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THE AMNESTIC SYNDROMES: Disturbances in Coding?

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The limits of my language mean
the limits of my world.

Wittgenstein, *Tractatus Logico-Philosophicus*, 1922

I. Introduction

I want to take this opportunity to dispel the myth that experimentally produced local brain lesions (especially ablations) do not affect memory functions, that is, learning and remembering. This conception, like so many in neuromythology, derives its strength from the fact that it is a half-truth. In this instance the idea rests largely on Lashley's (1929) contribution, *Brain Mechanisms and Intelligence*, and derives support from his later publication (1950), *In Search of the Engram*. Lashley presented evidence and made interpretations. I shall show here that his data have been superseded – thus the fanciful aspect of the current myth – but that his interpretations were extremely shrewd – thus the myth's persistence. To make the counterargument I will describe data from experiments made over the past 20 years. In my laboratories alone some 952 behaviorally tested rhesus monkeys have been subjected to selective brain operations during this period. These studies provide evidence that makes me think that

the impairments in memory functions produced by local experimental lesions are best subsumed as deficiencies in input processing, and I will describe the evidence that demonstrates that memory traces become distributed widely within a sensory projection system. I will then argue that the mechanism of remembering critically involves input coding, both during storage and retrieval.

II. Classification of Lesion-Produced Memory Disturbances

As noted earlier, the experimental analysis of subhuman primate psychosurgical preparations has, contrary to popular opinion, uncovered a host of memory disturbances. The initial technique by which these brain-behavior relationships were established is called the method of the "intersect of sums" (Pribram, 1954), an extension of what Teuber named the method of "double dissociation" of signs of brain trauma. The intersect of sums method depends on classifying the behavioral deficit produced by cortical ablations into *yes* and *no* instances on the basis of some arbitrarily chosen criterion; then plotting on a brain map the total extent of tissue associated with each of the categories *ablated:deficit* and *not ablated:no deficit*; and finally finding the intersect of those two areas (essentially subtracting the *noes* from the *yeses-plus-noes*). This procedure is repeated for each type of behavior under quantitative consideration. The resulting map of localization of disturbances is then validated by making lesions restricted to the site determined by the intersect method and showing that the maximal behavioral deficit is obtained by the restricted lesion. (See Table I and Fig. 1.)

Once the neurobehavioral correlation has been established by the intersect of sums technique, two additional experimental steps are undertaken. First, holding the lesion constant, a series of variations is made of the task on which performance was found defective. These experimental manipulations determine the limits over which the brain-behavior disturbance correlations hold and thus allow reasonable constructions of models of the psychological processes impaired by the various surgical procedures.

Second, neuroanatomical and electrophysiological techniques are engaged to work out the relationships between the brain areas under examination and the rest of the nervous system. These experimental procedures allow the construction of reasonable models of the functions of the areas and of the mechanisms of impairment.

Table I
Simultaneous Visual Choice Reaction[a]

Operates without deficit			Operates with deficit			Nonoperate controls		
	Pre	Post		Pre	Post		Pre	Post
OP 1	200	0	PTO 1	120	272	C 1	790	80
OP 2	220	0	PTO 2	325	F	C 2	230	20
OP 3	380	0	PTO 3	180	F	C 3	750	20
LT 1	390	190	PTO 4	120	450	C 4	440	0
LT 2	300	150	T 1	940	F			
H 1	210	220	T 2	330	F			
HA	350	240	VTH 1	320	F			
FT 1	580	50	VTH 2	370	F			
FT 3	50	0	VTH 3	280	F			
FT 4	205	0	VTH 4	440	F			
FT 5	300	200	VT 1	240	F			
FT 6	250	100	VT 2	200	F			
DL 1	160	140	VT 3	200	890			
DL 2	540	150	VT 4	410	F			
DL 3	300	240	VT 5	210	F			
DL 4	120	100						
MV 1	110	0						
MV 2	150	10						
MV 3	290	130						
MV 4	230	10						
MV 5	280	120						
CIN 1	120	80						
CIN 2	400	60						
CIN 3	115	74						
CIN 4	240	140						

[a]Pre- and postoperative scores on a simultaneous visual choice reaction of the animals whose brains are diagrammed in Fig. 2, indicating the number of trials taken to reach a criterion of 90% correct on 100 consecutive trials. Deficit is defined as a larger number of trials taken in the "retention" test than in original learning. (The misplacement of the score H 1 does not change the overall results as given in the text.)

Two major classes of memory disturbance have been delineated by these operations: *specific* and *contextual* amnesias.

III. The Specific Amnesias

Between the sensory projection areas of the primate cerebral mantle lies a vast expanse of parieto-temporo-preoccipital cortex. Clinical observation has assigned disturbance of many gnostic and language functions to lesions of this expanse. Experimental psychosurgical

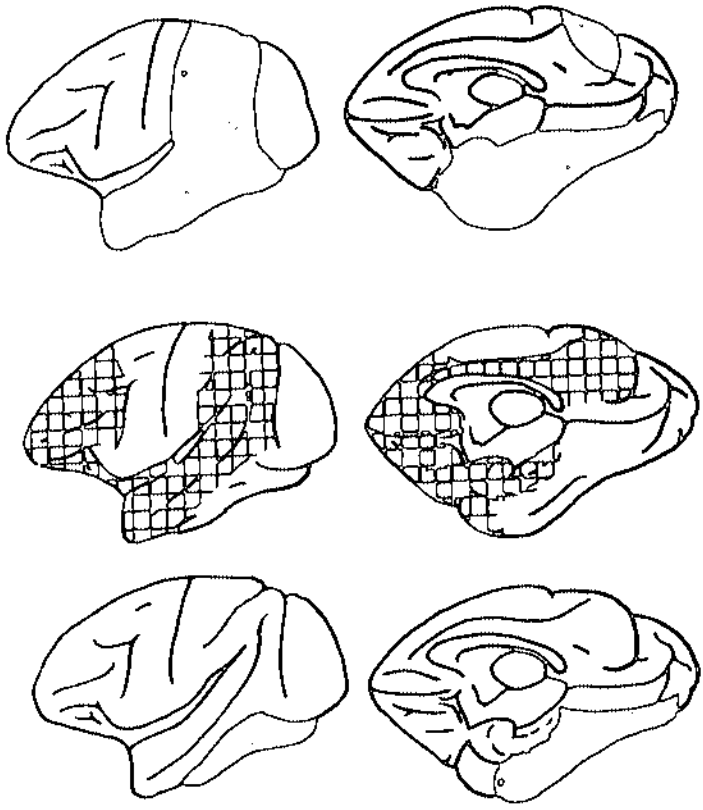

Fig. 1. The upper diagram represents the sum of the areas of resection of all of the animals grouped as showing deficit. The middle diagram represents the sum of the areas of resection of all of the animals grouped as showing no deficit. The lower diagram represents the intersect of the area shown in black in the upper diagram and that *not* checkerboarded in the middle diagram. This intersect represents the area invariably implicated in visual choice behavior in these experiments.

analysis in subhuman primates of course, is limited to nonverbal behavior; within this limitation, however, a set of sensory-specific agnosias (discrimination disabilities and losses in the capacity to identify cues) have been produced. Distinct regions of primate cortex have been shown to be involved in each of the modality-specific mnemonic functions: anterior temporal in gustation (Bagshaw & Pribram, 1953), inferior temporal in vision (Mishkin & Pribram, 1954), midtemporal in audition (Weiskrantz & Mishkin, 1958; Dewson, Pribram & Lynch, in press), and occipitoparietal in somesthesis (Pribram & Barry, 1956). In each instance discriminations learned prior to surgical interference are lost to the subject postoperatively and great difficulty (us-

ing a "savings" criterion) in reaquisition is experienced, if task solution is possible at all.

