewhere (i.e. an intracerebral steal phenomenon). Such a hypothesis is very unlikely to be correct because of the tremendous haemodynamic reserve of the brain (Heistad & Kontos 1983) and also because there is no one-to-one spatial or temporal correlation between increases and decreases (figures 1–6).

Second, these decreases are not confined to regions of the brain whose baseline activity significantly exceeds that of the overall brain average. For example, it has been shown that, in anticipation of stimulation, areas of somatosensory cortex outside the representation of the skin area that is the target of the expected stimulation exhibit marked reductions in activity as measured with PET (Drevets *et al.* 1995). These observations are thought

to reflect a model of spatial attention in which potential signal enhancement relies on a generalized suppression or filtering of background activity (Whang *et al.* 1991).

Third, the relatively large spatial extent of these regional decreases suggests the inactivation of specific systems within the cerebral cortex. The mechanism(s) by which this is achieved remain(s) to be determined. What is most important for our present purpose is identifying the functions with which these regions are associated. Whatever the functions, it seems reasonable to suggest that they must be suspended for proper task execution.

With regard to the posterior cingulate cortex and adjacent precuneus, animal studies suggest that it is involved in orientation within and interpretation of the environment (for a recent review, see Vogt *et al.* (1992)). The response of posterior cingulate neurons to visual stimuli, for example, is crucially dependent upon the physical characteristics of the stimulus. Small spots of light to which a monkey may be attending and responding do not elicit neuronal responses in this area. In contrast, large, brightly textured stimuli elicit responses even if they are totally irrelevant to tasks the animal is performing. Lesions of the posterior cingulate cortex also disrupt spatial working memory. From the studies reviewed by Vogt and his colleagues (Vogt *et al.* 1992), it is not possible to separate, cleanly, spatial working memory functions from functions concerned with evaluation and interpretation of the environment.

Additional light is shed on the function of the posterior cingulate cortex and adjacent precuneus by the work of Carol Colby (Colby *et al.* 1988), John Allman (Baker *et al.* 1981) and their colleagues. Both of these studies call attention to the fact that elements of the dorsal stream of extrastriate visual cortex (area M in the owl monkey and area PO in the macaque) are part of a network of areas concerned with the representation of the visual periphery. These areas are primarily located along the dorsal midline and can be distinguished experimentally in various ways from those areas of the visual system of the monkey that represent the fovea (i.e. the central ten degrees of the visual field). From these data and those reviewed by Vogt *et al.* (1992) emerges a specific hypothesis. Activity within the posterior cingulate cortex and adjacent precuneus in the baseline state in humans is associated with the representation (monitoring) of the world around us (i.e. our environment or our visual periphery). The hypothesis further predicts that efficient processing of items in the centre of our visual field requires generalized suppression or filtering of this background activity (Whang *et al.* 1991). This is operationally achieved by reducing activity of the posterior cingulate cortex and precuneus. As has been shown by Shulman *et al.* (1997*a*), attention to centrally presented stimuli is accompanied by enhanced responses in areas of the visual system concerned with their processing at the same time that posterior cingulate and precuneus are shut down (Shulman *et al.* 1997*b*).

Behavioural evidence in humans provides additional support for the above hypothesis. Mackworth (1965) has shown that increased foveal load leads to decreased extrafoveal information acquisition. He termed this phenomenon ‘tunnel vision’. This work has been confirmed and extended by a number of workers (see, for

example, Henderson & Ferreira 1990). Older adults are more affected by foveal load than younger adults (Owsley *et al.* 1995). Although no studies have been done to relate this decrement in performance with normal aging to reductions in the activity of the posterior cingulate and adjacent precuneus, recent studies in patients with Alzheimer's disease provide an intriguing perspective.

As reported recently by Kuhl and associates (Minoshima *et al.* 1994, 1997), reduction in the activity of the posterior cingulate gyrus is the earliest metabolic abnormality detected in patients with Alzheimer's disease with PET. Abnormalities in the processing of extrafoveal information have been noted in patients with dementia of the Alzheimer's type (Benson *et al.* 1988), but no systematic study has been performed on this group of patients in the light of the recent findings of Kuhl and associates (Minoshima *et al.* 1994, 1997).

