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THE ROLE OF PREFRONTAL LOBES IN PSYCHONERVOUS MEMORY IN VERTEBRATES

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Abstract. The memory phenomena are classified into image memory, emotional memory and conditioned reflex memory. It is assumed that prefrontal area is critically involved in the image memory, and in particular, in short-term image memory. On the other hand, both emotional and conditioned reflex memory do not depend on the prefrontal area but they are controlled by other parts of the neocortex and by paleocortex. The intimate nature of both short-term and long-term memory is discussed.

Introduction

We started studying memory in vertebrates as early as 40 years ago when the animal's psychonervous behavior became the object of our investigation. During the last decade I, together with my co-workers at the Institute of Physiology of the Georgian Academy of Sciences and at the Department of Physiology of the Tbilisi State University, conducted a systematic investigation of memory.

For a long time we have been studying memory mainly in mammals: rabbits, cats and dogs; in lower vertebrates (fish, amphibian, reptiles, birds) a systematic study of memory was begun in the last 10 years. And only recently have we started experiments on higher vertebrates — primates.

In all species, experiments were carried out under conditions of free locomotion. The experiments were designed to reveal the animals' ability to remember a new location of food, which is the object of vital importance. A hungry animal was confronted with a food-object, placed in a new location, perceived either with one sense organ or with a complex of organs. We have established the maximal length of delay after which the animal was able to approach the place in which the food had been presented. Memory of this kind was called by us image memory, since the animal's alimentary behavior was controlled by the image of food location.

We have also made a thorough study of memory in respect to the location of an external noxious agent, or of very unpleasant inedible food. We call this memory emotional, since it is mainly determined by emotional experience produced by the object perceived.

When the animal is repeatedly fed in the same place the animal learns to go there, i.e. involuntary (automatic) motor response to that place is established. Thus, being repeatedly exposed to this place, the animal runs there on the stimulus-response principle. Memory of this kind is called by psychologists the motor memory. whereas I call it conditioned-reflex memory, since it is established o nthe basis of temporary connections.

All types of memory based on cortical processes, responsible for perception of the external world, images, and emotional experience are called by us psychonervous memory. Conditioned reflex memory is also called psychonervous, since all the habits and learned movements are established through the formation of temporary connections in higher vertebrates on the basis of image-driven behavior and on the basis of image-directed and conscious activity in man.

As you know, psychologists and physiologists distinguish short-lasting or short-term, and long-lasting or long-term memory. I conventionally denote memory as short-term, if the animal remembers the perceived object for a short time, and this memory is not carried over to the following day. Memory is called long-term, if it is manifested in the subsequent days and weeks and even later after a single perception.

For better understanding of the mechanism of memory we have first determined, by means of extirpation technique, which cortical areas or subcortical structures play an essential or auxiliary role in each of the two types of memory. The areas of the brain which were assumed to be the main substrates of memory were subjected to oscillographic investigation of electrical effects, to reveal physiological peculiarities of neural and neuroglial elements of these areas. On the other hand, these substrates were investigated morphologically by means of light and electron microscopes to establish intracellular and extracellular structural peculiarities of neural and glial elements in comparison with those in other brain areas.

Origin of short-term image memory

Image memory in higher vertebrates is thought to be a function of the neocortex.

We find that in the neocortex perception of an external object occurs through the activation of stellate neurons in layers IV and III of the perceptive areas in which an appreciable part of afferents from the receptors terminates. Perceptive areas are the so-called primary projection areas, e.g. field 17 in the visual area and medial part of the ectosylvian gyrus in the auditory area.

In higher vertebrates the axonal ramifications of a considerable part of stellate neurons terminate on their own dendrites. I think that excitation of these stellate neurons with pericellular axon net elicits subjective experience of that modality which corresponds to the stimulated receptor. The stellate neurons of this kind are called by us sensory. They have either no axonal connections with other stellate neurons, or these connections exist with regard to adjacent stellate neurons. In this way a glomerule of stellate neurons of the same sensory modality is formed. Owing to it, perception is not diffuse, but strictly corresponds to the object perceived.

