

11

The Hippocampal System and Recombinant Processing

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1. Introduction

1.1. The Enigma

Last night, during surgery, a graduate student, in discussing his future, made the comment that the hippocampus was the black hole of the neurosciences. Surveying the four volumes that Isaacson and I have edited on the subject, I began to wonder whether perhaps he was correct, especially when I recalled that these four volumes do not contain their own reviews of the prodigious efforts of Brenda Milner, Ross Adey, James Olds, Mortimer Mishkin, and the teams of Squire and Zola-Morgan and of O'Keefe and Nadell, all of whom were asked but for one reason or other could not participate.

As in the case of the cosmic black holes, ignorance is not the only fallout (or should I say, fall in?) to result from the experiments and analyses motivated by the "puzzle wrapped in an enigma," an older description of this beautiful piece of neuroarchitecture that is the hippocampus. Two approaches can be discerned in the research. One of these uses the hippocampus as a model system to study generalizable functions of neural networks; the other is addressed to the functions of the hippocampus *per se*.

In this chapter, my concern is only with the second of these approaches, which is implemented by reviewing the experiments performed in my laboratory and the theory developed on the basis of laboratory discussions of these experiments. My motivation is simple: despite several decades of

T-161

experimentation using monkeys, there is almost no mention in the current literature of the data we obtained (e.g., see Mahut, and also Gray and Rawlins, this volume, and Zola-Morgan *et al.*, 1982). The reasons for this neglect may be many, but one possibility is that the data and conclusions were presented in a form that could not be readily digested by those who did not participate in the experiments. In this chapter, I address this possibility.

Before reviewing this work in detail, the basic procedure by which the experiments were performed is set out briefly. Much of the work to be described was accomplished in the 1960s, when funding for basic research was ample. Thus, each of the experiments described below involved two to three groups of at least 4 monkeys each. In a typical experiment, one group of monkeys was subjected to hippocampectomy and another to amygdalectomy, and a third served as a control group, altogether a total of 12 monkeys. The experiments in which both the amygdala and the hippocampus were removed—the medial temporal lobe resections—used a minimum of 8 subjects. (In these experiments, *hippocampectomy* refers to removal of the entire hippocampal gyrus and thus includes, in addition to the hippocampus, the subiculum and the entorhinal cortex. The control group was given surgery identical to that performed in the operated groups except that no tissue was removed.)

Behavior was assessed quantitatively in a computer-controlled system that allowed us to automate an extensive battery of tests (Pribram, 1969). This system, called DADTA (for Discrimination Apparatus for Discrete Trial Analysis), consisted of a portable chamber within which the monkey could move about readily. The monkey was able to reach a 4×4 array of translucent Plexiglas panels through bars along one side of the chamber. Underneath these panels was a small food cup that delivered banana pellets. Visual patterns were projected onto the panels by digital display units, controlled by computer. The computer also kept track of the panel presses made by the monkeys, their reaction times, and whether the responses had been reinforced. In correct trials, the pattern reappeared each time in a new location (another panel) after a 5-s intertrial interval. Incorrect responses merely turned off the display without the delivery of a reinforcement and initiated (after 5 s) another trial. Simultaneous depression of two panels was not rewarded and delayed the next trial by 10 s. Failure to press any panel within 5 s resulted in a timeout of 10 s, during which the house lights were dimmed before the next trial was initiated.

For the most part, the tests were developed as modifications of paradigms that, in other hands, had been thoroughly analyzed so that the variables critical to performance were known. Nonetheless, modification entails the need for reinterpretation according to the specifics of the tasks as they are actually presented. As a result, the conclusions derived from the experiments

the paradigms themselves can emerge that provide biological grounding to hypotheses held at the behavioral level.

2. *Limbic versus Nonlimbic Learning and Memory*

2.1. *Alternation versus Discrimination*

The historical roots of the work reported here were reviewed in the introductory chapter of the first volume of this series (Isaacson and Pribram, 1975). The use of monkeys as subjects was motivated by the work of Klüver and Bucy (1938, 1939), who had removed the entire temporal lobe and had found a dramatic change in behavior to result. The monkeys were tamed and sexy and put all sorts of objects in their mouths. These findings were not entirely new, as similar results from temporal lobectomy in monkeys had been reported during the latter part of the nineteenth century by Sanger-Brown and Schäfer (1888). These early results became the basis for suggestions by Economo and Koskinas (1929) and Papez (1937) that Broca's *grande lobe limbique* (defined on the basis of a thick, and therefore white, first cortical layer) served as the forebrain system responsible for emotional experience and expression. In addition to these early findings, the Klüver-Bucy monkeys showed what they termed "psychic blindness" (1938).

In order to relate the variety of these behavioral phenomena to more specific brain regions, I began by making subtotal resections of various parts of the temporal lobe and was able to show that the visual disturbance was due to removal of the lateral portion of the temporal lobe (Blum *et al.*, 1950; Mishkin and Pribram, 1954), but that damage to the medial "limbic" structures, the amygdala and the hippocampus, produced taming (loss of fear as demonstrated by accelerated extinction in a conditioned avoidance procedure; Pribram and Weiskrantz, 1957); diminished aggression (as measured in a dominance hierarchy; Rosvold *et al.*, 1954); and oral changes in behavior (as determined by a Poppelreuter preference procedure and food intake measures; Pribram and Bagshaw, 1953).

The extent of the lateral temporal lesion was localized to the inferotemporal cortex by means of a multiple dissociation technique that involves the addition and subtraction of overlaps of location in terms of behavioral outcome. This technique is described in detail in Pribram (1954a, 1958a,b, 1960a; Pribram and Kruger, 1954). Many of these early experiments were performed before automation and involved a variety of discrimination tasks administered in various apparatuses such as Yerkes (Wisconsin) boxes and snooperscope television devices. We found that the entire posterior intrinsic "association" cortex could be subdivided according to sensory modality: Inferotemporal resections disrupted visual discriminations (Blum *et al.*, 1950;

resulted in deficits in taste discrimination (Pribram and Bagshaw, 1953); and posterior parietal damage resulted in tactile discrimination deficits (Blum *et al.*, 1950; Pribram and Barry, 1956; M. Wilson, 1957).

In clear contrast to the above results, resections of the amygdala and the hippocampus resulted in no discrimination deficit whatsoever. Instead, we found marked changes in conditioned avoidance (Pribram and Weiskrantz, 1957), dominance (Rosvold *et al.*, 1954), and oral (Pribram and Bagshaw, 1953) behaviors. In addition, and most important for the analysis pursued here, there was a marked deficit in the learning and performance of the delayed alternation task (Pribram *et al.*, 1962). Such deficits are also obtained when parts of the head of the caudate nucleus (Rosvold, 1972), the far-frontal (prefrontal; frontal granular), and cingulate cortices (Pribram *et al.*, 1952) are resected. As no such deficit appeared as a result of any of the lateral cortical resections, the frontal and limbic formations, including the medial temporal lobe structures, the amygdala, and the hippocampus, were classified together as frontolimbic and juxtaposed to the systems of the cortical convexity (Pribram 1954*a,b*; 1960*a,b*; 1971).

The essential characteristic of the discrimination tasks that we employed was that the monkey's choice of either one of two or more cues was consistently reinforced (or consistently not reinforced), and equally important, that the cues were continuously present until a choice was made. By contrast, in the delayed alternation task, choice cannot be guided by the specific cues present at the time. The correct choice always depends on what was done on the previous trial. This means that the cue-reinforcement contingencies are inconsistent. Jacobsen and Nissen (1937) termed this sort of task "one trial learning," and more recently, Mishkin (1978) referred to it as "trial unique."

2.2. *Henry M.*

While these experiments were in progress, a paradox emerged. When we compared our data to the neuropsychological studies on humans with far frontal lesions, as in the leukotomized (lobotomized) patients, there were consistent parallels between the effects in monkeys and those obtained with humans (see, e.g., Pribram, 1950, 1951; Poppen *et al.*, 1965). There were also similarities between the syndrome produced by amygdalotomy in humans and monkeys (Pribram, 1961*a,b*). However, when the entire medial extent of the temporal lobe, including amygdala and hippocampus, was resected in humans, no changes were observed in behaviors that could be described as emotional or motivational, such as in avoidance (fleeing), aggression (fighting), feeding, or sex (the Four Fs; see Pribram, 1960*a,b*). Instead, a very distressing and peculiar long-term defective memory was produced (Milner and Penfield, 1955; Scoville and Milner, 1957; for a review of the paradox, see Pribram, 1960*b*). My personal encounter with this paradox came as follows:

to take a look at H. M. because he seemed somewhat peculiar. I was eager to examine such a patient with a view to finding out how his emotional responses differed from those of unoperated subjects: we had just obtained our results in a conditioned avoidance experiment (Pribram, 1954a,b; Pribram and Weiskrantz, 1957), which was the first quantitative experimental deficit obtained from lesioning the hippocampus. Much to my surprise, therefore, H. M. responded normally in all respects. He discussed his relationship with his family; we had an interesting conversation about a subject we were both interested in, a possible trip from Capetown to Cairo, during which H. M. became quite animated. I tested him on recall of lists such as telephone numbers and again found him to be normal. At this point in the interview, I was called to the telephone. On my return, I tried to recall where we had left off, somewhat unsuccessfully, and so turned to H. M. for help. Had we been doing telephone numbers? Or were we doing subtractions? H. M. stared at me for some time and then asked, with a puzzled expression; "Doctor, have I seen you before?"

The distraction caused by the interruption had apparently produced a complete amnesia. H. M. had appeared so utterly normal to me that I had doubted that Scoville had succeeded in the surgery. I had seen no change in emotions, no change in memory (the Africa journey had been a pre-operative interest). Now the memory defect was striking. Distraction had, as it were, wiped the slate clean. Before I left him, I suggested to H. M. that he carry lists of activities to which he could refer whenever his memory failed him.

I knew that Brenda Milner had found similar disturbances of memory in patients operated on by Wilder Penfield at the Montreal Neurological Institute. I therefore asked Mortimer Mishkin, who knew Milner, to alert her to the existence of H. M. and to ask her if she might be interested in studying him. The rest is history. It has now been some 30 years that Milner has regularly interviewed and tested H. M. and obtained results that had to be taken into account in all of the subsequent experiments on the functions of the amygdala and the hippocampus in both humans and animals.