Finally, severe damage to the parietal cortex, when it extends medially to include the precuneus and the posterior cingulate region, produces a condition known as Balint's syndrome (Hecaen & Ajuriaguerra 1954), whose cardinal feature is the inability to perceive the visual field as a whole (i.e. severe tunnel vision). This is known as simultanagnosia (Rizzo & Robin 1990). It is of interest that simultanagnosia has been reported in patients with dementia of the Alzheimer's type (Benson *et al.* 1988). Of interest would be a study of the relationship between decrements in baseline metabolic activity in this region in patients with Alzheimer's disease and the development of simultanagnosia.

Thus, the posterior cingulate cortex and adjacent precuneus can be hypothesized as a region of the brain associated with the continuous gathering of information about the world around us. It would appear to be a default condition of the brain with rather obvious evolutionary significance. Successful performance on tasks requiring focused attention demand that such broad information-gathering is curtailed. We see this reflected in marked decreases in this region during focused attention. As a task becomes easier and requires less focused attention, activity in this area predictably resumes (figure 6, row 1).

The other midline region of the cortex exhibiting prominent decreases in activity during focused attention is the orbitofrontal cortex. As with the posterior cingulate and adjacent precuneus, these changes have not only been observed in the tasks discussed in this paper but also in a wide variety of other tasks requiring focused attention (Shulman *et al.* 1997*b*). In contrast to the behaviour of the posterior cingulate and adjacent precuneus, the decreases we observe in the orbitofrontal cortex not only decrease initially when reading tasks are novel and require focused attention, but actually decrease even further with practice (figure 6, row 2). Further analysis of these changes (Simpson *et al.* 1997) reveals a number of important features. First, the reductions observed in this region, as they increase with practice, are significantly correlated with improved performance as measured by improved reaction times on the verb generation task. Second, these changes represent correlated responses within a group of areas in the orbital and medial inferior prefrontal cortex and the hypothalamus. This is consistent with the connective anatomy of this region known from non-human primates (Carmichael & Price

1994, 1995, 1996). Third, the likelihood that these changes are related to the emotional aspects of novel task performance is supported by a parallel study of anticipatory anxiety in normal subjects (Simpson *et al.* 1997). Reductions similar to those seen in the verb-generation task were correlated with the degree of anxiety reported by the subjects. Less anxious subjects showed greater reductions in activity.

These observations occur against a background of considerable clinical and experimental data suggesting that the orbital and medial prefrontal cortex play an important role in emotional behaviour (Drevets *et al.* 1997), especially fear (for review, see LeDoux (1996)) and decision-making (Bechara *et al.* 1997; Damasio *et al.* 1994). These activities are based on converging information from multiple sensory modalities (Rolls & Baylis 1994) and connections to the amygdala, hypothalamus, brainstem and basal ganglia (Carmichael & Price 1996). Puzzling, of course, is the fact that the changes we observe are seen as reductions and, as discussed in detail earlier, they begin from a baseline level of activity that is significantly above the brain mean.

A broad view of the function of the prefrontal cortex suggests that it is active when new rules need to be learned and older ones rejected (Dias *et al.* 1997; Wise *et al.* 1996). The activation of regions within the prefrontal cortex during the naive performance of the verb-generation task (figure 1, row 4) would certainly be consistent with that view. When this same reasoning is applied to the orbital and medial prefrontal cortex one must confront the fact that activity in this region may be greatest in the baseline state. Thus, as we come to associate general monitoring of incoming sensory information with the posterior cingulate cortex and adjacent precuneus, we may also come to associate an evaluation of this information with the medial and orbital frontal cortices.

### (c) *Conclusions*

The main purpose of this paper was to present a functional brain-imaging strategy that isolates neural correlates of consciousness in humans. This strategy is based on skill learning. In the example presented (rapidly generating verbs for visually presented nouns) a cognitive skill is examined before and after practice. As shown, there are marked qualitative differences in the neural circuitry supporting performance of this task in the naive and practised state. William James succinctly captures the interpretation we wish to place on this transformation in performance and neural circuitry: 'habit diminishes the conscious attention with which our acts are performed' (James 1890). Areas active during naive performance become candidate neural correlates of consciousness.

