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The Prefrontal Cortex and Neurological Impairments of Active Thought

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Abstract

This article reviews the effects of lesions to the frontal cortex on the ability to carry out active thought, namely, to reason, think flexibly, produce strategies, and formulate and realize plans. We discuss how and why relevant neuropsychological studies should be carried out. The relationships between active thought and both intelligence and language are considered. The following basic processes necessary for effective active thought are reviewed: concentration, set switching, inhibiting potentiated responses, and monitoring and checking. Different forms of active thought are then addressed: abstraction, deduction, reasoning in well-structured and ill-structured problem spaces, novel strategy generation, and planning. We conclude that neuropsychological findings are valuable for providing information on systems rather than networks, especially information concerning prefrontal lateralization of function. We present a synthesis of the respective roles of the left and right lateral prefrontal cortex in active thought.



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Contents

INTRODUCTION	158
Overall Perspective	158
Why Neuropsychology?	159
The Neuropsychological Approach to Frontal Functions	160
BROAD-BRUSH ASPECTS OF ACTIVE THOUGHT	163
Dual System Brain-Based Models of Cognitive Control	163
Active Thought and Intelligence	163
Active Thought and Language	164
ESSENTIAL PREREQUISITES FOR ACTIVE THOUGHT	166
Volition and Concentration	166
Set Switching and Response Inhibition	167
Active Monitoring and Checking	167
Working Memory	168
FORMS OF ACTIVE THOUGHT	169
Abstraction	169
Deduction	170
Reasoning in Well-Structured and Less Well-Structured Problem Spaces	170
From Lateral Transformations to Strategy Shifts	171
Planning for Future Action	172
THEORETICAL CONCLUSIONS	173

INTRODUCTION

Overall Perspective

This review is concerned with what neuropsychological findings can tell us about the cognitive processes underlying active thinking. By active thinking, we refer to mental processes that allow us to confront situations where we do not respond routinely to the environment but, rather, effectively address problems that can be big or small. Active thinking entails a set of complex mental processes, for example, those involved in abstraction, deduction, and other forms of reasoning between alternative possibilities, switching lines of thought, selecting strategies, inhibiting obvious responses, and formulating and realizing plans. For example, organizing a dinner party would entail many active thinking processes, whereas daydreaming or implicit processes like priming would not be considered active thinking.

A number of well-known neuropsychological tests designed to assess prefrontal function require active thinking. Typical examples are tests such as Wisconsin Card-Sorting (switching lines of thought), Proverb Interpretation (abstraction), Stroop (inhibition), Tower of Hanoi (planning), and tests of fluid intelligence such as Progressive Matrices or Cattell Culture Fair (reasoning between alternative possibilities). Following frontal lobe lesions, performance on these tests is typically impaired. This suggests that the frontal lobes are critically involved in active thinking.

Impairments in active thinking are also exemplified by a number of frontal lobe syndromes that involve release of irrelevant environmentally triggered actions. Examples include the grasp reflex, where the patient whose palm is being stroked by a doctor grasps the doctor's fingers despite being repeatedly instructed not to (De Renzi & Barbieri 1992), or the somewhat analogous situation

where the patient is instructed not to move their eyes to a distracting light but does so anyway (Paus et al. 1991). At a higher level, there is utilization behavior, originally described by Lhermitte (1983). In this case, the patient makes a standard afforded action to one of the objects surrounding him, such as dealing from a pack of cards, without being told to do so or, in the so-called incidental form, when explicitly told to do something else (Shallice et al. 1989). These examples highlight behaviors that occur when active thinking processes are absent or impaired through brain injury. Interestingly, these syndromes have been most frequently described in patients with lesions involving medial frontal areas (see De Renzi & Barbieri 1992).

Prefrontal functions are involved in many different cognitive domains. They have been well reviewed fairly recently by Szczepanski & Knight (2014). This review, therefore, focuses only on those cognitive domains we consider critical for active thinking. Thus, we discuss individual cognition rather than social cognition and ongoing reasoning rather than (long-term) memory, learning, motivation, and emotion.

Our review is structured in the following fashion. The Introduction considers why we have chosen neuropsychological evidence, out of the many cognitive neuroscience techniques available, to be used for the review of the cognitive processes underlying active thinking. We then address the methodological approaches adopted for the neuropsychological investigation of prefrontal functions. The second section briefly outlines our theoretical framework for active thinking, which is largely based on the Norman & Shallice (1986) supervisory system model of prefrontal cortex (PFC) functioning. We also consider the relationship between active thinking and potentially overlapping cognitive domains such as intelligence and language. The third section will deal with processes that are prerequisites for active thinking, namely concentration, set shifting, thought inhibition, and monitoring and checking. In the fourth section, we discuss different types of core active thinking processes, including abstraction, deduction, novel strategy selection, insight, and planning. The final section aims to produce an overall theoretical synthesis.

Why Neuropsychology?

As cognitive processes become more abstract and distant from sensory and motor processes, it becomes increasingly difficult to investigate them adequately using behavioral means alone. Thus, discussing theorists working on reasoning about syllogisms, Khemlani & Johnson-Laird (2012, p. 453) wrote, “Thirty-five years ago they had only heuristic accounts that explained biases and errors, and so the domain appeared to be an excellent test case for cognitive science. There are now 12 sorts of theories of syllogisms and monadic inferences, and so skeptics may well conclude that cognitive science has failed.” A more powerful source of empirical findings seems to be required. Methodologies related to the brain are obvious candidates.

Within human cognitive neuroscience, there are two main classes of methodologies. The oldest class consists of those methodologies derived from lesion studies of neurological patients, which have recently been supplemented by transcranial magnetic stimulation (TMS) and, somewhat more conceptually distantly, by the study of the cognitive effects of individual differences in brain structure across the normal population. The second class consists of those methodologies where on-line measures are taken of brain processes while normal subjects carry out tasks; these methodologies include positron emission tomography (PET), functional magnetic resonance imaging (fMRI), electroencephalography (EEG), magnetoencephalography (MEG), and so on.

If one’s aim is to provide accurate anatomical correspondences for known cognitive processes or to provide real-time information on processing, the second class is much to be preferred. Despite

this clear advantage of the second class of methodology, the first class, especially neuropsychology, has complementary advantages for the development of cognitive theory. There are at least five reasons for this:

- If one takes cognitive theory to refer to models like classic box-and-arrow information-processing ones, then neuropsychological data can speak directly to cognitive theory. Appropriate inferences are derived from a set of simple assumptions, first formalized by Caramazza (1986). They are based on the idea of subtraction of components from an overall system. Of course, subtraction in reality is complicated by complex processes related to the recovery process (see Henson et al. 2016 for a good example). However, to a first approximation, subtraction is a plausible characterization of the effect of a brain lesion. So, this approach was much used in the heyday of cognitive neuropsychology. Moreover, the same set of assumptions can be used to relate such data to connectionist models, as well (Shallice & Cooper 2011). By contrast, methodologies of the second type require complex bridging assumptions, based on physics and physiology, to relate their data to cognitive theory.
- It is generally accepted that activation-based findings do not necessarily imply causal efficacy (see Gilaie-Dotan et al. 2015 for a particularly clear example). This possibility is of particular concern for lateralization of function. Thus, neuropsychological data show language functions to be strongly lateralized. Crossed aphasia is very rare. In a consecutive series of over 1,200 aphasics with unilateral lesions, only 4% had right-hemisphere lesions (Croquelois & Bogousslavsky 2011). However, neuroimaging studies of language processing often report bilateral activation patterns, although they are somewhat smaller in size in the right hemisphere (Jung-Beeman 2005). So, considering merely the presence or absence of activation may, in effect, hide real lateralization of function.
- Neuropsychological data provide additional sources of behavioral evidence that are not generally available from other cognitive neuroscience methods, namely, the nature of the responses and, in particular, the errors made. These can be very informative for specifying the function damaged. Below, we consider two examples, the concrete interpretation of proverbs and strategy-reflecting responses.
- When carrying out a cognitive neuroscience experiment on neurologically intact subjects, the investigators are entirely reliant on their own theoretical framework to set up the study. Neurological patients can produce behaviors that strikingly challenge theoretical preconceptions. Phineas Gage and HM are the most famous such cases, but there are many others. They facilitate serendipity.
- Some problem solving situations involve a single step change, where the subject makes a change in strategy in one trial. Examples are those involving insight (see the section titled From Lateral Transformations to Strategy Shifts). They cannot be effectively studied using standard activation-based methods that require summing over multiple trials because the critical situations cannot be reproduced; a repeat would no longer be novel. Instead, damage to the relevant systems may prevent strategy change occurring, thus allowing relevant investigation.