2.3. *Discrimination Reversal*

The paradox with which H. M. presented us made it necessary to examine closely the difference between the discrimination tasks that so clearly set apart the effects of resections of the posterior cerebral convexity and the alternation tasks that were disrupted by frontolimbic lesions. Discrimination tasks are particularly useful in the study of long-term memory, whereas delayed alternation and related delay tasks such as delayed response had been the standard for exploring short-term memory ever since their introduction by Hunter (1913) and their application to the analysis of brain function by Jacobsen (1928, 1936; Jacobsen *et al.*, 1935) and Jacobsen and

resections were especially sensitive to pro- and retroactive interference, a result that was extended by Pribram (1961) and that clarified considerably the nature of the short-term memory defect. It was possible that H. M.'s deficit reflected a reduction in an enhanced capability (compared with that of monkeys) of the human brain to resist interference. On the other hand, the manner in which we dichotomized memory into short-term and long-term may have been incorrect (see, e.g., Pribram in Kimble, 1967).

When there is a sharp dichotomy between the effects of brain lesions on two types of behavioral tasks, it is important to discover where the boundary between them may be drawn. Discrimination reversals in which animals must suddenly adjust to a new stimulus-reinforcement contingency provide a tool for titrating such a boundary. What effects would medial temporal lobe resections have on the learning and performance of discrimination reversals? The answer to this question ought to bring us closer to understanding the deficit shown by H. M.—in the sense that a sudden reversal may serve the same function as the distraction when I left the room. At the same time, a discrimination reversal deficit would relate the deficit in delayed alternation (a trial-to-trial reversal) to a wider range of behaviors.

Our initial expectation in undertaking a series of discrimination reversal experiments was that medial temporal lobe resections would influence the slope of the learning curve. This change in slope would, in turn, be increased by reversal. We were attempting to influence what is known as a "one-element" (at a time) model of learning. These models assume that animals (or humans) attend to only one feature of a complex stimulus, such as color or the slope of a line, at a time. A multistage model of this type properly described discrimination learning in unoperated, normal monkeys (Bleher, 1966, in our laboratory) as well as in humans (Zeaman and House, 1963). We found in our study that nonreinforced choices were *eliminated* one at a time from the response repertoire on a cue-by-cue basis.

In the series of experiments on discrimination reversal in temporal lobe lesioned animals, we used 11 naive monkeys, with 7 monkeys serving as controls and 4 receiving extensive resections of the entire medial portion of the temporal lobe, including the hippocampal gyrus and the amygdala. The surgery was performed before any testing. The monkeys were trained following surgery in the DADTA to discriminate between the numerals 2 and 7, which appeared in different locations (i.e., on different panels) on each trial. The monkeys were trained to criterion performance and were then given another 100 overtaining trials, were rested for 3 weeks, and were tested for retention.

For the discrimination reversal task, the numerals 0 and 5 were used, and reversal training was instituted as soon as the monkey reached criterion (90% on 100 consecutive trials). What we found was contrary to our expectations: the slopes of the learning curves were hardly affected by

aspects of these discrimination-learning tasks are a function of the posterior isocortex.

However, the amygdala-hippocampal resection markedly *slowed* learning nonetheless. The impairment was localized to the portion of the learning curve that is relatively flat (i.e., "stationary"). These periods of stationarity showed a marked prolongation, and even more severe disruption appeared during the cue-reinforcement contingency reversals. We interpreted these results in terms of an operant conditioning framework, in that "behavior during discrimination learning and reversal is under the control of two competing variables: the patterned cues to be discriminated and the noncontingent schedule of reinforcement" (Pribram *et al.*, 1969, p. 770). Further, the insights derived from this analysis helped to establish a relationship between the behavioral deficit and theories on incentive motivation and hypothesis formation. An excerpt from the discussion of this study summarizes this relationship:

Monkeys with limbic lesions . . . show a long plateau after their performance reaches a chance 50% level. Despite this, the slopes of the curves on either side of this plateau are comparable to those in original learning. It is difficult to explain these results in terms of an inability to discriminate between stimuli.

One way of considering the plateau is to suggest that the situation does not furnish sufficient incentive to alter the behavior of monkeys with lesions. This would conform to ideas that the limbic system is a substrate of motivation. However, no simple reference to the stimulus situation per se will provide a sufficient explanation. The cues remain the same; the overall probabilities of their being reinforced have not changed. *What has changed during reversal is the short-term probability that the monkey's response will be reinforced. Apparently, when this probability reaches 50%, a disposition or state is induced in the hip-am [monkeys with resections of the hippocampus and the amygdala] monkeys, but not the normals, which leads to a continuation of this relatively ineffective performance. The question is how best to characterize this state.*

The data and theories of Zeaman and House (1963) would appear to be relevant to present findings, and to offer a possible answer. Through the use of backwards learning curves these investigators have found results much like ours, in human retardate learning. That is, discrimination learning appears to involve a stationary period of varying length in which the subject is correct at only a chance probability. This is followed by an abruptly rising curve of relatively constant slope from one person or problem to the next. Their data, and our findings with many normal monkeys, indicate that the difference between a difficult and an easy problem or a fast and a slow learner is in the length of the stationary period prior to the take-off point. Furthermore, a stationary period is often found at the 50% point in reversal learning in human retardates. Zeaman and House suggest that the stationary period in a discrimination-learning problem is one in which the subject learns an observing response or, in other words, learns which aspects of the compound stimuli to attend to.

A long flat period might then indicate that the instrumental and observing responses have come under the control of different aspects of the reinforcement schedule. The stationary period during reversal training thus represents an extinction of the previously appropriate observing responses, while the instrumental responses are maintained by the 50% schedule. Apparently, the animal or retarded human is unable to . . .

problem had been presented. It is in this sense ["I give up"] perhaps that the limbic system can be said to play a role in incentive motivation.

The results can also be interpreted in "hypothesis formation" terms if observing responses are taken as indicators of hypothesis testing. When an organism's observing of a distinctive feature or stimulus dimension is reinforced, an hypothesis (attentive state) may be induced which increases the likelihood that this feature will be observed again. This hypothesis will be either confirmed or disconfirmed on subsequent trials. As already noted, two separate factors seem to be responsible for learning in the discrimination setting. One is likely to be related to the stimulus dimensions per se and, thus, probabilistically will distribute observing among dimensions. With no other mechanism than this, any subject could learn any problem in which the correct stimulus dimension has a finite probability of being observed. With low probability stimulus dimensions, however, this learning could be extremely protracted.

The second factor is likely to be related to the duration over which any hypothesis is held in the face of disconfirmation. It is this factor (a criterion for relinquishing the hypothesis) which is most likely to be regulated by limbic structures.

This study and earlier ones thus emphasize the fact that the distribution of attention is determined by at least two factors. One is directly related to stimulus dimensions; the other to the temporal organization of the learning situation. Only the second of these, the duration over which an hypothesis is held in the face of distraction and disconfirmation, is critically affected by amygdlectomy and hippocampectomy. This may explain why animals with hippocampal and amygdala lesion (or both) have their characteristic learning difficulties, and perhaps equally important, why they can readily solve most discrimination problems in which the reinforcing contingencies are not varied. (Pribram *et al.*, 1969, pp. 770-771)

This analysis directly invokes the theoretical framework of incentive motivation and hypothesis testing. What is suggested is that the monkeys with medial temporal lobe resections are insufficiently motivated to maintain a hypothesis in the face of disconfirmation; to maintain a behavior (a behavioral stance or set) in the face of distraction; and to resort to obtaining a low-benefit (50%) incidence of reinforcement when the cost (discriminating the cues) for obtaining a greater benefit (90%) becomes too high for them (though not for controls). Another way of stating this is to say that the difference between obtaining a 50% and a 90% reward is insufficient incentive for the monkeys with medial temporal lobe resections: they fail to "pay" attention to the discriminative stimuli in order to achieve the increased reward.

2.4. Effort

These conclusions were tested in a final experiment in the series involving the entire medial aspect (amygdala plus hippocampus) of the temporal lobe. In this experiment, we modified a signal-detection, decision-theory paradigm in an attempt to clearly separate behavior controlled by the stimulus ("detection") and that controlled by the reinforcing contingencies ("bias"). Eight monkeys were used: four subjected to surgery and four serving as controls.

The procedure consisted of pseudorandomly distributed reinforcement

screen. Discrimination learning and reversal training procedures were followed as in the previous experiment. One of the stimuli (*J*) was reinforced 90% of the time; the other (*S*) was reinforced on the other 10% of the trials. Thus, stimulus control was effected in a 90% probability reinforcement situation, and spatial location (position bias) came under the control of a 50% noncontingent schedule of reinforcement. Because monkeys readily succumb to position biases, the incentive of the 90% reinforcement schedule (for attending to the visually displayed cues) had to overcome this bias. (See Fig. 1.)

The results clearly demonstrated that the monkeys with resections of the medial portion of the temporal lobe (amygdala and hippocampus) succumbed to their position bias more readily than did the control subjects. The control monkeys learned more quickly to make the discrimination and accomplished the reversals much more quickly than the monkeys with the medial temporal lobe resections. The differences in behavior were limited to those portions of the learning and reversal curves where the monkeys were making a sufficient number of errors (misses) so that their schedule of reinforcement was around 50% (plus or minus 10%). Once the behavior reached the point where a discriminative stimulus was reinforced over 60% (and its mate was nonreinforced 40%), the learning and reversal curves of the lesioned and control monkeys were essentially indistinguishable. When response operator characteristic (ROC) curves were plotted, detection (d') was shown intact. The deficit in learning and reversal was due to a greater influence of position bias in the monkeys with the lesions than in the control subjects (which did demonstrate this bias as well, however). As in the previous experiment, the monkeys with medial temporal lobe resections succumbed more than their controls to the relatively effortless 50% noncontingent opportunity for obtaining reinforcement. The potentially more rewarding 90%/10% probability schedule, contingent on "paying" attention to the appropriate stimulus, failed to be as powerful an incentive for the lesioned monkeys as it was for their controls. The monkeys with the lesions did not as readily expend the "effort" to attend, a motivational, intensive aspect of attention delineated by Berlyne (1969), among others. The reasoning involved in reaching this conclusion was summarized in the report of the experiment by Spevack and Pribram (1973):

This hypothesis suggests that the major effect produced by bilateral amygdalotomy and hippocampectomy may be to alter the intensive aspects of attention (Berlyne, 1969). If hip-am subjects expend less effort than the intact monkeys for obtaining reward, they will show position preferences during a larger portion of discrimination and reversal trials than do intact controls. Whenever there is a reduction in the incentive value accruing to the stimulus dimension—as during the chance reward periods of reversal—the experimental monkeys resort to a period of position preference (chance levels of responding) more rapidly than do the intact controls. The resulting period of chance performance is more prolonged for the experimental animals because they