The neural correlates of consciousness for one task may not correspond, region for region, to those for another task. This is most directly demonstrated in our own data when comparisons are made between verb generation and maze tracing (Petersen *et al.* 1998). Thus, although a common theme emerges from the work reviewed here in terms of principles governing the neural instantiation of conscious and non-conscious behaviour of the same task, differences do exist among tasks in terms of the specific brain regions involved. Put another way, no single,

unique architecture emerges as a unifying feature of conscious, reflective performance (see also Shulman *et al.* 1997b). The cerebral cortex appears like the sections of a symphony orchestra. No one section or individual is at all times necessary for the production of the music. Likewise, in the brain, no one region (system) is necessary for consciousness under all circumstances. Rather, it is a distributed process with changing participants, some of which are identified through the strategy described. Relationships determine performance and performance can be infinitely variable.

The continuity of consciousness must also be kept in mind in pursuing the type of analysis presented in this paper. Consciousness does not cease when task performance changes from a naive, effortful, attention-focusing experience to a practised, effortless one requiring little attention. It is in this regard that it is important to consider the role of those regions of the brain whose activity ceases during naive task performance only to resume under baseline conditions. These task-induced deactivations from a baseline state provide important clues concerning neural correlates of consciousness in the baseline state. The recognition of these decreases probably represents a unique contribution of functional brain imaging to our understanding of human cortical physiology and should stimulate increased interest in the manner in which brain resources are allocated on a large systems level.

The material in this paper was presented, in part, as the 1997 Thomas William Salmon Lecture of the New York Academy of Medicine. I thank my many colleagues whose published data I have reviewed in this paper and, for generous support over many years, the National Institutes of Health of the USA, The McDonnell Center for Studies of Higher Brain Function of Washington University School of Medicine, The John T. and Katherine T. MacArthur Foundation and the Charles A. Dana Foundation.