We therefore primarily address findings from neuropsychological studies and consider other methodologies where their findings help interpret the results of such studies. Of course, neuropsychological methods have their own limitations, which we discuss in the next section.

The Neuropsychological Approach to Frontal Functions

Researchers concerned with making inferences about normal cognitive function from neuropsychological data have used three main approaches: the single case study (including its close relation,

the multiple single case study), the case series, and the group study. In the first approach, individual patients are selected for study depending on their theoretical interest. In the second and third approaches, all patients who fit the appropriate criteria are reported. In the second approach, each patient is treated as a separate test of relevant theories, whereas in the third approach, results are averaged across all patients in a group.

Historically, researchers have tended to favor one approach and reject others. In contrast, Shallice (2015) has argued that all three approaches are legitimate but have different potential problems and so are more powerful in combination. This statement needs to be qualified as far as prefrontal functions are concerned. Often, performance on paradigms sensitive to prefrontal lesions can have a large range in the normal population—consider, as an example, the Stroop test. Impairment, then, becomes more easily detected using group studies due to variance reduction with increased n .

In practice, the anatomically based group study, where the patient is allocated to a group according to their site of lesion, is the most widely used method for studying prefrontal functions. This type of study comes in two forms. In the more traditional approach, the anatomical regions are decided a priori. In the oldest such version, the classical approach, there is a simple comparison between patients with unilateral left and right frontal lesions. In a more refined approach (the Stuss-Alexander method), patients with frontal lesions are divided into those with left lateral, right lateral, superior medial, and inferior medial (including orbital) frontal lesions, this division being based partly on statistical grounds and partly on clinical ones (Stuss et al. 1998). In the modified Stuss-Alexander method, the two medial groups are combined.

The alternative approach (the critical lesion localization method) uses the range of performance produced by patients in a series. It determines whether there are patients with lesions in a particular region who perform worse than those with lesions elsewhere without specifying the region in advance. A package such as voxel-based lesion symptom mapping (VLSM)—now sometimes called lesion behavior mapping (Bates et al. 2003, Rorden & Karnath 2004)—is used.

Recently, Mah et al. (2014) have criticized existing methods of this type, which make the simplifying assumption that damage to any voxel is independent of that to any other voxel. Unfortunately, the assumption is flawed when applied to brain lesions caused by stroke. In this case, the arterial tree structure of the vascular system means that there will be a high correlation between damage to functionally critical and noncritical regions fed by the same artery. Mah et al. (2014) advocated a high-dimensional multivariate approach. However, to our knowledge, this approach has yet to be applied in an analysis of the effects of prefrontal lesions. Related criticisms may apply to brain tumors, but if they do, then the associated noncritical regions will not be the same as those for vascular damage. This makes replication, especially across etiology, very useful. This is also the case for a second problem—the existence of large silent regions due to insufficient patients for complete coverage.

In fact, for the purpose of drawing inferences about the separability of executive systems, the precise anatomical location of a critical area is not important. Performance on a given test requires many subprocesses. So, the inferential logic of cognitive neuropsychology depends on the relative performance of the patient across multiple tests. We adopt an analogous approach using groups. If the critical areas for one test do not overlap with those of another, then we take this as evidence that the two tests do not rely on the same set of subsystems. As we discuss in the section titled From Lateral Transformations to Strategy Shifts, two tests that appear to involve inhibition—the Stroop and the Hayling B Sentence Completion Test—lateralize differently in the PFC, and, therefore, the most critical processes for performing the two tests differ.

By contrast, lesions to an area can affect performance on more than one test. This, then, puts on the intellectual agenda the possibility that the resources required by test performance may overlap cognitively as well as anatomically. For example, Tsuchida & Fellows (2013) used VLSM on the performance of 45 frontal patients on three tests—task-switching, the Stroop, and a spatial search task. The authors found that similar left ventrolateral regions were critical for the first two tasks. A different, more medial region was critical for the spatial search task. The authors held that the existence of a common critical area for the first two tasks meant that “they are likely to be related to disruption of a single underlying process” (Tsuchida & Fellows 2013, p. 1797). We consider that this result provides suggestive evidence only.

Adopting a group study methodology is, however, beset with a host of methodological problems. Typically, patients differ widely in age and premorbid cognitive abilities. In addition, lesions vary greatly in etiology and size. Moreover, these two types of factors can interact in a complex fashion. Thus, Cipolotti et al. (2015b) examined two tests sensitive to prefrontal damage—Advanced Progressive Matrices and Stroop. Increasing age was found to exacerbate the effects of frontal damage, as measured using age-specific norms. This exacerbated age effect on executive performance in frontal patients was not ameliorated by proxies of cognitive reserve such as education or IQ (Macpherson et al. 2017). This suggests that any behavioral effect that a lesion has can only manifest itself when influenced by many strong confounding factors. Large samples of patients and well-matched subgroups are therefore required.

How, then, is one to proceed in practice? One approach is to limit the sample by, say, restricting selection to a particular type of etiology, such as vascular lesions. Thus, patients in subgroups should be better matched. In support of this view, Karnath & Steinbach (2011) argue that it is best to restrict patient samples to those suffering strokes and reject other etiologies, in particular, tumors. The authors suggest that the effects of tumors are too diffuse and not well localized. In fact, there are clear examples showing that postoperative tumors can give strong localization effects (for a particularly clear example, see Papagno et al. 2011). Moreover, if one was to include only patients with vascular lesions, collecting a large sample of frontal patients with well-matched subgroups for a new set of tests would, in practice, take much too long.

A common practice, therefore, is to mix different etiologies in the patient sample to obtain a large enough group. But are the effects of, say, strokes and tumors even roughly equivalent when affecting similar parts of the cortex? To answer this question, Cipolotti et al. (2015a) compared 100 frontal patients with four different types of etiology on four frontal executive tasks (Advanced Progressive Matrices, Stroop Color-Word Test, Letter Fluency-S, Trail-Making Test Part B). The four groups consisted of one vascular group and three with different types of tumor—high-grade gliomas, low-grade gliomas, and meningiomas. The groups did not differ significantly in size or location of lesion. Strong behavioral effects on performance of the frontal tests were found for age and premorbid cognitive abilities. However, only on one test—Trail-Making Part B—was a significant difference between etiologies obtained when age was partialled out in an analysis of covariance. Critically, the significance did not survive Bonferroni correction, as there was no reason to consider Trail-Making, which later research has shown to be not specific to frontal lesions (Chan et al. 2015), to be more susceptible to differences in etiology than the other three tests. We therefore conclude that it is acceptable practice to mix etiologies to overcome the great variability in the population under study.

