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AMYGDALOID COMPLEX OF THE MACAQUE

Antoni SMIAŁOWSKI

Department of Comparative Neuroanatomy, Jagiellonian University, Kraków, Poland

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The amygdaloid complex lies above the dorsomedial portion of the pyriform lobe, extending from the anterior commissure to the descent of the stria terminalis and the tail of the caudate nucleus. Dorsally it comes into contact with the anterior commissure, putamen, substantia innominata, and optic tract. Laterally to the amygdaloid complex are the ventral portion of the claustrum and the tail of the caudate nucleus, from which it is separated by bundles of fibres of the stria terminalis. The external capsule marks out the ventral and ventrolateral boundary, while on the ventromedial side the amygdaloid complex borders upon the pyriform cortex, severed from it by a layer of fibres, which are a continuation of the external capsule. The caudomedial and caudodorsal wall of the inferior corner of the lateral ventricle and Ammon's horn border the complex caudally.

The amygdaloid complex has been the object of interest of neuroanatomists for long. One of the first authors to work in this field was Völsch (1910), who described the amygdaloid complex of the ferret *Mustella putorius furo*, the lemur *Lemur catta*, and the macaque *Macacca mulata*. Craigie (1925), Guardijan (1947), and Brodal (1947) studied the amygdaloid complex of the rat, Humphrey (1944) did this for the short-tailed shrew *Blarina brevicauda* and adult man, and Maksymowicz (1963) made the wax model of the amygdaloid complex of the dog. Lauer (1945) and Castellanos (1949) described the amygdaloid complex of the macaque. They differentiated in it a number of nuclei using cytoarchitectural criteria.

MATERIAL AND METHOD

A model of the amygdaloid complex was made on the basis of a series of frontal sections of a macaque brain cut at 20 μ and stained by the methods of Klüver-Barrera and Nissl. A sagittal series stained by the same methods and

another series of frontal sections cut at 50 μ and stained according to the Weigert method were used to check the findings. Every 16th section was drawn magnified 20 times. The ready model was painted white and next the whole model and its particular nuclei were weighed and the relative size of each nucleus calculated as a percentage of the whole amygdaloid complex.

OBSERVATIONS

The amygdaloid complex of the macaque comprises the majority of nuclei described in other mammals. They differ in the size and stainability of cells and the density of fibres. The attempt of the present work was to distinguish the nuclei making up the amygdaloid complex and to make their wax model. This model may be of use in neurophysiological studies since the boundaries of the nuclei are very obscure and hard to mark out. The criteria of division were the size of cells, their stainability and arrangement in the nuclei, and the course of fibres within them.

Basal Nucleus (Figs. 1—9, NB)

The basal nucleus is the largest in the amygdaloid complex of the macaque. It is oval in shape and situated centrally. The weight of this nucleus forms 45% of the total weight of the macaque amygdaloid

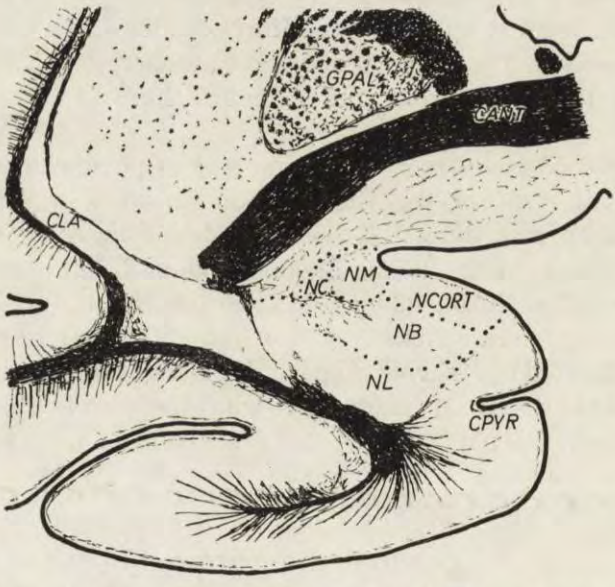

Fig. 1. Transverse sections through the macaque amygdaloid complex
The boundaries of the nuclei marked with dotted-lines

complex. Orally it is bounded by large intercalate nucleus I, which lies at the level of the anterior commissure in the anterior portion of the complex, and caudally reaches the level of the descent of the stria terminalis and the tail of the caudate nucleus. Laterally and ventrally the basal nucleus neighbours on the lateral nucleus and ventromedially it is separated from the pyriform cortex by a bundle of fibres of the external capsule. Dorsomedially the basal nucleus borders on the cortical nucleus, but this boundary is difficult to trace, there being only a small number of fibres on it. Dorsally the basal nucleus is accompanied throughout its length by the medial nucleus and laterally by the central except for the place where intercalate nucleus II appears among the medial, central, and basal nuclei.

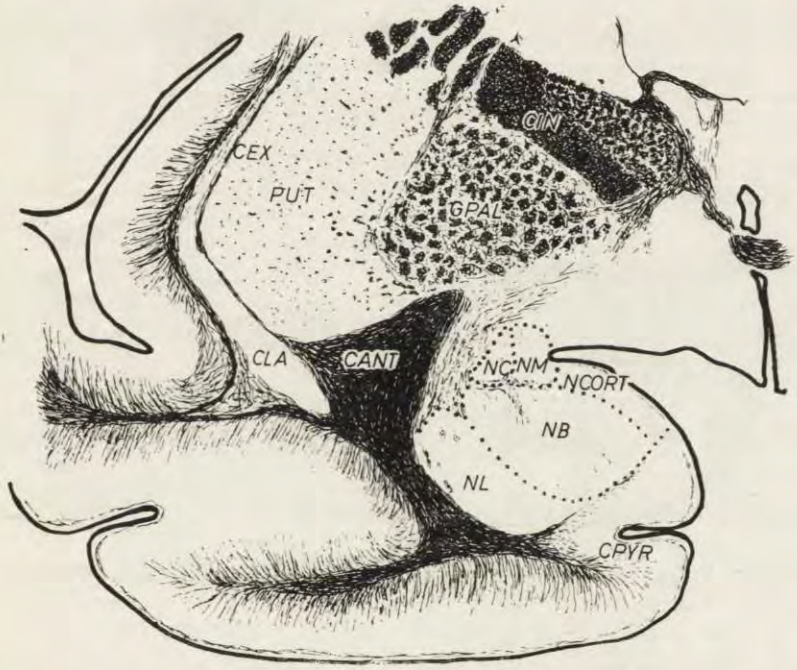

Fig. 2. Transverse sections through the macaque amygdaloid complex
The boundaries of the nuclei marked with dotted-lines

Cytoarchitecturally the basal nucleus can be divided into two parts: a large-celled ventrolateral portion and a small-celled dorsomedial portion. Many authors apply more complicated divisions of this nucleus in their studies. In the present work both of the parts were modelled together as a single nucleus. The cells of the large-celled portion are about 20 μ in diameter, those of the small-celled portion about 13 μ.

Cortical Nucleus (Figs. 1—8, NCORT)

The cortical nucleus is flat and lies in the dorsomedial part of the amygdaloid complex, on its medial surface. It is a sector of spherical cap resembling a trapezium in shape. Its weight makes about 11% of the total weight of the amygdaloid complex. The cortical nucleus is bordered by the pyriform cortex ventrally. On this boundary there is a group of cells, which many authors (Humphrey 1941, 1944, Lauer 1945, Castellanos 1949) described and called the cortico-amygdaloid transition area. This region is very interesting, for it is due to it that

