Does Damage to the Frontal Lobes Produce Impairment in Memory?

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ABSTRACT—*There has long been controversy about the function of the frontal lobes in memory. Historically, in lesion studies, the frontal lobes were discussed as if they represented a single functional unit, and little attention was paid to possible regional differences. In a series of experiments involving patients with focal frontal lobe lesions, we have demonstrated that different frontal regions affect strategic memory processes in unique ways. In addition, some regions of the frontal lobes are involved in nonstrategic memory encoding, likely through actual involvement of the limbic memory regions or through the impact of processing deficits related to the specific mode of the information to be learned (e.g., language). These findings converge with those of functional imaging studies showing the dissociation of memory processes within the frontal lobes, and are indicative of the complex roles subserved by the frontal lobes. Future research will need to explore how the different functions within the frontal lobes influence other dynamic cognitive systems.*

KEYWORDS—*frontal lobes; memory; localization; fractionation of processes*

The question posed by the title of this article has eluded easy answer. Most attempts to answer it have generated controversy. The frontal lobes are considered to be important for higher-level functions such as planning and organization. However, such functions, classified as strategic because of their role in controlling behavior, have been difficult to define operationally and test experimentally. Other reasons for the controversy are carried in the nature of the question. The reference to "frontal lobes" implies an assumption that this region of the brain functions as a single, homogeneous unit. Indeed, most research has implicitly accepted this characterization, largely ignoring potential regional functional differences. Moreover, memory is a complex phenomenon that involves numerous processes. In recent years, the domains of study have shifted from the more commonly examined aspects of memory, such as encoding and retrieval, to more strategic aspects, such as working memory (keeping information on-line to work on it), source memory (ability to remember the source of the information learned—e.g., where it was learned and who said it—independently of the fact itself), and monitoring of memory.

The controversies surrounding the topic of this article are evident even in the clinical reports of memory dysfunction after frontal lobe damage. Although early clinical reports suggested that memory dysfunction was an important index of damage to the frontal lobes in patients later shown to have frontal lobe tumors (reviewed in Stuss & Benson, 1986), a century of work with standard clinical memory tests indicated that even extensive damage to the frontal lobes does not often cause any deficits on these tests. The devastating loss of ability to learn new information known as classical amnesia is caused by bilateral destruction of the hippocampus (a part of the limbic system[1] that is key to memory formation and situated in the medial part of the temporal lobe) and inferior temporal cortex (located behind the frontal lobes), not by frontal damage.

A variety of hypotheses about how frontal lesions might affect memory, the majority implying some effect of impaired strategic processing, have been proposed to account for these disparate clinical observations. Hécaen and Albert (1978), for example, proposed that frontal lobe damage does not cause a primary

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[1]The limbic system is a group of brain structures (e.g., hippocampus, amygdala, septal areas) that are associated with functions such as arousal, motivation, emotions, and recent memory.

disturbance in memory, but somehow interferes with efficient use of memory functions: Patients "forgot to remember" (p. 333). Luria (1973) noted that the deficits in memory were secondary to strategic processes, such as switching from one memory to another and organizing information for efficient recall. And Moscovitch and Winocur (2002) argued that the frontal lobes "work with memory" (pp. 188–189); they are involved not in memory recollection but in mediating the strategic processes that support memory functions, such as attention, activation, and monitoring. It has often been claimed, or at least implied, that there is no deficit in recognition memory[2] after frontal lobe damage, because recognition testing minimizes strategy demands.

CAN THE ROLE OF THE FRONTAL LOBES IN MEMORY BE DEFINED AND DIFFERENTIATED?

The treatment of the frontal lobes as an amorphous unit must be questioned, considering the size and anatomical diversity of this brain region; the frontal lobes constitute some 25 to 33% of the brain, including at least 15 architectonically distinct regions. It is unlikely that such a diverse area would have one pervasive functional role. If different architectonic regions of the frontal lobes have different functions, then research that groups together patients with lesions in different frontal regions will fail to identify different functions. Much research into the effects of frontal lesions has failed to differentiate patients on the basis of where their lesions are located more specifically, and this accounts for much of the current limitation in understanding frontal functions. One goal of our frontal lobe research over the past two decades has been to define lesions with greater specificity to probe a variety of cognitive functions, including memory. This work has produced evidence that lesions in different frontal regions have different effects. Thus, a second goal presented itself: to isolate the underlying frontal processes that affect memory. If there are different strategic processes that operate on—"work with"—memory, can these be correlated with damage to distinct regions within the frontal lobes?

