Cortical Lesions and Attention

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ABSTRACT Neurological patients have historically provided important insights into the brain mechanisms of attentive behavior. The contribution of the lesion method to understanding attentional functions is discussed with particular reference to prefrontal cortex. This brain region is a central component of the distributed neural systems engaged during sustained and phasic attention to both external environmental events and to the internal mental state. Prefrontal cortex regulates sustained attention and working memory through both inhibitory and facilitory mechanisms. Phasic attention to novel events is dependent on a prefrontal-hippocampal network. Thus, many of the observed behavioral deficits subsequent to prefrontal damage may be due to impaired function in distant neural regions under prefrontal control. Delineation of the cellular and pharmacological substrates of those pathways could lead to treatment interventions for the attentional deficits observed after prefrontal damage.

For hundreds of years scientists and clinicians have made inferences about the location of cognitive functions in the human brain from observations of the behavioral deficits exhibited by persons who have suffered brain damage (Bouillard, 1825; Aubertin, 1861, as cited in Stookey, 1954; Harlow, 1868; Dejerine, 1892). Until recently, this approach—the lesion method—was one of the few techniques available for examining the neural basis of human sensory, cognitive, and motor functions.

The venerable tradition of neuropsychology entered the era of contemporary neuroscience with the advent of techniques that provide accurate, quantifiable images of the living human brain. The merger of information-processing accounts of the mind and parallel distributed processing concepts with the refined ability to localize lesions using magnetic resonance imaging (MRI) has added to knowledge of the distributed neural networks that mediate processes such as attention.

This chapter reviews the current status of the application of the lesion method to the study of attention, with special reference to the prefrontal cortex. The prefrontal cortex represents a critical component of distributed neural systems engaged during sustained and phasic attention to external and internal events.
THE LESION METHOD

Single-Case Versus Group Studies

Researchers disagree over the best way to design a research program in cognitive neuropsychology based on the lesion method. One debate concerns the importance of single-case studies versus group studies. A related issue that has generated controversy is the relative emphasis placed on localizing cognitive operations in the brain, which has been championed by those favoring the group studies approach, versus the emphasis placed on informing theoretical conceptions of normal cognitive function based on the existence of double dissociations in patients, which is a feature of the single-case approach. The single-case study camp maintains that averaging test results over a group of patients is inappropriate because brain damage can disrupt a cognitive system in a variety of ways (Caramazza, 1986, 1992; Sokol, McCloskey, Cohen, and Aliminos, 1991). Proponents claim that the single-case approach is more likely to produce strong evidence for making inferences about normal function.

An opposing position states that limiting studies to single cases is generally an ultracognitive approach (Shallice, 1988) that ignores the importance of biological evidence in developing theories of cognition (Kosslyn and Intriligator, 1992; Robertson, Knight, Rafał, and Shimamura, 1993). Advocates of group studies contend that "[single-case studies] are of limited value in constructing a general theory of human cognitive neuropsychology because there are serious difficulties in generalizing from the behavior of one person to the behavior of all people" (Kolb and Whishaw, 1990, p. 84).

Brain structure varies from person to person and, of course, people vary in their behavior and in their cognitive capabilities. The research presented in this chapter is based on group studies of patients with unilateral, focal brain lesions, primarily due to stroke. However, we also believe that one can learn a great deal about relationships between the brain and behavior from the single-case approach (e.g., Scoville and Milner, 1957).

Indirect and Compensatory Effects of Lesions

A second important issue that must be addressed whenever neurological patients are examined, whether in single-case or in group studies, is the indirect and compensatory effects of lesions on both brain function and behavior. Recovery of function after brain damage can change the neural circuits recruited for a specific cognitive task. Damage to a particular brain area may disrupt connections to and influence the function of remote regions. However, the observation of changes remote from the site of lesion can reveal information about connectivity and modulatory interactions. For example, frontal lobe lesions can influence visual processing in extrastriate occipitotemporal areas (Kosslyn et al., 1993; Knight, 1997; Swick and Knight.
Another advantage of the lesion method is that it allows determination of whether a particular brain region is necessary for a particular cognitive function. Intracerebral recordings from epilepsy patients have suggested that "full-employment is the brain processing policy" (Halgren et al., 1995, p. 246). Multiple cortical and limbic sites generate large potentials during simple sensory discriminations, for example, but many of those areas may be unnecessary for task performance.