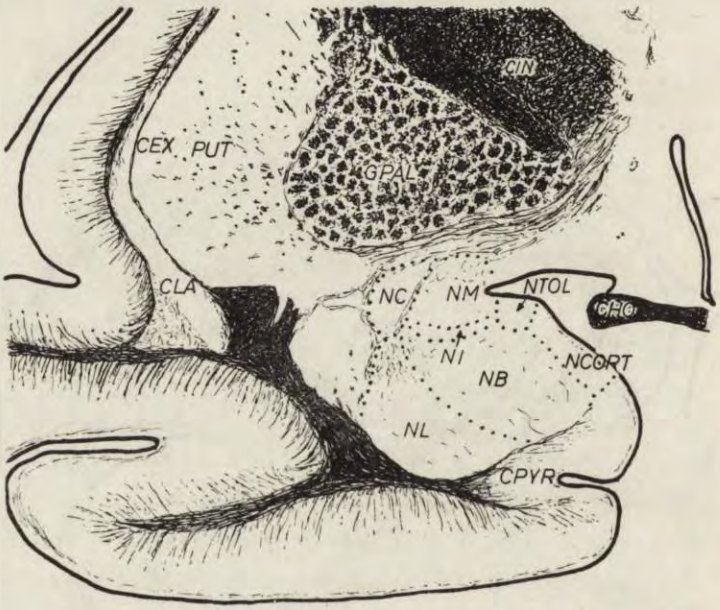

Fig. 3. Transverse sections through the macaque amygdaloid complex
The boundaries of the nuclei marked with dotted-lines

the connection between the amygdaloid complex and the pyriform cortex is maintained. It is present not only in the macaque, but also in other mammals. In this study the boundary between the amygdaloid complex and the pyriform cortex was marked out across the middle of this system, because it is difficult to determine definitely where it belongs. The cortical nucleus differs from the pyriform cortex mainly in its lack of the stratified arrangement of cells, which is typical of the cortex. The cells of the cortical nucleus are 10 μ in diameter and they show no regularity in arrangement. Ventrolaterally, the basal nucleus underlies the cortical

throughout its length except for the caudal part, as the cortical nucleus ends somewhat orally to the end of the basal nucleus. This boundary is hard to trace, there being hardly any fibres there. Dorsally to the cortical nucleus is the medial nucleus separated from it by some fibres of the

Fig. 4. Transverse sections through the macaque amygdaloid complex
The boundaries of the nuclei marked with dotted-lines

stria terminalis. This is not true of the region where the nucleus of the lateral olfactory tract comes in between the cortical nucleus and the medial. Dorsomedially the cortical nucleus neighbours upon the lateral ventricle, making its wall.

Medial Nucleus (Figs. 1—7, NM)

This is an elongate nucleus resembling a cylinder in shape. It begins in the anterior portion of the complex and extends throughout it, ending together with the basal nucleus in the rear. Its weight amounts to 9% of the weight of the amygdaloid complex. The medial nucleus lies in the dorsal portion of the complex and is bounded by the cortical nucleus ventrally and the substantia innominata dorsally. Laterally it is severed by a bundle of dorsoventral fibres from the central nucleus and medially adjoins to the optic tract, forming the medial corner of the ventricle more caudally. In the middle part of the amygdaloid complex the nucleus of

Fig. 5. Transverse sections through the macaque amygdaloid complex
The boundaries of the nuclei marked with dotted-lines

the lateral olfactory tract lies between the medial nucleus and the cortical and the flat intercalate nucleus II between the medial nucleus and the basal.

Central Nucleus (Figs. 1—6, NC)

The central nucleus extends in the dorsolateral portion of the amygdaloid complex. It lies between the basal nucleus on the ventral side and the substantia innominata and putamen on the dorsal side. Laterally it neighbours on the tail of the caudate nucleus, separated from it by some accumulations of fibres, and medially on the medial nucleus. The central nucleus is elongate, irregular in shape, and its orocaudal length is somewhat smaller than that of the medial nucleus. Its weight forms 5% of the weight of the amygdaloid complex.

Intercalate Nuclei (Figs. 3, 6, and 8, NINT, NI)

Among the nuclei of the amygdaloid complex there are small accumulations of nerve cells. Völsch (1910) described them as accumulations of glial cells. Johnston (1923), in conformity with the modern opinions, treats them as real nerve cells. Sanides (1957) regards the intercalate nuclei (massa intercalata) in man as fragments broken

off the island of Calleja and claims that they are scattered throughout the corpus striatum. Their nature is not quite clear. They are always connected with the accumulations of fibres, which indicates their associational nature. The number of fibres inside the intercalate nuclei is small.

The accumulations of the intercalate nuclei were described in man and in many lower mammals. In the macaque there are a few accumulations of cells of this type. In the anterior portion of the amygdaloid

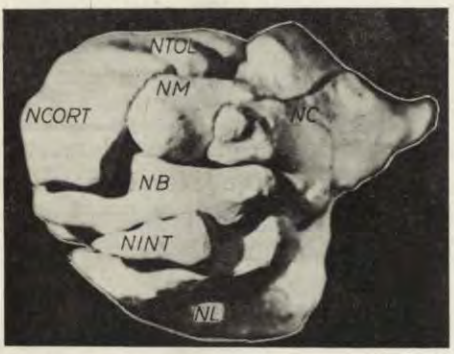

Fig. 6. A photograph of the model of the left amygdaloid complex of the macaque
Frontal view

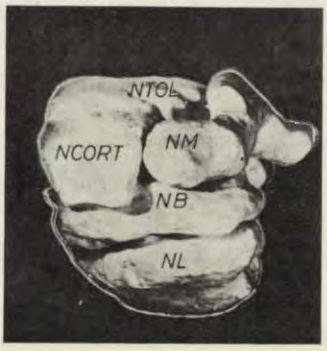

Fig. 7. The model of the left amygdaloid complex of the macaque with the central nucleus and intercalate nucleus removed

complex is large intercalate nucleus I (NINT), which forms the oral boundary of the basal and lateral nuclei. The other nucleus modelled is intercalate nucleus II (NI). It is smaller than the first and lies in the central portion of the amygdaloid complex, pressed in between the basal nucleus on the ventral side, the medial nucleus on the dorsal side, and the central nucleus on the lateral. Castellanos (1949) described a few other accumulations of intercalate mass between the lateral nucleus and the striatum. These, however, have been left out in accomplishing the model on account of their small size. The weight of intercalate nucleus I is 0.66% and that of intercalate nucleus II 0.2% of the weight of the amygdaloid complex.

Nucleus of the lateral olfactory tract (Figs. 3, 6, 7, and 8, NTOL)

This nucleus, being one of the smallest nuclei of the amygdaloid complex, is situated in its central part. Orally, caudally, and medially it is bounded by the cortical nucleus, while laterally it adjoins to the medial

nucleus. It lies dorsally to the basal nucleus. Its weight forms 0.2% of the weight of the amygdaloid complex. According to Lauer (1945) the size of this nucleus in the macaque is variable and its length in the rostrocaudal plane ranges from 0.5 to 1.1 mm.

Lateral Nucleus (Figs. 1—10, NL)

The lateral nucleus occupies the lateroventral part of the amygdaloid complex. It is irregular in shape and forms about 29% of the weight of the complex. In the anterior portion of the amygdaloid complex intercalate nucleus I lies in front of the lateral nucleus at the height of the anterior commissure and the fibres of the external capsule border it caudally and laterally. In the posterior portion of the complex, on the ventral side, the lateral ventricle cuts in between the lateral nucleus and the fibres of the external capsule. Dorsomedially the lateral nucleus neighbours throughout its length upon the basal nucleus and ventrally

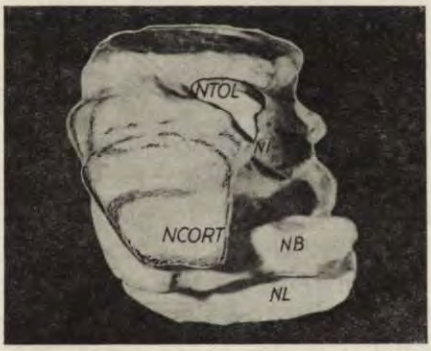

Fig. 8. The same as Fig. 7. In addition to the nuclei mentioned the medial nucleus has been removed

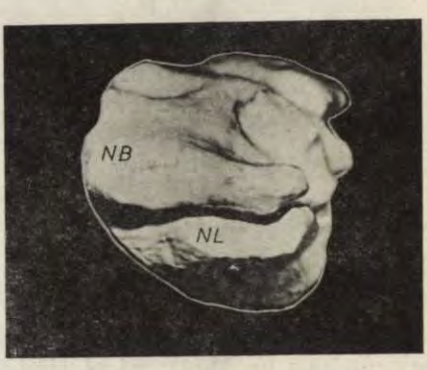

Fig. 9. The basal and the lateral nuclei of the macaque amygdaloid complex

it is separated from the pyriform cortex by the external capsule. In the posterior region of the amygdaloid complex the dorsolateral part of the lateral nucleus is accompanied by the tail of the caudate nucleus, which next penetrates between the hippocampus and the inferior corner of the lateral ventricle in the posterior portion of the telencephalon. The boundary between the lateral nucleus and the large-celled portion of the basal nucleus is distinct and marked out by the fibres running dorsomedially from the stria terminalis. The cells of the lateral nucleus are 7—10 μ in diameter. The investigations on the degenerations of the stria terminalis

in the cat carried out by Fox (1940) showed that, in contrast with the other nuclei of the amygdaloid complex, the lateral nucleus is not connected with the system of fibres of the stria terminalis but with that of the external capsule.