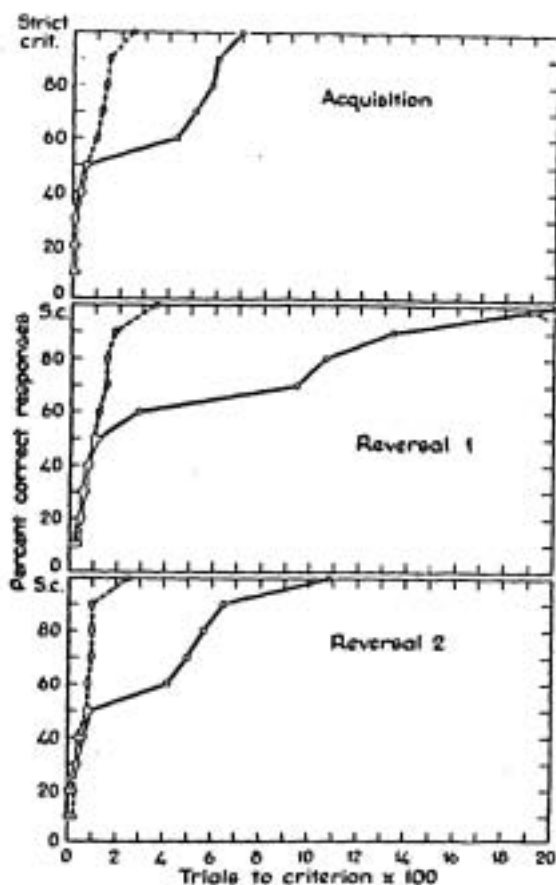


FIG. 1. (Above) Number of trials required for 10 percent increments in performance and the acquisition of the strict criterion after the last criterion during pattern discrimination learning and the first two reversals. (O—O): hip-am monkeys; (O---O): intact monkeys. (Facing page) Comparison using ROC curves of the performances of a typical hippocampal and a typical control subject during pattern discrimination and the first two reversals.

dimension. Even after the hip-am subjects do eventually begin to respond on the basis of the stimulus dimension, presumably because the intensity of their attentional state has been sufficiently altered, they still retain their increased tendencies to give up attending and resort to a position bias. This hypothesis also suggests an explanation for the difficulties of the hip-am monkeys to maintain a criterion level of performance, once they have already achieved the lax criterion. The same bias for position preference which caused the experimental animals to remain at a chance level of responding at the beginning of pattern discrimination learning and at the end of the extinction period of reversal, and to retard their achieving criterion is still present even after criterion

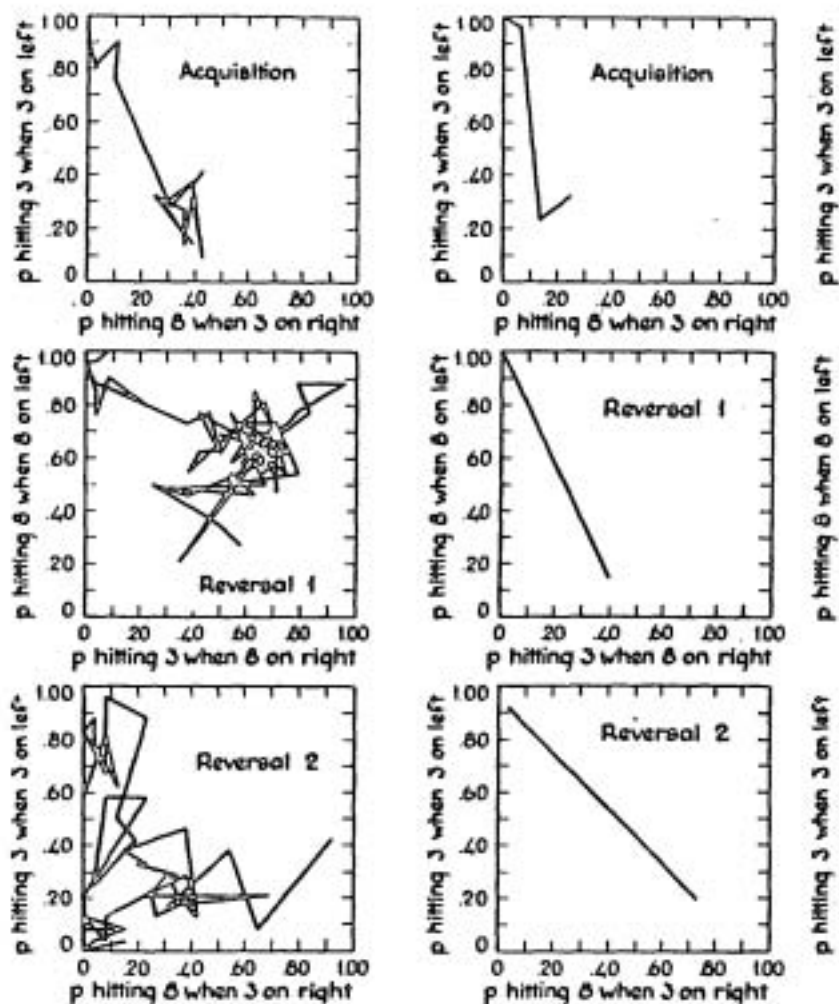


FIG. 1. (Continued)

to the stimulus dimension, have difficulties in maintaining criterion performance during three successive test days.

Signal detection analyses, therefore, have clearly demonstrated that the major difference between the hip-am and the intact subjects is in the intensive rather than the selective dimension of attention—or to put it more baldly, in the monkeys' motivation. Further, the analysis has shown that this motivational difference between the experimental and unoperated monkeys during discrimination and reversal learning, is a quantitative and not a qualitative one: the vinetized discrimination and reversal

2.5. Competence

At the conclusion of these experiments, it seemed to me that we had narrowed the apparent gap between the effects of medial temporal lobe resections in monkey and human. However, the terms *motivation*, *intensive dimension*, and *effort* (especially *effort*, as any such term derived from verbal reports of introspection) may not fully convey their technical meanings as they were developed in the laboratory and may well convey surplus meanings that are not intended. Specifically, as I hope to make clear, an increase in motivation (the intensive dimension of processing) is not due just to more "drive" (see also Miller *et al.*, 1960). In this instance, motivation involves an incentive to reorganize the processing capacity of the organism. Attention theorists use the term *effort* to describe a process that comes into play in overcoming the limited capability, the limited "span," that characterizes attention and the results of this limitation on performance (see Kahneman, 1973, for review). Most attention theorists conceive of an organism as having a fixed limitation in processing "capacity," but on the basis of experiments described below, McGuinness and I have argued that attention span is not fixed and that both external and internal flexible constraints are operating so that span can be expanded and contracted. *Competence* is a more accurate term to describe the span and its limitations. Competence, conceptualized in communication theory terms, is the reciprocal of equivocation, that is, the sum of noise and redundancy. "Effort can then be defined as the measure of attention 'paid' to increase or maintain efficiency by reducing equivocation, that is enhancing competency" (Pribram and McGuinness, 1975, p. 135). As we shall see in the following sections, *redundancy* and *noise* translate into "familiarity" and "novelty" with regard to the effects of amygdectomy and hippocampectomy.

Communication theory is based on measuring how much information in a communication is necessary to reduce uncertainty. The measure of both uncertainty and information is made in terms of the number of alternatives that describe the communication. Shannon and Weaver (1949) suggested that this measure be made in terms of a binary Boolean algebra, the *bit* (an acronym for *binary digit*), and this suggestion has been widely accepted. At the same time, Shannon pointed out that a communication is often made intelligible by repetition, which in the jargon of the theory is called *redundancy*. George Miller and his colleagues performed an extensive series of experiments on the role of redundancy in the intelligibility of a communication (see Miller, 1951) and the effect on memory and ease of processing of "chunking" or packaging information (Miller, 1956). Garner (1962, 1969) explored the relationship between such structuring and redundancy as explanatory of a host of perceptual and cognitive processes. In information measurement theory *per se*, this issue of combining and recombining chunking is handled by means of the concept of providing the *minimum variety* in the

From the results of the experiments, which distinguished the effects of resections of the posterior cerebral convexity from those of the frontolimbic formations, and from the model derived from them, it is possible to make a clear distinction between the brain systems involved in processing information *per se* and the redundancy and structuring that enhance processing. Pribram and Tubbs (1967) and Pribram *et al.* (1966) showed that resections of far-frontal and medial temporal lobes affected the operations of the structuring and redundancy processes, and not those directly concerned with information processing.

To illustrate this point, it is useful to cite an experiment seminal in this distinction between information and structuring redundancy that was performed by Smets (1973). In this experiment, he compared the effect on alpha-wave blocking and skin conductance (measures of arousal) of changing the amount of information in a display with the effect of altering the "complexity," the structure of redundancy of the display. Increases in the amount of information (the number of features) had little relationship to the measures of arousal. By contrast, arousal varied directly with the complexity of arrangements among the features displayed. As we shall see in the following sections, the same measures of arousal were dramatically altered by far-frontal and medial temporal lobe resections (see also Pribram and McGuinness, 1975, and McGuinness and Pribram, 1980, for review):

In short, we suggest that the controls [on processing] operate on the mechanisms of redundancy, on the constraints operating within and between channels rather than on the information being processed. The constraints . . . may be conceived of as operating on memory rather than on input information. Another way of stating this is to say that the controls operate on the context in which the informational content is processed. (Pribram and McGuinness, 1975, p. 156)

Several paragraphs follow that cite supporting evidence from the work of Anderson and Fitts (1958), Garner (1962), and Lindsay (1970), as well as from our own work (Pribram *et al.*, 1966).

The technical use of the term *effort* thus relates to the efficiency with which an input is processed and does not imply the inverse of laziness (a connotation in ordinary language). This efficiency is brought about by the restructuring of processing channels, a restructuring both within and between channels. Another term for restructuring is *recoding*. Thus, the binary code of machine language is recoded into octal and assembly languages for more efficient processing under certain conditions (constraints). Further recoding into operating systems and word-processing routines makes it possible for me to use the binary-coded machine operations to write this essay efficiently.

What appeared to be missing in both H. M. and our monkeys with resections of the medial portions of the temporal lobe was the ability to provide variety in the constraints, the contexts that make efficient coding of sensory input possible. The lesions impaired neither short- nor long-term

al. (1968) for H. M., and by Pribram and Douglas, who tested monkeys on the retention of a visual discrimination two years after original learning and found no deficit. As reviewed in the final chapters of the first two volumes of this series by Weiskrantz and Warrington (1975), and by Pribram and Isaacson (1975), it was *competence* (i.e., efficiency and processing span) that were impaired.

3. *Hippocampus versus Amygdala: Novelty and Familiarity*

3.1. *Factors That Influence Processing Span*

In the previous section, the effects of medial temporal lobe resections were conceptualized in terms of attention and information theory. This conceptualization helped to bring together to some degree the apparent discrepancies between the results of such resections in humans and in monkeys. Essentially, a distinction was made between information processing carried out by the neural systems of the posterior cerebral convexity, on the one hand, and the structuring of the context within which information is processed, which is carried out by the frontolimbic formations of the forebrain, on the other (see, e.g., Pribram, 1971, for review). The systems of the posterior cortical convexity were shown to be involved in processing invariants (which are the basis for alternatives, information) in organism-environment transactions. The frontolimbic formations, including the hippocampus and the amygdala of the medial surface of the temporal lobe, were shown to be involved in the competence (efficiency) with which processing proceeds. It was suggested that two factors influenced competence, redundancy and noise, and it was also suggested that competence involves structuring both the internal and the external constraints on the processing of information (in its technical meaning), producing flexibility in enhancing or limiting processing span.