The behavioral analysis of these "specific" amnesias is still underway, but an outline of the psychological process involved can be discussed. Perhaps the easiest way to communicate this outline is to detail the observations, thinking, and experiments that led to our present view of the function of the inferior temporal cortex in vision.

IV. Search and Sampling

All sorts of differences in the physical dimensions of the stimulus, for example, size (Fig. 2), are distinguished less after the lesion (Mishkin & Hall, 1955), but there is more to the disability than this—as illustrated in the following story:

One day while testing monkeys with such lesions at the Yerkes Laboratories at Orange Park, Florida, I sat down to rest from the chore of carrying a monkey the considerable distance between home cage and laboratory. The monkeys, including this one, were failing misera-

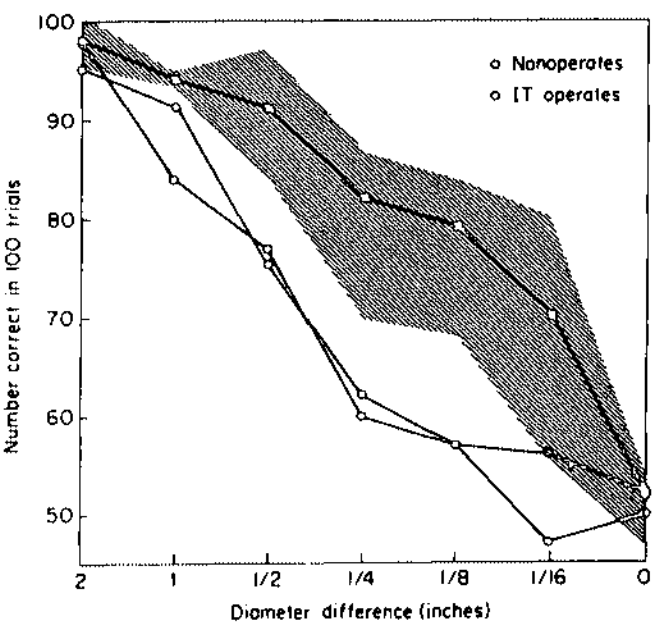

Fig. 2. Scores for two operates and four controls on the first run of size discrimination. Shaded area indicates the range of performance of the four nonoperate controls. IT operates = monkeys with resections of inferior temporal cortex.

bly at the visual discrimination tasks being administered. It was a hot, muggy, typical Florida summer afternoon and the air was swarming with gnats. My monkey reached out and caught a gnat. Without thinking I also reached for a gnat—and missed. The monkey reached out again, caught a gnat, and put it in his mouth. I reached out—missed! Finally the paradox of the situation forced itself on me. I took the beast back to the testing room: He was as deficient in making visual choices as ever. But when no choice was involved, the monkey's visually guided behavior appeared to be intact. This gave rise to the following experiment (Fig. 3), which Ettlinger (1957) carried out. On the basis of this particular observation we made the hypothesis that choice was the crucial variable responsible for the deficient discrimination following inferotemporal lesions. As long as a monkey does not have to make a choice, his visual performance should remain intact.

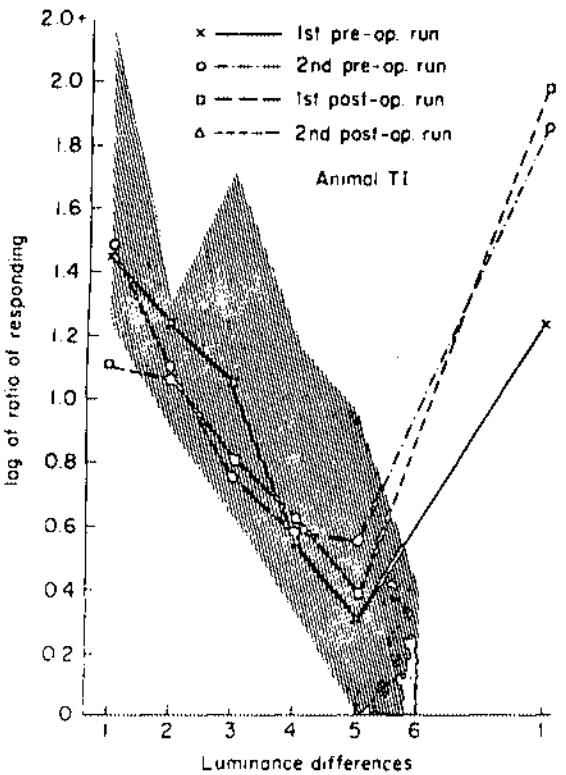

Fig. 3. Single manipulandum performance curves of a single animal in a varying brightness situation. Shaded area indicates variability among groups of four animals.

To test this hypothesis, monkeys were trained in a Gantzfeld made of a translucent light fixture large enough so the animal could be physically inserted into it. The animal could press a lever throughout the procedure but was rewarded only during the period when illumination was markedly increased for several seconds at a time. Soon response frequency became maximal during this "bright" period. Under such conditions no differences in performance were obtained between inferotemporally lesioned and control animals. The result tended to support the view that if an inferotemporally lesioned monkey did not have to make a choice he would show no deficit in behavior, since in another experiment (Mishkin & Pribram, 1954) the monkeys failed to respond differentially to differences in brightness.

In another instance (Pribram & Mishkin, 1955) we trained the monkeys on a very simple object discrimination test: an ashtray vs a tobacco tin (Fig. 4). These animals had been trained for 2 or 3 years before they were operated on and therefore were sophisticated problem-solvers; this, plus ease of task, accounts for the minimal deficit in the simultaneous choice task. (There are two types of successive discrimination: In one the animal has either to go or not to go, and in the other he has to go left or right.) When given the same cues successively the monkeys showed a deficit when compared with their controls, despite this demonstrated ability to differentiate the cues in the simultaneous situation.

This result further supported the idea that the problem for the operated monkeys was not so much in "seeing" but in usefully manipulating what they saw. Not only the stimulus conditions per se but the whole range of response determinants appear involved in specifying the deficit. To test this idea in a quantitative fashion we next asked whether the deficit would vary as a function of the *number* of alternatives in the situation (Pribram, 1959). The hope was that an informational measure of the deficit could be obtained. Actually something very different appeared when the number of errors was plotted against the number of alternatives (see Fig. 5).

If one plots repetitive errors made before the subject finds a peanut – that is, the number of times a monkey searches the same cue – vs the number of alternatives in the situation, one finds there is a hump in the curve, a stage where control subjects make many repetitive errors. The monkeys do learn the appropriate strategy, however, and go on to complete the task with facility. What intrigued me was that during this stage the monkeys with inferotemporal lesions were doing better than the controls! This seemed a paradox. As the test continued, however, after the controls no longer made so many errors, the le-

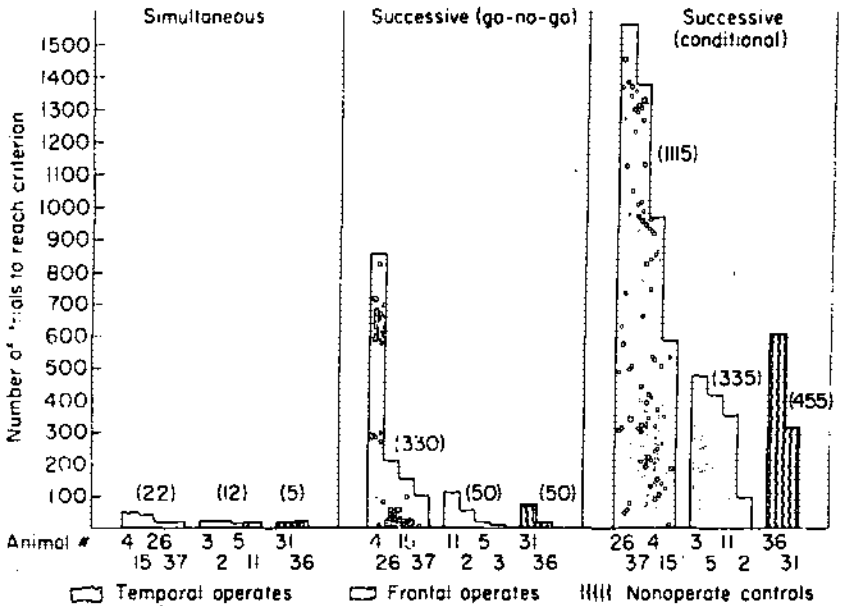

Fig. 4. Comparison of learning scores on three types of object discrimination by three groups of monkeys. Note that though the cues remain the same, changing the response which was demanded increased the deficit of the inferotemporal groups.