The Tail of the caudate nucleus (Figs. 4 and 5. CNC)

In the macaque the tail of the caudate nucleus descends together with the stria terminalis. It accompanies the amygdaloid complex, terminating in the proximity to its central portion. The tail of the caudate nucleus lies dorsolaterally to the lateral and basal nuclei, bordering medially on the central nucleus, dorsally on the substantia innominata, and laterally on the putamen. Its boundary with the central nucleus is clear-cut and easy to trace, there being a large number of dorsoventral fibres of the

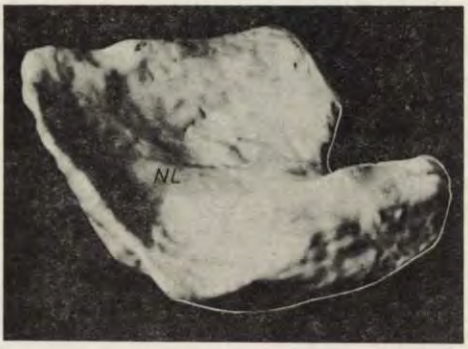

Fig. 10. The lateral nucleus of the macaque

stria terminalis running along it. The other boundaries are difficult to define. The cells of the tail of the caudate nucleus are small and agree in shape with the cells of the head of this nucleus. Lauer (1945) described the tail of the caudate nucleus in his paper on the amygdaloid complex of the macaque. This formation occurs only in the primates and in man, whereas the members of the other orders of mammals have merely the head of the caudate nucleus.

DISCUSSION

The nuclei distinguished in the amygdaloid complex of the macaque are identical with those in other species. However, I failed to find the putaminal nucleus, detected by Maksymowicz (1963) in the dog, in which it lies above the lateral nucleus in the fork of the external capsule.

So far this nucleus has not been found in any other species. It is likely that, in the course of evolution the putaminal nucleus may have undergone compression by the fibres of the external capsule and fused with the lateral nucleus. The nucleus E, described for the first time by Völsch (1910) in the ferret *Mustella putorius furo* and, most recently, by Maksymowicz (1963) in the dog, was not found in the macaque, either.

In the model of the amygdaloid complex of the macaque the division into nuclei corresponds in general to the divisions applied by other authors (Table). The present division resembles that used by Lauer (1945). The basal nucleus, in which Lauer distinguished six parts, is an exception and has been treated in this study as a whole.

Table

Identification of the nuclei of the amygdaloid complex

Crosby and Humphrey (1941) man	Crosby and Humphrey (1944) *Blarina brevicauda*	Lauer (1945) rhesus monkey	Castellanos (1949) rhesus monkey	Snider and Lee (1961) rhesus monkey	Maksymowicz (1963) dog	Śmiałowski (1965) rhesus monkey
lateralis	lateralis	lateral am. nucl.	lateral am. nucl.	n. am. lateralis	lateralis	lateralis
basalis	basalis	basal am. nucl.	basal am. nucl.	n. am. basalis	basalis	basalis
corticalis	corticalis	cortical am nucl.	cortical am. nucl.	n. am. corticalis	corticalis	corticalis
medialis	medialis	medial am. nucl.	medial am. nucl.	n. am. medialis	medialis	medialis
centralis	centralis	central am. nucl.	central am. area	n. am. centralis	centralis	centralis
intercalated cell masses	massa intercalata	massa intercalata	intercalated cell masses	XXX	inter-calatus	inter-calatus I II
n. lat. olf. tract	n. lat. olf. tract	n. tr. olf. lat.	n. lat. olf tract	XXX	n. tr. olf lat.	n. tr. olf. lat.
XXX	XXX	XXX	XXX	XXX	putamin-alis	XXX

Many authors divide the nuclei of the amygdaloid complex into two groups: the basolateral nuclei and the corticomedial ones. The first group includes the basal and the lateral nuclei, while all the other nuclei of the amygdaloid complex belong to the second group. This division was initia-

ted by Johnston (1923), who grounded it on the origin and the phylogenetic age of the nuclei. As a result of this interpretation Johnston distinguished the poorly differentiated nuclei, that is, the central, cortical, and medial nuclei as well as the nucleus of the lateral olfactory tract, and the second group of nuclei formed by convolution or by the immigration of cells, consisting of the basal and lateral nuclei.

Another interesting division of the nuclei of the amygdaloid complex was introduced by Miodoński (1965), who worked out the myeloarchitectonics of the amygdaloid complex of the dog. In addition, Miodoński showed that there are two types of the nuclei of the amygdaloid complex so far as their connections with other brain structures are concerned. The first type includes the nuclei connected with the system of the external capsule, namely, the lateral and the putaminal nuclei. In the second type Miodoński differentiated the nuclei which have connections with the system of the stria terminalis but not with the external capsule. This division is consistent with that made on the basis of the studies on degenerations of the stria terminalis in the cat (Fox 1943). Fox was the first to observe the association of the lateral nucleus of the cat with the external capsule.

The amygdaloid complex of the macaque, as compared with that of the dog, has undergone a shift and a swing by an angle of 45° mediad. The change in the size of the nuclei of the amygdaloid complex is probably associated with this shift as well as with the decrease of the role of smell in the primates.

The amygdaloid complex of the macaque much resembles that of man in its structure and position. In man, however, it has done a further swing of 22° mediad in relation to its position in the macaque, the main arrangement of the nuclei being unchanged. Humphrey (1941) distinguishes the same nuclei in the amygdaloid complex of man as have been found in most mammals. In man, the largest nucleus of this area is the lateral. It occupies the lowermost portion of the complex and, consequently, is often called the nucleus amygdalae ventralis. The basal nucleus comes in second as far as its size is concerned. In this nucleus Humphrey distinguishes four parts: the large-celled part, the small-celled one, and the accessory basal nucleus divided into the lateral and the medial portions. Basing on the cytoarchitecture of this nucleus, Lauer (1945) found as many as six parts in it. The myeloarchitectonics of the nucleus justifies its being divided only into the large-celled and the small-celled part. These parts have been modelled together because they may form a functional whole.

Many neurophysiological experiments have been made on animals

with lesions of the amygdaloid complex. Pribram and Bagshaw (1963) showed that the amygdaloid complex is associated with food intake and that the lesions localized in the cortex of the island and operculum produce a decrease of taste in monkeys. After the excision of the orbitofrontal area of the cortex in five goats, Bell and Lawn (1957) found long-lasting decrease in intake of food and water. Green, Clemente and de Groot (1958) observed hypophagia or hyperphagia in cats with lesions of the amygdaloid complex. Brutkowski, Fonberg, Kreiner, Mempel and Sychowa (1962) found a five-month aphagia and adipsia following the complete bilateral removal of the amygdaloid complex in the dog, the recovery being only partial. Basing on this evidence and on the observations of partial hyperphagia in animals in which a part of the amygdaloid complex has been removed, Brutkowski et al. (1962) conclude that there are some antagonistic mechanisms controlling the food intake in the frontotemporal region of the brain.

ABBREVIATIONS

CANT,	Commissura anterior.	NC,	Nucleus centralis.
CEX,	Capsula externa.	NCORT,	Nucleus corticalis.
CHO,	Chiasma opticum.	NINT,	Nucleus intercalatus I.
CIN,	Capsula interna.	NI,	Nucleus intercalatus II.
CLA,	Claustrum.	NL,	Nucleus lateralis.
CNC,	Cauda nuclei caudati.	NM,	Nucleus medialis.
CPYR,	Cortex pyriformis.	NTOL,	Nucleus tractus olfactorii lateralis.
GPAL,	Globus pallidus.	PUT,	Putamen.
HIPP,	Hippocampus.	TO,	Tractus opticus.
NB,	Nucleus basalis.	VL,	Ventriculus lateralis.