The current section addresses the issue of what constitute redundancy and noise in the processing of span and whether these two aspects of competence can be teased apart by restricting the medial temporal lobe resection to either the amygdala or the hippocampus. To this end, a series of experiments was undertaken in which amygdalotomized monkeys were compared to those with hippocampotomy and also to a sham-operated group. Modifications of the discrimination paradigm were used in which 70% versus 30% was substituted for the more usual 100% versus 0% schedule of reinforcement in order to make the tasks sensitive to frontolimbic damage.

3.2. *Discrimination Reversal*

As noted, discrimination reversal

reversal process consists of two stages; the loss of the familiar response and the acquisition of the new. In a new series of experiments (Douglas and Pribram, 1966) involving a dozen monkeys, we found that the amygdalectomized group of monkeys had no difficulty in the first stage of discrimination. During reversal, they were slightly superior to the sham-operated monkeys in eliminating the familiar (previously correct) response but had some difficulty in acquiring the new response with consistency (much as in the acquisition phase of the extinction experiment; see below).

Hippocampectomized subjects were slow to initiate the extinction of responses to the familiar cue and were equally slow in initiating the learning of the new response, a pattern similar to that obtained in the monkeys with the combined "hip-am" medial-temporal-lobe resection. It thus appears that the effect on discrimination reversal obtained with the medial temporal lobe resection is largely a result of the hippocampal component of that lesion. When the reinforcement ratio approximates 50% during the intermediate range of reversal—that is, when the monkeys have given up responding to the previously reinforced cue but have not as yet achieved responding correctly to the currently reinforced cue—the hippocampectomized monkeys remain stuck longer than do amygdalectomized monkeys and control subjects. Hippocampectomized monkeys apparently fail to process the change in the cue-reinforcement contingencies as efficiently as the other monkeys.

3.3. *Learning, Extinction, and Relearning*

From the fact that whenever the reinforcement ratio for performing without observing (discrimination) approaches chance, hippocampectomized but not amygdalectomized monkeys get stuck, we expected an even more marked and specifiable deficit in a discrimination procedure in which the reinforcements are distributed 70% versus 30% between the cues. Normal monkeys tend to maximize in the presence of such a probability distribution. This was also true of the monkeys with amygdectomy and hippocampectomy. During extinction, however, the hippocampectomized monkeys took longer than did the amygdalectomized or the control monkeys. What the probability-matching procedure brought out was the fact that the hippocampectomized monkeys responded most often to the more rewarded (70%) stimulus, whereas the amygdalectomized monkeys responded least often. This result provided a clue that was followed subsequently in tests involving reaction to novel stimuli (see below). Finally, when reaction times were plotted, it was discovered that the hippocampectomized monkeys showed the shortest latency of responding throughout extinction, whereas the amygdalectomized monkeys showed the longest. In fact, the amygdalectomized subjects showed more long-latency (over 2 s) responses than did controls, whereas the hippocampectomized monkeys showed fewer such "hesitation"

tomy. At this point in the experimental analysis, the effects of medial temporal lobe lesions on orienting and its habituation were clearly established:

The finding that the amygdalotomized Ss were more prone to make long latency responses on the rewarded trials may be related to Bateson's (unpublished data) observation that amygdalotomized monkeys cock their ears more often during the training procedure than do normal monkeys, which show a much greater decrement in ear movements as training progresses. This result may also be related to the observation reported by Schwartzbaum and Pribram (1960) that amygdalotomized Ss hesitate on test trials in a transposition task. (Douglas and Pribram, 1966, p. 210)

3.4. Paired versus Scattered Stimuli

The fact that hippocampectomized monkeys make few long-latency responses in our DADTA procedures was also demonstrated (Douglas and Pribram, 1966) in an experiment in which the cues were either closely paired on the DADTA display panels or displayed on panels more remote from each other. In this experiment, hippocampectomized monkeys made significantly more correct responses on the paired than on the scattered presentations, whereas no such effect was obtained in the amygdalotomized and control monkeys. When the stimuli were scattered, the hippocampectomized monkeys pressed the cued panel that happened to be within their line of gaze irrespective of the nonreinforcement history of that cue. This was the second experiment in which medial temporal lobe resection or hippocampectomy influenced the processing of nonreinforced elements in the stimulus array: the first was the experiment in which the multistage model of learning was tested (see Section 2.3, "Discrimination Reversal"). We therefore undertook another experiment in which we directly confronted the animal with a novel cue paired with a previously reinforced or a previously nonreinforced cue.

3.5. Massed versus Spaced Trials

But before I report the results on the pairing of novel cues, another relevant result needs to be interposed. In this experiment (Kimble and Pribram, 1963), the effects on learning of amygdalotomy and hippocampectomy were assessed under the conditions of massed and spaced trials. Control and hippocampectomized monkeys showed a steady and equal improvement in performance as the intertrial interval is lengthened up to 6 min. Amygdalotomized monkeys, on the other hand, learned more slowly as the intertrial interval increased.

It is assumed that, for normal subjects, the longer intervals reduce pro- and retroactive interference among successive reinforced and nonreinforced trials; thus, learning is enhanced. The result that amygdalotomy wiped out this advantage supported earlier evidence that amygdalotomized monkeys were considerably less sensitive to manipulations of CA.

fore, that the effects of medial temporal lobe resections on the redundancy factor that influences competence, the effect of pro- and retroactive interference, are a function of the amygdectomy rather than of the hippocampotomy portions of the lesion.

3.6. Reaction to Novel Stimuli

These results indicate that the two factors that influence competence, redundancy and noise, may be separately influenced by amygdectomy and hippocampotomy. Interference among redundant trials was shown to be affected by amygdectomy. In Pavlovian theory, the orienting reaction following a situation in which the organism has become habituated is paradigmatic for studying interference phenomena. The laboratory had undertaken a long series of experiments assaying the visceromotoric components of the orienting reaction as a function of the effects of amygdectomy (Kaada *et al.*, 1949; Bagshaw *et al.*, 1965; Kimble *et al.*, 1965; Bagshaw and Benzies, 1968; Bagshaw and Coppock, 1968) after we found that monkeys with these lesions failed to habituate to repetitions of a stimulus (Schwartzbaum *et al.*, 1961). It was therefore a natural next step to insert a novel stimulus into the current series of discrimination studies.

In these experiments, we compared the effects of amygdectomy to those of hippocampotomy on a task in which a novel cue was matched either to a cue that had been previously reinforced (70%) or previously nonreinforced (30%) after the animal had reached a criterion of 90% in 100 consecutive trials. We found that, after amygdectomy, the monkeys chose the novel cue and the previously reinforced cue at about 50% each, whereas hippocampotomized monkeys and control subjects chose the previously rewarded cue 80% of the time. Further, the amygdectomized monkeys chose the novel rather than the previously nonreinforced cues about 70% of the time, as did the control monkeys, whereas hippocampotomized monkeys responded 50% to each. The amygdectomized monkeys apparently attended to and remembered the nonreinforced cue as being nonreinforced, but they ignored or forgot the previously reinforced cue. By contrast, hippocampotomized monkeys chose the previously reinforced cue more than 80% of the time over the novel one, but they chose the novel and the previously nonreinforced cue about equally. The hippocampotomized monkeys had attended to and remembered the previously reinforced cue but had apparently failed to attend to the one that had been previously nonreinforced.

We concluded that amygdectomized monkeys learned by attending to the nonreinforced member of a pair whereas hippocampotomized monkeys learned by attending to the reinforced member. In the absence of a hippocampus, learning *not* to go to a *nonreinforced* cue (i.e., actively ignoring

to the more rewarded (70%) stimulus, whereas the amygdalectomized monkeys responded least often.

3.7. *Errors of Omission and of Commission*

We tested our conclusion regarding the effect of hippocampectomy on normally occurring active ignoring of nonreinforced elements in a task by presenting another group of monkeys a discrimination in which there was only one reinforced cue, but in which the number of nonreinforced cues varied from one to four. The control (and amygdalectomized) subjects quickly learned to ignore the nonreinforced cues; the hippocampectomized monkeys did not (Douglas *et al.*, 1969).

4. *The Hippocampus and Competence*

4.1. *Orienting and Habituation*

The experimental analyses reviewed in the previous section devolved on teasing apart the variables responsible for enhancing competence and extending span by increasing flexibility in processing. As noted, in information measurement theory, the critical variables for controlling "requisite variety" in the processing channels are redundancy and noise. In the analysis of the effects of resection of the medial temporal lobe, these variables translate into familiarity and novelty: We noted that with respect to familiarity, amygdalectomy reduces pro- and retroactive interference. Other studies using the orienting reaction further specified the nature of the involvement of the amygdala in processing familiarity and are reviewed in other publications rather than here because this chapter primarily addresses the functions of the hippocampus (Bagshaw *et al.*, 1965; Kimble *et al.*, 1965; Pribram *et al.*, 1966, 1979; Bagshaw and Benzies, 1968; Bagshaw and Coppock, 1968; Pribram and McGuinness, 1975). Other paradigms explored other facets of this relationship (Schwartzbaum and Pribram, 1960; Hearst and Pribram, 1964a,b; Bagshaw and Pribram, 1965; Barrett, 1969).

In essence, these studies showed that the visceromotoric components of orienting were markedly attenuated by amygdalectomy and that habituation of the behavioral components failed to take place. I interpreted these findings to mean that the novel stimulus had failed to "register" (to become familiar) and that a visceromotoric "booster" was required for registration. Considerable convergence with the work of McGaugh and Hertz (1972) on some facets of "consolidation" of the memory trace has been pointed out (Pribram, 1984). Failure to register a novel experience was shown to be reflected in a failure to transfer training in transposition paradigms (Bagshaw and Pribram, 1965); at the same time, stimulus generalizations remain

This section concerns the relationship between the hippocampus and the other component of competence, the processing of "noise." As we shall see, hippocampectomy influences monkeys' responses to distraction and in general reduces the flexibility of behavior in problem-solving situations. In a sense, the momentarily irrelevant aspects of a problem-solving situation constitute its noise. Changes in the situation, in the contexts that enhance their relevance, constitute novelty. Thus, in any situation that is characterized by variability, effort is expended in processing momentary irrelevancies and their subsequent emergence as novelties. The experimental analysis reviewed in this and the following sections is aimed at showing that hippocampectomy influences a process that operates on irrelevancy, a mechanism that is involved in the development of a context, the internal and external constraints, that defines novelty. The flexibility provided by this mechanism allows the same stimulus, the same memory, and the same intent to be experienced as novel when, under other conditions, it is experienced as familiar. The reasoning that led to this conclusion did not proceed simply but came as a result of testing hypotheses that were, in several critical instances, disconfirmed.