We therefore include all types of neuropsychological methods in our review but concentrate on the *a priori* groups approach. We note the number of relevant patients, as the results of studies with small group sizes are especially likely to be biased by the idiosyncrasies of a few patients or by imperfect matching across subgroups.

BROAD-BRUSH ASPECTS OF ACTIVE THOUGHT

Dual System Brain-Based Models of Cognitive Control

Within the literature on reasoning, a variety of so-called dual system models have been put forward. Most of them differentiate between a fast, automatic, and unconscious mode of processing and a slow, deliberate, conscious one (Kahneman & Frederick 2002). In the reasoning field, the two are often called the products of system 1 and of system 2, respectively (Stanovich 1999).

Before the development of dual system models of reasoning, the Russian neuropsychologist Alexander Luria (1966) argued that neuropsychological evidence supports a theoretical framework in which the PFC contains a system for the programming, regulation, and verification of activity—adopting the terminology of the reasoning literature, a system 2. This prefrontal system implements its functioning by calling upon a more posterior system in the cortex—a system 1. A number of neuroscientists have adopted a related type of dual system model framework for conceptualizing PFC function in information processing terms (see Shallice 1982, Miller & Cohen 2001, Duncan 2010). In this review, we adopt Norman & Shallice's (1986) framework.

Contention scheduling—the system 1 of this framework—is the lower-level control system that can effect routine thought and action operations. It operates in a production-system fashion, including selecting action and thought schemas involving more posterior dedicated processing systems and connections (Cooper & Shallice 2000). The syndromes discussed in the Introduction as examples of nonactive thought, such as utilization behavior, represent contention scheduling operating in isolation.

If contention scheduling cannot cope with a nonroutine situation, a second, higher-level control system comes into play, the supervisory system, believed to be in the PFC. The supervisory system is responsible for the control mechanisms that modulate contention scheduling top down by boosting relevant action and thought schemas to allow novel goal-directed behavior. The supervisory system is loosely equivalent to the executive system or control processes in other theoretical frameworks. Where it differs is in being more specific about what it modulates and how. It is the key system involved in active thinking.

Another major brain-based model descending intellectually from Luria's ideas is the multiple demand network approach of Duncan (2010). Using neuroimaging, Duncan & Owen (2000) found that more difficult tasks in many different domains—such as perception, response selection, and working memory—activate the same set of regions, mainly in the frontal and parietal cortices, so-called multiple demand regions. These regions are held to have the function of programming other regions of the brain to carry out nonautomatic tasks. This is a similar function to that held to be carried out by a supervisory system. Duncan (2013, p. 41) also argues that “the fMRI literature contains little consensus on clear repeatable functional distinctions” between different regions within the multiple demand network. We address how the neuropsychological evidence relates to the two models and to equipotentiality below.

Active Thought and Intelligence

Duncan et al. (2000) also argued that the multiple demand regions are the seat of fluid intelligence, *g*. Thus, they made a major link to another cognitive domain, intelligence, and aimed to support *g* as a solid scientific concept.

The neuropsychological literature does not support the idea that a reduction in *g* is sufficient to explain frontal patients' executive impairments. Roca et al. (2010) showed that it is for some tests (e.g., Wisconsin Card-Sorting). However, for others, such as the Hayling B, both Roca et al. (2010) and Cipolotti and colleagues (2016) have demonstrated that frontal patients' impairment

cannot be fully explained by reduced *g*. Similarly, impairments in other executive tests, such as Stroop and Proverb Interpretation, were shown to be not accounted for by an effect on *g*.

However, Duncan & Owen's (2000) claim about *g* related specifically to multiple demand regions. To test this claim, Woolgar et al. (2010) gave the Cattell Culture Fair IQ test to 80 patients with cortical lesions. The volume of lesions both in multiple demand regions and outside those regions was assessed. For the group as a whole, there was a significant correlation between the IQ score and multiple demand volume, and the result remained highly significant when total lesion volume was partialled out. However, for the 44 pure frontal patients, the correlation was no longer significant if non-multiple demand volume was partialled out. So, as far as the PFC is concerned, the theoretical claim was not strongly supported by evidence from neuropsychology.

Active Thought and Language

Thought and language processes are intertwined in numerous complex ways (Gentner & Goldin-Meadow 2003), but in the mature adult brain, how independently can active thought take place without language? One potential line of evidence comes from aphasia: Can aphasics reason? This has been investigated in quite a number of aphasic patients in whom relatively preserved reasoning has been shown (Varley 2014). However, studies have tended to be rather loose, relying on essentially clinical reports or on a fairly crude analysis of the processing problems of the patients. An exception is the study of Varley et al. (2005), where three patients with severe problems in comprehension and production of syntax were given a variety of arithmetic and calculation tasks. Two of the patients were near ceiling on some calculation tasks with quasisyntactic aspects, such as three-figure subtraction, including problems with negative answers. They also performed adequately, but not perfectly, on problems involving interpretation of brackets. Thus, it appeared that the understanding and execution of syntactic operations could be relatively preserved in arithmetic when such operations were severely impaired in language.

Grammatical encoding is, however, part of what Levelt (1989) characterized as the formulator stage of language production. It can be inferred from such studies that the formulator and articulator stages operate relatively specifically within the language domain as opposed to the thought domain. The key issue, therefore, relates to the so-called conceptualizer stage, which precedes them in language production. It produces what Levelt (1989) calls the preverbal message, which, in our approach, requires active thought. However, can active thought occur without the involvement of conceptualizer-stage processes?

A relatively little-known aphasia syndrome bears on this question. This syndrome, called dynamic aphasia, is a subtype of the clinical category of transcortical motor aphasia and was first described by Luria (1970). He described two patients who could answer questions but were incapable of narrative speech. In dynamic aphasia, the inner mechanics of the language system—the formulator and articulator stages—appear to operate relatively normally, but the patient says little, especially in spontaneous speech. For instance, patient ROH of Costello & Warrington (1989), when asked to describe his last holiday, produced, in 30 s, only “I’m . . .” Typically, in sentence generation tasks, the patient failed to produce a response or was extremely slow. However, some direct questions could be answered appropriately, and any sentence that was produced was lexically, syntactically, and morphologically correct. What appears to be impaired is the conceptualizer stage.

About 10 other patients of this type have been described as single cases. A massive influence on the performance of these patients is the range of alternatives that are potentially available to the speaker (Robinson et al. 1998). When this is high, the dynamic aphasia patient typically cannot respond. But when the situation allows only a very restricted set of possibilities, the patient typically produces a correct sentence. For instance, patient ANG of Robinson et al. (1998) was

given a range of tasks that involved this contrast. Thus, when she was asked to produce a sentence including a common object, such as a telephone, that was shown as a picture, she scored 0/6. On the other hand, when presented with a simple scene to describe (e.g., a girl ice skating), she scored 34/34. When asked to produce a sentence including a single proper name (e.g., Hitler) she scored 26/28, saying, for instance, "Hitler is one of those wicked people that should never have been born." But given a single common word (e.g., sea), where the range of alternatives is greater, she scored only 14/28, saying, in this case, "No idea."

Related results were obtained at the same time by Thompson-Schill et al. (1998), using a task in which patients were asked to generate a verb given a noun. Nouns were divided into two groups according to the diversity of responses given by controls. Four patients with posterior left inferior frontal lesions had significantly more difficulty with high-selection (i.e., inconsistent) verbs than with low-selection verbs, compared with controls. Nine patients with lesions elsewhere in the frontal lobes did not have this problem.