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THE EFFECTS OF LESIONS WITHIN THE SENSORI-MOTOR CORTEX UPON INSTRUMENTAL RESPONSE TO THE „SPECIFIC TACTILE STIMULUS"

Czesława DOBRZECKA, Barbara SYCHOWA and Jerzy KONORSKI

Department of Neurophysiology, The Nencki Institute of Experimental Biology, Warsaw 22, Poland

(Received October 5, 1964)

In previous papers of this series (Dobrzecka and Wyrwicka 1960, Dobrzecka and Konorski 1962), it was shown that the alimentary type II CR established to a tactile stimulus administered to the leg participating in the instrumental response (hereinafter called „specific tactile stimulus", STS) has a number of properties differing it from the type II CRs established to other stimuli. First, the instrumental response to the STS is established much more easily than to other stimuli, both auditory and tactile, administered to other parts of the body. Then, if a type II CR is first established to the STS and afterwards to an auditory stimulus, the formation of the CR to the latter stimulus is much handicapped and the reflex permanently remains weaker than in normal condition. Third, the resistance to extinction of the STS, both acute and chronic, is much stronger than that to other CSi. Finally, if the animal is given food *ad lib.* before the experimental session, the instrumental response to the STS disappears much later than that to the auditory stimuli.

It has been shown that all these peculiar properties of the STS may be explained by an assumption that the connections between the STS center and the center of the corresponding motor act are stronger than the connections between other CSi and the latter center (cf. Dobrzecka and Konorski 1962, Fig. 5). This increased strength of the connections was attributed to the organisation of the sensori-motor cortex in which the sensory area representing the given limb lies in close vicinity to the corresponding motor area and these two areas are presumably interconnec-

ted. The dependence of the placing reflex on the integrity of this region is one of the manifestations of these interconnections.

Therefore, the problem arose what might be the effect of lesions produced in the sensori-motor cortex on the instrumental response to the STS executed by the contralateral limb. The most logical way of studying this problem was to produce such lesions which would simply separate the sensory and motor areas of the cortex by small incision through the grey matter of the cortex and underlying white matter. Besides this most crucial operation it was thought useful to remove separately the sensory and the motor cortex representing the limb participating in the instrumental response.

Much evidence has recently been provided that, in the dog, the motor and sensory areas are separated one from another, the boundary between them lying along the small dimple called „central sulcus", situated roughly half-way between the cruciate and ansate sulci and its prolongation both medially and laterally (Fig. 1a).

This evidence is brought forth by the study of Pinto Hamuy et al. (1956) in which the sensory cortex in dog has been mapped. Then, in acute experiments of Tarnecki and Konorski (unpublished) it has been shown that moving the stimulating electrode longitudinally from the rostral to the caudal points of the sensori-motor cortex, there is a sudden raise of threshold at the central sulcus line, although the movement evoked remains roughly the same. Even more clear distinction between the sensory and motor area is provided by the ablation studies. Stępień and Stępień (1959), Stępień et al. (1960), Dobrzecka and Konorski (in preparation) have shown that the symptoms produced by lesions in both these areas strikingly differ from each other. While the ablation of the motor cortex produces a hypermotility of the affected limb, ablation of the sensory cortex, on the contrary, produces its hypomotility. The atactic symptoms are rather characteristic for the sensory lesions, while paretic symptoms are characteristic for the motor lesions. Furthermore, the placing reaction is more affected by the sensory than by the motor ablations. Accordingly, the sensory and the motor area in dog may be considered separate structures, the more so that their ablations produce different patterns of subcortical degenerations, which will be shown in the present paper.

MATERIAL AND METHOD

Experimental procedure. Experiments were performed in a sound-proof CR chamber on 8 mongrel dogs 1.5 to 3 years old, weighing 10 to 18 kg. During testing, each animal was situated in a Pavlovian stand facing a foodtray containing 10 bowls which could be remotely, put into position.

In the preliminary training the animals were taught to lift the right foreleg (in one dog also the left foreleg) and place it on the foodtray to one of the following three stimuli: buzzer (B), metronome (M) and rhythmic tactile stimulus, administered to the wrist of the trained leg (STS). The method used for obtaining the instrumental response was that of passive movements being reinforced by the presentation of food. The number of presentations of each CS in the preliminary training was roughly the same. The animals were then overtrained and performed the instrumental response in 100%. Eight or nine trials separated by 3/4 to 2 min. intervals were given in each session.

The test used in this study was exactly the same as that applied in our previous paper (Dobrzecka and Konorski 1962). It was the test of chronic extinction. The experimental procedure was that in an extinction series two non-reinforced trials were interspersed among 8 reinforced trials in partially random order. The stimuli subjected to extinction were B and STS. Either of them was given once daily for 5 sec without reinforcement in such a way that, alternately, either first B and then STS was presented, or *vice versa*. The extinction series was carried out to criterion of three successive no-responses to the presentation of the CS which appeared more resistant to extinction. Then the CRs to both CSi were restored.

The sound of M was always a positive CS, i.e. it was associated with food reinforcement during the entire period of testing. However, during extinction sessions the animals occasionally decreased the performance to the M presentations. In these cases the food was offered „gratis" after 5 sec of CS operation to avoid disturbing the normal course of experiments.

The course of experiments was not quite identical in all our dogs. Since, according to our previous data (Dobrzecka and Konorski 1962), in normal dogs the resistance to extinction of the CR to the STS is always much stronger than that to the auditory stimulus, the preoperative control was thought to be superfluous. And so, most animals were trained before operation in instrumental CRs to B, M and STS, and the extinction series was carried out only after operation. In some of the dogs extinction series were performed twice, separated by a long time intervals, either before and after operation, or only after operation, to see the remote effects of the surgery. In one dog the training began only after operation.

Surgery. All the operations were performed with aseptic precautions in nembutal anaesthesia. The sensori-motor area was unilaterally exposed, the sulci and gyri identified and the planned operation performed. Then the dura matter was sewed, as well as muscles, subcutaneous tissue and skin. In all the dogs the postoperative period was uneventful and after a few days the animals were suitable for CR experimentation.

As mentioned before, three types of surgery were made: (1) the separation of the sensory and motor area, (2) the partial removal of the sensory area, and (3) the partial removal of the motor area. All the operations were performed contralaterally to the foreleg trained within the foreleg area only.

(1) After the identification of the central sulcus an incision was made by a sharp knife along its course. The incision was about 5mm deep and 7mm and reached the coronal sulcus (Fig. 1b).

(2) The sensory area for the foreleg (Fig. 1c) between the ansate sulcus, coronal sulcus and central sulcus was removed by suction. The white matter was spared.

(3) The lesion in the motor area was made around the cruciate sulcus (Fig. 1d) up to the middle of its length on the dorsal surface of the cortex.

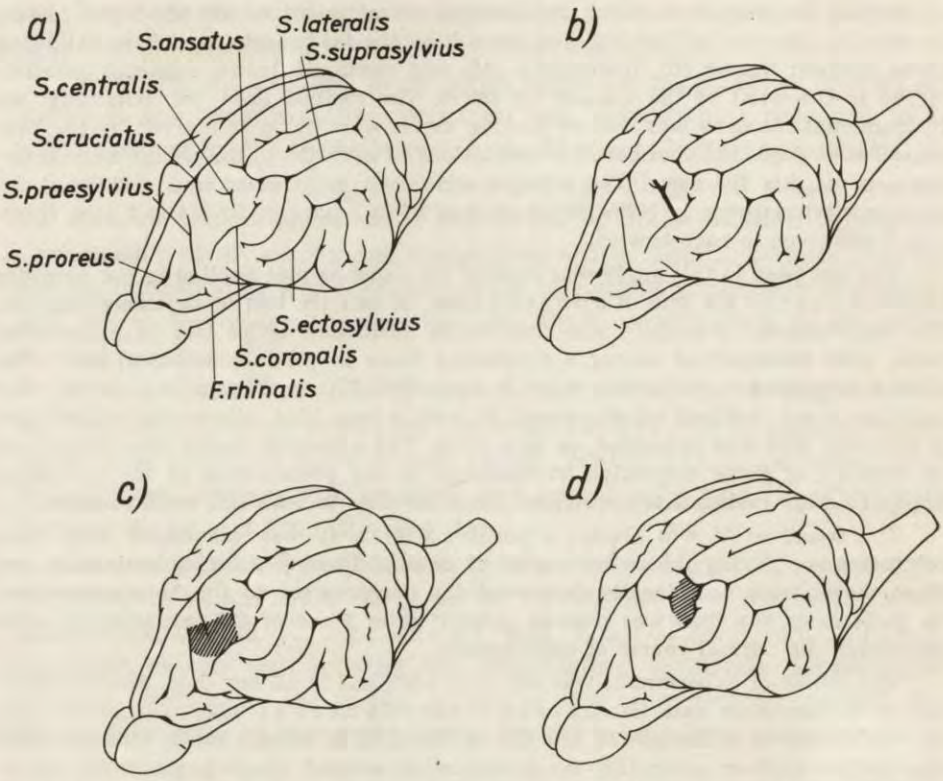

Fig. 1. The left hemisphere of the dog's brain with indication of the sustained lesions

a, normal cortex; b, incision between sensory and motor cortex; c, removal of the motor area; d, removal of the sensory area

Anatomy. After the postoperative series of experiments had been terminated and at least half a year had elapsed from the operation, the dogs were sacrificed, their brains perfused with 10 per cent formalin, embedded in paraffin and sectioned. Each fourth section was stained alternately by the Klüver and Nissl methods. The degenerations in the thalamus and brain white matter were carefully studied.

