

IN SEARCH OF THE ENGRAM*

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'When the mind wills to recall something, this volition causes the little [pineal] gland, by inclining successively to different sides, to impel the animal spirits toward different parts of the brain, until they come upon that part where the traces are left of the thing which it wishes to remember; for these traces are nothing else than the circumstance that the pores of the brain through which the spirits have already taken their course on presentation of the object, have thereby acquired a greater facility than the rest to be opened again the same way by the spirits which come to them; so that these spirits coming upon the pores enter therein more readily than into the others.'

So wrote Descartes just three hundred years ago in perhaps the earliest attempt to explain memory in terms of the action of the brain. In the intervening centuries much has been learned concerning the nature of the impulses transmitted by nerves. Innumerable studies have defined conditions under which learning is facilitated or retarded, but, in spite of such progress, we seem little nearer to an understanding of the nature of the memory trace than was Descartes. His theory has in fact a remarkably modern sound. Substitute nerve impulse for animal spirits, synapse for pore and the result is the doctrine of learning as change in resistance of synapses. There is even a theory of scanning which is at least more definite as to the scanning agent and the source of the scanning beam than is its modern counterpart.

As interest developed in the functions of the brain the doctrine of the separate localization of mental functions gradually took form, even while the ventricles of the brain were still regarded as the active part. From Prochaska and Gall through the nineteenth century, students of clinical neurology sought the localization of specific memories. Flechsig defined the association areas as distinct from the sensory and motor. Aphasia, agnosia, and

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apraxia were interpreted as the result of the loss of memory images, either of objects or of kinaesthetic sensations of movements to be made. The theory that memory traces are stored in association areas adjacent to the corresponding primary sensory areas seemed reasonable and was supported by some clinical evidence. The extreme position was that of Henschen, who speculated concerning the location of single ideas or memories in single cells. In spite of the fact that more critical analytic studies of clinical symptoms, such as those of Henry Head and of Kurt Goldstein, have shown that aphasia and agnosia are primarily defects in the organization of ideas rather than the result of amnesia, the conception of the localized storing of memories is still widely prevalent (Nielson, 1936).

While clinical students were developing theories of localization, physiologists were analysing the reflex arc and extending the concept of the reflex to include all activity. Bechterew, Pavlov and the behaviourist school in America attempted to reduce all psychological activity to simple associations or chains of conditioned reflexes. The path of these conditioned reflex circuits was described as from sense organ to cerebral sensory area, thence through associative areas to the motor cortex and by way of the pyramidal paths to the final motor cells of the medulla and cord. The discussions of this path were entirely theoretical, and no evidence on the actual course of the conditioned reflex arc was presented.

In experiments extending over the past 30 years I have been trying to trace conditioned reflex paths through the brain or to find the locus of specific memory traces. The results for different types of learning have been inconsistent and often mutually contradictory, in spite of confirmation by repeated tests. I shall summarize today a number of experimental findings. Perhaps they obscure rather than illuminate the nature of the engram, but they may serve at least to illustrate the complexity of the problem and to reveal the superficial nature of many of the physiological theories of memory that have been proposed.

I shall have occasion to refer to training of animals in a variety of tasks, so shall give a very brief description of the methods used. The animals studied have been rats and monkeys with, recently, a few chimpanzees. Two lines of approach to the problem have been followed. One is purely behavioural and consists in the analysis of the sensory excitations which are actually associated with reactions in learning and which are effective in eliciting the learned reactions. The associated reactions are similarly analysed. These studies define the patterns of nervous

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activity at receptor and effector levels and specify certain characteristics which the memory trace must have. The second approach is by surgical destruction of parts of the brain. Animals are trained in various tasks ranging from direct sensory-motor associations to the solution of difficult problems. Before or after training, associative tracts are cut or portions of the brain removed and effects of these operations on initial learning or postoperative retention are measured. At the termination of the experiments the brains are sectioned and the extent of damage reconstructed from serial sections. The brains are also analysed for secondary degeneration, so far as available histological methods permit.

ELIMINATION OF THE MOTOR CORTEX

I first became sceptical of the supposed path of the conditioned reflex when I found that rats, trained in a differential reaction to light, showed no reduction in accuracy of performance when almost the entire motor cortex, along with the frontal poles of the brain, was removed. This observation led to a series of experiments

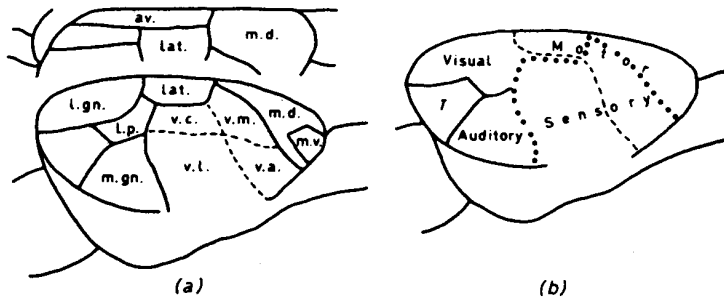


Figure 1. Functional divisions of the rat's brain. (a) The projection fields of the principal thalamic nuclei: av., anteroventral; lat., lateral; l.gn., lateral geniculate; l.p., lateral, pars posterior; m.d., median dorsal; m.gn., median geniculate; m.v., median ventral; v., the various divisions of the central nucleus. The projection fields of the median nuclei (m.d., m.v.) correspond to the prefrontal areas of primates. (b) Location of visual, auditory, and overlapping sensory-motor areas (after Lashley, 1944). The region marked T is probably homologous with the temporal association area of primates

designed to test the part played by the motor cortex or Betz cell area in the retention of various habits. The matter can be tested either by removing the motor cortex or by severing its connections with the sensory areas of the brain. Both methods have been used with the rat and the monkey.

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The sensory and motor areas of the brains of these animals have been mapped by anatomic methods and by electric stimulation. Figure 1 shows the principal areas of the rat's brain, the separate auditory and visual areas and the overlapping sensory and motor areas. Figure 2 is a composite from several sources of the chief sensory and motor areas of the brain of the macaque monkey.