4.2. *Alternation versus Delayed Response*

An important early finding seminal in the analyses reviewed in this section is the fact that the effects of brain resections can dissociate variations of the delayed response and the delayed alternation procedures and can even produce a dissociation between delayed response and delayed alternation in their classical form. Mishkin and I had used the delayed response task in our early localization experiments (Mishkin, 1954; Mishkin and Pribram, 1954) and had found no deficit after hippocampal resection. The classical form (also called the *direct form*) of delayed response performance (which is severely affected by far-frontal resections) consists of having a monkey recall which of two boxes had been baited 5 s previously with a peanut while it watched. A screen is interposed during the delay. As noted earlier, Malmö (1942) had shown that it was this screen that acted as a distractor (resulting in pro- and retroactive interference), because when the delay is created by darkening the testing chamber for 5 s, the monkeys with frontal resections show no deficit.

The classical form of delayed alternation consists of initially baiting both boxes out of sight of the monkey. The monkey chooses one box and is rewarded. After the imposition of an opaque screen, the monkey has another choice and, in order to receive the reward, must choose the box it had not emptied on the previous trial. To do this, it must learn a win-shift strategy. On successive trials, alternate boxes are baited out of view of the monkey (i.e., while the screen is down). A correction procedure is used: the same box remains baited until the monkey chooses it. (Alternation without correc-

Resections of far-frontal cortex result in deficits in the learning and performance of these forms of the delayed alternation as well as of the delayed response task. But hippocampectomy, although it produces a complete deficit in this classical form of delayed alternation (Pribram *et al.*, 1962), fails to impair delayed response learning or performance (Mishkin and Pribram, 1954; Mahut, 1971).

Because all frontolimbic (far-frontal, cingulate, orbitofrontal, temporal polar, and amygdala, as well as hippocampal) lesions produce defective performance in delayed alternation tasks, I had come to the hypothesis that such lesions interfere with the sequencing of (instrumental) behavior (Pribram, 1954*b*; 1958*a,b*). Performance on the delayed response task demands the carrying out of a sequence (observing and reaching), although limited to a single trial. There was therefore the need to distinguish between the types of sequencing involved in the two tasks.

The fact that both tasks involve a delay seemed to rule out this element as critical to the distinction. Nonetheless, because the memory loss in H.M. appeared to partake of an intermediate-range short-term (primary) memory, and because both delayed response and alternation involve short-term memory, we performed two rather different experiments in which intermediate lengths of delay were a factor. As reviewed earlier, in an experiment using the DADTA, we investigated the effect of hippocampectomy on discrimination learning under massed versus spaced trial conditions. There was no effect (Kimble and Pribram, 1963). In the other experiment, I used a 15-min fixed-interval procedure and again obtained no effect (Pribram, 1963*a,b*). Clearly, the delay factor *per se* could not account for the deficit produced by hippocampectomy in monkeys.

4.3. Internally versus Externally Ordered Sequences

We next inquired directly into the distinction between a sequence where observing is followed by one instrumental response and a sequence that requires two different instrumental responses. The distinction appeared to depend on whether the sequencing was cued externally (visually) to the organism or whether an internal (i.e., kinesthetic) cue was critical. To this end, we tested monkeys in the DADTA on one task (which we labeled *externally ordered*) in which the sequence of panel presses necessary to receive a reward within that trial was specified by the stimulus display, and on another (which we called *internally ordered*) in which the monkeys were free to determine their own sequence, provided they did not choose a stimulus that, during that trial, they had chosen previously. We found that hippocampectomy disrupted performance on both the internally and the externally ordered sequence (Kimble and Pribram, 1963) when the monkeys were relatively inexperienced, but not when they had been overtrained.

Similar results were obtained when resections were made of other

alysis of the factors involved in producing the deficit (Brody *et al.*, 1977; Brody and Pribram, 1978) showed that a continual shift in the spatial location of the stimuli (the pseudorandomization of cues across the 12 panels of DADTA) distracted all subjects, but especially those with frontolimbic resections (Douglas and Pribram, 1965; Grueninger and Pribram, 1969).

The results of these experiments focused our attention once again on the distraction caused by distributing cues among the 12 panel locations of DADTA. *This distracting effect had both good and bad consequences: learning was often slowed but the range of problems that the monkeys could learn was enhanced considerably by the fact that the resort to position habits was discouraged. Distraction, when properly processed, as in the experienced monkey, enhances competence.*

4.4. Spatial versus Nonspatial Tasks

Alterations in the processing of distractors underlie the deficits in both attention and learning discussed so far. Such alterations also confound another issue that has plagued the study of the effects of hippocampectomy: the relevance of spatial as opposed to nonspatial cues. I wish therefore to present in some detail a set of experiments performed over 15 years ago that remained unpublished because spatial effects and distractibility were confounded. The reason for detailing them now is that, more recently, others have come up against this difficult problem, and their studies as well as ours have provided plausible explanations for the findings (see, e.g., Mahut and Moss, Chapter 8, this volume).

The spatial aspect of the deficit following hippocampectomy has been repeatedly emphasized by O'Keefe and Nadel (1978) and by Mahut (see Chapter 8, this volume). In fact, Schäfer, in the 1900 edition of his *Text-book of Physiology*, devoted over three pages to this issue. He reported that Ferrier and Munk had described changes in tactile sensibility following lesions of the hippocampus and the gyrus fornicatus (including the cingulate cortex). However, working with Horsley and with Sanger-Brown, Schäfer was unable to confirm these results.

In our experiments, we used modifications of delayed alternation and sensory discrimination procedures. As noted earlier, such modifications allow inquiry into the basic variables that characterize the deficit produced by the cerebral resections, variables that are only superficially represented in the impairment of task performance. Specifically, when the successive (go, no-go) form of the delayed alternation procedure is used in addition to the classical spatial (right-left) form, frontal and amygdala resections produce different results: frontal lesions drastically impair right-left delayed alternation, leaving go, no-go alternation virtually intact, whereas amygdalectomy has a greater effect on performance of the go, no-go version than of the spatial form of the task (Mishkin and Pribram, 1955, 1956; Pribram *et al.*

tony might also be different when different versions of the delayed alternation procedure were used. This expectation was enhanced by the fact that performance of spatial delayed response is spared by this lesion. Our results had shown that neither the delay nor the spatial aspect of the spatial delayed alternation task appeared to be the critical variable basic to the deficit produced by the resection.

This finding left the possibility that alternation *per se* is the basic variable disrupted by hippocampectomy. To test this hypothesis, we returned to the delayed alternation and visual discrimination tasks, but we used them not only in their classical spatial guise but also in a successive go, no-go form. Monkeys were trained on both alternation and discrimination tasks, each given in both spatial and go, no-go versions.

Eight rhesus monkeys were divided into two groups of four subjects each. One group was given bilateral hippocampal resections; the other received the identical surgery except that no tissue was removed. The testing was performed in the DADTA. For the simultaneous discriminations and reversal, a red and green circle (or, for the second test, the numerals 3 and 8) were distributed in pseudorandom sequence (no more than four repetitions) over the 12 panels. For the classical spatial alternation, white zeros were displayed in the two center panels of the DADTA. For the successive (go, no-go) discrimination, both panels were illuminated by the same pattern (red circle or green circle), and the correct response consisted of pressing either (go for green)—or *neither* (no-go for red)—panel. In the go, no-go alternation, the panels were always illuminated with white zeros, and the monkey had to alternately press either panel or withhold a response for 5 s. For all tasks, incorrect responses were followed by a repetition of the trial (correction procedure).

The behavior of the monkeys was shaped before surgery so that they would sustain panel pressing at a 50% overall reinforcement schedule. After surgery, the tests were administered in the following order (no attempt was made to balance for order effects): simultaneous red-versus-green discrimination; reversal of the red-green discrimination; go, no-go red-green discrimination and its reversal. Then the classical right-left spatial alternation was presented, followed by the go, no-go alternation.

A deficit in the spatial, simultaneous form of the red-green discrimination was produced by hippocampectomy. Thus, the possibility arose that such a deficit was due to invasion of or damage to the adjacent inferotemporal cortex. In order to assess this possibility, a more difficult discrimination (a 3-versus-8) was administered, as were a set of discrimination reversals to these cues. Damage to the inferotemporal cortex produces severe deficits on such difficult discrimination tasks and impairs the development of reversal learning sets (Christiansen and Pribram, 1979).

The results of the first set of these experiments are clear-cut, as can be seen from Tables 1 and 2. Discrimination

TABLE 1
Spatial Alternation, Discrimination, and Reversal

	Right-left alternation	Right-left red-versus- green discrimination	Right-left disc reversal		Right-left 3-versus-8 discrimination	Right-left reversals
	Control					
<i>N</i>				<i>N</i>		
352	1150	200	450	352	100	1100
353	750	200	200	353	100	700
354	1100	150	300	354	150	600
361	800	350	450	361	250	650
	Hippocampal					
351	1500F	550	600F	351	800	850
355	1500F	500	600F	355	400	750
358	1500F	600	600F	358	700	1000
359	1500F	550	600F	359	100	500

alternation nor with the discrimination, or its reversals. By contrast, the monkeys that had been given hippocampal resections failed spatial right-left alternation completely (in 1500 trials) and were retarded (no overlap with the sham-operated control group) in the initial simultaneous red-versus-green discrimination, which they also failed to reverse (in 600 trials). This deficit in simultaneous discrimination learning was confirmed with subsequent more difficult 3-versus-8 discriminanda. However, the deficit was no more severe than on the initial task, despite the greater difficulty of the 3-versus-8 discrimination. In fact, one subject had no deficit at all.

TABLE 2
Spatial Alternation, Discrimination,
and Reversal

Go, no-go alternation	Go, no-go red-versus-green discrimination	Go, no-go disc reversal
	Control	
1800	400	250
600	200	200
1050	150	150
900	250	100
	Hippocampal	
1200	300	150
800	250	150

This deficit in discrimination performance was surprising (the study by Mahut, 1971, was carried out at my urging to confirm or disconfirm this result) and discomforting in view of the repeated failure to find such a deficit when the testing was done in the spatial, simultaneous fashion with only two manipulanda. Only when we performed the paired-versus-scattered-cue experiment described above (Douglas and Pribram, 1966) and compared the performance of the same monkeys in the classical (Verkes/Wisconsin) apparatus and showed that the deficit was due to the randomization of cues across the 12 panels of the DADTA (Brody *et al.*, 1977) did we obtain a plausible explanation for our result.