With the strengths and weaknesses of the lesion method in mind, careful neuroanatomical studies in human patients have made substantial contributions to elucidation of the neural substrates of perception, attention, memory, and language (Damasio and Damasio, 1989). A series of assumptions underlies all methods used by cognitive neuroscientists, and each method has its limitations. Ultimately, converging evidence from multiple techniques will yield the most integrated and insightful models of attention. This review focuses on neuropsychological and neurophysiological data that link the frontal lobes to attention and to the control of sensory and cognitive processing. Some of the evidence implicates additional regions that comprise distributed networks for orientation and the novelty response.

DORSOLATERAL PREFRONTAL CORTEX AND ATTENTION

Dorsolateral prefrontal cortex (Brodmann’s areas 6, 8, 9, 10, 44, 45, and 46) is critical for a broad range of processes, including language, motor control, attention, working memory, and executive functions. Given the extensive bidirectional connections between prefrontal cortex and numerous cortical, limbic, and subcortical regions (Goldman-Rakic, Selemon, and Schwartz, 1984; Seltzer and Pandya, 1989; Friedman and Goldman-Rakic, 1994), dorsolateral prefrontal lesions can result in a variety of cognitive disturbances. With early damage from tumors or degenerative disorders, subtle deficits in creativity and mental flexibility can be observed. Behavioral problems are more pronounced with bilateral damage or with the progression of unilateral disease, producing impairments in attention, temporal coding, metamemory, planning, judgment, and insight. Acute infarcts of prefrontal cortex are associated with a transient syndrome of attention abnormalities and global confusion. Right hemisphere lesions involving areas 8 (which includes the frontal eye fields), 9, and 46 can result in hemispatial neglect (Heilman, Watson, and Valenstein, 1994; also, see Rafal, chapter 22, this volume).

Moreover, prefrontal cortex (particularly areas 9 and 46) is crucial for the control of sustained and phasic attention to environmental events (Stuss and Benson, 1986). Knight and colleagues studied the attention, orienting, and memory abilities of neurological patients with focal prefrontal lesions using behavioral and event-related potential (ERP) recording techniques (Knight, 1984, 1991; Knight, Hillyard, Woods, and Neville, 1981; Knight, Scabini, and Woods, 1989; Knight, Scabini, Woods, and Cloyworth, 1989; Swick and Knight, 1994, 1996; Yamaguchi and Knight 1990, 1991a). The
primary impairments in these patients include problems with inhibitory control of sensory inputs, deficits in sustained attention, and abnormalities in the detection of novel events. The inability to gate irrelevant inputs and sustain attention, coupled with deficits in novelty detection, impairs the coding and processing of discrete external events. Similar to the role it plays in attention to external events, prefrontal cortex is crucial for attention to the internal mental representations that presumably contribute to working memory, to the use of strategies in experimental (and everyday) settings, to planning, and to decision making (Knight and Grabowecky, 1995; Stuss, Eskes, and Foster, 1994).

**Sensory Gating and Prefrontal Cortex**

The attention deficits and perseveration observed in patients with frontal lesions have been linked to problems with inhibitory control of posterior sensory and perceptual mechanisms (Lhermitte, 1986; Lhermitte, Pillon, and Serdaru, 1986). This relatively early sensory gating deficit, combined with abnormalities in the detection of novel events, can lead to deficits in higher-order cognitive processes such as executive control. For instance, the inability to inhibit internal representations of previous responses that are no longer correct may cause poor performance on the Wisconsin card-sorting task and on the Stroop task (Shimamura, 1995; Vendrell et al., 1995). Physiological data indicate that the lack of inhibitory control may begin with early sensory processing in primary cortical regions. Suppression of a prefrontal-thalamic gating system in cats increased the amplitudes of evoked responses in primary auditory cortex (Skinner and Yingling, 1977; Yingling and Skinner, 1977).