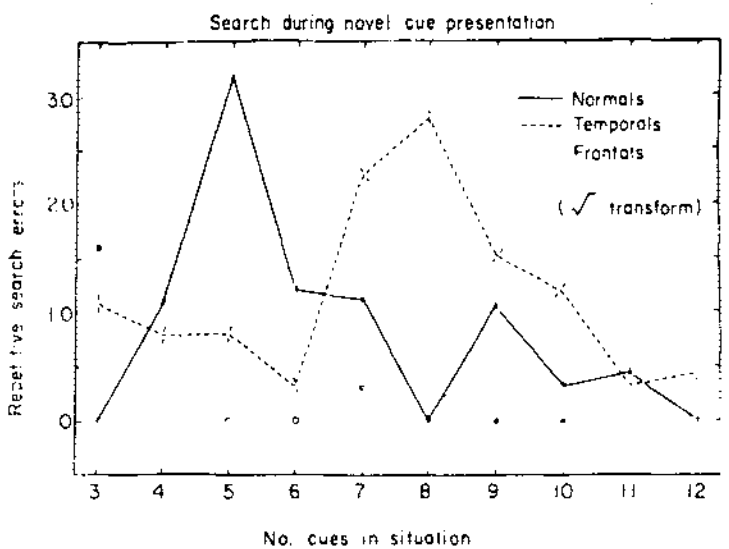

Fig. 5. Graph of the average number of repetitive errors made in the multiple object experiment during those search trials in each situation when the additional, that is, the novel, cue is first added.

sioned subjects began to accumulate an error hump even greater than that shown earlier by the controls.

When a stimulus sampling model was applied to the analysis of the data, a difference in sampling was found (Fig. 6). The monkeys with inferotemporal lesions showed a lowered sampling ratio; they sampled fewer cues during the first half of the experiment. Their defect can be characterized as a restriction in the visual field; however, the limitation is not in the visual-spatial field but in the information-processing field, that is, in the number of alternatives they can sample or handle at any one time.

In short, the modality-specific defect that results from a posterior "association" system lesion appears to produce an information-processing defect best described as a restriction on the number of alternatives searched and sampled.

V. The Contextual Amnesias

The second major division of the cerebral mantle to which mnestic functions have been assigned by clinical observation lies on the medial and basal surface of the brain and extends forward to include the poles of the frontal and temporal lobes. This frontolimbic portion of the hemisphere is cytoarchitecturally diverse. The expectation that different parts might be shown to subserve different functions therefore is even greater than that entertained for the apparently uniform posterior cortex. In the case of the posterior cortex the diversity of lesion effects nonetheless allowed classification: Differential discriminations were always involved, and the defects turned out to be sensory-mode specific. In the same manner, lesions of the frontolimbic region, irrespective of location (dorsolateral frontal, cingulate-medial frontal, orbitofrontal-caudate, temporal polar-amygdala, and hippocampal) have been shown to produce disruption of "delayed alternation" behavior. The alternation task demands that the subject alternate his responses between two cues (for example, between two places or between two objects) on successive trials. On any trial the correct response is dependent on the outcome of the previous response. This suggests that the critical variable which characterizes the task is its temporal organization. In turn, this leads to the supposition that the disruption of alternation behavior produced by frontolimbic lesions results from an impairment of the process by which the brain achieves its temporal organization. This supposition is in part con-

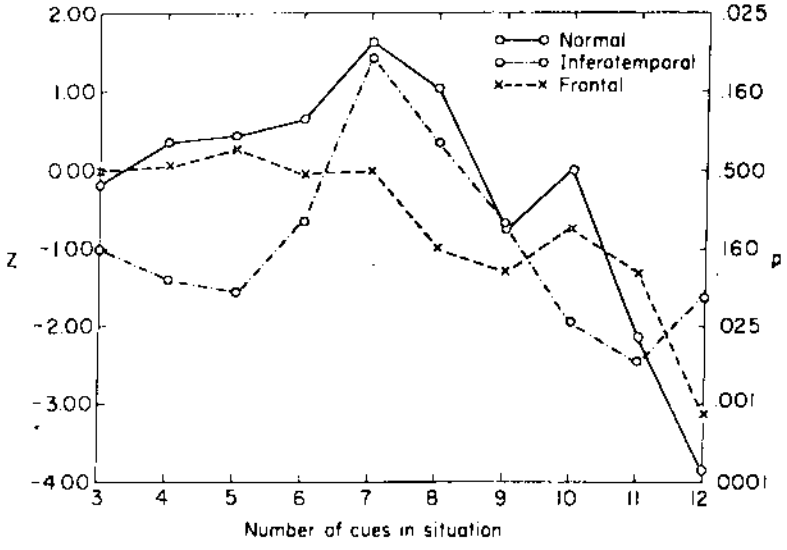

Fig. 6. Graph of the average proportion of objects (cues) that are sampled (except novel cue) by each of the groups in each of the situations. To sample, a monkey had to move an object until the content or lack of content of the food well was clearly visible to the experimenter. As was predicted, during the first half of the experiment the curve representing the sampling ratio of the posteriorly lesioned group differs significantly from the others at the 0.024 level (according to the nonparametric Mann-Whitney U Test).

firmed by further analysis, but severe restrictions on what is meant by "temporal organization" arise. For instance, skills are not affected by frontolimbic lesions, nor are discriminations of melodies. Retrieval of long-held memories also is little affected. Rather, shorter term mnestic processes are singularly involved. In animal experiments these are demonstrated especially clearly when tasks demand matching from memory a cue (as in the delayed response problem) or outcome (as in the alternation task) that in the past has shown some complexity in the regularity of its recurrence. Rather than identify an item, the organism must fit the present event into a "context" of prior occurrences, only some of which relate directly to the situation at hand.

As noted, different parts of the frontolimbic complex would, on the basis of their different structure, be expected to function somewhat differently within the category of short-term mnestic processes. Indeed, different forms of contextual amnesia are produced by different lesions. For instance, resection of the primate hippocampal formation (Douglas & Pribram, 1966) results in relative insensitivity to the non-

reinforced aspects of the environment (the $S\Delta$ of operant conditioning; the negative instances of mathematical psychology). In their first experience with a discrimination learning situation these subjects show a peculiar retardation provided there are many nonrewarded alternatives in that situation: In a computer-controlled automated testing apparatus (DADTA) we face the subject with 16 panels; on only two of these are cues displayed, and pressing only one of them is rewarded. The site of display is randomized from trial to trial. Hippocampectomized monkeys press the unlit panels for thousands of trials after their unoperated controls have ceased responding to these "irrelevant" items. It is as if in the normal subject "ground" is established by progressively stronger "inattention" to those aspects of the situation that do not become "figures." This "inattention" is an active, evaluating process. For example, in a discrimination reversal task, when the demand is to notice the previously nonreinforced cue, unsophisticated subjects in our situation will press on almost any part of their cage and the testing apparatus before making an often-by-chance response to the nonrewarded cue.