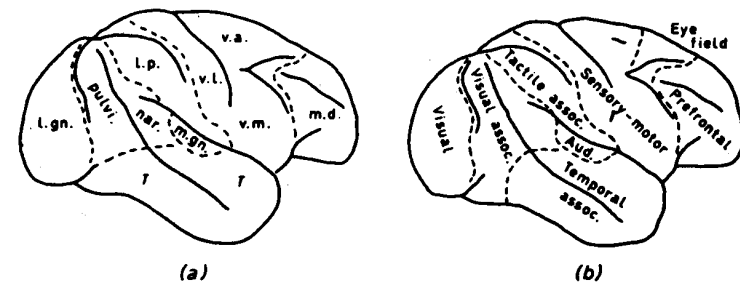


Figure 2. Functional divisions of the monkey's brain. (a) The projection of the principal thalamic nuclei. Abbreviations as in Figure 1. The homologies between the divisions of the central and lateral nuclei are uncertain. (b) Location of functional areas

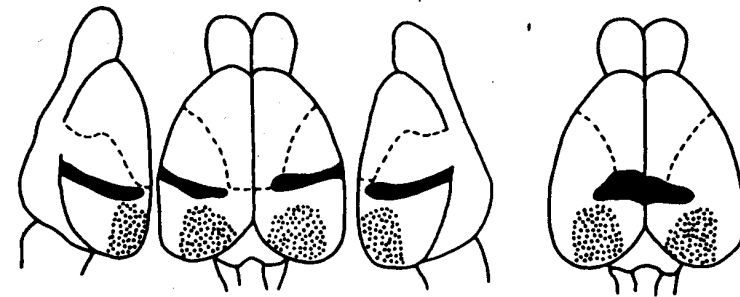


Figure 3. Lesions partially separating the visual area (stippled) from the motor areas (outlined by dashes) of the rat's brain without disturbing visual learning

Incisions were made through the cortex and underlying fibres of the rat's brain such as to sever the visual areas more or less completely from the motor regions of the brain. The rats were then trained in what I have called the conditional reaction. They are taught to jump to a white triangle and to avoid a white x when both figures are on a black background, but to choose the x and avoid the triangle if the background is striped; the direction of

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choice is conditional upon the character of the background. This is the most difficult visual generalization that we have been able to teach the rat. Animals with incisions like those shown in *Figure 3*, which practically separate the motor regions from the visual, were able to learn this reaction as quickly as did normal controls (Lashley, 1942b).

Monkeys were trained to open various latch boxes. The motor areas were then removed, as shown in *Figure 4*. Note that these lesions involved both the Betz cell area and the premotor area, including parts of the eye fields around the arcuate sulcus. This operation produces a temporary paralysis, but after 8 to 12 weeks this paralysis recovers to such an extent that the animals are

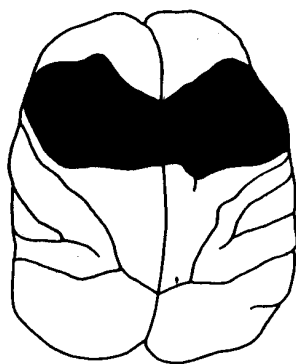


Figure 4. Extent of cortical lesion which did not abolish latch-box habits. The lesion is bounded caudally by the central fissure and extends forward to include the arcuate sulcus

capable of the movements required to open the boxes. During this recovery period they did not have access to the training boxes. When sufficiently recovered, they were tested and opened the boxes promptly without random exploratory movements. The tasks require both visual recognition of the latches and semiskilled movements, such as turning a crank. Removal of the motor areas did not produce a loss of memory for the movements (Lashley, 1924). Jacobsen has since confirmed these observations with a chimpanzee from which the motor cortex was removed (Jacobsen, 1932).

These experiments seem to rule out the motor cortex or Betz cell area as containing any part of the conditioned-reflex arc. The traditional view of the function of this area regards it as the region of final integration of skilled voluntary movements. My own interpretation, to which few neurologists would subscribe, is that it has no direct concern with voluntary movement, but is a part of the vast reflex postural system which includes the basal nuclei,

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cerebellar and vestibular systems. Certainly there is no evidence that it forms a part of the conditioned reflex circuit.

For the rat the experiments rule out the whole frontal region of the brain from participation in visual habits. In the monkey there remains another possibility. The so-called visual associative area (area 18) has direct connection with the cortex of the arcuate sulcus (area 8), and this in turn with the premotor cortex (area 6). This last area is also motor and perhaps equivalent in function with the Betz cell area (Bucy, 1934). The cortex of the arcuate sulcus and of a considerable surrounding area was removed from five monkeys that had been trained in a variety of visual discriminative reactions. After the operations they showed perfect retention of all their visual habits (Lashley, 1948). Jacobsen (1932) has reported loss of certain latch-box habits in monkeys after removal of area 6, but there are indications that this may be a kinaesthetic-sensory area (Gay and Gellhorn, 1948; Walker, 1948), and the loss cannot be ascribed to disturbance of its function as a final common motor path. I have removed it in combination with area 4 without disrupting motor habits (Lashley, 1924).

I have occasionally seen the type of defect reported by Jacobsen after prefrontal lobe lesions, as also reported by Kennard (1939), but it has not occurred consistently and its occurrence remains unexplained. I did not find it after removal of area 6 in conjunction with the Betz cell area.

TRANSCORTICAL CONDUCTION

There is evidence, not only that the motor cortex does not participate in the transmission of the conditioned-reflex pattern, but also that the transmission of impulses over well-defined, isolated paths from one part of the cortex to another is inessential for performance of complicated habits. The maze habit of the rat almost certainly involves the utilization of several sensory modalities, visual, tactile and kinaesthetic. In a rather complicated set of experiments I attempted to test the importance of connections across the cortex for maze performance. Rats were trained on the maze, then knife cuts were made through the cortex and underlying fibres, separating different functional areas or cutting through functional areas. The incisions were long, averaging half of the entire length of the cerebral hemispheres. After recovery the animals were tested in retention of the maze habit. In other experiments the incisions were made before training and their effect upon the rate of initial learning was tested. In neither

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initial learning nor in retention could any certain effect of separating the various parts of the cortex be demonstrated. If the incisions interrupted sensory tracts to the cortex, there was loss of the habit, but uncomplicated separation of cortical areas produced no effect on performance.

Both the anatomic evidence of Le Gros Clark (1941) and the physiological evidence from strychninization of the cortex (Bonin, Garol and McCulloch, 1942) show that the primary visual area has direct axon connections only with the immediately adjacent cortex.

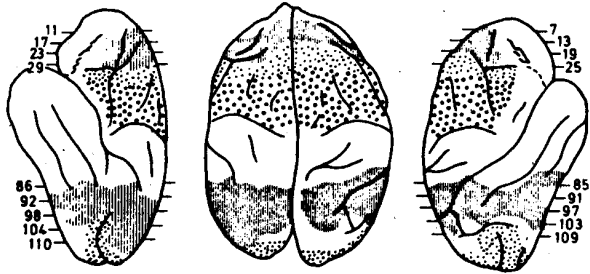


Figure 5. Lesions, marked by hatching, which destroyed the greater part of the so-called visual associative areas in a monkey without affecting visual functions

In experiments which I shall report in more detail in considering the function of associative areas, I removed the greater part of this band of cortex surrounding the visual areas from five monkeys that had been trained in a variety of visual habits (Figure 5). This operation almost certainly destroyed all the relay connections across the cortex from the macular fields. It produced no loss of visual habits based on discrimination of the colour, brightness, or form of objects (Lashley, 1948).

Miss Wade trained monkeys in habits which are abolished by destruction of the frontal lobes and which require visual, tactile and kinaesthetic adjustments. I cut the transcortical fibres of the frontal lobes in these animals, leaving only the projection fibres for the area. There was no disturbance of performance after the operations (unpublished experiments).