RESULTS

1. Separation of the sensory and motor cortex. Experiments were performed on 4 dogs. In two of them (Nos. 2 and 4) the control extinction series was performed before operation and the test extinction series after the operation. The interval between two series was 5 and 8 months respectively. In dog No. 1 the CR training began only after the operation. In dog No. 4, in addition to the incision along the central sulcus, an incision along the cruciate sulcus was made unintendedly.

The general symptoms of the lesion were very insignificant. The animals ran and walked quite normally, jumped without any difficulty on

the stand and behaved normally. In dog No. 3 slight ataxia of the right foreleg was seen. The placing reaction of the right foreleg was abolished in all the dogs for about one month.

In dogs Nos. 2 and 3, the instrumental CR was fully preserved. In dog No. 4, the CR disappeared after operation to all the CSi. However, it recovered without training after a few months of break in experimentation.

The training of the instrumental CR in dog No. 1 began after operation. It took more time than in normal animals, but once established it was skillful and prompt.

The results of extinction series of the CRs to STS and B are summarized in Table I, and the typical course of extinction both before and after the operation is shown in Fig. 2. It is seen that the exceedingly strong

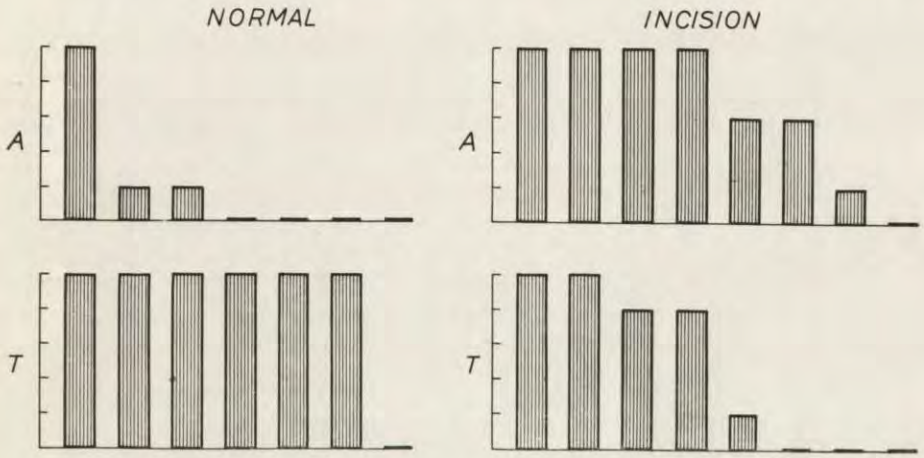

Fig. 2. The course of extinction series before (left) and after (right) separation of sensory and motor cortex in dog No. 2

A, auditory stimulus (Buzzer); T, specific tactile stimulus. Each column denotes the number of positive responses in 5 trial bock. Note the weak resistance to extinction to the auditory CS and strong one to the STS before operation and the partially reverse situation after operation

resistance to extinction of the CR to the STS observed under normal conditions disappeared completely after operation, and it became even slightly weaker than that to the auditory stimulus. This was not only owing to the decrease of the resistance to extinction of the response to the STS, but even more so owing to the increase of the resistance to the auditory CS. Another finding clearly shown in Table I is that indicating a radical change of the CR to M which has never been extinguished. As indicated in our previous paper, the instrumental CR to auditory CSi are suppressed by the mere presence of the CR to the STS. This was seen, among

Table I

The rate of extinction of auditory and tactile CR after incision between sensory and motor cortex

Dog No.	The total number of extinction trials of each CS	The numbers of trials till complete extinction		Extinction rate of STS in % of that of buzzer	The total number of positive trials in extinction series	The number of responses to positive CS	The percentage of positive response
		Buzzer	STS				
Before operation							
1							
2	32	7	30	429	224	51	23
3							
4	36	6	28	467	252	189	75
$\bar{x}$	34	6.5	29	448	238	120	49
After operation							
1	13(12)	12(5)	8(7)	67(140)	98(91)	98(91)	100(100)
2	35	27	19	70	245	245	100
3	34	26	29	112	238	238	100
4	19	13	11	85	103	95	92
$\bar{x}$	25	19	17	83	171	169	98

Numbers in parenthesis denote the results of the second extinction series.

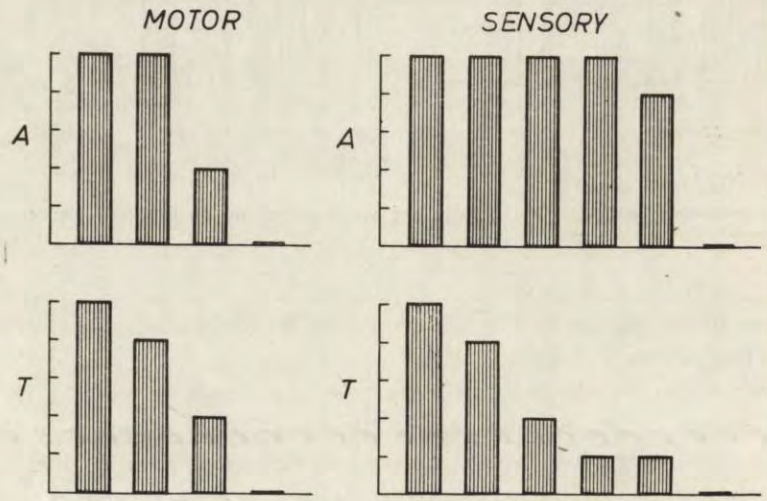

Fig. 3. The course of extinction series after the motor ablation in dog No. 5 (left) and after the sensory ablation in dog No. 8 (right)

Denotations as in Fig. 2. Note the weak resistance to extinction to both stimuli after motor ablation, and only to STS after sensory ablation

other things in the instability of the CR to the reinforced CS, during the chronic extinction series. After the separation of the sensory and motor cortex this instability was abolished and the instrumental CR to M was elicited in 100 per cent.

The *post mortem* examination of the brains revealed that in dogs Nos. 1 and 2 the incision resulted in the degeneration of white matter beneath the lesion and the reduction of fibers in fasciculus subcallosus in the anterior dorsal part of the lateral ventricle (Figs. 4 and 5). In dog No. 2 the reduction of fibers in cingulum was also seen. No changes were found in the internal capsule, peduncle and thalamus.

Fig. 4. Sagittal section of the brain of dog No. 1 to show cortical incision (x) s.c., cruciate sulcus; s.a., ansate sulcus; n.c., caudate nucleus; c.g.l., lateral geniculate body. Note the fiber degeneration underneath the place of lesion

Fig. 5. Sagittal section of the brain of dog No. 2 to show cortical incision (x) s.c., s.a., n.c., as in Fig. 4; th, thalamus; A, artefact ablation of the scar. Note reduction of fibers in white matter indicated by white circles

In dog No. 3, the incision was made in front of the central sulcus (because it was situated more caudally as usually) and it was larger than that in the first two dogs (Fig. 6). There was found some degeneration of projective fibers in the internal capsule (Fig. 6b), which, however, could not be traced to the lower parts of the brain. Also, degeneration of U-fibers running to the frontal cortex was seen. Slight reduction of fibers in the fasciculus subcallosus. No changes in the thalamus and the peduncle.