I interpret these and many similar results to indicate that the hippocampal formation is involved in an evaluative mechanism by which "ground" or context is established.

VI. Expectancy, Novelty, and Registration

However, context formation, by itself, is of little use to an organism. Events must be fitted to context. A series of experiments on the orienting reaction to novelty and its habituation have pointed to the amygdala as an important locus in the "context-fitting" mechanism. Our experiments took off from those of Sokolov (1960).

Sokolov's experimental demonstration went as follows: Human subjects were exposed to a tone beep of a certain intensity and frequency, repeated at irregular intervals. Galvanic skin response (GSR), heart rate, finger and forehead plethysmograms, and electroencephalograms were recorded. Initially these records showed the perturbations that are classified together as the orienting response. After several repetitions of the tone, these perturbations diminish and finally vanish. This is habituation, a process that had been thought to reflect a *lowered* sensitivity of the central nervous system to inputs. But Sokolov now *decreased* the intensity of the tone beep, leaving the other parameters unchanged. Immediately the subjects again showed full-

blown orienting responses. Sokolov reasoned that the central nervous system cannot be *less* sensitive – it is only less sensitive to *sameness*; to *differences* the central nervous system has become *more* sensitive. He tested this idea by rehabituating his subjects and then shortening the tone beep without changing any other parameter. As predicted, his subjects now oriented to the unexpected silence.

The orienting reaction and habituation are thus sensitive measures of an organism's expectancy process – the process by which context is organized. We therefore initiated a series of experiments to analyze in detail the neural mechanisms involved in orientation and habituation. This proved not as easy as it at first seemed. The dependent variables – behavior, GSR, plethysmogram, and electroencephalogram – are not as dependable as is desirable. As others have found, dissociation between them is readily observed when one makes one or another experimental variation. In our hands, forehead plethysmography turned out to be especially tricky. We finally settled on behavior, the GSR, heart and respiratory responses, and the electrical brain manifestations as most reliable.

The results of the first of these experiments (Schwartzbaum, Wilson, & Morrissette, 1961) indicate that, under certain conditions, removal of the amygdaloid complex can selectively affect the persistence of locomotor activity in monkeys by minimizing or retarding decrements that normally occur. The lesion thus produces a disturbance in the habituation of motor activity (Fig. 7).

The results of the experiments on the habituation of the GSR component of the orienting reaction (Bagshaw, Kimble, & Pribram, 1965) also indicate clearly that amygdalectomy has an effect (Fig. 8). The lesion interferes with the GSR in a situation in which the GSR is ordinarily obtained as part of the orienting reaction, although the GSR per se is not abolished. Concomitantly, deceleration of hearbeat, change in respiratory rhythm, and some aspects of the EEG indices of orienting also are found to be absent (Bagshaw & Benzies, 1968). From Schwartzbaum (1960a,b) and Bateson (in press) we know that the habituation of behavior is severely altered by these lesions. Putting the results together, one could conclude that the GSR component of orienting and heart and respiratory rate changes are in some way crucial to subsequent behavioral habituation. We therefore identified the process indicated by the autonomic components of the orienting reaction as "registering" the novel event.

However, the registration mechanism is not limited to novelty. Bagshaw (Bagshaw & Coppock, 1968) extended her work to a classical conditioning situation. Using the GSR as a measure of conditioning,

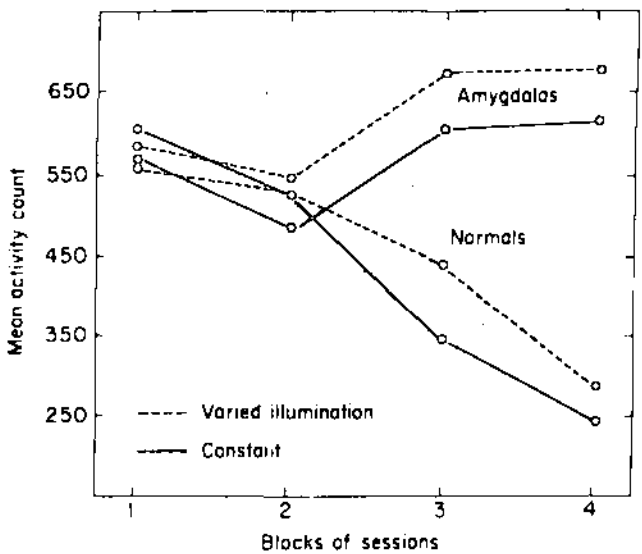

Fig. 7. Postoperative activity scores of normal and amygdalectomized monkeys for successive blocks of three sessions under conditions of constant illumination and more intense, varied illumination.

she found that normal monkeys not only condition but give more and more, as well as earlier and earlier, anticipatory GSR's in the situation. Amygdalectomized subjects fail to make such anticipatory responses. This observation suggests that registration entails some active process akin to rehearsal – some central mechanism aided by viscero-autonomic processes that maintains and distributes excitation over time.

Behavioral experiments support this suggestion. Amygdalectomized monkeys placed in the situations described above for testing the effects of resection of the hippocampal formation fail to take proper account of reinforced events. This deficiency is dramatically displayed whenever punishment, that is, negative reinforcement, is used. For instance, an early observation showed that baboons with such lesions will repeatedly – and this means day after day and week after week – put lighted matches in their mouths despite showing obvious signs of being burnt by them (Fulton, Pribram, Stevenson, & Wall, 1949). These observations were quantified in tasks measuring escape from and avoidance of shock (Pribram & Weiskrantz, 1957). The results of these two experiments have been confirmed in other laboratories and with other species so often that the idea has taken hold that loss of fear based on altered pain sensitivity is the primary difficulty that follows amygdalectomy. Bagshaw and Pribram (1968)

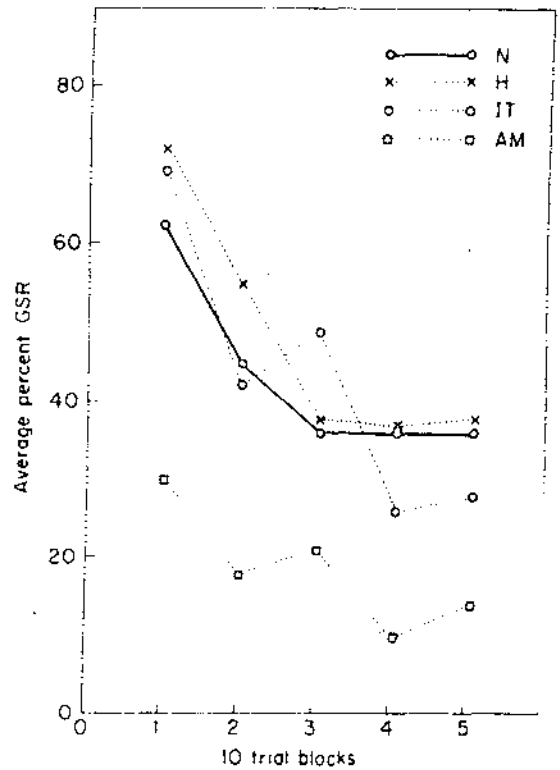

Fig. 8. Curves of percent GSR response to the first 50 presentations of the original stimulus for the normal (N) and three experimental groups (H, IT, AM), i.e., hippocampal, inferior temporal, and amygdala resected monkeys.

put this hypothesis to test and showed that the GSR threshold to shock, far from being elevated is, if anything, reduced by the ablation. This experimental result makes it possible to ascribe the observations that amygdalectomy produces a "loss of fear" directly to a mnestic disturbance—a disturbance of "registering" the noxious event and placing it in context—so that its recurrence will not on each occasion again be experienced as "novel."