Our approach was simple—test patients with damage in specific frontal areas (lesion approach), using a range of memory measures so that we might be able to map specific impairments onto specific frontal areas. The lesion approach identifies regions that are essential, in some structural sense, to a function. Functional imaging techniques, in contrast, identify regions that are involved in a function; even with very finely tuned test methodology, critical regions can only be inferred. To avoid treating the frontal lobes as functionally homogeneous, we included patients with pathology in varied frontal regions. In addition, we used separable measures of memory encoding and retrieval, as well as of the putative strategic processes, so that our results would not point to an overly simplified model of episodic memory (memory of personal experience).

Our initial memory study focused on a population of convenience: patients who had undergone frontal lobotomies. This group showed highly consistent damage to an inferior medial frontal region. The patients were not amnesic in any sense; their performance on the Wechsler Memory Scale (a commonly used test for diagnosing memory impairment) was actually above average. This group was quite impaired, however, on one specific memory task: recalling three consonants after varying delay periods during which they performed a conflicting task (see Stuss & Benson, 1986). Thus, under certain conditions of high demand for working memory or managing divided attention, damage to this inferior medial region of the frontal lobes impaired memory.

MEMORY PROCESSES RELATED TO SPECIFIC FRONTAL REGIONS

In our next study of memory in patients with frontal lobe lesions, we classified the lesions as in the left frontal lobe, in the right frontal lobe, or bifrontal (a term used to indicate damage to both frontal lobes)—an advance at that time but in retrospect a crude classification (Stuss et al., 1994). The patients were asked to learn a list of 16 words that was presented four times. After each presentation, their free recall of the words was tested, and later they were given a recognition test. The results were unexpected. Two of the three groups of patients (i.e., those with left and bilateral damage) had a significant deficit in free recall. But, in contrast to conventional wisdom from earlier research, these same two groups also had a recognition memory deficit compared with a normal control group (albeit their deficit was not as severe as that of amnesic patients with hippocampal injury).

In an attempt to understand why our results were so different from what other researchers had found, we took a performance-based approach. Instead of using the a priori anatomical groupings of left, right, and bifrontal, we ranked the patients by performance and discovered that the recognition scores of approximately half the patients were equivalent to those of the normal control group (which likely explains why earlier studies, which did not consider thoroughly the location of the frontal lobe damage, did not find a recognition impairment). The other half had very significant impairment.

With closer inspection of lesion sites and supporting evidence from other tests, further reasons for the earlier confusion became clear: There were two separate reasons for recognition memory impairment, each related to a separate brain region and to a separate psychological process. Some patients with recog-

[2]Memory can be assessed in different ways. Recognition memory is tested by presenting material learned earlier along with new items not seen before and asking participants to identify (recognize) the items presented earlier. This type of recall has the least demands on strategic processing, because the learned words are provided. Cued recall is tested by requesting recall of previously learned information and assisting participants by presenting a retrieval cue such as the type of information (category) or the initial letter of the word. In tests of free recall, participants are asked to spontaneously recall previously learned information without the benefit of any types of cues or prompts.

nition memory impairment had inferior medial frontal lesions (many of the patients in our original bifrontal group were in this category) with damage extending back to the limbic regions (septum) that are part of the memory system. Their recognition memory deficit was secondary to an encoding problem in binding new information into memory. Other patients had damage to a limited region of the left frontal lobe, the left dorsolateral area (the more posterior part of the left frontal lobe), and exhibited mild deficits in naming objects. This group also had an encoding problem, as measured by recognition memory scores, but their deficit in recognition memory correlated with their language difficulties, suggesting that their impairment in encoding had a language basis and was distinct from the binding problem of the patients with damage to the limbic memory system.

The original right frontal group was not significantly different from the control group in either recognition performance or the total number of words they could recall, but did have specific deficits in retrieval processes, showing inconsistency in words recalled from one test to another and repeating already recalled words within a given test. All groups with frontal lesions were impaired on one specific measure of strategy, Sternberg and Tulving's (1977) subjective-organization score, which is thought to reflect higher-order and subjective organization. (Subjective organization is the ability to organize information as learned so that words are recalled in connected pairs, regardless of their order of presentation on the recall test.) This experiment illuminated many of the reasons why prior research pooling all patients with frontal lesions, whatever their site, into a single group had failed to show distinct effects of frontal damage on memory.

In the same year that we published our results for patients with lesions (Stuss et al., 1994), Tulving, Kapur, Craik, Moscovitch, and Houle (1994) demonstrated, using positron emission tomography (PET), that the left frontal region was activated when subjects encoded information, and the right frontal area was activated when subjects retrieved information. Thus, their study and ours, although taking two different approaches, converged on the same general conclusion about the roles of different frontal regions—still coarsely defined—in memory. The left frontal region is associated with encoding, and the right frontal area with retrieval (their results did not assess the role of the inferior medial regions).