Prefrontal cortex can thus exert an inhibitory, top-down influence on neural activity within primary sensory cortices. Additional support for such a mechanism has been obtained from ERP recordings in stroke patients. ERPs are brain potentials that are time-locked to the occurrence of sensory, motor, or cognitive events and that are extracted from the ongoing electroencephalogram (EEG) by signal-averaging techniques (Hillyard and Picton, 1987). Because of their excellent temporal resolution, ERPs provide a valuable index of the timing of covert sensory and cognitive processing in humans that complements both the behavioral measures of cognitive psychology and the superior spatial resolution of functional neuroimaging techniques (see Corbetta, chapter 6, this volume). Application of the ERP methodology to studies of attention is discussed by Luck and Girelli (chapter 5, this volume). Constraints upon localizing the neural generators of ERP components have been obtained from lesion studies in both animals and humans (for a review, see Swick, Kutas, and Neville, 1994).

Task-irrelevant auditory and somatosensory stimuli (i.e., monaural clicks or brief electric shocks to the median nerve) were presented to patients with comparably sized lesions in dorsolateral prefrontal cortex, in the temporal-
Somatosensory

Auditory

Parietal

P27

Temporo-parietal

N20

Frontal

CONTROL

LESION

0 10 20 30 40 50 60 msec

1uV

0.5uV

Figure 8.1 Primary cortical somatosensory and auditory evoked responses in control subjects (solid line) and patients (dashed line) with focal damage in lateral parietal cortex (top, n = 8), temporal-parietal junction (middle, n = 13), or in dorsolateral prefrontal cortex (bottom, n = 11). Reconstructions of the extent of damage in each patient group are shown on the left. Somatosensory potentials were elicited by square-wave pulses delivered to the median nerve at the wrist and recorded from area 3b (N20) and areas 1 and 2 (P27). Auditory evoked responses generated in the inferior colliculus (wave V) and the primary auditory cortex (P30) were elicited by clicks delivered at a rate of 15/s and a 50 dB HL intensity level. Prefrontal lesions resulted in a selective increase in the amplitudes of the P27 and P30 responses (shaded areas). See color plate 7.

parietal junction, or in lateral parietal cortex. Evoked responses from primary auditory (Kraus, Ozolamar, and Stein, 1982) and somatosensory (Leuders, Leser, Harn, Dinner, and Klem, 1983) cortices were recorded from these patients and from age-matched controls (figure 8.1 and color plate 7). Not surprisingly, damage to primary auditory or somatosensory cortex reduced the early-latency (20–40 ms) ERPs generated in those regions. Posterior association cortex lesions that spared the primary sensory regions had no effect on the amplitudes or latencies of the early potentials; thus, the patients with posterior association cortex lesions served as a brain-lesioned control group. Prefrontal damage produced disinhibition of both the primary auditory and somatosensory evoked responses (Knight, Scabini, and Woods, 1989; Yamaguchi and Knight, 1990). Spinal cord and brain stem potentials were not affected by prefrontal damage, suggesting that the amplitude enhancement was due to abnormalities in either prefrontal-thalamic or direct prefrontal-sensory cortex mechanisms.
Chronic disinhibition of sensory inputs may contribute to many of the behavioral sequelae of prefrontal damage. Distractibility has been proposed to be a major component of the delayed response deficit in animals with prefrontal lesions (Malmo, 1942; Bartus and Levere, 1977). The inability to suppress irrelevant information can lead to difficulties in target detection and match-to-sample paradigms. For example, patients with frontal resections were impaired at detecting multiple visual targets embedded among distractors (Richer et al., 1993). Likewise, patients with lesions confined to dorsolateral prefrontal cortex were impaired at matching two environmental sounds only when distractors intervened between cue and target (Chao and Knight, 1995).