VII. The Parsing Problem

The structures in the polar and medial part of the temporal lobe of primates are not the only ones concerned in short-term mnestic processes. Classically, disturbance of "immediate memory" has been ascribed to lesions of the frontal pole. Anterior and medial frontal resec-

tions were the first to be shown to produce impairment on delayed response and delayed alternation problems. In other tests of context-formation and fitting, frontal lesions also take their toll. Here also impairment of conditioned avoidance behavior and of classical conditioning and of the orienting GSR is found. Furthermore, error sensitivity was tested in an operant conditioning situation (Fig. 9). After several years of training on mixed and multiple schedules, 4 hrs of extinction were run, that is, the reinforcement (peanuts) was no longer delivered, although everything else in the situation remained the same. Note that the frontally lesioned animals failed to extinguish in the 4-hr period, whereas the control monkeys did (Pribram, 1961).

This failure in extinction accounts in part for poor performance in the alternation already described (Fig. 10): The frontally lesioned animals again make many more repetitive errors. Even though they do not find a peanut, they go right back and keep looking (Pribram, 1959).

This result was confirmed and amplified in a study by Wilson (1962). He analyzed the occasions for error – Did errors follow alterna-

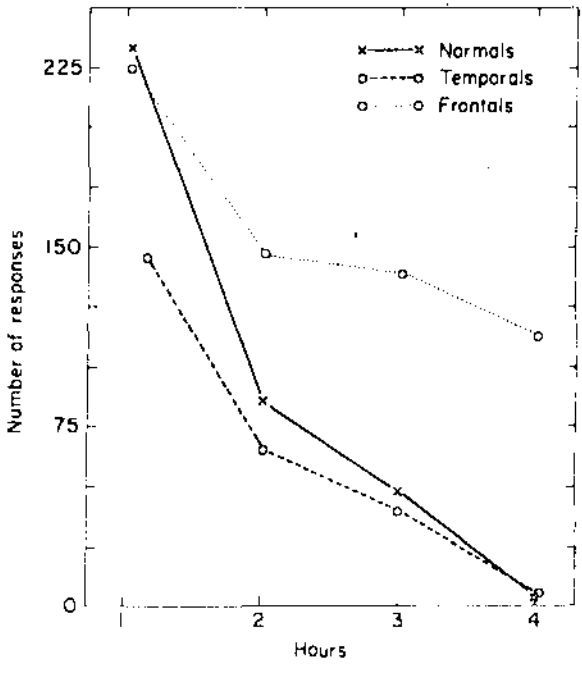

Fig. 9. Graph of performance of three groups of monkeys under conditions of extinction in a mixed schedule operant conditioning situation. Note the slower extinction of the frontally lesioned monkeys.

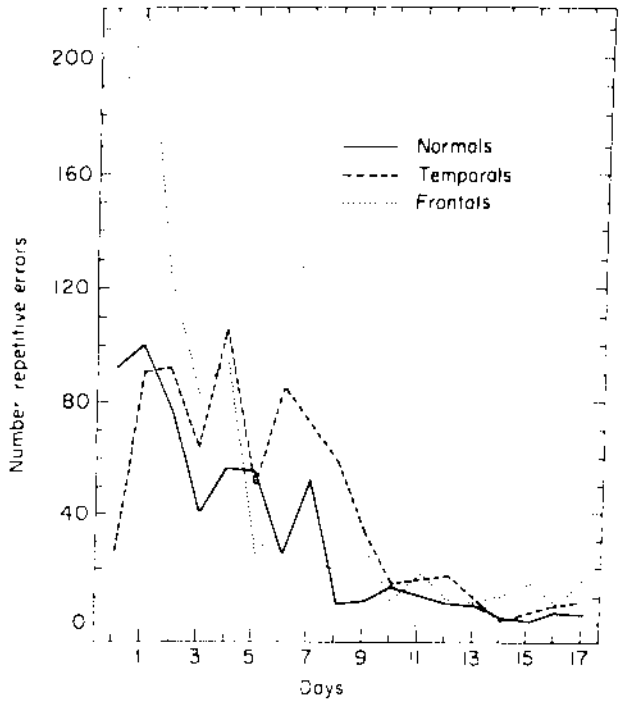

Fig. 10. Graph showing the differences in the number of repetitive errors made by groups of monkeys in a go, no-go type of delayed reaction experiment. Especially during the initial trials, frontally operated animals repeatedly return to the food well after exposure to the "nonrewarded" predelay cue. Note, however, that this variation of the delay problem is mastered easily by the frontally operated group.

tion or nonreinforcement? To determine which, he devised a situation in which both lids over the food well opened simultaneously, but the monkey could obtain the peanut only if he had opened the baited well. Thus the monkey was given "complete" information on every trial and the usual correction technique could be circumvented. With this apparatus the procedure was followed with four variations: correction-contingent, correction-noncontingent, noncorrection-contingent, and noncorrection-noncontingent. The contingency referred to is whether the position of the peanut depended on the prior correct or incorrect response of the monkey or whether its position was alternated independently of the monkey's behavior. Wilson then analyzed the relationship between an error and the trial preceding that error. Notice (Table II) that for the normal monkey the condition of reinforcement and nonreinforcement of the previous trial makes a differ-

Table II
Percentage of Alternation as a Function of Response and Outcome of Preceding Trial[a]

	Preceding trial[b]			
S	A-R	A-NR	NA-R	NA-NR
Normal				
394	53	56	40	45
396	54	53	36	49
398	49	69	27	48
384	61	83	33	72
Total	55	68	34	52
Frontal				
381	49	51	41	43
437	42	46	27	26
361	49	48	38	35
433	43	39	31	32
Total	46	46	33	33

[a]Comparison of the performance of frontally ablated and normal monkeys on alternations made subsequent to reinforced (R) and nonreinforced (NR) and an alternated (A) and nonalternated (NA) response.

[b]A, alternated; NA, did not alternate; R, was rewarded; and NR, was not rewarded.

ence, whereas for the frontally lesioned monkey this is not the case. Alternation affects both normal and frontal subjects about equally. In this situation, frontal subjects are simply uninfluenced by rewarding or nonrewarding consequences of their behavior.

Now let me return to the multiple choice experiment discussed earlier (Pribram, 1959). Here also this inefficacy of outcomes to influence behavior is demonstrated; it is illustrated (Fig. 11) by an increased number of trials to criterion after the monkeys have first found the peanut. The procedure calls for the strategy of return to the same object for five consecutive times, that is, to criterion. The frontally lesioned animals are markedly deficient in doing this. Again, we see that the conditions of reinforcement are relatively ineffective in shaping behavior once the frontal eugranular cortex has been removed, so that the monkeys' behavior is relatively random when compared to that of normal subjects (Pribram, Ahumada, Hartog, & Roos, 1964). Behavior of the frontally lesioned monkeys thus appears to be minimally controlled by its (repeatedly experienced and therefore expected) consequences.