ANG, too, had a left inferior frontal gyrus lesion. This localization of the main form of dynamic aphasia was supported by a group study. Robinson et al. (2010) found that a subgroup of 12 patients with lesions involving the left inferior frontal gyrus performed significantly worse than 35 patients with other frontal lesions and normal controls in generating a sentence from a high-frequency word but not in generating a sentence from low-frequency words, where there would be fewer selection requirements.

These findings all fit with the idea that the dynamic aphasic patient is impaired in constructing the preverbal message at the conceptualizer stage. This shows up behaviorally when the process is at all difficult, such as when there are many alternative possibilities. Is this a problem that affects active thought processes in situations where language is not required? Individual dynamic aphasic patients can apparently perform much better on reasoning tasks. For instance, patient CH (Robinson et al. 2005), a patient with dynamic aphasia similar to that of ANG, although somewhat less severe, performed in the high average range on the IQ test Advanced Progressive Matrices and in the superior range on WAIS Block Design. However, such a comparison involves many disparate cognitive components. It is not comparable to the Varley et al. (2005) study of syntactic aspects of arithmetic, where there was excellent matching between verbal and nonverbal tasks.

One type of task that requires active thought and has been studied in both verbal and nonverbal forms in the same patients is that of fluency—generation of items defined by a particular criterion. Phonemic fluency, i.e., generating as many words as possible in a fixed time beginning with a particular letter, has been extensively studied by neuropsychologists since the pioneering work of Brenda Milner (1964). This type of fluency is usually much impaired in dynamic aphasic patients. In Robinson et al.'s (2012) study, performance on this test was compared with that on seven other fluency tasks. In a sample of 40 frontal patients, out of the 11 who performed worse than any healthy control on phonemic fluency, 6 had left inferior frontal gyrus lesions, as one would expect if dynamic aphasia leads to poor phonemic fluency.

Patients with left lateral lesions in this sample did not generally have word production impairments. On a naming test, their scores were similar to those of right lateral lesion patients and not significantly different from those of normal controls. Yet, on phonemic fluency, they produced only just over 50% of the number of words that right lateral patients did. By contrast, on a task requiring them to produce as many designs as they could given certain constraints, they performed equally well as right lateral patients. Thus, CH, for instance, was well within the normal range. Even more surprising, the left lateral patients performed similarly to the right lateral patients in the ideational fluency task—e.g., "How many uses you can think of for a brick?" In comparison with right lateral lesion patients, their fluency deficit was restricted to verbal material. We assume that a phonemic fluency deficit, if word production processes are intact, is a sign of impairment in

the production of the preverbal message by the conceptualizer stage. Thus, it would appear that this process, at least in part, is purely in the language domain and not basically reliant only on general active thought processes.

ESSENTIAL PREREQUISITES FOR ACTIVE THOUGHT

Volition and Concentration

In this section, we deal with the processes that might be considered the nuts and bolts of active thought. We start with the most basic prerequisites for active thought, volition and concentration. Clinically, syndromes such as apathy and akinetic mutism, the failure to initiate actions or speech (Cummings 1993), which represent the extreme loss of volition, have been associated with lesions to the medial PFC.

Formal neuropsychological testing supports the idea of a weakening of processes underlying volition in superior medial prefrontal lesions. In the so-called ROBBIA set of studies (Stuss & Alexander 2007, Shallice & Gillingham 2012), the Stuss-Alexander subdivision of the frontal cortices was adopted with approximately 40 frontal patients. These studies included simple reaction time, two versions of choice reaction time, task switching, and go-no-go. In none of these paradigms was the left or right lateral or the inferior medial group significantly slower than the normal controls. In all of them, however, the members of the superior medial group were significantly slower than normal subjects and, in most, significantly slower than the other patient groups. Moreover, the effects were large. Thus, in one task, the healthy control group took, on average, 607 ms, and three of the four frontal patient groups took from 533 to 643 ms, but the superior medial group took 821 ms. In addition, in the more difficult conditions, such as the switch condition in task switching, which is more difficult than the repeat condition, the superior medial group were disproportionately slowed.

Stuss et al. (1995, 2005) argued that the primary impairment of the superior medial group in these tasks is one of energization. They argued that, in the supervisory system model, contention scheduling operating alone would not be optimal in reaction time tasks. For instance, a selected schema would gradually lose activation over several seconds. Thus, for better performance, top-down boosting of lower-level action schemas would be needed. Energization, then, is seen as the process required to initiate supervisory system operations. This closely corresponds to a number of characterizations of the function of the anterior cingulate derived from functional imaging, such as those of Posner & DiGirolamo (1998) and Kerns et al. (2004). Energization may be seen as the material substrate of volition and the basis of concentration.

In this approach, impairments following superior medial lesions should be found much more widely, even on cognitively simple tasks. They are. Thus, MacPherson et al. (2010) investigated the performance of 55 frontal patients, subdivided into subgroups with medial, orbital, and lateral damage, on the Elevator Counting subtest (Manly et al. 1994). This test assesses the ability to sustain attention by presenting a long series of tones at a slow rate. Optimally, one simply counts the tones. The medial and left lateral groups were significantly impaired on the task compared to healthy controls, with the medial group making errors 13% of the time in comparison to the controls' 1.6% error rate. In contrast, the right lateral patients were not impaired.

Energization impairments could also account for certain medial frontal findings reported in some studies discussed above. In Robinson et al.'s (2012) fluency study, discussed in the previous section, the medial frontal group, unlike the lateral frontal groups, was impaired on all eight fluency tasks, so an energization account is more plausible than a purely cognitive one. Medial frontal lesions are also the predominant site for the grasp reflex and utilization behavior, discussed

in the Introduction, where the task is simple and all that is required is to realize the will to carry it out. In lay terms, the superior medial region can be seen as the locus of the system producing volition and concentration.

Set Switching and Response Inhibition

A second prerequisite for active thought is flexibility. Classically, the best-known deficit following prefrontal lesions was, indeed, difficulty switching sets. This deficit leads to a consequent increase in perseveration, as in the Wisconsin Card-Sorting test, which loads heavily on the ability to switch from responding to one perceptual dimension to another (Milner 1963).

Such clinical tests are, however, complex and have multiple components, including discovery. Much cleaner are so-called task switching paradigms, in which two simple tasks that use the same stimuli are carried out repeatedly in a rapid random ordering. Three studies have used such paradigms with 35 or more frontal patients (Aron et al. 2004, Shallice et al. 2008, Tsuchida & Fellows 2013). All three studies showed left frontal patients to have either increased error rates early in learning (Shallice et al. 2008) or increased reaction times each time the task switched. Aron et al. (2004) suggested that what is impaired in these patients is top-down (supervisory) control of task set (action schema). Regarding the critical anatomical areas, a VLSM analysis carried out by Tsuchida & Fellows (2013) was in agreement with a meta-analysis of functional imaging studies carried out by Derrfuss et al. (2005), suggesting that the left inferior frontal junction is critical for task switching.

However, Aron et al. (2004) also reported increased error rates in task switching in patients with right ventrolateral lesions. They attributed this to impairment in response inhibition. However, no such effect was found by either Tsuchida & Fellows (2013) or Shallice et al. (2008). Aron et al. (2003) had previously used a standard response inhibition task from human experimental psychology, namely, the stop signal task, with the same 17 right frontal patients but, unfortunately, no other frontal group. For five right frontal subregions, the correlation between amount of damage to the subregion and poor performance on the task was examined. For three of the regions, the correlation was significant, but for one—the inferior frontal gyrus—it was very high. The authors argued that this was the critical region involved in response inhibition, with the other significant effects arising due to correlations between the amount of damage in a region and that in its neighbor.