In dog No. 4, two deep incisions were made, one in the central sulcus and the other in the precruciate cortex. Degeneration in the centrum semiovale, cingulum and internal capsule. Fasciculus subcallosus degenerated in the antero-dorsal part. Some degenerated fibers could be found in the peduncle, but in the thalamus no changes were observed.

2. Lesions in the motor area. Experiments with unilateral ablation of the motor cortex were performed in 3 dogs, Nos. 2, 5 and 6.

In dog No. 2, which had been in the experiments described in the previous section, a new instrumental CR was established, consisting in lifting the left foreleg and placing it on the foodtray in response to two auditory

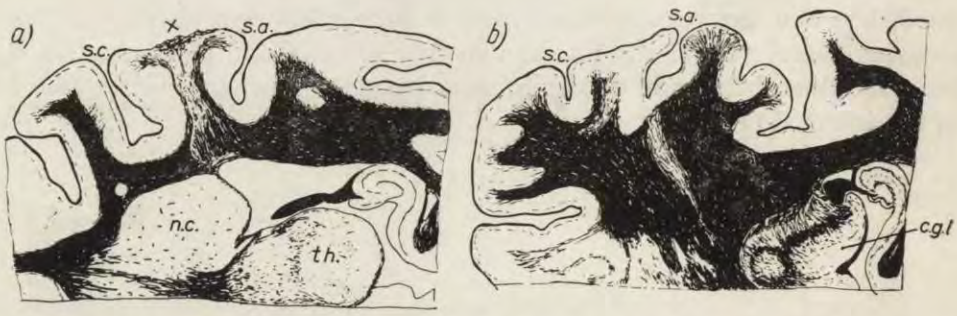

Fig. 6. Two sagittal sections of the brain in dog No. 3 to show cortical incision (x) and fiber degenerations

Connotations as in Figs. 1 and 2. Note degenerated bundles of fibers and slight reduction of fibers indicated by white circle

CSi, the sounds of a whistle (W) and bubbling of water (Bu), as well as to the STS applied to the wrist of the left foreleg. Then the preoperative extinction series of Bu and STS was performed. Thereafter, the right motor area corresponding to the left foreleg was removed and after the recovery of CRs another extinction series to STS and Bu was carried out, W being the background positive CS.

In dogs Nos. 5 and 6, after the normal training of instrumental CRs to B, M and STS, the motor cortex for the right foreleg was removed, and after the recovery from the operation the extinction series of CRs to B and STS was performed with M as the background positive CS.

The alterations of gross behavior following the removal of the motor cortex were very insignificant and evanescent. The only permanent symptom was the hypermotility of the affected leg especially manifested in dog No. 6. Due to this hypermotility the placing reaction could not be reliably examined.

The instrumental response was present from the very beginning in dogs Nos. 5 and 6, while it was temporarily absent in dog No. 2. Occasionally, dog No. 2, instead of lifting the left foreleg, performed the trained response with the right foreleg. This interesting symptom will be described and discussed in detail in a separate paper. However, after a short retraining period the instrumental CR in this dog became normal.

The results of the extinction series are presented in Table II, and the

typical course of experiments is shown in Fig. 3. It is clear that the resistance to extinction was after this operation nearly the same for STS as for the auditory stimulus. What is even more peculiar is that in this group of dogs the resistance to extinction of both CSi was weaker than that in the preceding group (in average 11 versus 20 trials). The CR to the reinforced CS was quite normal.

Table II

The rate of extinction of auditory and tactile CS after lesion in motor cortex

Dog No.	The total number of extinction trials of each CS	The number of trials till complete extinction		Extinction rate of STS in % of that of buzzer	The total number of positive trials in extinction series	The number of responses to positive CS	The percentage of positive response
		Buzzer	STS				
Before operation							
2	29	16	25	150	203	203	100
5							
6							
After operation							
2	17	8	7	87	119	119	100
5	17	12	11	92	119	119	100
6	19(12)	13(4)	11(4)	85(100)	133(84)	133(84)	100(100)
$\bar{x}$	18	12.5	11	88.5	124	124	100

Numbers in parenthesis denote the results of the second extinction series.

In dog No. 6, the second extinction series performed after one year manifested the same exceedingly weak resistance to extinction of both B and STS.

The post mortem examination of the brains revealed the similar picture in all three dogs (Fig. 7). The lesion involved the anterior and posterior sigmoid gyri around the lateral part of the cruciate sulcus. Extensive degeneration of U-fibers beneath the cruciate sulcus was seen. The degeneration of projective fibers from the place of the lesion could be traced in the peduncle. Degeneration was also found in cingulum and fasciculus subcallosus. No changes in the thalamus were found.

3. Lesions in the sensory area. Two dogs (Nos. 7 and 8) were used for these experiments. After establishing the instrumental CRs to M, B and STS, the ablation of the sensory cortex for the right foreleg was made and after the recovery two extinction series separated by a period of one year were carried out in each dog.

The neurological symptoms in both dogs consisted in a slight ataxia of the right foreleg and in total absence of placing for the period of at least several months.

The instrumental CR was present to all the CSi immediately after operation. In dog No. 7, however, the CR to the STS became weaker postoperatively than that to M and B: it was less energetic and had a latency of 3 to 4 sec. *versus* 1 sec. latency to other CSi.

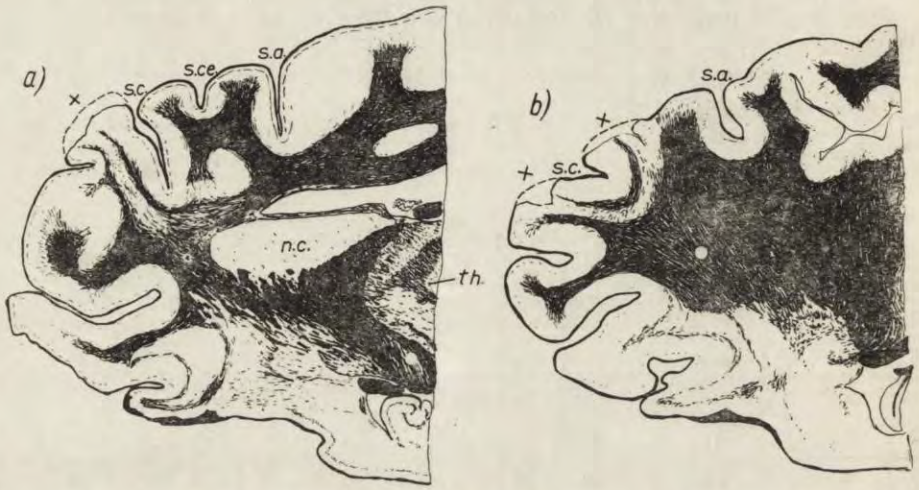

Fig. 7. Two sagittal sections of the brain in dog No. 2 (right hemisphere) to show cortical ablation (x) and fiber degenerations

Denotations as in preceding Figs; s.ce., sulcus centralis. Note gross degenerations of projective, longitudinal and U fibers traced in centrum semiovale and peduncle (white circles)

In the extinction series in both animals exactly the same results were observed (Table III and Fig. 3). The resistance to extinction of the CR to

Table III

The rate of extinction of auditory and tactile CS after lesion in sensory cortex

Dog No.	The total number of extinction trials of each CS	The number of trials till complete extinction		Extinction rate of STS in % of that of buzzer	The total number of positive trials in extinction series	The number of responses to positive CS	The percentage of positive response
		Buzzer	STS				
After operation							
7	19	16(25)	6(27)	37(108)	133(266)	133(266)	100(100)
8	28	24(18)	13(14)	54(77)	196(16)	196(161)	100(100)
$\bar{x}$	23(30)	20(21)	9(20)	45(94)	164(213)	164(213)	100(100)

Numbers in parenthesis denote the results of the second extinction series.

the STS became much weaker than that to the auditory CS. It is worth emphasising, however, that during the second extinction series conducted one year after operation, the difference between the effects of both stimuli disappeared.