**Visual Attention and Prefrontal Cortex**

Visual stimuli elicit a prominent, attention-sensitive N170 (N1) scalp potential that is maximal over temporal-occipital sites. Topographic and dipole modeling studies have suggested an N170 source in extrastriate cortex (Gomez Gonzalez, Clark, Fan, Luck, and Hillyard, 1994; Johannes, Munthe, Heinze, and Mangun, 1995). In the auditory modality, the presence of frontal lesions reduced the N1 attention effect in a dichotic listening task (Knight et al., 1981). A recent experiment examined the influence of prefrontal cortex on the visual N1. Control subjects and patients with frontal lesions performed a visual detection task while viewing centrally presented triangles, inverted triangles, and irrelevant novel stimuli (Knight, 1997). In control subjects, N170 amplitude was largest for target stimuli. Dorsolateral prefrontal damage decreased N170 amplitude over the lesioned hemisphere for all visual stimuli, with maximal reductions seen at posterior temporal sites (figure 8.2 and color plate 8). However, the degree of target-related N1 enhancement was comparable to controls over the extrastriate cortex of both lesioned and intact hemispheres (Knight, 1997). The N2 component to targets was eliminated over the lesioned hemisphere.

The reduction of N170 in frontal lesion patients was also observed in tasks using verbal stimuli (Swick and Knight, 1996). Subjects read centrally presented words and pronounceable nonwords and performed lexical decision or recognition memory tasks. For control subjects, both stimulus types elicited a focal N170 that was maximal at posterior temporal and occipital electrodes (figure 8.3). N170 was significantly larger over the left hemisphere in both tasks, similar to previous studies with words (Neville, Kutas, Chesney, and Schmidt, 1986; Curran, Tucker, Kutas, Posner, 1993). N170 amplitude was reduced in frontal lesion patients ipsilateral to damage, but peak latency was unaffected.

Those two experiments suggest that dorsolateral prefrontal cortex provides an ipsilateral facilitory input to neural processing in extrastriate cortex that begins within 120 ms post-stimulus. Additional support for prefrontal
PFCx - Visual Modulation

Figure 8.2 Prefrontal cortex modulates the visual N170 component. (a) Topographic maps display the scalp voltage distribution (in μV) of the N170 to targets. The extrastriate focus of the N170 in controls is reduced ipsilateral to prefrontal damage. (Inset) The gray shading on the brain shows the area of maximum lesion overlap, while the star indicates a putative N170 generator in extrastriate cortex. (b) Group averaged ERP's for target stimuli in controls and frontal patients (n = 11). Waveforms are from posterior temporal electrodes (T5/T6 in controls), ipsilateral (ipsi) and contralateral (contra) to the lesion. The N1 (N170) and N2 components are labeled. In this and subsequent figures, negative is up, stimulus onset occurs at 0 ms, and the scale is given in microvolts (μV). See color plate 8.

modulation of visual processing in extrastriate areas during sustained attention and spatial memory comes from blood flow data in humans (Roland, 1982), network analyses of PET results (McIntosh et al., 1994), and single-unit and lesion data in monkeys (Fuster, Bauer, and Jervey, 1985; Funahashi, Bruce, and Goldman-Rakic, 1993). Combined with the auditory ERP findings (Knight et al., 1981), these data suggest that dorsolateral prefrontal cortex is involved in multimodal control of sustained attention. However, caution is needed in comparing the current ERP results to those reported in prior visual attention studies (for a review, see Mangun, 1995). Most studies have employed lateralized stimulus arrays and divided or cued attention paradigms. Those designs allowed comparisons between attended and unattended stimuli. That design was not employed in our studies, both of which used central
presentation and either target detection or responses to all stimuli. Lateralized stimulation could conceivably result in signal detection deficits in the visual field contralateral to the lesioned hemisphere.

**Phasic Attention and Frontal-Hippocampal Circuits**

The P300 component of the human ERP is a prominent scalp-recorded response that is widely utilized to study phasic attention and memory mechanisms. The P300 potential was first reported in 1965 (Sutton, Braren, Zunin, and John, 1965; Desmedt, De Becker, and Manil, 1965) and since then has been the subject of extensive cognitive research in normal, neurological, and psychiatric populations. P300-like potentials have been described in rats (Ehlers, Wall, and Chapin, 1991), cats (Buchwald and Squires, 1982), and monkeys (Arthur and Starr, 1984; Neville and Foote, 1984; Pineda, Foote, Neville, and Holmes, 1988), supporting a broad ethological significance and leading to systematic investigations of possible neural substrates (Paller, 1994; Swick et al., 1994).