In the mammalian cortex there exist also sensory stellate neurons with pericellular network whose axons leave the cell and terminate on the stellate cells of Cajal and on the pyramidal cells of Meinert. Axons of these cells leave the boundary of the cortex and terminate in the middle brain in the coordinating apparatus of the neck and eye muscles. This implies that these sensory neurons participate in the performance of orientation movement of the head and eyes (*see* Beritov 1965, 1969).

It is assumed by us that subjective experience, or sensation, caused by excitation of stellate cells does not depend on pericellular network, but on peculiar intracellular molecular and submolecular processes. The pericellular network has probably been developed for repeated self-excitation of the cell which, perhaps, regulates the intensity of subjective experience.

This concept may be supported by the character of the intracellular structure of stellate neurons. In fact, electron microscopic study of sensory stellate neurons in different cortical areas, made by our co-workers, has shown that the fine structure of stellate neurons differs from that of other cortical nerve cells, especially of the pyramidal neurons. Cytoplasm of stellate cells is light and small in volume; the nucleus and nucleolus, on the contrary, are much larger in comparison with the volume of the cytoplasm; the cytoplasm contains a few polysoma and small mitochondria. Presence of flattend cisterns of various length is rather typical. There is a great number of wide pores in the nuclear sheath. In general, there are fewer synapses on the soma of stellate cells as compared with pyramidal cells. However, on the contrary, in layer IV of the visual and auditory areas more synapses are on the sensory stellate cells than on the pyramidal ones (Mikeladze and Kakabadze, in press).

All these peculiarities of the fine structure of stellate cells indicate that their basic function is not the integration of excitation, as is the case with pyramidal neurons, but a higher function consisting in subjective experience produced by the perceived objects.

We attach considerable importance to the occurrence of a large number of synapses on the soma of sensory stellate cells in layer IV of the perceptive areas. This lends support to our concept, as it will be pointed out below, that stellate cells are being excited not only by afferent impulses from the receptors, i.e. by perception, but also through the associative and internuncial pyramidal neurons from the entire cortex during reproduction of images.

There are also stellate cells with no pericellular network. They are encountered in all the cortical areas and in all nuclei of the brain, as well as in the spinal cord. These cells, like internuncial pyramidal neurons, serve to transmit excitation from afferent to efferent neurons.

Afferent pathways from the receptors terminate in the primary perceptive area not only on the stellate cells but also on internuncial pyramidal neurons, axonal branches of which end on the adjacent sensory stellate neurons. Owing to this, perception of an object produces activation of the internuncial pyramidal neurons together with the sensory neurons, providing the integration of the excited sensory neurons. Therefore, these internuncial pyramids may also mediate unitary subjective experience evoked by an acting object. These internuncial neurons are connected by collaterals, on the one hand, with the Cajal and Meinert cells responsible for the orientation reaction, and on the other hand, with adjacent associative pyramidal neurons which send axons to the appropriate secondary zones — to field 18 in the visual area, or to sylvian and suprasylvian gyrus in the auditory area. In these areas internuncial pyramidal neurons become activated and convey excitation to the associative neurons, whose axons end in the primary area and activate the same stellate and pyramidal neurons which have been activated by afferent impulses. The excited associative neurons again convey excitation to the secondary zones. Thence excitation again recurs through axons of the association neurons into the primary area, and this reverberation of excitation proceeds continuously in a high rhythm up to 50 per sec and upwards. Reverberation of excitation in the given nervous circuits may last after cessation of stimulation, until under the influence of a new external agent reverberation of excitation is elicited in other nervous circuits. Then the previous reverberation is discontinued due to inhibition of its nervous circuits through collaterals of the newly excited circuits.

Since reverberation of excitation in the nervous circuits outlasts stimulation of receptors, the sensory stellate neurons continue to be excited after this stimulation is over. *Thus the subjective experience, which is* *the image of the object perceived, is retained throughout the reverberation of excitation.* This reverberation in the nervous circuits produces an increase of the transmitter released from presynaptic vesicles, which, by acting on postsynaptic membrane causes its activation. It is known that the accumulation of presynaptic vesicles increases during reverberation of excitation and it is maintained for several minutes after stimulation (Smirnov 1967). Thus it may be suggested that their operation continues for some time after reverberation has been ceased. This does not produce excitation, but causes a prolonged increase of excitability of synaptic apparatus. Owing to this, the nervous circuits and the relevant stellate neurons may become activated some time after perception. It is this period of reveberation of excitation between the primary and secondary areas and the subsequent period of increased excitability within the activated synaptic apparatus of associative neurons that is supposed to underlie short-term memory (Beritov 1971).