In some respects, therefore, the frontal resection produces mnestic disturbances characteristic of both hippocampectomy and amygdalec-

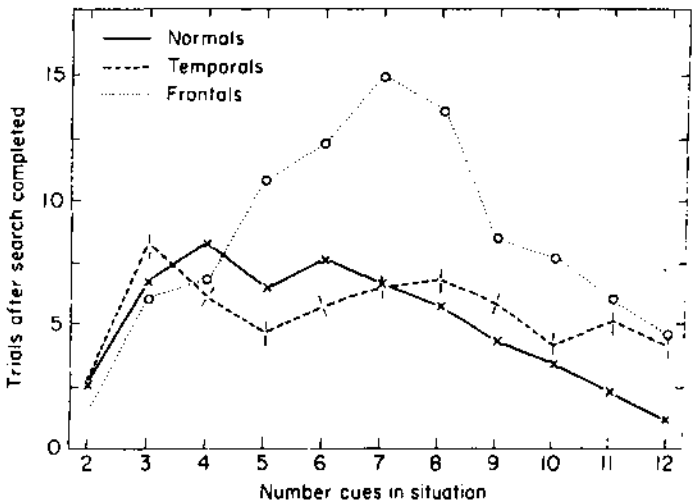

Fig. 11. Graph of the average number of trials to criterion taken in the multiple object experiment by each group in each of the situations after search was completed, that is, after the first correct response. Note the difference between the curves for the controls and for the frontally operated group, a difference that is significant at the .05 level by an analysis of variance ($F = 8.19$ for 2 and 6 df) according to McNemar's procedure performed on normalized (by square root transformation) raw scores.

tomy, though not so severe. Where temporal lobe ablations impair context formation and fitting, frontal lesions work their havoc on yet another contextual dimension. This is best demonstrated by manipulating the alternation task in a special way: Instead of interposing equal intervals between trials (R5" L5" R5" L5" R5" L5" . . .) as in the classic task, couplets of RL were formed by extending the intertrial interval to 15" before each R trial (R5" L15" R5" L15" R5" L15" . . .). Immediately the performance of the frontally lesioned monkeys improved and was indistinguishable from that of their controls (Pribram & Tubbs, 1967). I interpret this result to mean that for the subject with a bilateral frontal ablation the alternation task becomes something like what this page would seem were there no spaces between words. The spaces, and the holes in doughnuts, provide some of the structure, the parcellation, parsing of events (doughnuts, alternations, and words) by which they become codable and decipherable.

VIII. How the Brain Controls Its Input

Recently much of our effort has been channeled into an attempt to clarify the neural mechanism disturbed by brain ablations. To this end

a series of experiments was undertaken to find out how the brain cortex might affect the processing of visual information. It is appropriate to begin with some facts—or rather lack of facts—about the neuroanatomical relationships of the inferotemporal cortex. There is a dearth of neurological evidence linking this cortex to the known visual system, the geniculostriate system. There are no definitive anatomical inputs specific to the inferotemporal cortex from the visual cortex or the geniculate nucleus. Of course, connections can be traced via fibers that synapse twice in the preoccipital region, but connections also exist between the visual cortex, and the parietal lobe, the excision of which results in no change in visual behavior (as shown earlier). In addition, massive circumsection of the striate cortex does not impair visual discrimination (Chow, 1954; Pribram, Blehert, & Spinelli, 1966). Further evidence that these "corticocortical" connections are not the important ones can be seen from the following experiment. I performed (Table III) a crosshatch of the inferotemporal cortex much as Sperry (1959) had done earlier for the striate cortex and found no deficit either in visual learning or in performance. On the other hand, undercutting the inferotemporal cortex made a vast difference: It precluded both learning and performance of visual tasks. This suggests that the relationships of this cortex essential to visual behavior must come from somewhere below.

However, another proposal can be tested, viz., that the essential relations of the posterior association cortex are centrifugal, or efferent

Table III
Comparison of the Effects of Undercutting and Crosshatching Infero-Temporal Cortex of Monkeys on Their Performance in Several Discriminations

	Animal	3 vs 8	R vs G	3 vs 8
Crosshatch	158	380	82	0
	159	180	100	0
	161	580	50	0
	166	130	0	0
Undercut	163	[1014]	100	300
	164	[1030]	200	[500]
	167	704	50	0
	168	[1030]	150	[500]
Normal	160	280	100	0
	162	180	100	0
	165	280	100	0
	170	350	100	0

(Pribram, 1958). There is anatomical evidence to suggest and support such a notion. Some time ago two brains with inferotemporal resections were studied by Dr. Walle Nauta in his laboratory. These showed an efferent tract leading to the region of the superior colliculus, ending either within its substance or in the surrounding reticular formation (Nauta & Whitlock, 1954). No such fibers could be traced to the lateral geniculate nucleus. In support of this finding is a report by Kuypers (1962), who has also traced temporo-collicular fibers in monkey. The idea of an efferent mechanism "gating," or otherwise "partitioning," the input to the geniculostriate system has some backing as an explanation for the process of selective attention. How would an efferent mechanism of this sort work? To find out we performed the following experiment.

Instead of making ablations or implanting an epileptogenic lesion, we now chronically and continuously stimulate the brain. Dr. D. N. Spinelli in my laboratory designed the stimulator (Fig. 12) and the recording equipment (Spinelli & Pribram, 1966). The stimulator is sufficiently small so that it can be implanted under the scalp. It puts out a square-wave bidirectional pulse, 1 msec in duration and about 3 V in amplitude. The frequency of stimulation is approximately 8-10 pulses/sec. The batteries that drive the stimulator are rechargeable.

Records were made in the awake monkey (Fig. 13). Paired flashes are presented, and recordings are made from electrodes implanted in the occipital cortex. The response to 50 such paired flashes are accumulated on a computer for average transients. The flash-flash interval is varied from 25 to 200 msec. All are records from striate (visual) cortex. The top traces were recorded prior to the onset of stimulation and the lower ones after stimulation of the inferotemporal region had begun. Note that with cortical stimulation the recovery function is depressed, that is, recovery is delayed.

Figure 14 shows the average of such effects in five subjects. Chronic stimulation of the inferotemporal cortex produces a marked increase in the processing time taken by cells in the visual system.

A parallel experiment in the auditory system was done in collaboration with Dr. James Dewson. In this study, made with cats, removals of the auditory homologue of the inferotemporal cortex were performed. This homologue is the insular-temporal region of the cat. Dewson (1964) had shown that its removal impairs complex auditory discrimination (speech sounds), leaving simple auditory discriminations (pitch and loudness) intact. Removal, in addition, alters paired-click recovery cycles recorded as far peripherally as the cochlear nucleus. Bilateral ablation shortens the recovery cycle markedly. Of

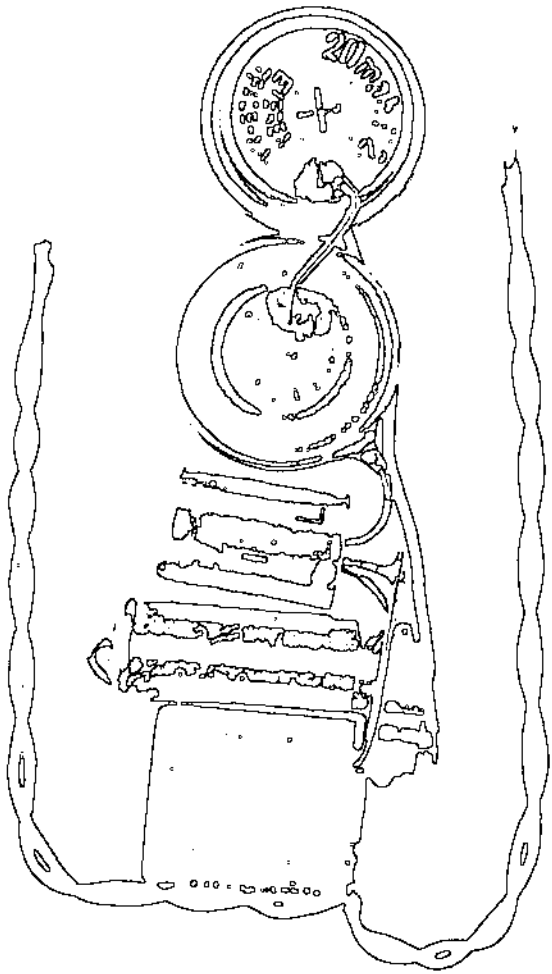

Fig. 12. Stimulator and batteries for chronic brain stimulation. Batteries are rechargeable nickel-cadmium and are available in different sizes from the manufacturer.

course, control ablations of the primary auditory projection cortex and elsewhere have no such effect. Thus we have evidence that chronic stimulation of the "association" cortex selectively prolongs, while ablation selectively shortens, the recovery time of cells in the related primary sensory projection system.