Subcomponents of the P300 have been proposed to measure engagement of early attention and working memory mechanisms. Voluntary detection of
a task-relevant stimulus in the visual, auditory, or somatosensory modalities generates a large P300 response that is maximal over parietal scalp regions (P3b). P3b amplitude and latency are responsive to stimulus probability, subjective probability, stimulus meaning, and task relevance (Donchin and Coles, 1988; Johnson, 1988) and have been related to a range of cognitive processes, including context updating, information delivery, stimulus categorization, and cognitive closure. Delivery of an unexpected and novel stimulus elicits an earlier latency P300 response (P3a), which is recorded over widespread anterior and posterior scalp sites. The P3a potential has a more frontocentral scalp distribution than the P3b in all sensory modalities and has been proposed as a central marker of the orienting response (Sokolov, 1963; Courchesne, Hillyard, and Galambos, 1975; Knight, 1984; Yamaguchi and Knight, 1991b).

No clear consensus has emerged on the cognitive underpinnings of the P300 (Verleger, 1988), primarily due to the fact that P300 is not a unitary brain potential arising from a discrete brain region or cognitive process, as was initially theorized. Instead, scalp positivities generated from 300 to 700 ms post-stimulus measure activation of multiple neocortical and limbic regions dependent upon the particular stimuli and tasks used. For instance, late positive components differing in scalp topography and latency have been linked to voluntary and involuntary attention and to different aspects of memory processing. Support for these conclusions is derived from scalp data in control subjects (Courchesne et al., 1975; Squires, Squires, and Hillyard, 1975; Ruchkin, Johnson, Grafman, Canoune, and Ritter, 1992; Rugg, 1995), intracranial recording in epileptic patients (Smith, Stapleton, and Halgren, 1986; McCarthy, Wood, Williamson, and Spencer, 1989; Pupe, Andrewes, Berkovic, and Bladin, 1991; Halgren et al., 1995), and lesion studies in neurological patients (Knight, 1984, 1997; Knight, Scabini, et al., 1989; Yamaguchi and Knight, 1991a; Johnson, 1995).

Lesion data recorded from patients with focal damage in dorsolateral prefrontal cortex, in temporal-parietal junction, or in lateral parietal cortex (figure 8.4) have indicated that P300 has multiple neural generators. Lesions of the temporal-parietal junction result in marked reduction of P3a and P3b at posterior scalp sites in both the auditory (Knight, Scabini, et al., 1989; Verleger, Heide, Butt, and Kompi, 1994) and somatosensory modalities (Yamaguchi and Knight 1991a), but not in the visual modality (Knight, 1997). Lateral parietal lesions had no effect on either P3a or P3b. Additionally, these studies demonstrate that modality-specific regions contribute to the scalp P3b.

Prefrontal damage produces differential effects on P3a and P3b (figure 8.4). The parietal P3b is unaffected by prefrontal damage in simple sensory discrimination tasks. However, reductions are observed in more difficult tasks, particularly when the lesions include posterior prefrontal cortex (Swick and Knight, 1994). The novelty P3a response is decreased in prefrontal patients.
Figure 8.4  Summary of the target P3b (left) and novelty P3a components (right) in controls and three patient groups with focal cortical damage. The area of maximum lesion overlap in each group is drawn in black (far left). ERPs are shown for electrodes with the largest responses (Pz for targets, Fz for noveltys) to stimuli in the auditory, visual, and somatosensory modalities. Prefrontal (top) and lateral parietal damage (bottom) did not affect the latency or amplitude of P3b in simple detection tasks of any modality. Conversely, temporal-parietal lesions (middle) reduced P3b amplitude in the auditory and somatosensory modalities, with only partial reductions in the visual modality. Prefrontal and temporal-parietal lesions produced multi-modal reductions of the novelty P3a, while lateral parietal lesions had no significant effects.