## REFERENCES

- Ackerman, R. F., Finch, D. M., Babb, T. L. & Engel, J. Jr 1984 Increased glucose metabolism during long-duration recurrent inhibition of hippocampal cells. *J. Neurosci.* **4**, 251–264.
- Baker, J. F., Petersen, S. E., Newsome, W. T. & Allman, J. M. 1981 Visual response properties of neurons in four extrastriate visual areas of the owl monkey (*Aotus trivirgatus*): a quantitative comparison of medial, dorsomedial, dorsolateral, and middle temporal areas. *J. Neurophysiol.* **45**, 397–416.
- Batini, C., Benedetti, F., Buisseret-Delmas, C., Montarolo, P. G. & Strata, P. 1984 Metabolic activity of intracerebellar nuclei in the rat: effects of inferior olive inactivation. *Expl Brain Res.* **54**, 259–265.
- Bechara, A., Damasio, H., Tranel, D. & Damasio, A. R. 1997 Deciding advantageously before knowing the advantageous strategy. *Science* **275**, 1293–1295.
- Benson, D. F., Davis, J. & Snyder, B. D. 1988 Posterior cortical atrophy. *Archs Neurol.* **45**, 789–793.
- Biral, G., Cavazzuti, M., Porro, C., Ferrari, R. & Corazza, R. 1984 [<sup>14</sup>C]Deoxyglucose uptake of the rat visual centres under monocular optokinetic stimulation. *Behav. Brain Res.* **11**, 271–275.
- Bridgeman, B., Hijiden, A. H. C. V. d. & Velichovsky, B. M. 1994 A theory of visual stability across saccadic eye movements. *Behav. Brain Sci.* **17**, 247–292.
- Carmichael, S. T. & Price, J. L. 1994 Architectonic subdivision of the orbital and medial prefrontal cortex in the macaque monkey. *J. Comp. Neurol.* **346**, 366–402.
- Carmichael, S. T. & Price, J. L. 1995 Limbic connections of the orbital and medial prefrontal cortex of macaque monkeys. *J. Comp. Neurol.* **368**, 615–641.
- Carmichael, S. T. & Price, J. L. 1996 Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys. *J. Comp. Neurol.* **371**, 179–207.
- Chen, L. L. & Wise, S. E. 1995a Neuronal activity in the supplementary eye field during acquisition of conditional oculomotor associations. *J. Neurophysiol.* **73**, 1101–1121.
- Chen, L. L. & Wise, S. E. 1995b Supplementary eye field contrasted with frontal eye field during acquisition of conditional oculomotor associations. *J. Neurophysiol.* **73**, 1121–1134.
- Colby, C. L., Gattass, R., Olson, C. R. & Gross, C. G. 1988 Topographic organization of cortical afferents to extrastriate visual area PO in the macaque: a dual tracer study. *J. Comp. Neurol.* **238**, 1257–1299.
- Crick, F. & Koch, C. 1998 Consciousness and neuroscience. *Cerebr. Cortex* **8**, 97–107.
- Damasio, A. R. 1995 Knowing how, knowing where. *Nature* **375**, 106–107.
- Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M. & Damasio, A. R. 1994 The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science* **264**, 1102–1105.
- Dias, R., Robbins, T. W. & Roberts, A. C. 1997 Dissociable forms of inhibitory control within prefrontal cortex with an analog of the Wisconsin card sort test: restriction to novel situations and independence from ‘on-line’ ‘processing’. *J. Neurosci.* **17**, 9285–9297.
- Donders, F. C. 1969 On the speed of mental processes. *Acta Psychol.* **30**, 412–431.
- Drevets, W. C., Burton, H., Videen, T. O., Snyder, A. Z., Simpson, J. R. Jr & Raichle, M. E. 1995 Blood flow changes in human somatosensory cortex during anticipated stimulation. *Nature* **373**, 249–252.
- Drevets, W. C., Price, J. L., Simpson, J. R. Jr, Todd, R. D., Reich, T., Vannier, M. & Raichle, M. E. 1997 Subgenual prefrontal cortex abnormalities in mood disorders. *Nature* **386**, 824–827.
- Fiez, J. A. & Petersen, S. E. 1998 Neuroimaging studies of word reading. *Proc. Natn. Acad. Sci. USA* **95**, 914–921.
- Fox, P. T. & Raichle, M. E. 1986 Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proc. Natn. Acad. Sci. USA* **83**, 1140–1144.
- Fox, P. T., Perlmuter, J. S. & Raichle, M. E. 1985 A stereotactic method of anatomical localization for positron emission tomography. *J. Comput. Assist. Tomogr.* **9**, 141–153.
- Fox, P. T., Raichle, M. E., Mintun, M. A. & Dence, C. 1988 Nonoxidative glucose consumption during focal physiologic neural activity. *Science* **241**, 462–464.
- Frith, C. D., Friston, K., Liddle, P. F. & Frackowiak, R. S. J. 1991 Willed action and the prefrontal cortex in man: a study with PET. *Proc. R. Soc. Lond. B* **244**, 241–246.
- Georgopoulos, A. P., Kalaska, J. F., Caminiti, R. & Massey, J. T. 1982 On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J. Neurosci.* **2**, 1527–1537.
- Hecan, H. & Ajuriaguerra, J. 1954 Balint’s syndrome (psychic paralysis of gaze) and its minor forms. *Brain* **77**, 373–400.
- Heistad, D. D. & Kontos, H. A. 1983 Cerebral circulation. In *Handbook of physiology. The cardiovascular system*, vol. 3 (ed. J. T. Sheppard & F. M. Abboud), pp. 137–182. Bethesda, MD: American Physiological Society.
- Henderson, J. M. & Ferreira, F. 1990 Effects of foveal processing difficulty on the perceptual span in reading: implications for attention and eye movement control. *J. Exp. Psychol.: Learn. Mem. Cogn.* **16**, 417–429.