Such results are certainly puzzling. They leave us with almost no understanding of the function of the associative fibres which extend across from one part of the cortex to another. The results are difficult to accept, yet they are supported by various other lines of evidence. Smith (1947) and Akelaitis (1944) have reported careful studies of human patients in whom the corpus callosum

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(the great commissure of fibres connecting the two hemispheres) had been severed in an effort to stop the spread of Jacksonian epilepsy. These investigators were not able to demonstrate any effects of the operation except a slight slowing of reaction time, which was equally great, whether the reaction was on the same or opposite side of the body to that stimulated. Sperry (1947) has divided the arm motor and sensory areas of the monkey's brain into a number of small square divisions (Figure 6) by careful subpial section. Although the operations were intended to sever only the intrinsic fibres of the cortex, they actually destroyed most of the longer loop fibres as well. Such animals do not show any postoperative incoordination of the movements of the different segments of the arm and use the arm efficiently in the performance of habitual movements.

It is difficult to interpret such findings, but I think that they point to the conclusion that the associative connections or memory traces of the conditioned reflex do not extend across the cortex as well-defined arcs or paths. Such arcs are either diffused through all parts of the cortex, pass by relay through lower centres, or do not exist.

There is the possibility that the chief associative connections between functional areas of the cortex are by connections through the thalamus. I doubt this for two reasons. The techniques

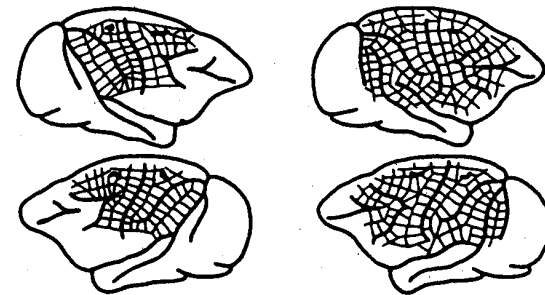


Figure 6. Pattern of incisions in the motor and sensory areas of two monkeys which did not produce incoordination movements (after Sperry, 1947)

that have been used to demonstrate cortical efferents to the thalamus, the Marchi stain and strychninization of the cortex, are unreliable indices of the direction of fibres. The supposed cortico-thalamic fibres follow the paths of the afferent fibres and may not be efferent. Secondly, in the rat at least there is little evidence of an elaborate system of intrathalamic association fibres. After

a cortical injury thalamic nuclei degenerate completely without leaving a residue of internuncial cells. The question of the importance of intrathalamic association is not settled, and none of the available anatomic or physiological techniques is capable of giving conclusive evidence.

A few experiments by Ingebritsen (1933) on the spinal cord suggest that the essential pattern of a learned reaction can be transmitted by a diffuse nervous network. Ingebritsen made double hemisections of the spinal cord of rats, severing one half at the second, the other at the fifth cervical level. These lesions cut all long fibres connecting the brain with the spinal motor centres of the limbs. Nevertheless, such rats retained maze habits and were able to learn to operate latch boxes requiring that they rise on the hindfeet and depress a lever with the forepaws. . . . There are no long fibres, either sensory or motor, crossing over between the two levels of these sections. Habit patterns cannot be acquired by the isolated spinal cord (Kellogg and colleagues, 1947). Somehow, the control of the motor pattern essential for the performance of the complex acts traverses the network of short internuncial cells of the spinal cord.

THE PROBLEM OF THE 'ASSOCIATION AREAS'

In anatomic theories of the memory trace the association areas of the cortex have played a major part. Frontal, parietal, occipital and temporal associative areas have been distinguished as regions of the cortex, relatively lacking in massive connections with the lower centres of the brain. On the basis of some clinical evidence, but chiefly because of their anatomic relations, these areas have been considered as associative and as the storehouses of memory images of sensations derived from the adjacent sensory areas. Thus areas 18 and 19 of Brodmann's questionable divisions have been called the visual associative areas, areas 5 and 7 tactile associative, and areas 20, 21, and 22 of the temporal lobe the auditory association areas. The prefrontal area was considered by Hitzig to be a higher integrative region because he believed that it showed the greatest evolutionary growth in the primate brain. Special memory functions were also ascribed to it, however.

Franz (1907) reported that the removal of the frontal association areas of cats destroyed recently formed habits but left old, well-established habits unaffected. The actual observation was that the cats lost their habits of opening latch boxes but would still come when called. His operations destroyed much of the motor areas as well as the prefrontal cortex. I later trained monkeys on

latch boxes and removed the prefrontal cortex, in an experiment designed to test the influence of the operation on learning ability. During the period allowed for recovery one of the animals found the experimental boxes piled in the corner of the room and promptly opened them. Tests of the other animals showed perfect retention of the manipulative habits. There was no indication that the recently acquired habits had been lost. Jacobsen took up the problem at this point and carried it further. He found that visual discriminative habits and simple habits of latch-box manipulation are unaffected by loss of the prefrontal association areas. Habits requiring a series of acts, such as opening a box with several independent latches, may be lost. This is not, however, a simple removal of memory traces. The animals are incapable of relearning the functions which they have lost. They fail because of a difficulty in going on from one task to the next, not from loss of memory of the individual items of the task (Jacobsen, 1936).

Loss of the delayed reaction after removal of the prefrontal lobes of the monkey has been interpreted as a loss of immediate memory. However, this task and others, which are affected by prefrontal injury, all involve a series of conflicting actions. Difficulty in maintaining a constant set or attitude is the real basis of the loss. Such an interpretation fits better with clinical findings than does the hypothesis of memory defect.

We have recently been testing the relation of other associative areas to memory functions in the monkey. Five spider monkeys were trained on a variety of visual tasks. A band of cortex surrounding the primary visual areas and including the visual associative areas of Campbell and Brodmann was then removed (*Figure 6*), and the animals were tested for retention of habits based on discrimination of colours, of geometric forms, and of a number of familiar objects, such as visual recognition of their home cages, of the caretaker, and the like. No loss of any visual memories could be demonstrated (Lashley, 1948).

Similar experiments with habits of tactile discrimination are now being completed. The monkeys are required to reach through a hole in a partition and to distinguish variously shaped covers of food dishes by touch alone. They learn readily such tasks as to choose a cylinder and reject a prism, if both are smooth, but to choose the prism, if both are coated with sandpaper. When they had reached a standard criterion of accuracy, the parietal associative areas (Brodmann's areas 5 and 7) were removed. No animal has shown significant loss of the habits based on tactile discrimination after removal of these areas alone (Dr. Josephine Blum).

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Removal of the lateral surfaces of the temporal lobes alone has also not affected visual or tactile habits.