with reductions observed throughout the lesioned hemisphere. Frontal lesions produce comparable P3a decrements in the auditory (Knight, 1984), visual (Knight, 1997), and somatosensory modalities (Yamaguchi and Knight, 1991a). These findings suggest that prefrontal cortex plays a critical role in the detection of novel stimuli. Furthermore, the results illustrate the importance of distributed interactions between prefrontal and posterior regions during both voluntary and involuntary attention (Mesulam, 1981).

Neural modeling (Metcalfe, 1993) and PET data (Tulving, Markowitsch, et al., 1994; Tulving, Markowitsch, Craik, Habib, and Houle, 1996) have recently implicated prefrontal and mesial temporal structures in novelty detection. Unilateral damage centered in the posterior hippocampal region has minimal effect on parietal P3b activity generated in response to auditory, visual, and somatosensory targets, but reduces front-central P3a activity to novel stimuli in all modalities (see figure 8.5 and color plate 9 for visual P3), with reductions most prominent at frontal sites (Knight, 1996). These observations
support involvement of a prefrontal-hippocampal system in the detection of deviances in the ongoing sensory stream. Reciprocal intra- and interhemispheric pathways (Amaral, Insausti, and Cowan, 1984; Goldman-Rakic et al., 1984) coursing through retrosplenial cortex or the cingulate may provide the anatomical substrates for prefrontal-hippocampal interactions during novelty detection. Prefrontal-hippocampal interactions during orientation to novel stimuli may underlie the classic von Restorff effect, wherein novel or out-of-context stimuli are better remembered (von Restorff, 1933; Karis, Fabiani, and Donchin, 1984; Metcalfe, 1993). Taken together, these ERP experiments provide further evidence that P300 subcomponents reflect distributed neural activity in corticocerebral regions engaged during voluntary and involuntary responses to discrete environmental events.

Figure 8.5 Visual P300 effects in patients with lesions centered in the posterior hippocampus. (a) The target P3b (left) and novelty P3a responses (right) from control subjects and patients. Hippocampal lesions produced reductions in the P3a while sparing the P3b. (b) Scalp voltage maps illustrate the widespread decrease in the novelty P3a after hippocampal damage. See color plate 9.
One difficulty with precise definition of the role of the frontal lobes in higher cognitive functions is deciding whether an observed impairment is a primary effect of frontal lobe damage or is secondary to deficits in more basic processes. For example, neuropsychological studies have implicated the frontal lobes in various types of human memory, including free recall (Lecina della Rocchetta and Milner, 1993; Janowsky, Shimamura, Kritchovsky, and Squire, 1989; Jetter, Posner, Freeman, and Markowitz, 1986), source memory (Janowsky, Shimamura, and Squire, 1989), and memory for temporal order (McAndrews and Milner, 1991; Shimamura, Janowsky, and Squire, 1990). However, deficits in attention and sensory gating could contribute to an inefficient use of encoding and retrieval strategies (Gershberg and Shimamura, 1995; Stuss, Alexander, et al., 1994). Distractibility and interference effects have been cited as major contributors to the types of memory problems exhibited by frontal lesion patients (Knight, 1991; Shimamura, Jurica, Mangels, Gershberg, and Knight, 1995).

A proliferation of functional neuroimaging experiments has reported blood flow changes in frontal regions during the performance of various memory tasks (for a review, see Buckner and Petersen, 1996). Positron emission tomography (PET) studies have observed blood flow activations in right anterior prefrontal cortex during memory retrieval in word stem cued recall (Buckner et al., 1995; Squire et al., 1992), verbal recognition (Tulving, Markowitz, Kapur, et al., 1994; Andreasen et al., 1995), and retrieval of previously studied category exemplars (Shallice et al., 1994). Other PET investigations that scanned subjects during memory encoding yielded activations in left inferior prefrontal cortex (areas 45, 46, 47, and 10; Kapur et al., 1994). Given that set of observations, the hemispheric encoding/retrieval asymmetry model (Tulving, Kapur, Craik, et al., 1994) proposed that left prefrontal cortex is preferentially involved in the encoding of novel information into episodic memory, whereas right prefrontal cortex is more involved in episodic memory retrieval.