We then undertook a meta-analysis (a statistical analysis combining results of numerous studies) of memory studies of patients with single frontal lesions that were limited in extent (i.e., focal lesions). The meta-analysis supported our finding: Patients with frontal lobe damage had difficulties not just in free recall, but also in recognition (Wheeler, Stuss, & Tulving, 1995). The studies in the meta-analysis most often did not, unfortunately, report finer anatomical distinctions.

In our most recent investigation of frontal injury and memory, we again used a word-list learning task, the California Verbal Learning Test (CVLT; Alexander, Stuss, & Fansabedian, 2003). The study involved 33 patients with focal frontal lesions, so there was greater representation of different frontal brain regions than in our previous studies, which involved smaller groups of patients. The performance-based methodology generated six frontal-lesion subgroups, each associated with a particular pattern of performance. Superimposed on the general division of left, right, and bifrontal lesion locations was a more specific division dependent on whether the lesion was more to the front (anterior) or back (posterior) part of the frontal lobes. In addition, we differentiated medial from lateral regions of the right and left lobes. The six subgroups were as follows: anterior left lateral, posterior left lateral, anterior right lateral, posterior right lateral, anterior inferior medial, and posterior inferior medial. (The patients in the inferior medial subgroups often had bifrontal damage.) Patients in the posterior inferior medial subgroup had damage extending back to involve the limbic areas involved in memory, much as the patients in the inferior medial subgroup of our previous study did (Stuss et al., 1994).

We confirmed that only the left posterior lateral and posterior inferior medial groups had impaired learning and recall. The left posterior lateral group also had an abnormal response bias in recognition—they often "recognized" words that in fact they had not learned. Several groups had monitoring deficits (indexed by perseveration—the repetition of words already recalled). These finer differentiations of memory impairment within the frontal lobes are illustrated in Figure 1.

LESSONS LEARNED

So, does damage to the frontal lobes produce impairments in memory? No and yes. How the frontal lobes relate to memory depends on the process in question, and the brain region being investigated. Damage in many areas of the frontal lobes does not impair the intrinsic workings of episodic memory, such as encoding. At the same time, lesions in other frontal regions do impair some aspects of memory (e.g., encoding). In addition, some frontal areas are involved in strategic processes, such as monitoring, setting thresholds to discriminate information previously learned from information not learned, and imposing subjective order on the fly. These latter regions are not involved in the representational processes of memory (which are likely more posterior in the brain), but are involved in the strategic, control processes. In earlier work, several authors postulated some role of the frontal lobes in memory. What we have done is indicate what these roles are and which specific regions of the frontal lobes they appear to involve. One implication of our results is that the frontal lobes are involved in multiple strategic processes. Imaging studies support the proposal that different subregions of the frontal lobes are involved in different functions supporting episodic memory (e.g., Henson, Rugg, Shallice, & Dolan, 2000).