A number of experiments with the rat have shown that habits of visual discrimination survive the destruction of any part of the cerebral cortex except the primary visual projection area. Similarly for auditory habits and the auditory cortex. There is no indication of specialized memory areas outside the primary sensory fields. Although there are not clearly distinguished associative areas in the rat's cortex, I have become somewhat sceptical of the existence of any great difference in the extent of associative areas, as between the rat and monkey. The best anatomic index that we have of the functional differentiation of a cortical area is its connections with the thalamus. The prefrontal cortex of man is the projection field of the dorsomedial and ventromedial nuclei. The corresponding nuclei in the rat's thalamus project to a large frontal region, perhaps proportionately as large as the prefrontal lobes of man (Lashley, 1941). This region also includes the electrically excitable points for the head and part of that for the forelegs. It has therefore been classed as motor, but it is equally justifiable to class it as corresponding to the human prefrontal cortex.

It has been claimed that the differentiation of a number of cerebral areas contributes to man's superior intelligence by avoiding confusion of functions, but, if the anatomic relations in man and the rat were reversed, it would be concluded with equal assurance that, because intellectual activity requires close integration of different functions, the advantage lies with the brain in which functional areas are not sharply set off. Such *post hoc* arguments based on anatomic grounds alone have little value for functional interpretations. Many current conceptions of cerebral physiology are based upon just such dubious inferences from anatomic data.

The outcome of the experiments involving removal of the associative areas of the monkey was unexpected, in spite of the fact that it confirms the earlier results with the rat. The conclusion, which seems to be forced by the accumulated data, runs counter to the accepted tradition concerning the organization of the cerebral cortex. Memory traces, at least of simple sensory-motor associations, are not laid down and stored within the associative areas; at least not within the restricted associative area supposedly concerned with each sense modality. Memory disturbances of simple sensory habits follow only upon very extensive experimental destruction, including almost the entire associative cortex. Even combined destruction of the prefrontal, parietal, occipital and temporal areas, exclusive of the primary sensory cortex, does

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not prevent the animal from forming such habits, although pre-existing habits are lost and their reformation is greatly retarded.

These results, showing that the so-called associative areas are not essential to preservation of memory traces, have been obtained with rats and monkeys. Is there a greater cortical differentiation in anthropoid apes and man? We have experimental data only on the prefrontal associative cortex of the chimpanzee and of man. Bilateral removal of the entire prefrontal granular cortex in five chimpanzees in our laboratory has not resulted in any memory defect. One 2-year-old animal, lacking prefrontal and parietal areas, removed in early infancy, falls well within the normal range in all aspects of development. Adult chimpanzees, trained in such complicated habits as choosing an object, like a model shown, retain the habits after removal of the entire prefrontal cortex. We have not been able to demonstrate loss of any memory or, in fact, of any function after such operations.

Clinical data, with amnesias following apparently small lesions, seem to contradict such experimental findings. However, lesions in the human brain are mostly the result either of tumor growth or of severe traumatism, both of which probably produce widespread changes in addition to the local injury. The surgical removal of parts of the frontal lobes in the recent topectomy studies has not produced such severe defects as usually result from traumatic destruction of the lobes (Mettler, 1949).

THE ROLE OF SUBCORTICAL STRUCTURES

Perhaps we have been looking in the wrong place for the conditioned-reflex arcs or memory traces. Are they formed somewhere else than in the cortex? Experiments on the thalamus and other subcortical structures are technically difficult, and there is little direct evidence on this question. Since the classical experiments of Goltz a number of investigators have studied the capacity of the totally decorticate animal to learn. The outcome of these experiments is that such animals can form simple sensory-motor associations, although with extreme slowness in comparison with the rate of the normal animal (Girden and colleagues, 1936; Poltyrew and Zeliony, 1930). We must ask, however, whether such learning occurs when the cortex is intact.

When the sensory or associative areas of the cerebral cortex are destroyed, the corresponding nuclei of the neo-thalamus degenerate, so this portion of the subcortex is eliminated from consideration by the same experiments which rule out the cortical association areas. The only experiments bearing upon the

participation of other subcortical centres suggest that subcortical learning does not occur when the cortex is functioning.

Fischel (1948) has maintained, solely from comparative psychological studies, that the basal ganglia are the seat of the space-coordinate elements of motor habits. I have destroyed the greater part of these structures in rats, trained in the discrimination box, without producing loss of orientation. The animals may perform forced circus movements but, in spite of this, they maintain their orientation in the problem box (Lashley, 1921b). The basal ganglia in man are subject to various degenerative diseases. The symptoms of such diseases are, in general, tremors and other disturbances of coordination at a primitive level, but without evidence of apraxia or other disorder of the learned patterns of motor coordination. The evidence seems conclusive that in mammals the basal nuclei are not an essential link in the patterning of learned activities.

It has been widely held that although memory traces are at first formed in the cerebral cortex, they are finally reduced or transferred by long practice to subcortical levels. The evidence for this has been the apparently greater fragility of recently formed habits than of old habits; the supposedly greater resistance of the latter to brain injuries. The amnesias following electroshock therapy indicate that it is the age of the trace and not the amount of practice that has built it up which determines its survival, and a difference of a few minutes in the age of memories may suffice to determine their loss or survival. This is scarcely evidence for reduction to lower levels of the nervous system. The chief argument for the dropping out of memory traces from the cortex has seemingly run somewhat as follows: Consciousness is a function of the cerebral cortex; long-practised habits become automatic and are performed without conscious control; therefore they are no longer mediated by the cerebral cortex. Both premises of this syllogism are probably false, and the conclusion would not follow if they were true.

When rats are trained in a habit based upon the discrimination of intensities of light, to choose a brightly lighted alley and avoid a dimly lighted one, the removal of the striate cortex completely abolishes the habit. The animals are able to relearn the reaction and require as much practice as they did for initial learning. One group of animals was trained in this habit and given 1,200 trials of overtraining, daily practice for a period of three months. Their behaviour strongly suggested automatization of the habit. The striate areas were then removed. The habit was lost, just as in the case of animals which are operated as soon as they give

evidence of the presence of the habit. The long overtraining did not eliminate the participation of the cortex (Lashley, 1921a).

This visual habit can be formed in the absence of the visual cortex, and the rates of learning with and without the visual area are exactly the same. The average for 100 normal animals is 125 trials; for nearly 100 without the visual areas it is 123 trials. After such animals, lacking the visual cortex, have learned the brightness reaction, any other part of the cerebral cortex may be destroyed without disturbing the habit. Apparently no other part of the cortex takes over the learning function (Lashley, 1922). If, in addition to removal of the striate areas, the pretectile region of the thalamus and the optic tectum are destroyed, the animals cannot learn the discrimination reaction (Lashley, 1935b). These facts indicate that, in the absence of the visual cortex, the learning of the brightness reaction is carried out by the optic tectum. However, so long as the visual cortex is intact, removal of the tectum has no effect whatever upon the performance of visual habits. The tectum apparently does not participate in visual learning so long as the cortex is intact (Lashley, 1935b).