As noted, the possibility also existed that the visual discrimination deficit was due to an unintended invasion of the inferotemporal cortex. Against this interpretation are (1) the histological findings, which showed that invasion of the inferotemporal cortex was minimal; (2) the excellent performance on the successive form of the discrimination; and (3) the relatively good performance on the 3-versus-8 discrimination, which monkeys with inferotemporal resections ordinarily find extremely difficult (e.g., Mishkin and Pribram, 1954; Pribram *et al.*, 1966).

An alternative, more parsimonious description is that the hippocampal resection failed to interfere with go, no-go performances while producing dramatic impairments of spatial tasks, whether discrimination or alternation. Taken in isolation, the obvious interpretation of this finding is that the hippocampal lesion impairs performance in which spatial cues must be learned. This is the interpretation espoused by O'Keefe and Nadel (1978) in their extensive and penetrating review of the results of experiments on rats. Against this interpretation is the fact that hippocampal lesions fail to impair delayed response performance, which has a strong spatial component. Furthermore, explanations in terms of spatial learning have been invoked to explain defective behavior following frontal (Oscar and Wilson, 1966; Mishkin *et al.*, 1969; Oscar-Berman, 1975) and parietal (H. Pribram and Barry, 1956; Wilson, 1957) lesions. If, in fact, the effects of hippocampal lesions are to be explained in terms of spatial learning, it will still be necessary to distinguish the type of spatial processing disrupted by these lesions as contrasted to those of other brain regions.

A possible alternative explanation of the selective effects of the hippocampal resections that does not ignore the spatial attributes of simultaneous tasks could be made in terms of processing distractors. As noted, Douglas and Pribram (1969) showed that hippocampectomy alters a monkey's susceptibility to distraction. In those experiments, it was also demonstrated that, in these tasks, spatial cues were more distracting to all monkeys than visual (or auditory) cues. Because the spatial factor plays such a large role when tasks are presented in the simultaneous form, the proposal may be entertained that the effects of the hippocampal lesion are primarily on the ability to process distractors and, because of the monkeys' tendency to position habits

All of the experiments reviewed in the previous section had pointed to an obvious conclusion: Monkeys with hippocampal lesions are impaired when problem solving depends on actively ignoring (processing) a nonreinforced cue (a potential distractor). How, then, do we explain the fact reviewed in the present section that learning and performance on the go, no-go versions of alternation and discrimination remain intact? An answer may be derived from two observations: Normal subjects make a very large number of repetitive errors on the no-go trials, so that the difference between them and the hippocampectomized monkeys is washed out. (In the tables, non-repetitive errors are presented; the monkeys in this experiment and those in others with frontolimbic lesions made approximately twice as many repetitive errors as did their controls; however, the learning curves of elimination of the repetitive errors were essentially parallel; i.e., the difference in the curves was early, before the process of elimination, much as in the effects on discrimination and reversal described in the previous section; see, e.g., Pribram, 1962.) Also, the nature of the no-go trials makes them difficult to ignore. These results also clearly demonstrate the fact that it is not the withholding of responses that is impaired by hippocampectomy; it is active ignoring.

Only in the spatial situation is there a cue that initially acts as a distractor in the performance of the task. Control subjects learn to eliminate the errors due to nonreinforcement because their hippocampus is involved in learning to actively ignore nonreinforced events. Hippocampectomized subjects continue to be distracted by the spatial cues until the elimination process has had a chance to work.

4.5. *Hippocampal Electrical Activity*

The hypothesis that the hippocampal deficit on spatial alternation and discrimination could be accounted for by a deficiency in processing spatial distractors received support from several other experiments performed in the laboratory. For instance, it was shown that the effects of resection of far-frontal cortex resulted in a similar deficiency, especially in the presence of spatial distractors (Grueninger and Pribram, 1969). However, as in the case of frontal lesions in humans, the failure to adequately process distractors can lead to perseveration as well as to distractibility, depending on the situation (Pribram *et al.*, 1964). Thus, we needed to discover what the conditions were in which hippocampectomy enhanced distractibility. Obviously, the spatial forms of the alternation and discrimination tasks were critical. Could it be, as suggested in the previous section, that withholding a response, as in the go, no-go versions, produces such a striking behavioral effect that ignoring is fostered and distraction is prevented? In order to test this hypothesis, we examined the electrical activity generated in the hippocampus during spatial and go, no-go alternation performance. Hippocampal

and "intentional" activity in rats and dogs (Vanderwolf, 1969; Black *et al.*, 1970). However, theta activity was not apparent in the ordinary recordings that had been reported from monkey hippocampus.

We found, however, that spectral analysis of hippocampal activity by computer established beyond doubt that a considerable amount of theta activity occurred in the record of primate hippocampal activity. Further, we found that the amount of theta was different during the go and the no-go trials of alternation performance: during the no-go trials (correctly performed), theta was distinctly more prominent. This prominence of theta activity developed gradually during learning. Further, the theta increase was present immediately after stimulus presentation and did not persist; hippocampal electrical activity recorded later in the trial did not show any systematic differences between trial categories or problems.

We fully expected that the electrical activity recorded during the spatial version of the task would resemble the activity recorded during the go trials of the go, no-go procedure. After all, the spatial task demanded a go response on each trial. But once again, we were surprised. Hippocampal theta activity recorded during trials on the spatial task resembled that recorded during no-go trials. With respect to hippocampal function (not the function of the rest of the brain, however), spatial alternation is a differentiation of no-go behavior (Crowne *et al.*, 1972). Clearly, the hippocampus is involved in those aspects of processing that lead to active ignoring and nonresponding, the context within which selective (information) processing occurs. The comprehensive program of research undertaken by Richard Thompson and his collaborators is relevant here (see Berger *et al.*, this volume). The results of this research show that a "neuronal model" of the time course of a response is constructed in the hippocampus, a model necessary to the performance of a classical (Pavlovian) conditional response *whenever there is prolonged delay* between the conditional stimulus (CS) and the unconditional stimulus (UCS). The neuronal model apparently serves as a temporal bridge to enhance withholding a premature response, to enhance the span over which the conditioning process can proceed. Perhaps, the construction of this sort of neuronal model is the basis of the effort expended to enhance the processing span in the more cognitive types of performances reviewed here.

4.6. Mechanism

These experimental results pointed once again, as had the earlier ones, to the hippocampus as a structure involved in processing those aspects of situations that demand active ignoring. Pavlov had conceptualized such processes as resulting from "internal inhibition" and Kinble (1969) developed a model of hippocampal function based on this concept. Douglas (1966) and Pribram (1969b) extended this model to include relevant new data from the laboratory.

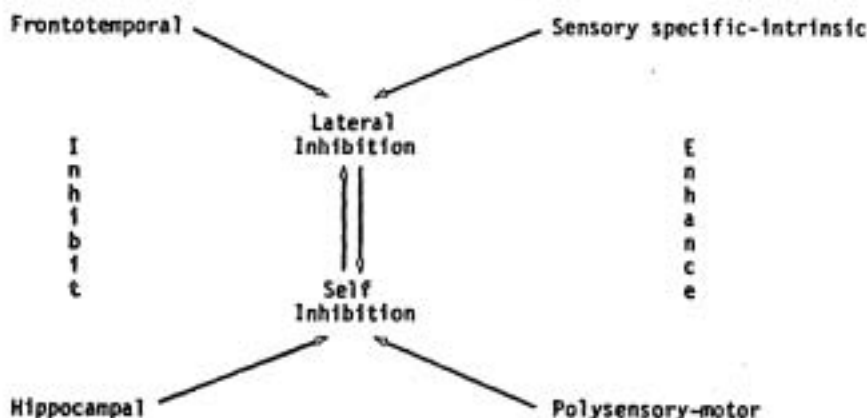


FIG. 2. Diagram of the relationship among excitatory and inhibitory neural interactions and the place of the hippocampus in this scheme. See text for the database upon which the diagram is constructed.

primary projection systems were controlled by the frontolimbic formations and by the precentral motor and intrinsic association systems of the posterior cerebral convexity. The controls on processing were demonstrated by the corticofugal effects of electrical excitation of these systems on recovery cycles within the sensory channels as assayed by successive sensory stimulations (Spinelli and Pribram, 1967). The dependent variables used were variability in the amplitudes of the channel response to sensory stimulation, as well as the speed of recovery.

The effects were interpreted (Pribram, 1967) as operating on reciprocal inhibitory mechanisms within the sensory channels: lateral inhibition (corresponding to Pavlov's external inhibition) and self-inhibition (corresponding to Pavlov's internal inhibition). Four controlling processes were delineated: those of the precentral motor and intrinsic systems of the posterior cerebral convexity operated by enhancing self- and lateral inhibition respectively; those of the frontotemporal (amygdala) and the hippocampus produced disinhibition of the basic inhibitory processes (see Fig. 2). Note that the effect of hippocampal excitation operates to disinhibit self-inhibition (inferred from the fact that the variability of the sensory evoked response is increased). Disinhibition of internal inhibition allows the processing of situations that would ordinarily induce internal inhibition; that is, inhibitory process would gate out these situations. Increased variability increases the opportunity for flexibility in processing.

Parenthetically, disinhibition of lateral inhibition by excitation of the amygdala and related frontal cortex results in the registration of an "orienting

rupted by amygdala or frontal lesions, with the result that habituation (familiarization) of the behavioral components failed to take place (Pribram, 1975).

To summarize: The deficits produced by frontolimbic resections and the effects of electrical excitation of frontolimbic formations (Kaada *et al.*, 1949) can be readily distinguished from the effects of resection and of electrical excitation of the sensorimotor and associated systems of the posterior cortical convexity. Manipulations of the posterior convexity influence behaviors that are characterized by invariant relationships between the organism and the environment. Manipulations of frontolimbic formations influence behaviors that are characterized by the more evanescent relationships of familiarity and novelty in the relationship between organism and environment. Thus, habituation of the orienting response is actively promoted by the amygdala and related frontal cortex. Once habituation has taken place, the hippocampal system makes possible the active processing of the habituated, ostensibly ignored stimulus.