Very different results were, however, obtained by Picton et al. (2007), who studied 43 frontal patients with another response inhibition task—go-no-go. They found that the critical areas for false alarms were left areas 6 and 8, areas Aron et al. (2003) did not investigate. The four patients with lesions in these areas made 30% false alarms. By comparison, the 13 patients with right ventrolateral lesions made only 12% false alarms, not significantly different from the controls (8%). Moreover, the effects found in Aron et al.'s (2004) right frontal patients did not replicate in the two other task switching studies. The neuropsychological evidence fits better overall with a different perspective from neuroimaging that suggests that the role of the right inferior PFC in such tasks is bottom-up attention rather than inhibition (Hampshire et al. 2010). When a stop signal occurs after the initiating stimulus, attention must then be switched to the new stimulus. This is not required in go-no-go tasks.

Active Monitoring and Checking

Error detection is an ubiquitous aspect of human active thought, especially when a new skill is being acquired. It begins with a mismatch between actuality and expectation, but this can be detected

by a variety of means, some very subtle (Rizzo et al. 1995). Thus, monitoring and checking are basic processes late in the time course of active thought. Neuropsychologically, these processes have long been thought to be controlled by dorsolateral PFC systems (Petrides 1994).

Neuropsychological evidence suggests that they are at least partly lateralized to the right. Stuss et al. (2005) asked 38 frontal patients, divided into groups based on the four Stuss-Alexander anatomical regions, to carry out reaction time tests in which the stimulus was preceded by a warning signal that occurred randomly from 3 s to 7 s before. For the simple reaction time condition, controls responded 30 ms to 40 ms more rapidly to the long than to the short warning intervals—the so-called foreperiod effect. This is to be expected, as the conditional probability of the stimulus occurring in a particular interval increases with the foreperiod. Three of the four frontal patient groups behaved in an identical fashion. The one exception was the right lateral group, which was actually slower in the long foreperiod condition. By contrast, when the foreperiod was fixed over a block of trials, the right lateral group behaved normally. Stuss et al. (2005) argued that, in the variable foreperiod condition, the right lateral group failed to monitor the fact that no stimulus had occurred and so did not increase preparation. When monitoring was not required because the foreperiod was constant over a block, they behaved normally. Thus, active monitoring was held to occur in the right lateral frontal area.

Qualitatively similar results have been obtained by Vallesi et al. (2007b) in a TMS study in which stimulation of the right dorsolateral PFC was contrasted with stimulation of the left dorsolateral PFC and the right angular gyrus. In a more direct attempt to replicate the precise paradigm used by Stuss et al. (2005), Vallesi et al. (2007a) studied 58 patients with fairly focal tumors. They obtained a partial replication. Premotor patients and parietal patients had foreperiod effects of the order of 30–55 ms both before and after operation, the same as normal controls. Left prefrontal patients showed a reduced foreperiod effect of 15–25 ms both before and after operation. The right prefrontal patients, however, were completely normal before operation, with a foreperiod effect of 55 ms, but this was drastically reduced to 10 ms after operation.

A number of neuroimaging studies point to a similar conclusion with respect to the involvement of the right rather than left PFC. Thus, Fleck et al. (2006) found that the right lateral PFC was also more active in low-confidence judgements, where more monitoring was needed, than in high-confidence ones in both memory and perceptual tasks (see also Sharp et al. 2004, Chua et al. 2006, Yokoyama et al. 2010; for another neuropsychological example, see Reverberi et al. 2005; note that only Sharp et al. and Reverberi et al. find a specifically lateral localization within the right PFC). Overall, there is some support for the idea that lateral regions within the right PFC are the most critical for active monitoring processes.

Working Memory

The reader may be surprised that an obvious requirement for active thought that has not yet been mentioned is working memory. Working memory has been associated with the lateral PFC since the neurophysiological work of Fuster & Alexander (1971) and Goldman-Rakic (1988). However, these classic neurophysiological experiments typically involved a monkey holding one position in space for up to a minute. Human working memory tasks involve the subject making operations on the much greater contents of a short-term store.

When short-term memory tasks are given to patients with frontal lesions, they can exhibit no deficits if operations do not need to be carried out on the contents of the relevant short-term memory store. Thus, D'Esposito & Postle (1999) reviewed all the studies they could find that compared groups of patients with lateral frontal lesions with normal controls on tasks that only loaded on short-term store capacity and did not involve operations. There were eight such studies for

digit span and four for spatial span; none showed a significant difference between the two groups. Thus, although working memory tasks can produce deficits in frontal patients, the impairment does not appear to be one of storage, but rather one of monitoring or manipulation, as argued by Petrides (1994). We discuss monitoring in the previous section. In the next section, we discuss how manipulation can take different forms, each associated with different prefrontal regions.

FORMS OF ACTIVE THOUGHT

Abstraction

A key human ability for much higher-level thinking is the ability to abstract. Goldstein (1936), having worked with soldiers with war wounds, particularly wounds affecting the frontal cortex, described them as having a loss of abstract attitude. Goldstein's concept abstract attitude was rather complex. However, it can be operationalized with a clinical test: the interpretation of proverbs. Murphy et al. (2013) tested 46 patients with frontal lesions, subdivided into groups with left lateral, right lateral, and medial lesions, using a proverb interpretation test (PIT) adapted from Delis et al. (2001). This test assesses the ability to interpret a statement in an abstract rather than a concrete sense. Thus, for "Rome was not built in a day," a generalized understanding is that any great achievement takes patience and time to complete. A concrete understanding may refer to the time it takes to complete buildings or infrastructure or even to establish the Roman Empire. Medial frontal patients were the only frontal subgroup significantly impaired on the PIT relative to healthy controls. However, their most frequent responses were partially correct ones (e.g., "Things take time, but you will get there in the end"), so an energization deficit seems plausible. However, of the errors made by the left lateral group, 45% were concrete, indicating an inability to produce an abstraction. By contrast, only 12% of right lateral errors and 8% of those made by healthy controls were concrete. McDonald et al. (2008) made the related finding that epileptic patients with a left frontal focus produced poorer abstraction responses on this test than those with a right frontal focus. The left lateral region seems to be critical for abstraction, at least in the verbal domain.

Neuropsychological studies have not yet produced a tighter localization of any abstraction process in the comprehension of so-called figurative language. Imaging studies are not entirely consistent, but the most common site is the left inferior frontal gyrus (e.g., Rapp et al. 2004; see also Papagno et al. 2009 for convergent TMS evidence). Shallice & Cooper (2013) have argued that the representation of abstract concepts requires a neural architecture that supports the construction of hierarchical structures and that this is carried out in the left inferior frontal gyrus.

Of course, abstraction also occurs in nonverbal domains. For instance, it is an important component process in carrying out nonverbal IQ tests, such as the Progressive Matrices or the Cattell Culture Fair. However, tackling these tests requires many other processes, as well, so they cannot easily be used to localize nonverbal abstraction. One study that begins to address this issue is that of Reverberi et al. (2005). They tested 40 frontal patients on the Brixton task (Burgess & Shallice 1996a), where subjects must abstract the rules of how a blue circle moves across successive cards, each containing a 2×5 array of circles. Left lateral patients were impaired even with good working memory, but this was not the case for the other frontal groups. Recently, Urbanski et al. (2016) used analogy tasks, which are somewhat simpler than *g* tests but require abstraction. Patients were requested to find an analogy between a source set and one of two candidate sets of colored letters of varying size. Using VLSM, the critical region for impairment was found to be the anterior lateral PFC, again on the left. However, only 27 patients were included in this study, so coverage of the frontal lobes was rather patchy.