Dunlap (1927) has advanced the hypothesis that complex serial habits, such as those of maze running, playing a musical passage, or speaking a sentence, are at first chains of sensory-motor reactions in which excitations from muscular contractions in one movement of the series serve as stimuli to elicit the next. He holds that, with continued practice, there is a short-circuiting of these conditioned reflex pathways through the cerebellum and that the peripheral elements drop out. McCarthy and I (Lashley and McCarthy, 1926) attempted to test this hypothesis by training rats in the maze, removing the cerebellum, and testing for retention. The operations greatly disturbed the motor coordination of these animals. Some of them practically rolled through the maze, but they rolled without entering the blind alleys. There was no loss of memory of the sequence of turns in the maze.

These few experiments are, of course, by no means conclusive. They constitute, however, the only direct evidence available, and they definitely point to the conclusion that, if the cerebral cortex is intact, the associative connections of simple conditioned reflexes are not formed in the subcortical structures of the brain.

The studies which I have reported thus far point to the conclusion that habits based upon visual discrimination are mediated by the striate areas, by the primary visual cortex, and do not involve the activity of any other part of the cerebral cortex. The conduction of impulses is from the retina to the lateral geniculate nuclei, thence to the striate areas, and from them down to some subcortical

nervous mechanism. The path beyond the striate cortex is unknown. It may be direct to the spinal cord. There is some evidence that the pyramidal paths contain many fibres from all parts of the cerebral cortex, not from the Betz cell area only.

It seems probable that the same restriction of simple discriminative habits to the primary sensory areas holds also for other sensory modalities. The evidence is less complete, but what there is is consistent with the data on the visual system.

The evidence thus indicates that in sensory-motor habits of the conditioned reflex type no part of the cerebral cortex is essential except the primary sensory area. There is no transcortical conduction from the sensory areas to the motor cortex, and the major subcortical nuclear masses, thalamus, striatum, colliculi and cerebellum, do not play a part in the recognition of sensory stimuli or in the habit patterning of motor reactions.

THE ENGRAM WITHIN SENSORY AREAS (EQUIPOTENTIAL REGIONS)

The experiments reported indicate that performance of habits of the conditioned reflex type is dependent upon the sensory areas and upon no other part of the cerebral cortex. What of localization within the sensory areas? Direct data upon this question are limited, but point to the conclusion that so long as some part of the sensory field remains intact and there is not a total loss of primary sensitivity, the habit mechanism can still function. Thus, in a series of experiments attempting to locate accurately the visual cortex of the rat, parts of the occipital lobes were destroyed in a variety of combinations. In these experiments it appeared that, so long as some part of the anterolateral surface of the striate cortex (the projection field of the temporal retina corresponding to the macula of primates) remained intact, there was no loss of habit. Any small part of the region was capable of maintaining the habits based on discrimination of intensities of light (Lashley, 1935b).

In a later experiment an attempt was made to determine the smallest amount of visual cortex which is capable of mediating habits based upon detail vision. The extent of visual cortex remaining after operation was determined by counting undegenerated cells in the lateral geniculate nucleus. Discrimination of visual figures could be learned when only one-sixtieth of the visual cortex remained (Lashley, 1939). No comparable data are available on postoperative retention, but from incidental observations in other experiments I am confident that retention would be possible with the same amount of tissue.

In an early study by Franz (1911) the lateral surfaces of the occipital lobes of the monkey were destroyed after the animals had been trained in pattern and colour discrimination. These operations involved the greater part of what is now known to be the projection field of the macula. There was no loss of the habits. I have destroyed the cortex of the retrocalcarine fissure (the perimacular field) without destroying visual memories. The results with monkeys thus support the more ample data for the rat; the visual memory traces survive any cortical lesion, provided some portion of the field of acute vision remains intact.

This lack of definite habit localization might really have been predicted from psychological data alone. Analysis of the effective stimuli in discriminative learning reveals that the association is independent of particular sensory nerve fibres. It is a response to a pattern of excitation which may vary widely in position on the sensory surface and consequently in cortical projection. The reactions involved in motor habits show the same sort of functional equivalence; a motor habit is not a predetermined set of muscular contractions but is a series of movements in relation to bodily posture and to the complex pattern of the environment. The writing of one's name, for example, is not a stereotyped series of contractions of particular muscles but is a series of movements in relation to the body planes which can be performed with any motor organ and with any degree of amplitude.

I have not time here to report in detail the experiments which justify the conclusion that neither the afferent path nor the efferent is fixed by habit. The mass of evidence accumulated by gestalt psychologists shows conclusively that it is the pattern and not the localization of energy on the sense organ that determines its functional effect. Similar motor equivalence is demonstrated by a variety of less systematic evidence. The psychological studies, like the more limited direct experiments on the brain, point to the conclusion that the memory trace is located in all parts of the functional area; that various parts are equipotential for its maintenance and activation.

FACILITATIVE FUNCTIONS IN LEARNING AND RETENTION (MASS ACTION)

The experiments thus far reported have been concerned almost entirely with discriminative habits requiring only an association between a single sensory stimulus and a motor response. A very different picture develops in experiments with other types of learning. If rats are trained in the maze and then have portions of the cortex removed, they show more or less loss of the habit. If a

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small amount of cortex is destroyed, 5 to 10 per cent, the loss may be scarcely detectable. If large amounts, say 50 per cent or more, are destroyed, the habit is completely lost, and relearning may require many times as much practice as did initial learning. The amount of loss, measured in terms of the practice required for relearning, is, on the average, closely proportional to the amount of cortex destroyed. Figure 7 shows the relation for one group of rats on a relatively difficult maze with eight culs de sac. There is some evidence that the more difficult the task, the greater the relative effect of the larger lesions (Lashley, 1929; Lashley and Wiley, 1933). Similar results have been obtained with latch-box learning and retention (Lashley, 1935a). So far as it is possible to analyse the data from more than 200 diverse operations, the amount of loss from a given extent of cortical destruction is about the same, no matter what part of the cerebral hemispheres is destroyed, provided that the destruction is roughly similar in both hemispheres.

The explanation of this quantitative relationship is difficult. In learning the maze the rat certainly employs a variety of sensory cues, visual, tactile, kinaesthetic, olfactory, possibly auditory. Brain injuries destroy various sensory fields and the larger the lesion the greater the reduction in available sense data. The production of different amounts of sensory deficit would thus appear to be the most reasonable explanation of the quantitative relation between habit loss and extent of lesion (Finley, 1941; Hunter, 1930). Sensory deficit certainly plays a role in it. In the experiment on effects of incisions through the cortex, which was described earlier, the severity of loss of the maze habit correlated highly with the interruption of sensory pathways, as determined from degeneration of the thalamus.