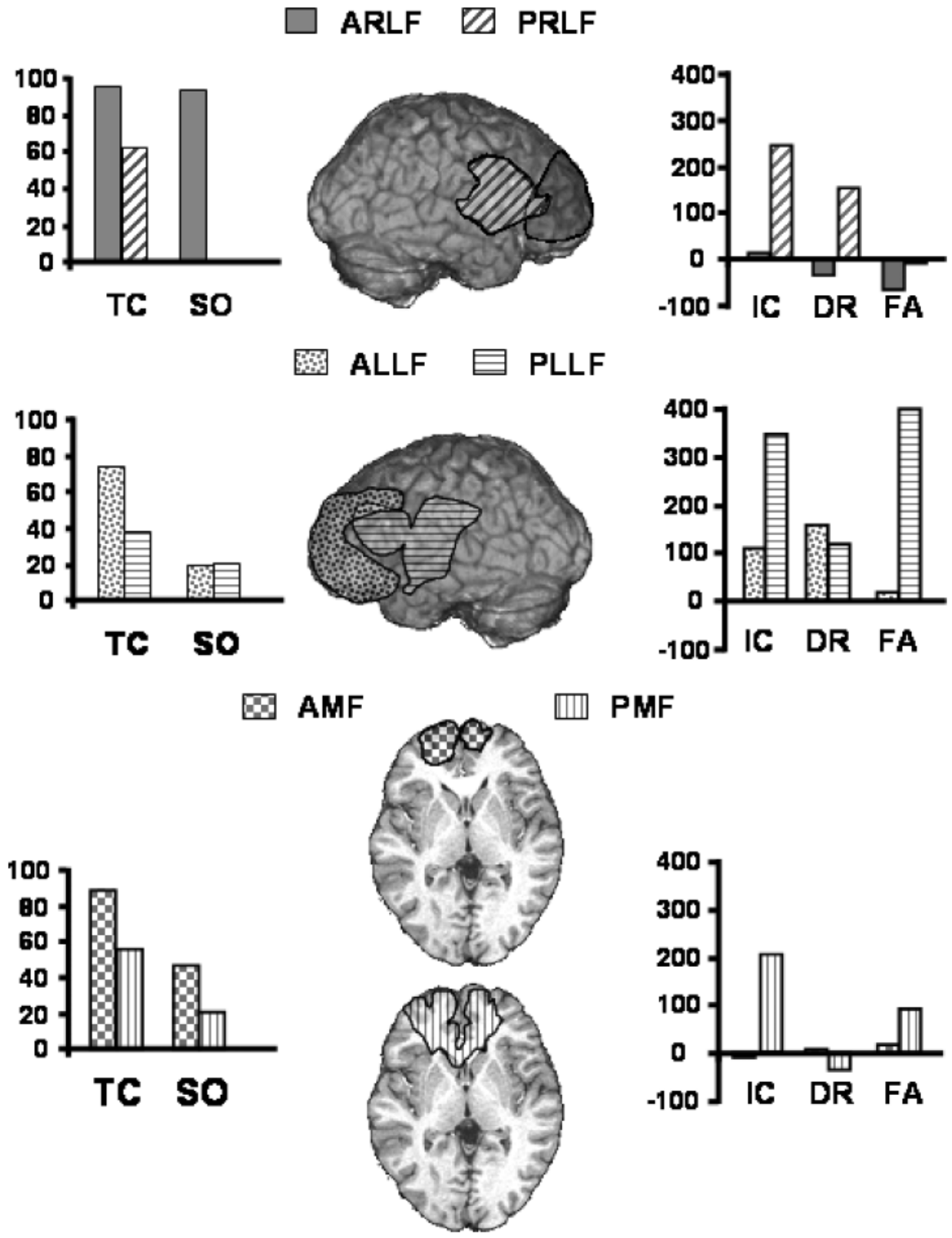

Fig. 1. Memory performance in six subgroups of patients with frontal lesions (Alexander, Stuss, & Fansabedian, 2003). The illustrations in the center of the figure show damaged areas in each of the subgroups: anterior right lateral frontal (ARLF), posterior right lateral frontal (PRLF), anterior left lateral frontal (ALLF), posterior left lateral frontal (PLLF), anterior inferior medial frontal (AMF), and posterior inferior medial frontal (PMF). The involvement of discrete memory processes within the frontal lobes can be seen by comparing the results across groups. Results are reported as percentages of the control group's scores. The graphs on the left show total number of items correct (TC) and subjective-organization (SO) scores; the graphs on the right show scores for inconsistency (IC; failure to recall an item on one trial after successfully recalling it on the previous trial), double recalls (DR; recall of a word a second time after it has already been presented as recalled), and false alarms (FA; identification of a nonlearned word as a learned word; also called a false positive). The operational definitions of the measures are presented in the original report (Alexander et al., 2003).

We have been successful in dissociating specific cognitive processes within relatively discrete frontal regions for several reasons. First, we have assembled sufficient numbers of patients that reasonably represent different frontal regions (at some risk to the speed of completion of projects). Second, we have used measures of memory sufficiently sensitive to isolate distinct processes. Third, the performance-based approach has enabled the data, not our a priori biases, to differentiate processes critical to memory and their relation to specific frontal brain regions.

FUTURE DIRECTIONS

Our sample sizes have been relatively small, although larger and more diverse than most, so replication of our findings and continued refinement of the identified anatomical regions and processes are both essential.

Once a study of a particular cognitive domain links an impaired process to a lesion in a particular frontal region, it might be possible to demonstrate similar impairments in that process in entirely different cognitive domains. We have already demonstrated this possibility with tasks that have no apparent similarity: target detection and learning a list of words. The CVLT study isolated lesions in the left posterior lateral frontal region as a cause of poor criterion setting (abnormal bias to identify nonlearned material as previously learned). We have demonstrated a similar criterion-setting problem (bias in identifying a nontarget as a target) in a reaction time task among patients with lesions in the same region (Stuss, Binns, Murphy, & Alexander, 2002). The memory studies have demonstrated that right frontal lateral lesions impair monitoring of responses to a task (see also Henson, Shallice, & Dolan, 1999). In a parallel manner, similar impairments in monitoring mental activity may be seen in other nonmemory tasks, such as those that demand sustained attention to ongoing stimuli (Stuss et al., 2002).

As the components of a functional system become better understood, it becomes possible to investigate the functioning of the entire system. To achieve this broader understanding of memory (and other cognitive domains), lesion and imaging studies provide a formidable combination for studying which brain regions are involved, and how necessary their involvement is.

Recommended Reading

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