Deduction

Induction is the process by which one produces a novel conclusion from the information currently available, prototypically in the articulation of a new scientific theory. Producing a novel abstraction, the process discussed in the previous section, is a key aspect of induction. The complement to induction within reasoning is deduction, where conclusions follow logically and certainly from the assumptions, or premises. Deduction is, however, somewhat difficult to isolate neuropsychologically, as tests typically involve multiple premises. So, in addition to language comprehension, it relies heavily on working memory. Although the effect of this factor can be mitigated by allowing premises to remain visible, it is difficult to eliminate completely.

With functional imaging, the complex stages of processing involved in deduction can be tracked over time. Thus, Reverberi et al. (2010) used a clever complex design to attempt to isolate the moment in time when subjects, following interpretation of premises, were making logical inferences. Activation increased particularly in left areas 44 and 45. This result is broadly consistent with earlier functional imaging studies of deduction (e.g., Goel et al. 2000). However, the complexity of this study would make converging neuropsychological data valuable. Yet lesions to the putatively critical areas typically produce aphasic problems, which interfere with the interpretation of individual premises. Probably one of the most extensive studies of classical deduction in frontal patients was conducted by Reverberi and colleagues (2009), who tested 36 frontal patients on their ability to process one-, two-, or three-premise syllogisms. However, aphasic patients were excluded, and this resulted in no patients having lesions overlapping the critical left areas 44 and 45. Notably, however, the performance of right lateral patients was indistinguishable from healthy controls, unlike that of left lateral and medial patients. Deduction, like abstraction, is a left frontal process, at least when the stimuli used are verbal.

Reasoning in Well-Structured and Less Well-Structured Problem Spaces

A well-structured problem space is one where, as in games like chess or puzzles like the Tower of Hanoi, the start position and goal are clearly specified. The consequences of selecting one from the finite set of alternatives available at any stage of problem solution are also well specified in advance. By contrast, a less well-structured problem space, more typical of real life, is a problem situation where at least one of these conditions does not hold, as in planning the cooking of a meal for guests.

Tower tasks involve moving balls on pegs to achieve a goal position in the minimum number of moves. They constitute a nonverbal well-structured domain and have been extensively investigated neuropsychologically. The two studies involving the most patients are a Tower of London study by Shallice (1982), with 61 patients, and a Tower of Hanoi study by Morris et al. (1997), with 59 patients. Both tasks included conflict situation trials in which, early in the solution, the subject must move a ball in the opposite direction of its eventual goal peg. The two studies used the classical group approach, and both found a selective impairment in left frontal patients. Of particular interest, in the Morris et al. (1997) study, the impairment was found only for conflict situation trials occurring relatively early in the testing period.

Tasks such as these require what Petrides (1994) called manipulation of working memory contents, which he localized in the dorsolateral PFC. In particular, these tasks involve, among other processes, updating the contents of working memory (Miyake & Friedman 2012). The two Tower studies discussed in the previous paragraph do not speak to the specific localization within the left frontal lobe. More recently, functional imaging studies of these tasks have generally supported Petrides' view (Kaller et al. 2011, Crescentini et al. 2012). Thus, processes that are different from those underlying verbal deduction are presumably involved.

If we return to the issue of less well-structured problem spaces, Goel et al. (2007) used tasks that either were explicitly spatial or could be mapped onto a spatial dimension through the use of ordinal scale comparisons, such as, “Mary is smarter than John. John is smarter than Michael. Mary is smarter than Michael. Does it follow?” For half of the problems, the conclusion did not follow. Of these, half again were indeterminate, e.g., “Sarah is prettier than Heather. Sarah is prettier than Diane. Diane is prettier than Heather.” The problems were given to 18 frontal patients. Goel and colleagues (2007) found that, for the determinate problems, both valid and invalid (e.g., Michael is smarter than Mary), the left frontal group performed worse than either healthy controls or the right frontal group. However, for the indeterminate problems that were not well structured, it was the right frontal group that performed much worse than either of the other two groups, which did not differ.

Goel et al. (2007) used the mental models approach of Johnson-Laird (1983) and held that the indeterminate problems require the construction of at least two models for the alternative possibilities, as well as holding the information that one or the other can be correct. They further argued that the left frontal lobe is adept at constructing determinate and unambiguous representations, whereas the right frontal lobe is needed to maintain “fluid, indeterminate, vague and ambiguous representations” (Goel et al. 2007, p. 2249). The study of Goel et al. is rather small for strong theoretical conclusions, but, as we discuss in the next section, its results resonate with other findings.

From Lateral Transformations to Strategy Shifts

In a single case study of an architect who had had a right frontal meningioma removed, Goel & Grafman (2000) made a different, if related, contrast between the functions of the left and right PFC. Despite having an IQ of 125 and a maintained ability to carry out the basic skills of his profession, the patient was unable to operate effectively as an architect. Goel & Grafman (2000) argued that he had retained the ability to make what they called vertical transformations, namely, more detailed versions of the same idea. What he had lost was held to be the ability to make lateral transformations, where one moves from one idea to a different type of idea, which the authors held to be a function of the right frontal lobe.

Support for a similar idea comes from a rather surprising source. In an attempt to develop a task requiring cognitive inhibition, Burgess & Shallice (1996b) invented the Hayling Sentence Completion Test. In section B of this test, subjects are presented with a sentence frame, such as “The ship sank very close to the . . .” The task of the subject is to give a word unrelated to the completion of the sentence or to any word in the sentence. “Banana” would be an example of such a word. In an initial study of 91 patients, the Hayling B test proved to be highly sensitive to frontal lesions. Patients with anterior lesions produced more than double the error score of either posterior-lesioned patients or healthy controls. No significant lateralization effects were found.

This result looks like a difficulty with inhibition. However, it was noted that, after a few trials, healthy controls tended to develop a strategy of looking around the room to select an object or of making an association with their previous response. Their aim was to produce a word before the sentence frame was presented. They then no longer had to inhibit the completion; they merely had to check that their already generated word did not, by chance, relate to the sentence frame. Anterior-lesioned patients gave far fewer responses that fitted either of these two strategies than did posterior-lesioned patients or healthy controls. They did not generate an effective strategy to circumvent the difficulty of the task.

Three studies have indicated surprising right frontal involvement in this entirely verbal task. Roca et al. (2010) examined the extent to which *g* scores could explain frontal deficits in several tasks with 44 frontal patients. As discussed above, they found that, for five tasks, one of which was

a much shortened version of the Hayling test, the frontal deficit could not be explained merely as a consequence of impairment in fluid IQ. Six patients performed particularly badly on this set of tasks. Five of them had right frontal lesions.

In another study using the full Hayling test, Volle et al. (2012) tested 45 patients with focal cortical lesions. They then used two critical lesion localization procedures. For both clinical measures of Hayling B, that of reaction time and that of errors, the critical lesion sites were in the right frontal lobe. For the more sensitive lesion localization procedure, the reaction time slowing localized to right lateral areas 45 and 47 and increased errors to right orbitofrontal area 11.