These results have been extended in both the auditory and visual modes. Electrode studies have shown alterations of visual receptive fields recorded from units at the optic nerve, geniculate and cortical levels of the visual projection systems produced by electrical

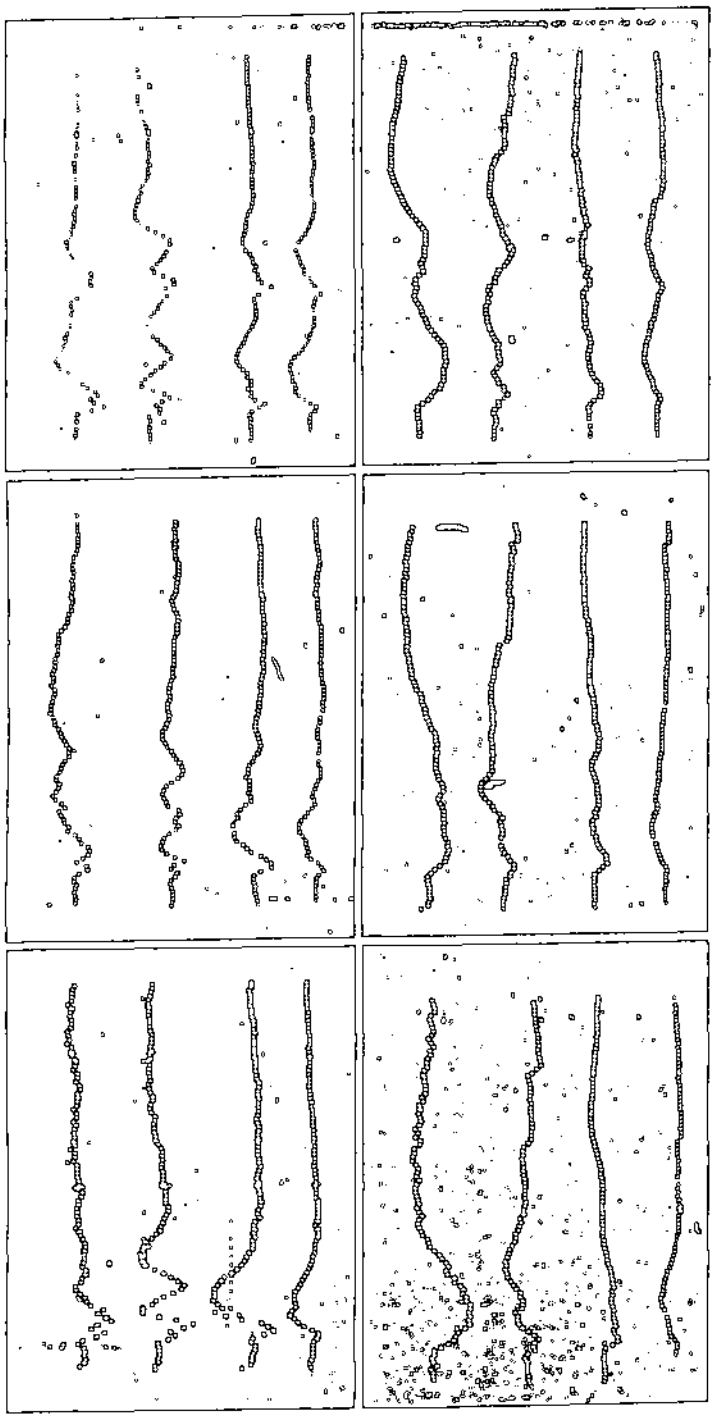

Fig. 13

stimulation of the inferior temporal cortex. The anatomy of the corticofugal pathways of these controls over sensory input also is under study. In the auditory system the fibers lead to the inferior colliculus and from there (in part via the superior olive) to the cochlear nucleus (Dewson, Noble, & Pribram, 1966). Definitive results as yet have not been achieved in our studies of the visual pathways, but preliminary indications lead to the pretectal-collicular region as the site of interaction between the corticofugal control mechanism and the visual input system.

The contextual amnesias only recently have become subject to neurophysiological analysis. Again, as in the case of the specific amnesias, cortico-fugal, efferent control mechanisms have been demonstrated. Results obtained in my laboratory show that in many instances these controls are the reciprocals of those involved in the sensory-mode specific processes (Spinelli & Pribram, 1967). Others (*Brain Res.*, 1967) have shown that the most likely pathways of operation of the frontolimbic mechanisms involve the brainstem reticular formation. Here, however, as in the case of the specific amnesias, control can be exerted as far peripherally as the primary sensory neuron (Spinelli & Pribram, 1967; Spinelli, Pribram, & Weingarten, 1965).

In general terms, the model derived from these experiments states that the operation of efferents from sensory-specific posterior systems tend to reduce, and those from the frontolimbic systems tend to enhance, redundancy in the input channels, that is, the primary projection systems. This presumably is accomplished by inhibition and disinhibition of the ongoing interneuronal regulatory processes within the afferent channels, both those by which neurons regulate the activities of their neighbors and those which decrease a neuron's own activity.

IX. The Distribution of Information in the Brain

This is not the first time in the history of experimental brain research that data have led investigators of complex mnestic disorders to

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Fig. 13. A representative record of the change produced in visually evoked responses by chronic stimulation of the inferotemporal cortex. Upper set of records was taken before stimulation; lower set, during stimulation. All traces were recorded from the visual cortex; the first set in response to a single flash, the second, to flashes separated by 75 msec, and the third, to flashes separated by 150 msec. Actually this was the first of our series of experiments that called our attention to the changed recovery phenomenon. Note here also the change in wave form of the response even when a single flash was presented. However, this change did not appear in all of our subjects.

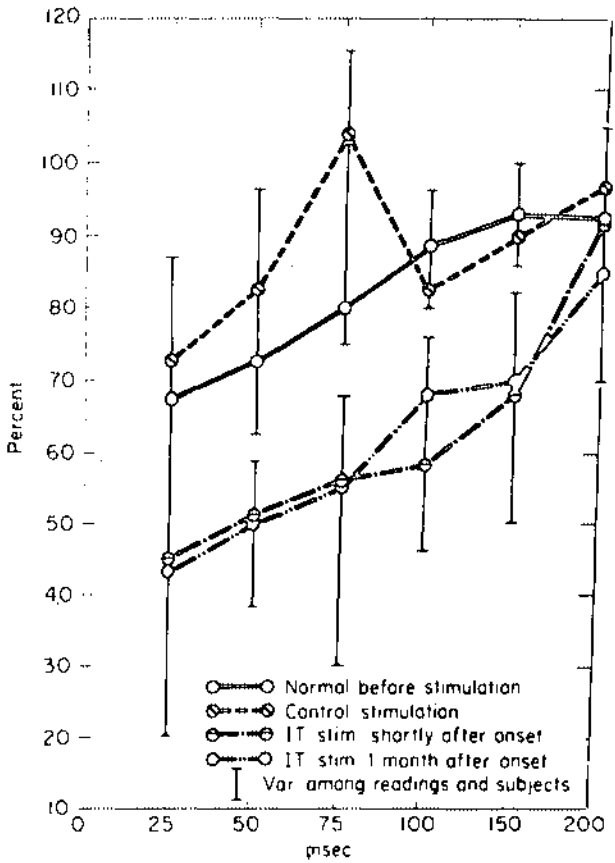

Fig. 14. A plot of the recovery functions obtained in five monkeys before and during chronic cortical stimulation: relative amplitude of the second response as a function of interflash interval.

focus on the primary projection systems. Munk (1881), von Monakov (1914), and Lashley (1942) pursued this course from an early emphasis on the "association" to a later recognition of the importance of the organization of the input systems. Of special interest in this pursuit are the experiments of Lashley that demonstrated that pattern vision remains intact after extensive resection—up to 85%—of the optic cortex. These results make it imperative to assume that input information becomes widely distributed within the visual system. Two types of mechanism have been proposed to account for such distribution (Pribram, 1969); here I want to present evidence that it indeed does occur.