Active ignoring and the active processing of ostensibly ignored situations form the processing span, that is, the context, the setting, and the apperceptive mass within which the invariances that make up perceived experience and ordinary behavior take place. With respect to the hippocampus, these results of analysis were stated in the summary of the first two volumes of this series as follows:

Pribram (1971) has distinguished the organization of appetitive-consumatory and other well-ingrained habitual behaviors which depend on the basal ganglia (and the nigrostriatal system) from attentional-intentional behaviors which depend on the hippocampal and cerebellar circuits for their controlling operations. Isaacson (1974) emphasized the same distinction by attributing instinctive and well-trained behaviors to the "reptilian complex" of the brain (as the term was used by MacLean, 1970) which includes the basal ganglia and associated brain systems. Appetitive-consumatory and habitual behaviors are regulated primarily by closed-loop, homeostatic feedback mechanisms. Attentional and intentional behaviors are characterized by parallel processing, open-loop, feedforward control systems. Habituation can be conceived as a change [in the hippocampus, among other systems] from an "and" gate state (in which a response depends on the convergent action of inputs) to an "or" gate (in which responses of complex spike cells are activated by any variety of inputs occurring at different times). Essentially this means that in the presence of these cell inhibitory activity, the complex spike channels are kept independent of each other. The system is maximally sensitive. Input systems can therefore act in parallel. (Pribram and Isaacson, 1975, p. 453)

4.7. *Context-Sensitive Recombinant Processing*

As indicated by the review thus far, the theoretical basis for our results centered for the most part on information measurement theory, on signal detection and sampling theories, on Pavlovian theory, and on models derived from computer-programming procedures. What has emerged is a consideration of hippocampal function in terms of the concept of a recombination

virtue of processing by an amygdala-frontal system. Coding was conceived of as a process, concomitant with storage, that "packaged" information into more-or-less redundant "chunks" that could be variously combined and recombined to facilitate retrieval. Possibilities we considered among the laboratory group as models of this process were "hash coding" in computer programming, the pagination necessary to store and retrieve information in a computer program, bandwidth limiting in holography, and the "parsing" of a communication, all of which were conceived of as providing a context within which information is processed. Without such contextual aids, input into the brain would be processed into one set of programs by sheer repetition, and into other programs that were responsible for skilled performances but that failed to allow the flexibility necessary for retrieval triggered by a particular need or episode.

For the most part, these concepts were developed with regard to the very similar, if not identical, functions of the far-frontal cortex and were related to the work of others in review articles and books: The concept of a working memory was introduced in *Plans and the Structure of Behavior* (Miller *et al.*, 1960) to describe the process involved in performing delayed alternation. Olton has since applied this concept extensively to the functions of the hippocampus (see Chapter 9, this volume). Shortly after its introduction, this concept was made more precise by specifying that the nature of working memory was a list structure that could be flexibly rearranged, a "flexible noticing order" (Pribram, 1961a). Somewhat later, these flexible noticing orders were developed into executive routines in time-sharing systems used with large "main-frame" computers, and "working memory" was conceived of as operating as an executive process for the functions of the rest of the brain (Pribram, 1973).

The distinction between the memory-processing functions of the fronto-limbic formations and the information processing performed by the systems of the posterior cerebral convexity was initially framed in terms of context-dependent and sensory-specific processing mechanisms (Pribram, 1966, 1971). More recently, the evidence for a hierarchical organization of components of these categories of memory and learning was reviewed: The components of sensory-specific processing, now identified as referential learning and memory, include sensory and motor skills, search, sampling, and categorizing. The components of contextual processing include registration of orienting to an episode and its subsequent habituation (or extinction, if conditioning or learning has taken place), processes considered basic to "event" or "episodic memory." To this form of processing was added probability estimation to complete the roster of components of context-dependent processing (Pribram, 1984; see Fig. 3).

One of the more influential of these attempts at modeling the mechanism involved in contextualization based on the laboratory's activities was that of

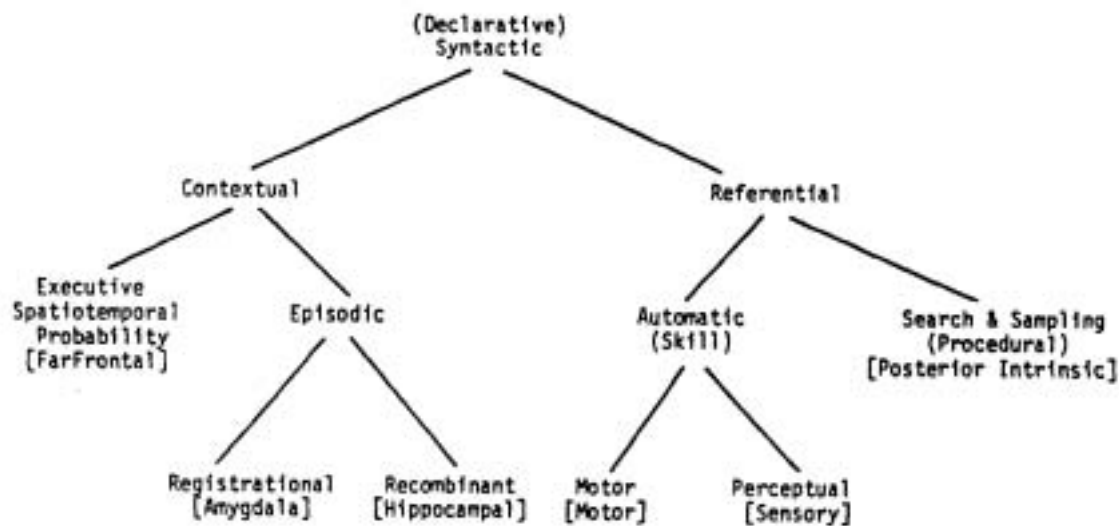


FIG. 3. A tentative diagram of relationships among various forms of memory processing to indicate the place of hippocampal mechanisms in a larger context. Brackets indicate anatomical structures; parentheses enclose other terms which have been used to label the process.

cue which refers to but is not necessarily described within the information that is retrieved." Such information is stored directly as a function of the invariant relationships between cues and responses, as in the discrimination tasks given to our monkeys. Hirsh went on to describe what is meant by *context*:

This concept has strong implications for theories of how the brain controls behavior. Understanding these implications requires defining and exploring the metaphysiological concept of the performance line. A performance line is defined as a system mediating the series of events or processes initiated by the overtly observable stimulus and resulting in the occurrence of the overtly observable response. It is considered to exist in real time and real space, and ultimately be physiologically observable.

S-R theories, as usually interpreted by physiological psychologists, hold that memory is stored upon the performance line. The stimulus is defined as activated by an environmental event of a neural system sensitive to it. Memory, or more exactly, learning, is held to result from the formation of a functional connection between the neural elements sensitive to the stimulus and those responsible for producing the response. This connection becomes the key part of the performance line for that particular combination of stimulus and response elements and is unique to it.

Retrieval of information stored upon the performance line can be described with associative logic. The memory consists of S-R, and the occurrence of the S, described within the information to be retrieved, results in performance of the described behavior. The concepts of retrieval and description are useful here only for comparative purposes. It suffices to say that the occurrence of the stimulus causes the occurrence of the response. Contextual retrieval has no role in such a system.

When contextual retrieval is present it is no longer necessary to store acquired information upon the performance line. Information can be stored in a sequestered place or state free from interference by information processing being carried out on the performance line. The next paragraphs describe how this happens after first discussing the nature of information storage. (Hirsh, 1974, pp. 422-425)

The relationship of this formulation to hippocampal function is then delineated by both experiment and further theorizing by Hirsh (1970, 1973, 1974; Hirsh and Segal, 1972), Mahut (Chapter 8, this volume), and Mishkin (Mishkin and Petri, 1984; Mishkin *et al.*, 1984). One inference to be made from this quotation is usually ignored, however: If processing of the performance line occurs in real time, contextualization must proceed in fast time, that is, ahead of processing the performance line (see Pribram, 1971). This inference is supported by the data obtained by Richard Thompson (Chapter 7, this volume), which demonstrate that the temporal shape of the nictitating response is constructed within the hippocampus *before* its emergence in the peripheral response.

Additional relationships between this formulation and other data sets and their analyses have been pointed out. One interpretation close to that presented here is developed by Jeffrey Gray (see this volume for review). The variables that define "anxiety" in Gray's theory are almost identical to the ones that define "effort" in the work reported here. There are some differences as well, however, and these were reviewed in 1989 by Pribram

inhibition" theory: "The safest conclusion for the moment, then, is that the septo-hippocampal system among its functions includes participation in the behavioral inhibition system." In fact, anxiety is defined in terms of "behavioral inhibition." Gray does suggest, however, that perhaps it is not "behavior" per se that is "inhibited by the system but motor programs or plans." Talland (1965), by contrast, had suggested that the hippocampus is involved in the active construction of plans. Several pieces of evidence support Talland against Gray. The first is the fact that whether hippocampectomized subjects are more distractible than control subjects depends on whether they are already engaged in carrying out a task. If response inhibition refers to inhibition of distraction, then in at least some situations the subjects with hippocampal resections show an increase in response inhibition. Even more clear-cut is the finding in nonhuman primates (Pribram, this volume; Mahut, 1971; Chapter 8, this volume) and other species that hippocampectomized subjects, while deficient in performing spatial alternation, show absolutely no deficiency whatsoever in go/no-go alternation. They show no increase in errors on no-go trials, which of all task responses demand behavioral inhibition in its clearest form. Finally, there is Richard Thompson's (Chapter 7, this volume) electro-physiological evidence, which shows that a neuronal model of the nictitating response of rabbits is formed prior to the occurrence (not the inhibition) of that response.

The question then arises of how to relate the Talland "construction of plans" to "anxiety" or "effort" (and also to memory) rather than an "inhibition of plans." This problem is dealt with in a step-by-step fashion (the steps are taken from one set of data to the next) by Pribram and Isaacson (1975). Critical to this analysis is a view of the hippocampus as a comparator between "attentional" (input-regulating) and "intentional" (behavior-regulating) systems. Comparison may take effort as in "paying" attention; "thoughtful" retrievals from memory; or "intentional" inhibition of an impulsive response to distractors.

Perhaps, as shown by these examples, the major fault in *Anxiety* lies in its narrowness of focus. As Pribram and McGuinness (1975) detailed, the hippocampal system cannot be understood without reference to two systems represented in the forebrain by several basal ganglia: the amygdala of the limbic formations and the striatum (caudate/putamen). It is these systems which are primarily involved in orienting reactions (distraction) and their habituation—the stop [and go] mechanisms which Gray attributes to the hippocampus. The hippocampus, by contrast, mediates between stop and go.