- Howard, D., Patterson, K., Wise, R., Brown, D., Friston, K., Weiller, C. & Frackowiak, R. 1992 The cortical localizations of the lexicons: positron emission tomography evidence. *Brain* **115**, 1769–1782.
- Jackson, J. H. 1874 On the nature of the duality of the brain. *Med. Press Circ.* **1**, 19, 41, 63.
- James, W. 1890 *Principles of psychology*. New York: Henry Holt & Company.
- Kwong, K. (and 12 others) 1992 Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc. Natn. Acad. Sci. USA* **89**, 5675–5679.
- LeDoux, J. 1996 *The emotional brain*. New York: Simon & Schuster.
- Lichtheim, L. 1885 On aphasia. *Brain* **7**, 433–484.
- McCarthy, R. & Warrington, E. K. 1984 A two-route model of speech production: evidence from aphasia. *Brain* **107**, 463–485.
- Mackworth, N. H. 1965 Visual noise causes tunnel vision. *Psychonom. Sci.* **3**, 67–70.
- Minoshima, S., Foster, N. L. & Kuhl, D. E. 1994 Posterior cingulate cortex in Alzheimer's disease. *Lancet* **344**, 895.
- Minoshima, S., Giordani, B., Berent, S., Frey, K. A., Foster, N. L. & Kuhl, D. E. 1997 Metabolic reduction in the posterior cingulate cortex in very early Alzheimer's disease. *Ann. Neurol.* **42**, 85–94.
- Mitz, A. R., Godschalk, M. & Wise, S. P. 1991 Learning-dependent neuronal activity in the premotor cortex: activity during the acquisition of conditional motor associations. *J. Neurosci.* **11**, 1855–1872.
- Norman, D. A. & Shallice, T. 1986 Attention to action: willed and automatic control of behavior. In *Consciousness and self-regulation* (ed. R. J. Davidson, G. E. Schwartz & D. Shapiro), pp. 1–18. New York: Plenum Press.
- Nottebohm, F. 1991 Reassessing the mechanisms and origins of vocal learning in birds. *Trends Neurosci.* **14**, 206–211.
- Ogawa, S., Lee, T. M., Kay, A. R. & Tank, D. W. 1990 Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc. Natn. Acad. Sci. USA* **87**, 9868–9872.
- Ogawa, S., Tank, D. W., Menon, R., Ellermann, J. M., Kim, S.-G., Merkle, H. & Ugurbil, K. 1992 Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc. Natn. Acad. Sci. USA* **89**, 5951–5955.
- Owsley, C., Ball, K. & Keeton, D. M. 1995 Relationship between visual sensitivity and target localization in older adults. *Vision Res.* **35**, 579–587.
- Passingham, R. E. 1993 *The frontal lobes and voluntary action*. (Oxford Psychology Series.) Oxford University Press.
- Paus, T., Marrett, S., Worsley, K. J. & Evans, A. C. 1995 Extraretinal modulation of cerebral blood flow in the human visual cortex: implications for saccadic suppression. *J. Neurophysiol.* **74**, 2179–2183.
- Petersen, S. E., Fox, P. T., Posner, M. I., Mintum, M. & Raichle, M. E. 1988 Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature* **331**, 585–589.
- Petersen, S. E., Fox, P. T., Posner, M. I., Mintum, M. A. & Raichle, M. E. 1989 Positron emission tomographic studies of the processing of single words. *J. Cogn. Neurosci.* **1**, 153–170.
- Petersen, S. E., Fox, P. T., Snyder, A. Z. & Raichle, M. E. 1990 Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. *Science* **249**, 1041–1044.
- Petersen, S. E., Mier, H. v., Fiez, J. A. & Raichle, M. E. 1998 The effects of practice on the functional anatomy of task performance. *Proc. Natn. Acad. Sci. USA* **95**, 853–860.
- Plum, F. & Posner, J. B. 1980 *The diagnosis of stupor and coma*. (Contemporary Neurology Series.) Philadelphia, PA: F. A. Davis Company.
- Posner, M. I. & Pavese, A. 1998 Anatomy of word and sentence meaning. *Proc. Natn. Acad. Sci. USA* **95**, 899–905.