The examination of the brain was made in dog No. 8 (Fig. 8). It is seen that from the place of cortical lesion situated in the lateral part of

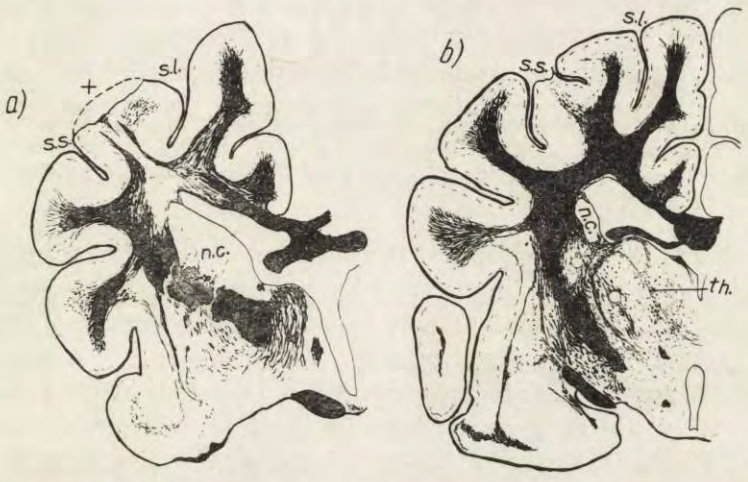

Fig. 8. Two frontal sections of the brain in dog No. 8 to show cortical ablation (x) and degeneration in projective fibers and thalamus (white circles)
s.s., sulcus suprasylvius; s.l., sulcus lateralis

the postcentral gyrus the degenerated bundles of fibers run to the internal capsule, to the adjacent gyri, to corpus callosum and cingulum. The degeneration of projective fibers can be traced to the nucleus ventralis postero-lateralis of the thalamus.

DISCUSSION

In our previous paper (Dobrzecka and Konorski 1962) it was supposed that the peculiar properties of the instrumental CR to the STS are due to the close intercortical relations existing between the sensory and the motor area of the cerebral cortex. This hypothesis brought us to the idea that the separation of these two areas by simple incision penetrating into the white matter might deprive the STS of its peculiar properties and convert this stimulus into a regular CS of an instrumental reflex.

This hypothesis has been fully confirmed by the present experiments.

It has been shown that separating the sensory and motor area of the cerebral cortex, producing quite insignificant and transient disorders of the motor responses of the affected leg, leads to a complete abolition of the peculiar characted of the STS. The resistance to extinction of STS becomes equal to, or slightly weaker than, that of the auditory stimuli, and what is even more interesting, the suppressing influence exerted by the STS upon the instrumental responses to other stimuli is totally removed. This is documented by the fact that the resistance to extinction of the auditory CSi, exceedingly weak before operation, increased after operation and that the instrumental CR to the reinforced background CS, being defective before operation, became quite normal postoperatively. Accordingly, it may be assumed that a small branch of the instrumental CR arc responsible for the particular strength of the CR to the STS was identified.

It is clear that the anatomical examination of the effects produced by the incisions has a great importance for the interpretation of our results, because it had to be verified whether the damage of projective fibers outgoing from, or ingoing to the cortex also took place. It seems that this examination gave a satisfactory result. In two dogs (Nos. 1 and 2) no impairment of the projective fibers in the internal capsule was found and the only slight degeneration was found in the longitudinal bundles running through the cingulum and tapetum (fasciculus subcallosus). In dog No 3, some slight degeneration of the projective fibers was found which, however, could not be traced in the thalamus or the peduncle. Only in dog No. 4 cannot the incision be considered as a pure one, because, in addition to the degeneration in the longitudinal bundles, the projective fibers were also affected which could be traced till the peduncle. This degeneration was undoubtedly due to the incision in the precruciate area. Since, however, the damage to the projective fibers was incomparably smaller than that produced by ablations of the motor cortex, this dog was left within the incision group.

Considering the results obtained in each dog we find that the resistance to extinction both of the auditory CS and the STS was considerable in dogs Nos. 2 and 3, and rather weak in dogs Nos. 1 and 4. The weak resistance to extinction in dog No. 1 may be due to the fact that the CRs were trained in this dog only after operation and, therefore, they could be not as strong as those trained before operation. This supposition is supported by the fact that the establishment of the CRs in this dog was undoubtedly more difficult than in normal dogs. On the other hand, the low resistance to extinction in dog No. 4 may be compared to that observed after the motor lesions.

The results of our experiments with incision of the cortex have raised a new problem, namely, that concerning the role of the sensory and motor areas themselves in instrumental CRs produced by the STS. This problem can also be explained on the basis of our results.

The lesions in the motor area produced „equalization" of the resistance to extinction of the auditory stimulus and the STS on a low level. Indeed, the resistance to extinction of the auditory stimulus was in average much weaker after the motor lesion than either after the sensory lesion or the incision (12.5 trials *versus* 20 trials and 19 trials respectively). This means that the attenuation of the instrumental CR after the motor lesion is due to the impairment of the „final common path" of the instrumental CR. In earlier papers of this laboratory (Stępień, Stępień, and Konorski 1960, 1961) it was shown that the instrumental CR of placing the foreleg on a platform was not destroyed by the removal of the motor area. From the present experiments it is seen that this area, although not crucial for the preservation of the CR, plays nonetheless some facilitatory or supporting role in its occurrence. This conclusion will be convincingly confirmed by further data which will be presented in the next paper of this series.

The question may be asked as to why the lesion in the motor cortex producing a clearcut degeneration in the descendant pathways traced in the peduncle causes no visible retrograde degeneration in the ventro-lateral nucleus of the thalamus. The answer to this question is that probably the same neurons of the VL nucleus send their axons both to the motor and premotor cortex, thus preventing the development of the retrograde degeneration after removal of the motor cortex alone. In this respect the Rose's idea of the supporting innervation seems to be relevant (Rose 1955).

The lesions in the sensory area of the cortex produce a different effect. Here, the resistance to extinction of the STS, or, more generally, of all the tactile stimuli, is much reduced, showing a great impairment of the CRs to those stimuli. On the other hand, the resistance to extinction of the auditory CS is high, thus showing that the defect concerns only the stimuli of the somatic analyzer. And so we may conclude that the ablation of this area, not destroying completely the reception of the tactile stimuli, produces its significant attenuation. Of course, the retrograde degeneration in the VPL thalamic nucleus is in perfect agreement with this finding.

The comparison of the effects of each of the three lesions (incision, motor ablation and sensory ablation) is shown in Fig. 9.

In conclusion we can state that while the lesion in the sensory area

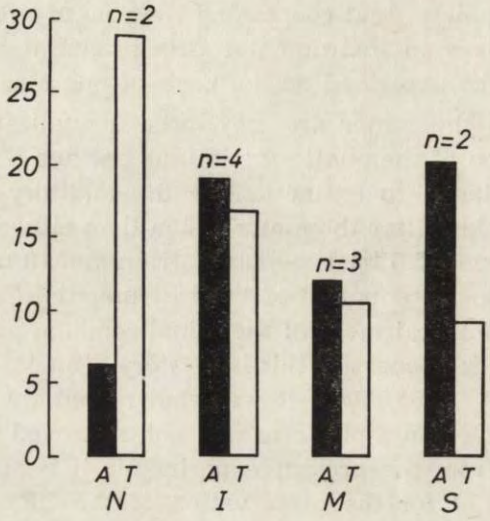

Fig. 9. Mean resistance to extinction to auditory (A) and specific tactile (T) stimuli in normal (N) dogs and in dogs with incision in the sensori-motor cortex (I), with motor (M) and sensory (S) ablation

Explanations in text

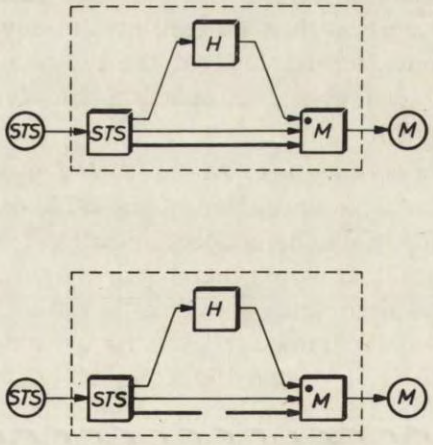

Fig. 10. Model of CR arc to STS

STS, receptor and center of specific tactile stimulus; H, hunger center, M, motor center and effector. The direct connection between STS and M has additional pathway which is cut by separation of the sensory and motor area

impairs the input of somatic CSi, and the lesion in the motor area impairs the output of the instrumental CRs to all stimuli, the incision between the two areas does not produce any of these effects; instead it changes the particular structure of the instrumental CR arc to the STS by depriving it of one branch responsible for its particular properties. These relations are shown diagramatically in Fig. 10.