On nervous substrate of short-term image memory

We made a thorough study concerning the problem of which areas of the cortex and which nervous elements in these areas have essential significance in the transient retention of the objects perceived. We have pointed out above that one of the cortical areas concerned is the secondary perceptive area.

However, the memory of the perceived food-objects even to a greater extent depends on other cortical areas, in particular, on the proreal gyrus of the prefrontal lobes. The homologous area in monkey is the prefrontal granular area, studied by us in *Papio Hamadryas.* Its cells are distinguished by slender processes and a great variety of the neuronal patterns, as compared with that in cats. Some of the cells are lighter and others darker. The lighter cells are round and more frequent than the darker cells. They are distinguished by their inner content; they are rich in mitochondria and crysts, lacking free ribosomes. The darker cells are triangular or more extended. The somas of lighter and darker cells, as well as their dendrites, are characterized by peculiar submolecular and molecular organization of synaptic apparatus (Mikeladze 1971). This peculiar structural organization of the granular area undoubtedly has a direct relevance to memory. Elucidation of particular functional significance of each particular structure is the subject of our future study.

The proreal gyrus in cats and dogs is one of the most converging sites in the neocortex. Afferent pathways from all the receptors impinge upon this area, mainly through the reticular formation. As seen from the oscillographic investigations, afferent impulses from the subcortical structures not only activate various neurons of the proreal gyrus, but also facilitate their spontaneous activity. These afferent impulses from different receptors activating various neurons frequently converge on the same neuron (Ioseliani et al. 1971, Gvilava 1971).

Oscillographic studies have demonstrated that the proreal gyrus, for its part, influence the activity of the cerebral cortex, as well as the subcortical structures (Akhmetelashvili 1971).

Bilateral connections between the cortex of the proreal gyrus and subcortical structures have been well established also morphologically by means of degeneration of corticofugal nerve fibers following the ablation of the proreal gyrus (Kiknadze 1968, Mikeladze and Kiknadze, in press).

Facilitatory influence of afferent innervation from the subcortical structures on the proreal neurons occurring simultaneously with their excitation via associative fibers from the receiving areas of the cortex seems to have an important role in the formation of nervous circuits which underlie the maintenance and reproduction of images of the objects perceived.

If the proreal gyrus is ablated in cats and dogs, or the prefrontal granular area is removed in monkeys, short-term memory for perception of food by any sense organ is strongly deteriorated for some time after surgery. It recovers with the lapse of time, but does not attain the preoperative level even in several months. It has been found that the impairment of short-term memory, depends, to some extent, on impairment of attention, increased motility, or motor perseveration. After recovery of attention and normal locomotion and disappearance of perseveration, short-term memory is partially restored (Beritashvili et al. 1968*ab*).

The recovery of short-term memory following ablation of the proreal gyri is probably due to the activity of other substrates of memory. Such deduction can be made from the following observation: if after ablation of the proreal gyri the secondary auditory area is also removed, the restoration of short-term memory for sound perception occurs to a considerably lesser degree, than after removal of the proreal gyrus alone (Aivazashvili 1971). From our experiment it is evident that ablation of the secondary visual or auditory perceptive areas leads to memory deficit only for perception of the corresponding modality. Thus, for instance, ablation of fields 18 and 19 in the visual cortex results in a temporary memory deficit only for visual perception of the food location. It is evident that after ablation of the proreal gyri restoration of memory takes place partially owing to the secondary perceptive areas.

Further on it has been shown that in dogs not only the proreal gyri, but also temporal lobes have an important role in the retention of the perception of the food-objects. Short-term memory becomes greatly impaired following bilateral ablation of sylvian gyrus and the middle and posterior portions of ectosylvian gyrus. The restoration of image memory for visual perception of food location took several months. Maximal length of delay after surgery was only 5 min as compared with 20 min pre-operatively. Short-term memory of a complex perception of food location is also severely impaired. The operated dogs approached the food location after the delay of 9–10 min, while the intact animals did it after 40 min (Natishvili and Sikharulidze 1969).