- Price, C. J., Wise, R. J. S., Watson, J. D. G., Petterson, K., Howard, D. & Frackowiak, R. S. J. 1994 Brain activity during reading: the effects of exposure duration and task. *Brain* **117**, 1255–1269.
- Price, C. J., Wise, R. J. S. & Frackowiak, R. S. J. 1996 Demonstrating the implicit processing of visually presented words and pseudowords. *Cerebr. Cortex* **6**, 62–70.
- Raichle, M. E. 1998 Behind the scenes of function brain imaging: a historical and physiological perspective. *Proc. Natn. Acad. Sci. USA* **95**, 765–772.
- Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A. M., Pardo, J. V., Fox, P. T. & Petersen, S. E. 1994 Practice-related changes in human brain functional anatomy during nonmotor learning. *Cerebr. Cortex* **4**, 8–26.
- Rayner, K. & Pollatsek, A. 1989 *The psychology of reading*. Englewood Cliffs, NJ: Prentice-Hall.
- Reason, J. & Mycielska, K. 1982 *Absent-minded? The psychology of mental lapses and everyday errors*. Englewood Cliffs, NJ: Prentice-Hall.
- Rizzo, M. & Robin, D. A. 1990 Simultanagnosia: a defect of sustained attention yields insights on visual information processing. *Neurology* **40**, 447–455.
- Rolls, E. T. & Baylis, L. L. 1994 Gustatory, olfactory, and visual convergence within the primate orbitofrontal cortex. *J. Neurosci.* **14**, 5437–5452.
- Shallice, T. 1988 *From neuropsychology to mental structure*. Cambridge University Press.
- Shiffrin, R. & Schneider, W. 1977 Controlled and automatic human information processing. II. Perceptual learning, automatic attending and a general theory. *Psychol. Rev.* **84**, 127–190.
- Shulman, G. L., Corbetta, M., Buckner, R. L., Raichle, M. E., Fiez, J. A., Miezin, F. M. & Petersen, S. E. 1997a Top-down modulation of early sensory cortex. *Cerebr. Cortex* **7**, 193–206.
- Shulman, G. L., Fiez, J. A., Corbetta, M., Buckner, R. L., Miezin, F. M., Raichle, M. E. & Petersen, S. E. 1997b Common blood flow changes across visual tasks. II. Decreases in cerebral cortex. *J. Cogn. Neurosci.* **9**, 648–663.
- Siesjo, B. K. 1978 *Brain energy metabolism*. New York: Wiley.
- Simpson, J. R. J., MacLeod, A. K., Fiez, J. A., Drevets, W. C. & Raichle, M. E. 1997 Blood flow decreases in human medial inferior prefrontal cortex and hypothalamus correlate with anxiety self-rating and with practice-related changes on a cognitive task. *Soc. Neurosci. Abstr.* **23**, 1317.
- Steriade, M. 1996a Arousal: revisiting the reticular activating system. *Science* **272**, 225–226.
- Steriade, M. 1996b Awakening the brain. *Nature* **383**, 24–25.
- Sutherland, N. S. 1996 The biological causes of irrationality. In *Research and perspectives in neurosciences* (ed. Y. Christen), pp. 145–156. Berlin: Springer.
- Vogt, B. A., Finch, D. M. & Olson, C. R. 1992 Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. *Cerebr. Cortex* **2**, 435–443.
- Weiskrantz, L. 1986 *Blindsight. A case study and implications*. (Oxford Psychology Series No. 12.) Oxford University Press.
- Weiskrantz, L. 1997 *Consciousness lost and found. A neuropsychological exploration*. Oxford University Press.
- Whang, K. C., Burton, H. & Shulman, G. L. 1991 Selective attention in vibrotactile tasks: detecting the presence and absence of amplitude change. *Percept. Psychophys.* **50**, 157–165.
- Wise, S. P., Murray, E. A. & Gerfen, C. R. 1996 The frontal cortex–basal ganglia system in primates. *Crit. Rev. Neurobiol.* **10**, 317–356.