However, sensory loss will not account for all of the habit deterioration. There is evidence which shows that another more mysterious effect is involved. In the first place, destruction of a single sensory area of the cortex produces a far greater deficit in maze or latch-box performance than does loss of the corresponding sense modality. A comparison was made of the effects on retention of the latch-box habits of combined loss of vision, vibrissae touch, and the anaesthesia to touch and movement produced by sectioning the dorsal half of the spinal cord at the third cervical level. This latter operation severs the columns of Gall and Burdach, which convey tactile and kinaesthetic impulses, and also severs the pyramidal tracts which have a dorsal position in the rat. The combined peripheral sense privation and section of the pyramids produced less loss of the latch-box habits than did destruction of

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a single sensory area of the cortex (Lashley, 1935a). Secondly, when blind animals are trained in the maze, the removal of the primary visual cortex produces a severe loss of the habit with serious difficulty in relearning, although the animals could have used no visual cues during the initial learning (Lashley, 1943).

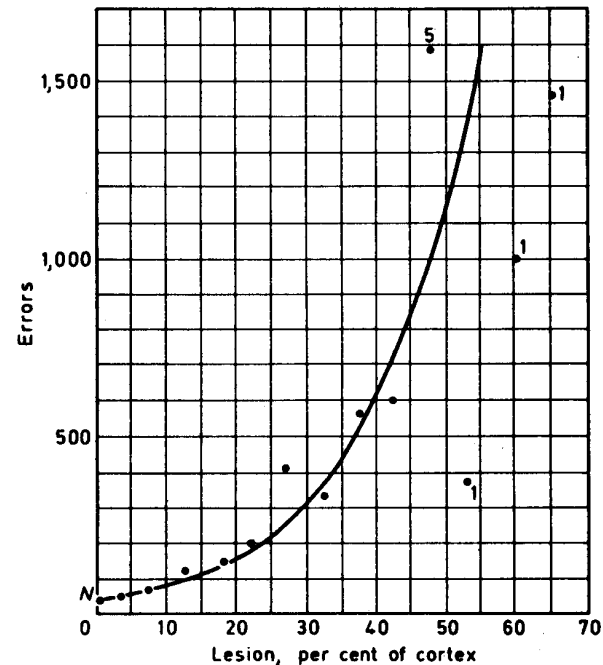


Figure 7. The relation of errors in maze learning to extent of cerebral damage in the rat. The extent of brain injury is expressed as the percentage of the surface area of the isocortex destroyed. Data from 60 normal and 127 brain-operated animals are averaged by class intervals of 5 per cent destruction. The curve is the best fitting one of logarithmic form. For lesions above 45 per cent the number of cases (indicated by numerals on the graph) is too small for reliability (after Lashley and Wiley, 1933)

A possible explanation of this curious effect was that the rat forms concepts of spatial relations in visual terms, as man seems to do, and that the space concepts are integrated in the visual cortex. The visual cortex might then function in the formation of spatial habits, even when the animal loses its sight. To test this Tsang (1934) reared rats blind from birth, trained them as adults

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in the maze, then destroyed the visual cortex. The resultant loss of the maze habit by these animals was as severe as in animals which had been reared with vision. The hypothesis concerning the formation of visual space concepts was not confirmed.

Our recent studies of the associative areas of the monkey are giving similar results to those gained with rats. Visual and tactile habits are not disturbed by the destruction singly, either of the occipital, parietal, or lateral temporal regions, so long as the primary sensory fields remain. However, combined destruction of these regions, as shown in *Figure 8*, does produce a loss of the habits with retarded relearning. Higher level functions, such as the conditional reaction, delayed reaction, or solution of the multiple stick problem, show deterioration after extensive damage

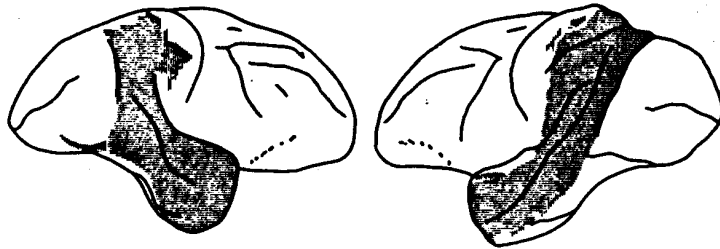


Figure 8. Minimal lesion which produces disturbances in tactile or visual memory in the monkey

in any part of the cortex. The capacity for delayed reaction in monkeys, for example (to remember in which of two boxes food was placed); may be seriously reduced or abolished by removal either of the prefrontal lobes or of the temporal lobes. That is, small lesions, embracing no more than a single associative area, do not produce loss of any habit; large lesions produce a deterioration which affects a variety of habits, irrespective of the sensory-motor elements involved.

Results such as these have led me to formulate a theory of mass action or mass facilitation. It is, essentially, that performance of any function depends upon two variables in nervous activity. The reaction mechanism, whether of instinctive or of learned activity, is a definite pattern of integrated neurons with a variable threshold of excitability. The availability of such patterns, the ease with which they can be activated, is dependent upon less specific facilitative effects. This facilitation can come from a variety of sources. Some instinctive behaviour seems to require hormonal activation, probably a direct chemical effect upon specific nervous

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elements. Emotional facilitation may produce a temporary activation. Continued activity of related mechanisms may facilitate the whole group of associated reactions; a sort of warming up effect.

There are indications (Krechevsky, 1936), although little systematic evidence, that the severity of postoperative amnesia varies with the intensity of motivation. Rats trained in a discrimination without punishment with electric shock for errors may show loss of the habit after lesions which do not produce loss in animals which were trained with punishment. The greater effects of cortical lesions in monkeys than in rats may be in part a result of the greater difficulty in getting consistent motivation in the higher animals. In man an amnesia often seems to be a difficulty rather than impossibility of recall; recall may be possible but only with extreme effort and fatigue. I believe that the evidence strongly favours the view that amnesia from brain injury rarely, if ever, is due to the destruction of specific memory traces. Rather, the amnesias represent a lowered level of vigilance, a greater difficulty in activating the organized patterns of traces, or a disturbance of some broader system of organized functions.

In interpreting apparent loss of memory after cerebral damage, extreme caution is necessary. The poor performance in tasks may be due to the destruction of specific associative connections, but is instead generally, I believe always, the result rather of interference with a higher level functional patterning. Some experiments of Dr. Klüver's (personal communication) illustrate this point. Monkeys were trained in a variety of discriminative reactions calling for use of different sense modalities by a method that required them to pull in the stimulus objects by attached strings. Extensive lesions in different cortical areas all caused loss of these habits. The monkeys simply pulled the strings at random. They were retrained in the discrimination of weights. When this was learned, the habits based on other sense modalities (reactions to intensities of light, for example) returned spontaneously. What had been disturbed by all the operations was the set or attitude to compare stimuli, not the specific memory of which one was correct.

This example perhaps illustrates at a primitive level the characteristic of amnesias as seen clinically. Apparent loss of memory is secondary to a disorder in the structuring of concepts. Some physiological mode of organizing or integrating activity is affected rather than specific associative bonds.