To test that hypothesis, cued recall performance was evaluated in a group of 16 frontal lesion patients (Swick and Knight, 1996). To control for possible strategy deficits, a simple organizing framework was provided. All subjects were told they could complete the items in any order and could fill in the items they remembered first. Patients were selected on the basis of focal prefrontal cortex lesion (11 patients had lesions on the left, and 5 had lesions on the right hemisphere) and were divided into three groups (figure 8.6 and color plate 10). Left superior frontal lesions were restricted to areas 6, 8, 9, 10, and superior 46; left inferior frontal lesions also included inferior areas 44, 45, and 46; right frontal lesions included areas 6, 8, 9, 10, or 46. Left frontal lesion patients (collapsed across superior and inferior groups) recalled fewer words than did controls in the first but not in the second experiment (figure 8.7). The right frontal lesion patients were not impaired with either

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**Figure 8.6** Lesion and lesion variability through the lateral frontal lesion resection, inferior as color plate 10.
The text continues:

...and their primary role in working memory. 

Several studies have investigated the role of the frontal lobes in working memory. For example, Squire, Tulving, and Zola-Morgan (1984) reported that patients with damage to the dorsolateral prefrontal cortex had difficulties with tasks requiring working memory. 

Mangels, one of the early researchers in this field, reported that patients with damage to various parts of the cerebral cortex showed reduced activation in the corresponding areas. 

Figure 8.6 Lesion reconstructions for frontal patients in the cued recall study, showing the degree of overlap and lesion variability. The scale refers to the percentage of patients in each group with lesions in that area. Lines through the posterior view show the level of the axial cuts from ventral (1) to dorsal (7). (Top) Patients with left frontal lesions restricted to areas 6, 8, 9, 10, and superior 46. (Middle) Patients with left frontal lesions that included inferior areas 44, 45, and 46. (Bottom) Patients with damage to right frontal areas 6, 8, 9, 10, or 46. See color plate 10.

list. Thus, the regions of prefrontal cortex activated in PET studies of young control subjects were not necessary for memory retrieval in these patients. Right prefrontal cortex could be activated by several strategic aspects of the cued recall paradigm (operating under time constraints, switching between recall of old words and generation of new words, etc.) that were minimized in our study. Hence, brain reorganization, a change in cognitive strategies, or both could be responsible for their intact performance.

CONCLUSIONS

Damage to dorsolateral prefrontal cortex produces impairments in sustained and phasic attention abilities, as well as deficits in inhibitory control of external stimuli and internal cognitive processing. Thus, the prefrontal lesion patient operates in a noisy internal environment deficient in the critical regulatory mechanisms necessary for the maintenance of working memory,
executive control functions, and the use of strategies. Prefrontal cortex appears to have both inhibitory and facilitatory influences on sensory and cognitive processing. Early input to primary sensory cortices is modulated by net inhibitory, prefrontal-controlled mechanisms. Conversely, later processing in association cortices is dependent on a facilitory prefrontal input. Little is known about the cellular or pharmacological substrates of these systems. This is a crucial area of research, because it has the potential to lead to treatment intervention for regulatory deficits in remote cortex secondary to prefrontal damage.

In addition to these sensory control mechanisms subserving sustained attention and working memory, a prefrontal-hippocampal network is selectively engaged during processing of novel stimuli. Based on anatomical connectivity, Nauta (1971) suggested that the prefrontal cortex is ideally suited to generate and evaluate internal models of action. It is proposed that in addition to that function and its role in sustained attention and working memory, a prefrontal-hippocampal system is crucial for detecting changes in the environment and for discriminating between internally and externally derived models of the world (Knight and Grabowecky, 1995). Deficits in those abilities may be responsible for most of the cognitive consequences of prefrontal lesions.

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REFERENCES


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