The key concepts (stop and go) relate to Gray's discussion of the two theories regarding monoamine transmitters involving serotonin and the dorsal ascending noradrenergic bundle. We suggested that the properties of these two systems may best be conceptualized as an interrupt or stop system mediated via the serotonergic pathway and an activating go system mediated by norepinephrine and dopamine. These designators fit the data reviewed by Gray . . . and are in accord with his conclusions. However, the anatomical and physiological data point to two separate systems which converge on the hippocampus rather than some unitary septo-hippocampal behavior-inhibition function. In addition, newer data show that the hippocampus, more than any other structure in the brain, contains receptors for adrenocortical hormones. While the stop and go functions are primarily indole (serotonergic) and catechol (norepinephrine and dopaminergic) aminergic and so are neuroregulatory, the hippocampus is seen as playing a critical role in the pituitary/adrenal "stress" system which modulates, by way of ACTH and related peptides derived from lipotropin (such as the β -enkephalins), the aminergic neuroregulatory mechanisms. Because of this higher order of modulation the functions of the hippocampal system are difficult to disentangle from those it modulates. This, we contend, is the reason why all the data reviewed by Gray do not fit a theory based solely on the septo-hippocampal system: a problem

5. Whither Now?

5.1. Issues

Experimental and theoretical analyses can never be completely dissociated: The data reviewed above were all guided by theory in the sense that the choice of the experimental paradigm tied the results to a body of knowledge in the behavioral sciences. Thus, the use of a fixed-interval task and the issue of whether the behavior of the hippocampectomized monkeys is under the control of the discriminative stimulus or a 50% schedule of reinforcement imply the response-reinforcement theory of operant conditioning. When probability-matching techniques are used and the data are presented in terms of response to previously reinforced versus previously nonreinforced cues, the sets of positive and negative instances of mathematical psychology come to mind. And when response operator characteristic (ROC) curves are used to determine whether d' (detection) or B (bias) is influenced by hippocampectomy, the theory of signal detection is invoked.

The problem for neuropsychology is essentially a twofold problem: (1) the reconciliation of disparate databases (in the case of medial temporal lobe lesions, the difference between what is found in humans and what is found in different species of animals) and (2) the reconciliation of the different theoretical frames within which the data were gathered. These problems, though they create a number of pitfalls and difficulties, also present opportunities for reaching a new level of understanding.

5.2. Disparate Interpretations of Related Databases

The pitfalls and opportunities are illustrated by the recent surge of interest elicited by experimental results obtained with monkeys, which appear to reconcile the animal and human data sets. Mahut and her co-workers (Mahut *et al.*, 1982; Mahut, 1985; Mahut and Moss, Chapter 8, this volume), Gaffan (1974, 1985), and Mishkin (Mishkin *et al.*, 1984; Mishkin and Petri, 1984) have used several modifications of a task that they adapted from human cognitive experimental psychology, a task that purports to test "recognition." For the monkey, this task is a trial-unique delayed nonmatching from sample. As such, it is a cross between the indirect version of delayed response (delayed matching from sample) and delayed alternation (the nonmatching aspect) and thus partakes of all the factors involved in solving those tasks: delay *per se*, alternation (i.e., learning a win-shift strategy), response to novelty, and pro- and retroactive interference. The results obtained with this task are more-or-less intermediate between those obtained with delayed response and those obtained with delayed alternation, as might be expected.

For example, Gaffan (1985), in a section entitled "Impaired Habit Formation after Fornix Transection," concluded that

In the examples discussed so far fornix transection impaired the ability to change an established habit. Some further observations suggest that this impairment can be subsumed under a more general defect, namely impaired learning ability when one habit is to be formed in one set of circumstances and a different habit is to be formed in a different set of circumstances that is similar to the first and therefore liable to be confused with it. (p. 95)

This description fits with what I have here and elsewhere (e.g., Pribram, 1971) been calling the competence for recombinant context-sensitive processing. Further, Gaffan suggested that it is "instructive to consider the hypothesis that habits unmediated by memories are one of the direct products of learning." Here, Gaffan's analysis is reminiscent of Hirsh's. However, Gaffan used the term *memory* in a technically specific manner as it is used by cognitive psychologists and in human neuropsychology (where the term *amnesia* is similarly restricted and does not cover the "agnosias," which are deficits in "re-cognizing" the use to which objects are put). Finally, Gaffan emphasized the relationship between response and reward in the production of habits in a fashion similar to that suggested in one of the Nebraska Symposia on Motivation, where I (1963b) referred to it as "addictionance" (see also Pribram, 1980, "Cognition and Performance: The Relation to Neural Mechanisms of Consequence, Confidence and Competence).

These considerations enabled Gaffan (1985) to distinguish between recall and the motivation for it: "The habit of choosing stimuli that are associated in memory with non-reward in preference to stimuli associated in memory with reward can therefore proceed without any confusion or interference between the recall task and the motive for it" (p. 93). Was he here not proposing a formulation similar to that of Jeffrey Gray and consonant with that pursued in the analysis of the work of this laboratory—but with certain differences as well? Both Gray's and our interpretation would ground recall in incentive motivation, where Gaffan wishes to separate the two.

By contrast, Mishkin *et al.* (1984) clearly separated "memories" and "habits," with the hippocampus and amygdala being involved only in memory processes. In this, he followed Hirsh and the other analyses stemming from our laboratory more closely than those of Gaffan:

The first form of learning to be considered, the one here labeled memory formation, is the one that by nearly universal agreement has been attributed to the hippocampal system exclusively. This attribution is explicit in the quotes from Hirsh. The evidence from our research on the monkey, however, suggests that memory formation has a broader limbic substrate than this, one that includes the amygdaloid system as well. (Mishkin *et al.*, 1982)

But it must be made clear that Mishkin used the term *memory* in its technical sense as it is developed in cognitive psychology. The cognitive

guish new (i.e., the novel) from old (i.e., the familiar as this is displayed in tasks in which *recently* presented stimuli are imbedded in ones not recently presented). As a rule, the presentations are made with words or pictures that are clearly "re-cognized" as such in the terminology of neurology.

Where Mishkin and the analyses presented here disagree is in the characterization of discrimination learning as a process which he calls habit formation. Discrimination learning involves categorization and decision making (see Pribram, 1971, for review). Further, Mishkin (as I did in earlier formulations) lumps together the caudate nucleus and the putamen, which constitute the striatal (basal ganglia) system, when the evidence indicates that the head of the caudate nucleus is concerned with the learning and performance of delayed alternation (the basis of allocating "memory" to the fronto-lymbic systems), whereas the putamen is concerned with discrimination (reviewed by Mahut and Moss, Chapter 8, this volume; and by Pribram, 1977b).

5.3. *Theoretical Frames and the Problem of Conscious Cognizance*

It is therefore worth asking whether there is anything fundamental being currently added to our understanding of hippocampal function or to relating the animal database to that obtained on humans? I believe that there is but that the issue that is being addressed must still be made transparent. The data reviewed and the analyses performed here that relate medial temporal lobe lesions to changes in "competence," an enhanced processing span, go a long way toward explaining the fact that Brenda Milner's H. M. has failed to recognize her for the past 30 years. Our job now is to relate competence and processing span, as well as their basis in learning and performing trial-unique tasks, to *conscious cognizance*.

The fact is that hippocampectomized monkeys "re-cognize" a discriminative stimulus in an instrumental situation two years after having been last exposed to the stimulus, better than do their controls (96% vs. 87%) and that H. M. "re-cognizes" instrumentally a task that he has learned: he simply has no introspective cognizance of the fact. Finally, H. M., when not distracted by long lists in which pro- and retroactive interference operate, has little difficulty in performing the type of short-term memory tasks that characterize the trial-unique situations used in the monkey experiments. There may be, and I believe there probably is, a relationship between this failure in introspective cognizance and failure on trial-unique tasks, but this connection has not yet been adequately developed. On close scrutiny, the current surge of interest in the effects of medial temporal lobe resection stems as much from verbal magic centered on the term *recognition* as it does from the intuition that we may be on the threshold of explaining reflective (introspective) consciousness.

experimental psychology (Pribram, 1977a,b, 1981; Tulving, 1985). Just what is the relationship between the observing response of the operant conditioning paradigm and a d' obtained in a decisional paradigm? What is the relationship between research on short-term memory and research on attention? When we use a particular technique developed by experimental psychologists and obtain a change in behavior as a function of a neurological manipulation, how are we to interpret the data? With respect to hippocampal function, just how do we go about deciding which theoretical frame—and thus, which paradigm—is the most cogent? Only when we answer these questions will the layers of puzzles that wrap the enigma of the hippocampus be further removed. And perhaps in the process, the relationships between theoretical frames in the behavioral sciences will also become clarified.

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Index

- ACTH: *see* Adrenocorticotropin hormone
Acetylcholine, 44-45, 62, 137-140, 152
 receptors, 46, 139, 228
Acetylcholinesterase, 44, 66
3-acetylpyridine, 99, 120
Acquisition: *see* Learning
Adipsia, 112
Adrenal medulla, 136
Adrenal steroids: *see* Glucocorticoids,
 Corticosterone, Mineralocorticoids
Adrenalectomy, 140, 154
Adrenocorticotropin hormone (ACTH), 141,
 360
Afterhyperpolarization, 222
Alcohol, 160, 162
Alpha-adrenergic receptors, 89
Alveus, 95, 97
Alzheimer's disease, 65-66, 121, 282
Amnesia, 31-32, 35, 170, 181, 193, 241-243,
 265, 273, 281-282, 289, 299, 310, 324,
 325, 333
Amphetamine, 131
Amygdala, 96, 318, 321
 lesions of, 241, 288, 330-346, 350-364
Amygdalohippocampal lesions, 246, 250, 273,
 275
Anterior commissure, 59
Anxiety, 160, 164, 180, 359-360
 and anti-anxiety drug action, 160-164, 180,
 186, 188-190, 193, 195
Aplasia, 112
Apomorphine, 133
Arousal, 218-219, 325
Association cortex, 318
Atropine, 44, 46
 and theta rhythm, 167-169, 177
Attention, 164, 218-219, 337, 339-340, 342,
 349, 356, 360, 364
Barbiturates, 160, 162, 189
Basal ganglia, 130-133, 151-153, 356, 360,
 363
 see also Caudate nucleus
Behavioral inhibition system, 160-164, 171-
 172, 187
Behavioral priming: *see* Learning
Benzodiazepines, 160, 193-194
 see also specific drugs
 receptors, 162, 189
Blood-brain barrier, 159
Bretium, 144-151, 152-153
Caudate nucleus, 2, 5-7, 9, 28, 31-32, 95,
 130-133, 274, 332, 360, 363
 see also Basal ganglia
Cerebellum, 229-232
Chlordiazepoxide hydrochloride, 164, 190-
 193
 β -Chloroamphetamine, 84
Choline acetyltransferase, 44, 66
Choline chloride, 135-140, 151-152
Cingulate cortex, 2, 5-9, 11-20, 35, 95-96,
 166, 175-176, 231-232, 317-318, 321,
 332
 lesions of, 11-17, 24-27, 332, 348-349
Circadian cycle, 129
Classical conditioning, 65, 160, 203-235,
 294-295, 302, 322
Clausstrum, 98
Caudate nucleus, 225, 234
Colchicine, 99, 104, 117
Conditioned avoidance behavior, 97, 120,
 128, 134, 170, 322-323, 332-333
 see also Learning
 and discrimination, 5-6, 10-11, 14-16, 20
 neural correlates of, 1-35