Participation of the temporal lobes in mnestic phenomena has been shown also in monkeys. Ablation of the so-called inferotemporal region impairs the visual discrimination learning and retention (Pribram and Mishkin 1955).

In general, all those neocortical areas in which there occurs a convergence of afferent impulses from the receptors stimulated by the given object, are responsible for image memory of external objects. As a matter of fact, such convergence occurs, to some degree in every area of the neocortex. This obviously explains a total memory deficit, which does not recover at all, following ablation of the entire neocortex or by sectioning both ascending and descending cortical pathways, i.e. as a result of functional decortication of the animal.

On the basis of these observations we have come to the conclusion that in higher vertebrates the whole neocortex is responsible for image memory. It may be suggested that the pyramidal neurons in the proreal gyri in dogs, or in the prefrontal granular area in monkeys, and generally in all those areas where convergence of afferent pathways occurs, play an important role in short-term retention of images of the objects perceived. It is well known that like pyramidal neurons of the secondary projective areas, certain associative and internuncial pyramidal neurons of the proreal gyri are also excited by perception of the external world, both directly by afferent impulses from the receptors, and through the activated primary projective areas. Excitation of these associative pyramidal neurons of the proreal gyri recurs to the primary and secondary perceptive areas directly or through the internuncial pyramidal neurons. Between these cortical regions reverberation of excitation also occurs. This reverberation must produce stable functional changes in the synaptic apparatus of pyramidal neurons in the proreal, as well as in the secondary areas. Namely, reverberation produces a considerable increase in the number of presynaptic vesicles in the synaptic apparatus, and consequently, a more or less prolonged activation of the transmitter with a prolonged increase in neuronal excitability. At the same time certain projective pyramidal neurons in the proreal gyri are activated through these reverberating circuits, evoking the appropriate alimentary behavior through the caudate nucleus and other subcortical structures. On the other hand, certain sensory stellate neurons in the perceptive areas, responsible for the reproduction of the image of the perceived food-object and its location, become activated.

As long as the state of increased excitability in the synaptic apparatus of pyramidal neurons continues in the proreal gyri some elements of the food-object or its environment excite approximately the same reverberating circuits, reproducing the image of food and its environment and producing the same alimentary behavior; this would be a manifestation of short-term delayed response.

What has been said before does not imply that other regions of the brain, beside the neocortex, play no role in short-term image memory. In fact, all subcortical structures, like the caudate nucleus, archipaleocortex, thalamus, hypothalamus, reticular formation, or cerebellum, which have direct or indirect connections with the neocortex, are also involved in memory.

The length of short-term memory can be estimated in terms of delayed responses. Yet, the maximal retention length of image of a single perception of food location can hardly be judged by the maximal length of time elapsed between the perception and the onset of the relevant alimentary behavior. We know that when starting experiments on rabbits in a new experimental situation, the maximal duration of the delay period after visual perception of food is not longer than 20–25 sec. However, after a month's work in this situation, the delay period may be protracted till 2–3 min, and in later stage of training till 8–10 min. This indicates that although the animal may have the image of food location, this image cannot be utilized because stimulation from the new experimental situation results in general motor inhibition (Beritov 1965, 1969, 1971).

On the origin of long-term image memory

Long-term memory for food location is manifested only in those cases when perception of food occurs in an entirely new situation and elicits both orientation reaction and considerable emotional excitation. This occurs in case of complex perception of food, including its smell and taste. This memory, observed in birds and mammals, is directly associated with the development of the neocortex.

According to our view, the origin of long-term memory in higher vertebrates may be interpreted in the following way.

Both short-term and long-term memory is based on reverberation of excitation in the nervous circuits which connect perceptive neurons, through the associative pyramidal neurons, with the projective efferent pyramids, responsible for motor effects through the subcortical structures.

In case of visual perception of food, only the visual area is connected with these projective neurons, while in the case of a complex perception, the connection is established also with the olfactory and gustatory areas. It may be suggested that within the associative pyramidal cells stable molecular and submolecular changes with participation of nuclear and ribosomal RNA should take place. As a result, a special protein should be synthesized in the cell and certain enzymatic reactions should take place, regulating the changes of amine and electrolyte distribution (Kometiani, in press). Probably this process produces stable functional changes of the postsynaptic membranes, facilitating for a long time transmission of excitation from the synaptic terminals to the cell.