THE COMPLEXITY OF THE MEMORY TRACE

The experiments that I have reviewed deal with only a small part of the whole problem of the memory trace; with those aspects

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which can most readily be studied in experiments with animals. Immediate memory presents a different type of problem. It is highly probable that immediate memory is maintained by some sort of after-discharge of the originally excited neurons. Such persistent activity can scarcely be the basis of more permanent memory, although Ebbecke(1919) and Edgell(1924) have formulated theories of memory in terms of persistent states of excitation. It is by no means certain that all memory is mediated by a single type of mechanism; that motor skills and eidetic images, for example, have any physiological properties in common. The attempt to account for all memory by any single theory involves assumptions which are not supported by any evidence now available.

Much of learning theory has been based upon supposedly isolated and simple instances of association, on the assumption that these represent a primitive prototype of all memory. However, an analysis of even the conditioned reflex indicates that it is not the simple, direct association of stimulus and response that it has been thought to be. I served as experimenter and subject for several years in experiments employing both the salivary method of Pavlov and the motor reactions of Bechterew. The experience convinced me that, far from being a simple sensory-motor reaction, the conditioned reflex is very complicated (Lashley, 1916). The S-R diagram is misleadingly schematic. The effective stimulus is not only the object which the experimenter designates as S, but a whole background of other objects constituting the situation in which the experiment is conducted. Every stimulus has a space setting. When, for example, the rat is trained to react to a triangle, he fails to respond if the figure is rotated through more than 10 to 15 degrees (Fields, 1932). This means that the memory trace of the figure is tied in with the space coordinates of the animal's postural system. This system of space coordinates is a part of the postural reflex system which pervades every aspect of behaviour. There is scarcely a memory which does not have spatial orientation, either with reference to the planes of the body or to external space in addition.

Most skilled acts, from running a maze to playing a musical phrase or speaking a sentence, involve a timed series of actions which cannot be accounted for as a simple chain of conditioned reflexes (Lashley, 1951). The serial timing of actions is among the most important and least studied of behavioural problems. Almost all memories except those of automatized motor habits are dated, as Bergson (1896) has emphasized; that is, they have a temporal position in the series of memories which constitutes the individual's past. The memory trace is associated with this

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series as well as with the particular objects which make up its central core.

The conditioned reflex also includes an element of affective reinforcement. Corresponding to the nature of the conditioning stimulus, there is fear of electric shock, objectively demonstrable by cardiac and respiratory changes, anticipation of acid in the mouth with slight nausea, or expectation of food (Lashley, 1916). Unless this affective element is aroused, the conditioned reflex does not occur. So-called extinction of the conditioned reflex is not a weakening of the specific association, but a waning of this affective reinforcement. Other types of association also have dynamic aspects. The amnesic aphasias seem to be due less to a weakening of specific associations than to a reduction in some general form of facilitation. Henry Head has expressed this as a reduction of 'vigilance', without attempting to define further the nature of the function which is disturbed.

A variety of evidence (McGeoch, 1942) shows that, in a memorized series of nonsense syllables, associations are formed, not only between adjacent words but also between words remote from each other in the series. This, I believe, is an illustration at a primitive level of the fact that every memory becomes part of a more or less extensive organization. When I read a scientific paper, the new facts presented become associated with the field of knowledge of which it is a part. Later availability of the specific items of the paper depends upon a partial activation of the whole body of associations. If one has not thought of a topic for some time, it is difficult to recall details. With review or discussion of the subject, however, names, dates, references which seemed to be forgotten rapidly become available to memory. Head (1926) has given instances of such recall by multiple reinforcement in his studies of aphasia. Although there are no systematic experiments upon this 'warming-up' effect, it is a matter of common experience and is evidence, I believe, that recall involves the subthreshold activation of a whole system of associations which exert some sort of mutual facilitation.

All this is by way of indicating the probable complexity of the memory trace of even the simplest associations. The engram of a new association, far from consisting of a single bond or neuron connection, is probably a reorganization of a vast system of associations involving the interrelations of hundreds of thousands or millions of neurons.

SOME QUANTITATIVE CONSIDERATIONS

It has been customary to assume that, since the nervous system contains so many millions of neurons, there must be a large

reservoir of cells or of synaptic connections which can be modified and reserved for specific memory functions. Dunlap (1930) has expressed the view that every individual has far more brain cells than he is ever called upon to use, and has urged this as an argument against any congenital restriction of ability. A similar view has been implied in the identification of intelligence as the individual's number of unpreempted and available memory bonds. However, only the vaguest sort of anatomic data have been available to support such theories. Analysis of actual cell numbers involved in a reaction system gives little indication of a reserve of unused connections and raises a very difficult question as to the way in which the same system can mediate different functions.

I have counted or estimated the number of cells at different levels in the visual system of the rat. The numbers, which I believe are correct within approximately 10 per cent, are given in Table 1. You will note that there is a marked concentration of paths from the retinal myoids to the lateral geniculate nucleus, such that an average of nearly 300 myoids feed into each thalamo-cortical path. At the cortical level there is some dispersion, but it is not great. In the receptive layer (lamina iv) there are fewer than four neurons for each afferent fibre, and in the whole visual cortex there are only nineteen neurons for each afferent fibre.

The rat's maximal visual acuity is about 30 min. of arc, as determined by behavioural tests and from the resolving power of the lens system. Because of the extreme curvature of the cornea and lens the visual field of one eye subtends about 210 degrees. If acuity were uniform throughout the retina, it would require more than 80,000 fibres to represent each acuity unit of the retina by one central fibre. The concentration of ganglion cells falls off from 130 per hundredth square millimetre at the fixation point to 65 at the ora serrata (Lashley, 1932). Assuming that acuity decreases proportionately, some 40,000 separate paths are required to represent each acuity unit at the cortex by a single afferent fibre. This corresponds fairly well to the 34,000 geniculo-striate paths actually counted. Since acute vision is continuous under light stimulation, it follows that all of the geniculo-striate cells must be firing constantly when the eye is stimulated by the usual lighted environment. Further, since there are not more than nineteen neurons in the visual area for each afferent fibre, it is almost certain that every cell in the striate cortex is firing during light stimulation. Certainly there is no large reserve of cells which can be set aside for excitation only in specific habits.

Corresponding counts of cells in the visual system of the monkey have recently been made by Chow and Blum (personal communi-

cation). The number of neurons in the lateral geniculate nucleus and visual cortex is enormously greater than in the rat, about 1 and 140 millions respectively, but the ratio of cortical cells to central pathways is only 140 to 1, so again there is no great reserve of cells for mnemonic purposes.

The rat is capable of retaining scores, probably hundreds, of visual habits involving discrimination of complex figures (Lashley, 1938), and retention may sometimes be demonstrated a year after training. As I reported earlier, there is good evidence that visual habits are dependent upon the striate cortex and upon no other

Table 1. The number of neurons at each level in the visual system of the rat (unilateral)

Level	Total no. of neurons	Ratio to fibres in radiation
Retinal cells		
Rods	9,180,000	273.0
Cones	120,000	
Bipolar	3,530,000	104.0
Ganglion	260,000	13.1
Lateral geniculate	34,000	1.0
Cortical cells		
Lamina vii	68,000	2.0
Lamina vi	135,400	4.0
Lamina v	147,700	4.3
Lamina iv (granular)	127,000	3.7
Laminae ii-iii	176,000	5.2
Total cortical	654,900	19.2

part of the cerebral cortex. The efferent path from the striate cortex is not known. It is not via cortico-tectile fibres. If by cortico-thalamic fibres, there are far fewer neurons within the thalamic nuclei than in corresponding cortical areas, and there is certainly no reserve of cells there for the storing of memories. There seems to be no justification for assuming that the specific shunting of nervous impulses constituting various memories occurs at some level beyond the visual cortex or that memory traces are stored elsewhere than in the cortex.