Robinson et al. (2015) gave the Hayling test to 90 focal frontal lesion patients and used the Stuss-Alexander grouping method. On the reaction time measure, it was the right lateral group that were grossly slow—performing more than four times worse than the healthy control group—while the left lateral group did not differ from controls. On the error measure, the right lateral group was, again, the only patient group that performed significantly worse than controls, with an error score more than three times as high as that of the control. Moreover, they made very few responses indicating use of an effective strategy. More specifically, the difference between the effects of left and right lesions lay, again, in the inferior lateral frontal cortex.

In a different, smaller set of right frontal patients, those with lateral lesions were compared on the Hayling test to those with orbitofrontal lesions. Right lateral patients were found to make many suppression errors, to produce very few strategy-connected words, and to require longer thinking times, all measures known to correlate with fewer strategy responses. In contrast, the orbitofrontal group performed normally. This supports the notion that it is the inferior right lateral cortex rather than the orbitofrontal cortex that is involved in strategy production (Cipolotti et al. 2015c).

A general inhibition problem is an implausible explanation of the right lateral impairment. Cipolotti et al. (2016) tested 30 frontal patients on both the Hayling task and the Stroop. The right frontal group performed much worse than the left frontal one on the Hayling task, but for the Stroop, there was an insignificant effect in the other direction.

By contrast, the notion that the right inferior lateral regions are critical for novel strategy production in problem solving has been supported by two studies, one employing functional imaging and the other cortical thickness differences across normal subjects. Both studies used problem solving tasks that involved an insightful lateral move to produce a novel strategy. One used Guilford's matchstick task (Goel & Vartanian 2005), and the other the so-called Nim or Subtraction game (Seyed-Allaei et al. 2017). Both found the critical area to be right area 47. Whether its role lies in the creation of a novel structure or plan or the realization of the inadequacy of an earlier strategy remains to be established.

Planning for Future Action

Reasoning needs to be implemented in action, often after a gap in time. Intentions need to be set up and then realized later. Typically, other tasks have to be carried out in the interval. Thus, planning for future action typically leads to a multitasking situation. Shallice & Burgess (1991) described three frontal patients who performed well on a wide range of clinical tests of frontal lobe function but were specifically impaired when given two tests of multitasking. Each of these tests—Six Elements and Multiple Errands—required patients to organize themselves to interleave a number of different tasks without cues as to when to switch, while obeying a set of simple rules written on a card in front of them. This study showed that multitasking was a separable frontal function. The one patient, AP, in whom the lesion could be well localized had a bilateral lesion of the frontopolar cortex (areas 10 and 11) (Shallice & Cooper 2011). Burgess et al. (2000) used another multitasking test, the Greenwich, which required three different tasks to be interleaved

over 10 minutes. When memory was not impaired, poor overall performance was associated with lesions to the more polar and medial aspects of areas 8, 9, and 10. Area 10 appears to be critical. Roca et al. (2011) compared seven frontal patients with area-10 damage to eight patients without this damage. The patients with area-10 damage were more impaired in multitasking but less so on response inhibition and abstract reasoning.

That the temporal aspect of setting up and realizing intentions may indeed be the core deficit of the multitasking impairment is shown by a study by Volle et al. (2011). With the assistance of a stopwatch, 45 patients with focal lesions had to press a spacebar every 30 s while carrying out another task. The eight patients with area-10 lesions pressed the spacebar once every 48 s, in comparison with the rate of once every 32 s for the other patients. On control tasks not involving time, the area-10 patients were unimpaired.

Functional imaging studies, too, have given strong parallel evidence for the involvement of bilateral area 10 in multitasking and, in particular, in the generation and realization of intentions (Koechlin et al. 1999; Burgess et al. 2001, 2011).

THEORETICAL CONCLUSIONS

In this review, we have focused on neuropsychological group studies of what we termed active thought and on the localization of the principal processing components of a variety of tasks involving it. We have assumed that different localizations imply different computational functions. The most basic conclusion one can draw from the neuropsychological literature is that the PFC has a complex computational structure with a large set of subsystems combining to realize active thought. This is because impairments at the supervisory level differ qualitatively on at least some combinations of lateral versus medial, left versus right, anterior versus posterior prefrontal, and dorsal versus ventral.

In addition, most frontal tasks involve many components. Thus, the complexity of the neurocognitive architecture could well be greater than neuropsychological group studies alone currently indicate. This is because these pick out one or a very few critical regions. For instance, we have shown that right lateral frontal systems for novel strategy selection are important in carrying out the Hayling task. Yet Robinson et al. (2016) have recently described two patients with different types of difficulty completing the task, with one type of difficulty being clearly related to inhibition. Both had left frontal lesions! The task undoubtedly involves multiple systems relevant for active thought.

In this case, why are neuropsychological studies valuable? They clearly show that the affected systems are crucial. In addition, though, they complement functional imaging findings informatively with respect both to lateralization of function and to the role of networks or their constituent subsystems. Regarding lateralization of functions, one frequently obtains the impression from the imaging literature that the two frontal cortices have basically equivalent functions; activation is often bilateral. The neuropsychological literature provides a different perspective. The two lateral PFCs appear to have markedly different functions with respect to active thought.

There are a number of different ways in which these contrasting functions have been characterized. Thus, Stuss & Alexander (2007) and Shallice & Gillingham (2012) contrast task setting and setting up a program (left lateral frontal region) with active monitoring (right lateral frontal region). The latter is well supported by the currently reviewed studies, the former by the Morris et al. (1997) study of the Tower of Hanoi task. Goel and colleagues (2000, 2007), instead, made the contrast between vertical operations in a well-structured problem space (left) and lateral ones in an ill-structured space (right). This fits the results on deduction and Tower tasks (left) and Hayling tasks well.

Computationally, one can combine these two sets of contrasts. The left lateral region becomes the site where Duncan's serially operating program is realized; this fits, too, with the task switching studies. The program then runs on systems in premotor and posterior cortices. By contrast, the right lateral region would be where processes operate in parallel either separately, to detect any of a range of potential errors (active monitoring), or in combination, to produce a novel strategy. This would fit with the left lateral region having a much higher degree of internal inhibition than the right because, at each stage, the left lateral region selects, top down, one from a range of possible thought and action schemas.

Within the left lateral frontal lobe, the contrasting localizations of deduction (ventrolateral) and Tower task operations (dorsolateral) fit roughly with a Petrides-like anatomical perspective. Cognitively, the contrast supports the view that rule-based mental logic and mental model-based reasoning both exist but rely on anatomically different systems (Goel 2007). As far as mental model-based reasoning is concerned, Knauff (2013) has argued that the model itself is parietally located, and the existence of a qualitatively organized representation of objects in space in the right parietal lobe (Buiatti et al. 2011) supports this.

Regarding the contrast between the findings of neuropsychology and those of functional imaging on the role of networks or their constituent subsystems, imaging provides evidence on the network of systems involved in task execution. Focal lesion patients provide evidence more often, if the lesion is small, on single systems. From this perspective, Duncan & Owen's (2000) frontoparietal multiple demand network may be seen as composed of a variety of special-purpose subsystems that combine to realize, for instance, mental model-based reasoning in tests of fluid IQ.

The clearest example of this functional distinction between parts of the network is the contrast between lesions to lateral and superior medial frontal regions. Both contain parts of the multiple demand network. However, lesions affect the two regions differently across a range of neuropsychological tests, including reaction time, fluency, and reasoning tasks. In the current approach, the superior medial PFC energizes supervisory operations, but the lateral PFC implements them; the two regions have different functions.

The impaired performance on different tasks demonstrated by patients with lesions in the same region can also give rise to theoretical questions. Consider the left inferior frontal region. We argue that it is involved in constructing the preverbal message but also in the representation of abstraction. Both of these require hierarchically organized structures relating to language. But do they involve the same system? We will not know until it is investigated whether dissociations can exist between tasks involving the two regions.