A particular image of the object perceived, is however not coded in those associative pyramidal neurons in which these intracellular changes of proteins and a prolonged facilitation of synaptic transmission have occurred, but rather within the system of associative neurons which have been activated by that object, through receptors (Kometiani, in press).

Such intracellular and membranous changes in the cortical associative neurons should occur in the effect of a single visual or auditory perception; these changes, however, are so short-lasting that the facilitatory influence on the conductivity of postsynaptic membranes in rare cases outlasts the accumulation of the synaptic transmitter. On those occasions when the membranous changes outlast this accumulation, the intracellular and membranous changes should also participate in long-term memory. Under certain circumstances, memory for visual perception of food location may be observed in dogs for several hours after perception, in monkeys for several days, thus indicating that visual memory is essentially long-lasting (Beritov 1969, 1971).

On nervous mechanism of emotional memory

Emotional memory has been studied by us in respect to the location of fear producing stimuli and very unpleasant inedible food in all species of vertebrates.

Fear emotion arises in an animal after the action of a painful stimulus. When the animal is repeatedly exposed to environment in which this stimulus was operating, the animal tries to avoid this environment.

We have studied emotion of fear of the location of noxious electrical stimulation delivered to the nose during eating. All vertebrates exhibited fear of the place of the food and its situation, following a single noxious stimulation delivered during eating. It is known to us that in mammals, following ablation of the neocortex, emotion of fear is exhibited as distinctly and strongly as in normal animals. It follows that in mammals the nervous substrate for the fear emotion, i.e. the sensory neurons responsible for subjective experience of fear, are located in the archi- and paleocortex, that is in the limbic system. Apparently, in the limbic system the integrative mechanism responsible for motor expressions of fear is localized (Beritov 1965, 1969).

We assume that any strong unusual stimulation results in activating both the sensory and integrative motor mechanisms of fear localized in the limbic system. But concomitantly the neocortex is activated too. As an effect, the image of external stimulus and its situation emerges. The activated neuronal complex in the neocortex is associated with a similar neuronal complex in the limbic system. These connections are steady, and they are based on the intracellular and membranous changes in the associative and projective neurons which convey excitatory impulses from the neocortex to the limbic system.

Our experiments have demonstrated that the substrate of long-term emotional memory of fear is, apparently, located in the proreal gyri and temporal lobes, since the fear reaction may be elicited by electrical stimulation of these structures (J. M. Aivazashvili, in preparation). It is evident from our experiments that the proreal gyri are connected by efferent primary pathways with the limbic system, where the sensorimotor centers for the fear reactions are localized (Kiknadze 1968).

Once the animal experienced fear in a certain situation, later on, perception of this situation, or its part, would produce the same fear emotion. It is clear that a prolonged retention of the fear emotion in mammals depends on long-term image memory for the location of the noxious agent. In cats and dogs fear emotion, produced by strong electrical stimulation in a given situation, can be elicited several weeks later (Bregadze 1948).

In contradistinction, when a weak noxious stimulation is delivered during eating, avoidance of the given feeder may be manifested only for several minutes. In this case we are confronted with short-term emotional memory, which, perhaps, is subserved by a prolonged increase of excitability in synaptic apparatus of integrative neurons situated in the archi-paleocortex responsible fo fear reaction.

After removal of the neocortex or undercutting its afferent and efferent pathways the disruption of both short-term and long-term image memory take place. On the other hand, only long-term emotional memory induced by the situation with noxious stimulation is impaired after these lesions, whereas short-term emotional memory, based on the increase of excitability of the synaptic apparatus of the archipaleocortex, is maintained.

Following ablation of the neocortex, noxious stimulation delivered at the time of eating results in the increase of excitability of the sensory neurons responsible for the fear reaction with a prolonged after-effect. Subsequently, repeated exposure to this situation may activate these sensory neurons and evoke fear reaction. It must be pointed out that the maximal length of delayed fear reaction in this case depends upon the intensity of stimulation. In ranges from several minutes to several hours. We have reasons to think that this maximal span of time in delayed fear reaction is accounted for by prolonged functional changes in the integrative neuronal mechanism of fear in the limbic system. These changes are supposed to consist in a prolonged increase in transmitter excitability of the synaptic mechanism.