If the data on the restriction of visual memory to the striate cortex are correct, and they are supported by a variety of experiments, the conclusion seems inevitable that the same cells which bear the memory traces are also excited and play a part in every other visual reaction of the animal. In all probability, the same

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sort of quantitative relations holds for the other sense modalities.

Even if the associative areas are functional in memory, they do not provide the supposed excess of cells. The visual cortex is directly connected only to a band of cortex directly adjacent, the visuopsychic area of Campbell. The boundaries of this are indeterminate, but it certainly contains no more cells than does the striate area, probably fewer. There is no geometrical multiplication of cells and pathways. Many millions of cells of the striate cortex must be firing constantly into the adjacent area, so that its cells also must be constantly bombarded with nervous impulses and constantly firing. The conclusion is justified, I believe, by such considerations and is supported by electrical studies, that all of the cells of the brain are constantly active and are participating, by a sort of algebraic summation, in every activity. There are no special cells reserved for special memories.

Lorente (1934) has shown that each neuron may bear a hundred or more end-feet or separate synapses. However, considering the enormous complexity of the nervous activity involved in performance of even the simplest habit, it is doubtful that even the multiplication of cell number by a hundredfold will provide separate connections that function only for single specific memories.

The alternative to the theory of preservation of memories by some local synaptic change is the postulate that the neurons are somehow sensitized to react to patterns or combinations of excitation. It is only by such permutations that the limited number of neurons can produce the variety of functions that they carry out. Local changes in the cell membrane, such that combined excitation by several synapses excite the cell, would provide a possible mechanism for such response to patterns, but speculation about this mechanism without direct evidence is likely to be as futile as speculation concerning changes in resistance in the synapse has been.

SUMMARY

This series of experiments has yielded a good bit of information about what and where the memory trace is not. It has discovered nothing directly of the real nature of the engram. I sometimes feel, in reviewing the evidence on the localization of the memory trace, that the necessary conclusion is that learning just is not possible. It is difficult to conceive of a mechanism which can satisfy the conditions set for it. Nevertheless, in spite of such evidence against it, learning does sometimes occur. Although the negative data do not provide a clear picture of the nature of the engram, they do establish limits within which concepts of its

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nature must be confined, and thus indirectly define somewhat more clearly the nature of the nervous mechanisms which must be responsible for learning and retention. Some general conclusions are, I believe, justified by the evidence.

(1) It seems certain that the theory of well-defined conditioned reflex paths from sense organ via association areas to the motor cortex is false. The motor areas are not necessary for the retention of sensory-motor habits or even of skilled manipulative patterns.

(2) It is not possible to demonstrate the isolated localization of a memory trace anywhere within the nervous system. Limited regions may be essential for learning or retention of a particular activity, but within such regions the parts are functionally equivalent. The engram is represented throughout the region.

(3) The so-called associative areas are not storehouses for specific memories. They seem to be concerned with modes of organization and with general facilitation or maintenance of the level of vigilance. The defects which occur after their destruction are not amnesias but difficulties in the performance of tasks which involve abstraction and generalization, or conflict of purposes. It is not possible as yet to describe these defects in the present psychological terminology. Goldstein (1940) has expressed them in part as a shift from the abstract to the concrete attitude, but this characterization is too vague and general to give a picture of the functional disturbance. For our present purpose the important point is that the defects are not fundamentally those of memory.

(4) The trace of any activity is not an isolated connection between sensory and motor elements. It is tied in with the whole complex of spatial and temporal axes of nervous activity which forms a constant substratum of behaviour. Each association is oriented with respect to space and time. Only by long practice under varying conditions does it become generalized or dissociated from these specific coordinates. The space and time coordinates in orientation can, I believe, only be maintained by some sort of polarization of activity and by rhythmic discharges which pervade the entire brain, influencing the organization of activity everywhere. The position and direction of motion in the visual field, for example, continuously modify the spinal postural adjustments, but, a fact which is more frequently overlooked, the postural adjustments also determine the orientation of the visual field, so that upright objects continue to appear upright, in spite of changes in the inclination of the head. This substratum of postural and tonic activity is constantly present and is integrated with the memory trace (Lashley, 1951).

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I have mentioned briefly evidence that new associations are tied in spontaneously with a great mass of related associations. This conception is fundamental to the problems of attention and interest. There are no neurological data bearing directly upon these problems, but a good guess is that the phenomena which we designate as attention and interest are the result of partial, subthreshold activation of systems of related associations which have a mutual facilitative action. It seems impossible to account for many of the characters of organic amnesias except in such general terms as reduced vigilance or reduced facilitation.

(5) The equivalence of different regions of the cortex for retention of memories points to multiple representation. Somehow, equivalent traces are established throughout the functional area. Analysis of the sensory and motor aspects of habits shows that they are reducible only to relations among components which have no constant position with respect to structural elements. This means, I believe, that within a functional area the cells throughout the area acquire the capacity to react in certain definite patterns, which may have any distribution within the area. I have elsewhere proposed a possible mechanism to account for this multiple representation. Briefly, the characteristics of the nervous network are such that, when it is subject to any pattern of excitation, it may develop a pattern of activity, reduplicated throughout an entire functional area by spread of excitations, much as the surface of a liquid develops an interference pattern of spreading waves when it is disturbed at several points (Lashley, 1942a). This means that, within a functional area, the neurons must be sensitized to react in certain combinations, perhaps in complex patterns of reverberatory circuits, reduplicated throughout the area.

(6) Consideration of the numerical relations of sensory and other cells in the brain makes it certain, I believe, that all of the cells of the brain must be in almost constant activity, either firing or actively inhibited. There is no great excess of cells which can be reserved as the seat of special memories. The complexity of the functions involved in reproductive memory implies that every instance of recall requires the activity of literally millions of neurons. The same neurons which retain the memory traces of one experience must also participate in countless other activities.

Recall involves the synergic action or some sort of resonance among a very large number of neurons. The learning process must consist of the attunement of the elements of a complex system in such a way that a particular combination or pattern of cells responds more readily than before the experience. The particular mechanism by which this is brought about remains unknown. From

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the numerical relations involved, I believe that even the reservation of individual synapses for special associative reactions is impossible. The alternative is, perhaps, that the dendrites and cell body may be locally modified in such a manner that the cell responds differentially, at least in the timing of its firing, according to the pattern of combination of axon feet through which excitation is received.

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