We trained monkeys to discriminate between a circle and a set of vertical stripes by pressing the right or left half of a plastic panel upon which the cues were briefly projected (for 0.01 msec). Transient electrical responses meanwhile recorded from small wire electrical response were related by computer analysis to the stimulus, response, and reinforcement contingency of the experiment (Pribram, Spinelli, & Kamback, 1967). Thus we could distinguish from the record whether the monkey had looked at a circle or at the stripes, whether he had obtained a reward or made an error, and whether he was about to press the right or the left leaf of the panel. Interestingly enough, not all of these brain patterns were recorded from all of the electrode locations: From some, input-related patterns were obtained best; from others, the reinforcement-related patterns were derived; and still others gave us the patterns that were response-related. This was despite the fact that all placements were within the primary visual system, which is characterized anatomically by being homotopic with the retina. It appears therefore not only that optic events are distributed widely over the system but that response and reinforcement-related events reliably reach the input systems. Such results surely shake further one's confidence in the ordinary view that input events must be transmitted to the "association" areas for associative learning to be effected.

X. The Mechanism of Remembering

The experimental findings detailed here allow one to specify a possible mechanism to account for the lesion-produced amnesias. On the basis of the neurobehavioral and neuroanatomical data, I had suggested earlier (Pribram, 1960b) that the posterior "association" cortex by way of efferent tracts leading to the brainstem [most likely to the colliculi or surrounding reticular formation (Pribram, 1958)] partitions the events that occur in the sensory-specific system and classifies these events according to one or another scheme. During the course of our joint work, Dr. Spinelli would repeatedly ask: "What do you mean by 'partitioning'? What is 'partitioning' in neurological terms?" Until we had accomplished our electrophysiological experiments, I really had no idea just how to answer. But once we saw the results of these experiments, the neurophysiological explanation became evident: Partitioning must work something like a multiplexing circuit. In neurophysiological terms, when the recovery time of neurons in the sensory projection system is increased by posterior "association" cortex

stimulation, fewer cells are available at any given moment to receive the concurrent input. Each of a successive series of inputs thus will find a different set of cells in the system available to excitation. There is a good deal of evidence that, in the visual system at least, there is plenty of reserve capacity—redundancy—so that information transmission is not, under ordinary circumstances, hampered by such "narrowing" of the channel (Attneave, 1954). Ordinarily a particular input excites a great number of fibers in the channel, ensuring replication of transmitted information. Just as lateral inhibition in the retina has the effect of reducing redundancy (Barlow, 1961), so the operation of the sensory-specific posterior "association" cortex increases the density of information within the input channel.

Conversely, the functions of the frontolimbic mechanism enhance redundancy, making more cells available at any given moment to concurrent input. This diminishes the density of information processed at any moment and enhances temporal resolution.

The model has several important implications: First, the nonrecovered cells, the ones that are still occupied by excitation initiated by prior inputs, will act as a context or short-term memory buffer, against which the current input is matched. A match-mismatch operation of this sort is demanded by models of the process of recognition and selective attention spelled out on other occasions by Craik (1943), Sokolov (1960), Bruner (1957), MacKay (1956), and myself (1960a, 1963a,b). These "occupied" cells thus form the matrix of "uncertainty" that shapes the pattern of potential information, that is, the "unexpectancy" that determines the selection of input signals that might or might not occur. The normal functions of the posterior cortex are assumed to increase the complexity of this context while those of the frontolimbic systems would simplify and thus allow readier registration and parceling.

Second, in a system of fixed size, reduction of redundancy increases the degree of correlation possible with the set of external inputs to the system, while enhancement of redundancy has the opposite effect. The number of alternatives or the complexity of the item to which an organism can attend is thereby controlled (Garner, 1962). This internal alteration in the functional structure of the classic sensory projection system thus allows attention to vary as a function of the spatial and temporal resolution that excitations can achieve, with the result that events of greater or lesser complexity can be attended to. The sharper the spatial resolution, the greater the "uncertainty" and, thus, the more likely that any set of inputs will be sampled for information. Conversely, the greater the temporal resolution, the more likely that

attention is focused, and that events become grouped, memorable, and certain. In the extreme, the sharpening of the appetite for information becomes what the clinical neurologist calls stimulus-binding. Its opposite is agnosia, the inability to identify events because they fail to fit the oversimplified context of the moment.

Third, this corticofugal model of the functions of the so-called association systems relieves us of the problem of higher and higher order infinite regress—an association area "homunculus" who synthesizes and abstracts from inputs, only to pass on these abstractions to a still higher "homunculus," perhaps the one who makes decisions, etc. Former ways of looking at the input-output relationships of the brain invariably have come up against this problem (implicit or explicit) of "little men" inside "little men."

According to the model presented here, there is no need for this type of infinite regress. The important functions of perception, decision, etc. are going on within the primary sensory and motor projection systems. Other brain regions such as the posterior sensory-specific associated systems and the frontolimbic systems exert their effects by altering the functional organization of the primary systems. Thus these *associated* systems are not "association" systems; they simply alter the configuration of input-output relationships processed by the projection systems. In computer language the associated systems function by supplying *subroutines* in a hierarchy of programs, subroutines contained within and not superimposed from above on the more fundamental processes. In this fashion the infinite higher-order abstractive regress is avoided. One could argue that in its place a downward regress of sub- and subroutines is substituted. I would answer that this type of regress, through progressive differentiation, is the more understandable and manipulable of the two.

A final advantage of the model is that the signal itself is not altered; the invariant properties of a signal are unaffected (unless channel capacity is overreached). It is only the organization of the channel itself—the matrix within which the signal is transmitted—that is altered. Thus the same signal carries more or less information, depending on the "width" of the channel. I am here tempted to extrapolate and say that the signal carries different meanings, depending on the particular structure or organization of the redundancy of the channel.

Concretely, the associated cortex is conceived to program, or to structure, an input channel. This is tantamount to saying that the input must be coded by the operation of this cortex. In its more fundamental aspects, computer programming is in large part a coding operation:

The change from direct machine operation through assembler to one of the more manipulable computer languages involves a progression from the setting of binary switches to conceptualizing combinations of such switch settings in "octal" code and then assembling the numerical octals into alphabetized words and phrases and finally parceling and parsing of phrases into sentences, routines, and subroutines. In essence these progressive coding operations minimize interference among like events by identifying and registering unique structures among the configurations of occurrence and recurrence of the events.

The evidence presented here makes it not unlikely that one function of the posterior and frontolimbic formations of the forebrain is to code events occurring within the input systems. As already noted, the distribution of information (dismembering) implies an encoding process that can reduplicate events without recourse to widespread random neural connections. Regrouping the distributed events (remembering) also implies some sort of coding operation – one similar to that used in decoding binary switch settings into an octal format.

An impaired coding process therefore would be expected to produce grave memory disturbances. The question is thus raised whether lesion-produced amnesias, specific and contextual, reflect primarily malfunctions of mechanism of coding and not the destruction of localized engrams.

XI. Summary

Experimentally produced local brain damage does demonstrably impair memory functions. However, the impairment apparently is not so much a removal of localized engrams as an interference with the mechanisms that code neural events so as to allow facile storage and retrieval. Thus, the evidence shows that anatomically the memory trace is distributed within a neural system by means of an encoding process, while as a function of decoding the engram is reassembled, that is, remembered. Thus, what and whether something is remembered is in large part dependent on how it is, and that it is, adequately coded.

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