Neuropsychological findings on active thought do not just show that certain brain systems are critical for task execution. They also complement findings from functional imaging in two different ways. First, rather than giving information on whole networks, they highlight the role of the systems of which these networks are composed. Second, rather than downplaying differential lateralization of function, they emphasize it. Whether they can also help answer the key question of how these supervisory subsystems interact remains to be seen.

SUMMARY POINTS

1. For active thought processes, neuropsychology provides valuable evidence on underlying functional subsystems and their lateralization.
2. For the medial PFC, the subsystems to which such evidence relates are critical for energizing supervisory processes.

3. For the left lateral PFC, these subsystems are critical for top-down schema activation, updating, deduction, and, more anteriorly, abstraction.
4. For the left ventrolateral PFC, these subsystems help to construct preverbal messages.
5. For the right lateral PFC, these subsystems underpin active monitoring and, more inferiorly, are critically involved in the production of novel strategies.
6. For the frontopolar PFC, these subsystems play a key role in the setting up and maintenance of intentions.

FUTURE ISSUES

1. For models of frontoparietal control networks, of which the multiple demand network is one, are the frontal components functionally different or functionally equivalent to the parietal components?
2. Does the left lateral PFC have stronger inhibition internal to the region than the right lateral PFC, as suggested above?
3. For some claimed processes (e.g., active monitoring) and even some tasks (e.g., Hayling B), there is a broad agreement across studies about which frontal lobe plays the more critical role, but there is disagreement over the specific parts of the lobe responsible. Is this due to variations across samples of patients tested or due to subtle differences in the cognitive processes employed to perform the particular version of the task used?
4. Abstraction and formation of a preverbal message both involve more anterior parts of the inferior left lateral frontal lobe. Do they have any processes in common? For instance, extrapolating from Hagoort's (2013) ideas on localization of so-called unification processes, could the region be required for the construction of multilevel structures (Shallice & Cooper 2013)?
5. Are impairments following lesions to the inferior lateral right frontal region in tasks like the stop task due to impairments to systems controlling response inhibition or to those controlling bottom-up attention?
6. What is the involvement of the right frontal region in novel strategy attainment tasks, such as Hayling B? Does this region contain systems that create a novel structure or plan, or systems that determine that the preceding strategy was inadequate and thus needs changing? Are there yet further possibilities?

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Contents

The Properties and Antecedents of Hedonic Decline <i>Jeff Galak and Joseph P. Redden</i>	1
How We Hear: The Perception and Neural Coding of Sound <i>Andrew J. Oxenham</i>	27
The Psychology of Music: Rhythm and Movement <i>Daniel J. Levitin, Jessica A. Grahn, and Justin London</i>	51
Multistable Perception and the Role of Frontoparietal Cortex in Perceptual Inference <i>Jan Brascamp, Philipp Sterzer, Randolph Blake, and Tomas Knapen</i>	77
Ensemble Perception <i>David Whitney and Allison Yamanashi Leib</i>	105
Neuro-, Cardio-, and Immunoplasticity: Effects of Early Adversity <i>Eric Pakulak, Courtney Stevens, and Helen Neville</i>	131
Prefrontal Cortex and Neurological Impairments of Active Thought <i>Tim Shallice and Lisa Cipolotti</i>	157
Infant Statistical Learning <i>Jenny R. Saffran and Natascha Z. Kirkham</i>	181
How Children Solve the Two Challenges of Cooperation <i>Felix Warneken</i>	205
Linking Language and Cognition in Infancy <i>Danielle R. Perszyk and Sandra R. Waxman</i>	231
Cognitive Foundations of Learning from Testimony <i>Paul L. Harris, Melissa A. Koenig, Kathleen H. Corriveau, and Vikram K. Jaswal</i> ...	251
Gender Stereotypes <i>Naomi Ellemers</i>	275
Attitudes and Attitude Change <i>Dolores Albarracín and Sharon Shavitt</i>	299

Persuasion, Influence, and Value: Perspectives from Communication and Social Neuroscience <i>Emily Falk and Christin Scholz</i>	329
Social Mobilization <i>Todd Rogers, Noah J. Goldstein, and Craig R. Fox</i>	357
Developmental Origins of Chronic Physical Aggression: A Bio-Psycho-Social Model for the Next Generation of Preventive Interventions <i>Richard E. Tremblay, Frank Vitaro, and Sylvana M. Côté</i>	383
Improving Student Outcomes in Higher Education: The Science of Targeted Intervention <i>Judith M. Harackiewicz and Stacy J. Priniski</i>	409
Why Social Relationships Are Important for Physical Health: A Systems Approach to Understanding and Modifying Risk and Protection <i>Julianne Holt-Lunstad</i>	437
Principles and Challenges of Applying Epigenetic Epidemiology to Psychology <i>Meaghan J. Jones, Sarah R. Moore, and Michael S. Kobor</i>	459
Psychology, Science, and Knowledge Construction: Broadening Perspectives from the Replication Crisis <i>Patrick E. Shrout and Joseph L. Rodgers</i>	487
Psychology's Renaissance <i>Leif D. Nelson, Joseph Simmons, and Uri Simonsohn</i>	511
Indexes	
Cumulative Index of Contributing Authors, Volumes 59–69	535
Cumulative Index of Article Titles, Volumes 59–69	540

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TABLE OF CONTENTS FOR VOLUME 1:

Introduction, Susan A. Gelman, Sandra R. Waxman

Eleanor Maccoby: An Abridged Memoir,
Eleanor Maccoby

**Using Developmental Science to Distinguish
Adolescents and Adults Under the Law**,
Laurence Steinberg, Grace Icenogle

**Adolescent–Parent Relationships: Progress, Processes,
and Prospects**, Judith G. Smetana, Wendy M. Rote

The Life Course Consequences of Very Preterm Birth,
Dieter Wolke, Samantha Johnson, Marina Mendonça

**Early Deprivation Revisited: Contemporary Studies
of the Impact on Young Children of Institutional Care**,
Megan R. Gunnar, Brie M. Reid

The Development of Cumulative Cultural Learning,
Cristine H. Legare

**Neighborhood Effects on Children's Development
in Experimental and Nonexperimental Research**,
Tama Leventhal, Veronique Dupéré

**Cognitive Aging and Dementia: A Life-Span
Perspective**, Elliot M. Tucker-Drob

**Brain Plasticity in Human Lifespan Development:
The Exploration–Selection–Refinement Model**,
Ulman Lindenberger, Martin Lövdén

The Pervasive Role of Pragmatics in Early Language,
Manuel Bohn, Michael C. Frank

**Early Development of Visual Attention:
Change, Stability, and Longitudinal Associations**,
Alexandra Hendry, Mark H. Johnson, Karla Holmboe

**Childhood Adversity and Neural Development:
A Systematic Review**, Katie A. McLaughlin,
David Weissman, Debbie Bitrán

**Social Relations Across the Life Span: Scientific
Advances, Emerging Issues, and Future Challenges**,
Toni C. Antonucci, Kristine J. Ajrouch, Noah J. Webster,
Laura B. Zahodne

**Safety Net Policies, Child Poverty, and Development
Across the Lifespan**, Benard P. Dreyer

The Development of Social Categorization,
Marjorie Rhodes, Andrew Baron

Developmental Effects of Parent–Child Separation,
Anne Bentley Waddoups, Hirokazu Yoshikawa,
Kendra Strouf