Nervous mechanism of conditioned reflex memory

Conditioned reflex memory has been studied primarily in respect to conditioned feeding behavior. This behavior was established by way of repeated reinforcement of indifferent stimuli — sound, or light — with presentation of food (unconditioned stimulus) in the same situation. In the presence of conditioned signal, the animal runs rapidly towards food due to the reproduction of image of its location. If the conditioned stimulus is repeatedly reinforced by food, structural and functional changes of the synaptic apparatus in the excited association circuits of the brain develop to such an extent that any stimulus accompanied by food intake becomes sufficient to activate these circuits resulting in the animal's approaching food location. In that case the image of the food location does also emerge, but it does not control any longer the alimentary behavior. If the experimental situation is changed, e.g., an obstacle is placed on the direct route to the food conditioned automatic response cannot be performed, being replaced by the image behavior: the animal approaches the location of the food according to the conditioned reflex mechanism until the obstacle is reached. At this moment, the conditioned reflex ceases to operate — the animal stops, and then goes around the obstacle reaching the location of food according to its image (Beritov 1965, 1969, 1971).

If automatized alimentary conditioned behavior is firmly established, it is preserved for days and months. We call this phenomenon conditioned reflex memory. The more numerous are the food reinforced trials in the given situation and the higher the animal's phylogenetic development, involving the better developed synaptic mechanisms in the excited neuronal circuits, the longer is this behavior preserved.

Nervous mechanism of conditioned reflex memory has been studied for defensive reflex of flexion of the dog's forepaw. We have studied structural and physiological changes of efferent part of forward temporary connections, i.e. motor cortical area, which mediated the conditioned flexion of the forepaw. It has been found that in the associative and projective pyramidal cells of the motor area there are observed definite morphological changes: bud-like outgrowths on presynaptic fibers and even newly grown nerve terminals (Kuparadze 1965, Kuparadze and Kostenko 1971, and in press). It was further found that during the formation of motor conditioned reflex of the forepaw flexion, the number of pyramidal cells with high concentration of RNA in the cytoplasm is increased in III and IV layers of the corresponding motor area, as well as in the giant pyramidal cells of Betz type in layer V. Simultaneously, the content of RNA is increased in the glial satellites of pyramidal cells (Svanidze et al., in press). In the same area, there occurs doubling of the number of capillaries and doubling or even tripling of the amount of glial elements (Kuparadze 1965, Kuparadze and Kostenko 1971, and in press). Obviously the intensified blood circulation plays an essential role in the development of synaptic apparatus. We have reasons to believe that the glial elements also play important role in the development of synaptic apparatus. It is suggested that myelinization of new presynaptic fibers, as well as intensified myelinization of the old ones is accomplished by glial satellite cells which envelope with their processes these nerve fibers (Roitbak 1969). As is well known, the thicker the myelin sheath, the higher is the conductivity of excitation in these nerve fibers.

All these structural changes provide better conditions for the excitation of pyramidal neurons in the motor area through the old and newly grown synaptic terminals, for the formation in these terminals of a large amount of transmitter, and for the transfer of the transmitter through the synaptic clefts and activation of postsynaptic membranes. All these structural changes are likely to play an important role in the formation of temporary connections and in their preservation in all types of conditioned reflexes including trained movements.

Thus, the main substrate of conditioned reflex memory with regard to defensive limb movement is the motor area in the neocortex.

Conditioned defensive reflexes are not impaired after bilateral ablation of the proreal gyri: the established reflexes are preserved and new reflexes are formed involving the same or different limbs as easily as in unoperated animals. Thus, it may be concluded that the proreal gyri are not essential in the formation of conditioned defensive reflexes.

Similarly, proreal gyri do not participate in the formation of conditioned alimentary behavior and in various kinds of learned instrumental movements performed in the course of this behavior. Following ablation of the proreal gyri, conditioned signals evoke alimentary behavior, i.e. running to the signalled feeder and the instrumental movements of its opening, as in normal animals. Delayed responses to these signals are, however, much impaired. During the first month after the operation the animals (dogs or cats) after being released from the cage do not run toward the feeder 10–15 sec after the cessation of the signal. Only in 3–4 month's do they respond to the signal with 3–4 min delay. Before the operation they were able to respond correctly after 10–12 min delay (Beritov 1969, 1971, Aivazashvili 1971).

The question arises which areas of the brain are responsible for the specific plastic changes involved in conditioned reflex memory for alimentary behavior.

It may be maintained that the structural changes, as pointed out above, occur in the first place in the synaptic apparatus of the associative and projective pyramidal cells (in the olfactory, gustatory, visual, motor and other analyzers of the cortex) which are excited at each food-intake. These excited cells interact with those associative and internuncial pyramidal neurons which have been excited by conditioned stimuli including the entire environment, where food-intake has taken place. Moreover, similar structural changes presumably take place in the synaptic apparatus of subcortical structures in which the axons of projective pyramidal neurons, excited through the temporary connections and responsible for alimentary behavior, terminate.

Since the prefrontal area includes also the orbital gyri where afferent fibers from the gustatory receptors terminate, and where the projective pyramidal neurons involved in the act of eating are located, it may be suggested that the structural changes of synaptic apparatus, which underlie the formation of temporary connections responsible for the act of eating occur in the orbital gyri.

Conditioned reflexes in cats and dogs, both alimentary and defensive, can be also established after ablation of the neocortex, but with more difficulty than in normal animals (Ordjonikidze and Nutsubidze 1959, 1961, Kvirtskhalia 1971). Temporary connections are formed in the archipaleocortex with the pyramidal neurons integrating emotional fear reactions (*see* Beritov 1965, 1969).

Apparently, during the formation of conditioned reflex flexion, structural changes of the synaptic apparatus occur in the integrative pyramidal neurons in archipaleocortex similar to those occurring in the sensorimotor cortex. It may be assumed that in normal animals during elaboration of conditioned defensive reflex temporary connections are established with the projective pyramids of the motor area in the neocortex, responsible for the flexion of the limbs, as well as with the integrative pyramids for the fear reaction in the archipaleocortex. Naturally, if the neocortex, or only the sensorimotor area is ablated, the isolated flexion of the limb and in general, instrumental movements of the foreleg are observed neither with conditioned nor unconditioned stimulations, for the motor reactions of this kind are mediated only through the sensorimotor area of the neocortex.

For instance, if a conditioned stimulus is combined with electrical stimulation of the foreleg eliciting flexion of that leg, the isolated conditioned leg flexion will not be extablished even after 150 trials; instead, the conditioned stimulus evokes only general motor excitement with extensor responses of the other limbs, thus, manifesting fear emotion (Khananashvili 1971).

Summary

The proreal gyri in cats and dogs, and the granular areas of the prefrontal lobes in monkeys are main nervous substrates of short-term image memory, lasting no more than several dozens of minutes.

It is suggested that short-term memory of a food-object of biological importance mainly depends on a prolonged increase of excitability in the synaptic apparatus of the nervous circuits excited by this object. This increase seems to occur in the effect of a prolonged and augmented action of a chemical transmitter, released during excitation from the presynaptic vesicles, on the postsynaptic membrane.

Long-term memory of the object of biological importance, preserved for days and weeks, depends on the formation of intracellular active protein in the pyramidal cells of the excited nervous circuits responsible for stable plastic changes of the postsynaptic membranes.

Both types of image memory are formed in mammals exclusively in the neocortex, the proreal gyri and inferotemporal lobes playing a main role. Following ablation of these gyri, short-term memory is impaired and partially recovers in several weeks; on the other hand, long-term memory is much less affected: it is present during a total absence of short-term memory.

Emotional memory produced by the action of a painful agent, preserved for days and weeks as the emotion of fear, is localized in neocortex and paleocortex. The permanence of this memory depends on the neocortex being concerned with the image of the spatial location of painful agent. The archipaleocortex, on the other hand, is responsible for emotional experience and its overt manifestations. Following ablation of the neocortex, long-term emotional memory is abolished, while short-term

memory is preserved; its duration depends on the strength of the noxious stimulation.

Prefrontal lobes are not critically involved in conditioned reflex memory, i.e. in the formation and preservation of conditioned reflexes or learned movements. Conditioned reflex memory depends on structural and functional development of synaptic apparatus in the activated nervous circuits responsible for the formation of the temporary connections. This occurs all over the cortex, being considerably weaker in the paleocortex.

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