An additional finding of this paper is related to the problem of restitution of the defects produced by the above cortical lesions after a lapse of time. This important problem was only slightly touched in the present paper, however, the preliminary results show that such a restitution takes in fact place. In two dogs in which the second extinction series was carried out about one year after the sensory lesion, partial recovery of the defect could be seen. This was, however, not true in respect to the lesion of the motor area; here the second extinction series manifested even the poorer resistance to extinction than the first one. This whole problem certainly needs a more thorough examination.

SUMMARY

1) The resistance to extinction of the instrumental food CR to the specific tactile CS and an auditory CS in chronic extinction series was investigated after (1) separation of the sensory and motor cortex, (2) removal of the motor area, and (3) removal of the sensory area. All operations were contralateral to the leg used in instrumental conditioning.

2) After separation of the sensory and motor area by incision made between them, the exceedingly strong resistance to extinction of the specific tactile stimulus manifested in normal dogs is abolished, as well as the suppressing effect of that stimulus on the CR to the auditory stimuli. In consequence the resistance to extinction of the two CSi becomes nearly equal.

3) After removal of the motor cortex the resistance to extinction of both CSi becomes equal and is weaker than in the preceding case.

4) After removal of the sensory area the resistance to extinction of the CR to the specific tactile stimulus becomes much weaker than that to the auditory stimulus.

5) The anatomical verification of lesions shows that after separation of the two areas only some degeneration of the longitudinal but not projective fibers are found; after removal of the motor area the degeneration of the projective fibers occurs traced in peduncles; after removal of the sensory area degeneration of projective fibers traced till nucleus postero-lateralis thalami is observed.

6) The physiological mechanism of the results obtained after each operation is discussed.

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THE RELATIONSHIP BETWEEN THE AVOIDANCE RESPONSE AND SUBSEQUENT CHANGES IN HEART-RATE[1]

A. H. BLACK and A. J. DALTON

Department of Psychology, McMaster University, Hamilton College, Hamilton, Ontario, Canada

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The relationship between the classically conditioned fear response (CFR) and the operant avoidance response plays a crucial role in many theories of avoidance conditioning. For example, Mowrer (1947), and Solomon and Wynne (1954) postulate that the CFR provides both motivational and discriminative stimuli for avoidance, and that the termination of the CFR reinforces avoidance responses; or, speaking more strictly, that the feedback from the CFR provides motivational and discriminative stimuli for the avoidance response while termination of this feedback acts as reinforcement.

Mowrer (1960) in a more recent theory emphasized the opposite side of the coin. In this theory, feedback from the avoidance response acts as a CS for a subsequent conditioned emotional response — the „relief" response. (The „relief" response is supposed to decrease the CFR). In avoidance conditioning the following steps are assumed to occur. First, the CFR is conditioned to the CS. Once this occurs, CS termination becomes a UCS for the unconditioned „relief" response. Since avoidances are paired with CS termination, feedback from avoidance then becomes a CS for the conditioned „relief" response.

Sołtysik and Kowalska (1960) have presented a theory of avoidance conditioning stemming from Konorski's (1948) earlier ana-

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lysis in which both types of relationship are involved. The CFR elicited by the CS is assumed to act as a motivator and discriminative stimulus for the avoidance response, and feedback from the avoidance response is supposed to act as a conditioned inhibitor of the CFR. In a recent paper, Sołtysik postulated that the feedback from avoidance becomes a conditioned inhibitor because it is paired with CS termination which in turn produces termination of the CFR (Sołtysik 1963).

From this cursory review of avoidance theories, it becomes clear that two types of chaining between the classically conditioned emotional responses and the avoidance response are assumed to occur. In one, feedback from the classical CFR acts as a discriminative stimulus for the operant avoidance response. In the other, feedback from the operant avoidance response acts as a CS for classically conditioned „relief" responses, or as a conditioned inhibitor of the CFR.

One area of theoretical conflict concerns the latter type of chaining — the relationship between the avoidance response and subsequent emotional responses. According to the first type of theory described above (Mowrer 1947, Solomon and Wynne 1954), the avoidance response is not important as a discriminative stimulus or CS for subsequent emotional responses. Only CS termination produces the decrement in the CFR (or if it occurs early enough, prevents the occurrence of a fullblown CFR). According to the second type of theory (Mowrer 1960, Sołtysik 1963), feedback from the avoidance leads to a decrement in the CFR or prevents its occurrence. In these latter theories two sources of decrement in the CFR are postulated; first, the termination of the CS, and secondly, the feedback from avoidance.

In the present paper we were interested in studying CS termination and feedback from the avoidance response as controllers of subsequent changes in the CFR. Heart-rate was employed as a measure of the CFR. d-tubocurarine chloride[2] was employed to control the occurrence of the avoidance response. The data which are reported in the present experiment were gathered in the course of another experiment on the effects of preventing avoidance responses and of delay of CS termination on the extinction of avoidance. Although many extinction trials were carried out, only the first extinction trial was employed in this paper since the heart-rate response could have been influenced differentially by the extinction procedures. That is, the test procedure itself could have influenced the heart-rate during an extended series of extinction trials.

[2] d-tubocurarine chloride was supplied by E. R. Squibb and Sons, of Canada, Ltd.

MATERIAL AND METHOD

Subjects and Apparatus: The subjects were 15 naive mongrel dogs. They were randomly assigned to three groups of five dogs each.

The dogs were confined in a hammock made of rubberized cloth and stood on a platform during training.

The CS was a white noise of 75 decibels. The UCS was an oscillating 60 cycle AC shock varying in intensity from 0 to 7 ma. A high resistance, high voltage circuit was employed in order to minimize the effects of changes in the dog's resistance. The shock was delivered through plate electrodes attached about six inches apart on the dog's right hind leg. The avoidance response was pressing a pedal with the left fore-leg.

d-tubocurarine chloride was used to paralyze the dogs. The doses varied from 18 to 24 milligrams. The drug was injected using a Harvard infusion pump through the polyethelene catheter which was inserted into the recurrent tarsal vein. A Harvard respirator was used to maintain respiration during curarization.

Measurements: The following behaviour was recorded on a Grass Polygraph. The vertical movement of the left fore-leg was recorded by attaching one end of a long lever to the leg and the other end of the lever to a variable transformer; changes in resistance were proportional to movement. The avoidance response was measured by a microswitch attached to the pedal. Also, EMG from the left fore-leg and EKG were recorded.

Procedure: On the first day of the experiment the dogs were given five presentations of the CS interspersed with five presentations of another t o n e of 60 decibels in order to determine the responses to these stimuli alone.

On the second day of the experiment, training of the avoidance response began. On each trial, the CS was presented and 10 sec. later the UCS (shock) followed. If no avoidance response was made during the 10 second CS-UCS interval, the shock remained on until the response occurred when the shock was terminated. If the dogs responded during the CS-UCS interval, the CS was terminated and shock avoided. Twenty trials a day were given; each dog was run until it made a series of twenty consecutive avoidances on any given day.

On the day after the acquisition criterion was reached, curarization took place. First, each dog was given ten avoidance trials in the normal state. Then the dog was curarized; the depth of curarization was such that EMG responses could occur, but little or no leg movements could be made.

For two groups of dogs the crucial trial — the first extinction trial — occurred under curare. Thus in these two groups no avoidance response could occur on the test trial. For one of these groups the CS was terminated when an EMG response of at least 50 microvolts occurred. For a second group of dogs the termination of the CS was delayed until a 5 second period had passed without an EMG response. The first group was called the „Reinforced EMG" group and the latter the „Reinforced No EMG" group. (These designations were used to make the extinction procedures which were employed in the main experiment clear.).

For the control group no special treatment occurred under curare; the dogs were simply allowed to rest. Then the first extinction trial was given in the normal state following recovery from curarization. On this trial the CS terminated when the avoidance response occurred.

RESULTS

The data which are relevant for our purposes are the last trial before curarization and the first extinction trial. In Fig. 1 data on these trials for a single dog from the „Reinforced EMG" group are shown, and in Figure 2 data for a single dog from the „Reinforced No EMG" group are presented. The first record shows data for the last trial in the normal state prior to curarization, and the second and third show the first and second trials under curare. In each record the upper channel shows the EMG. The second channel shows both the vertical leg movement and the avoidance response. (The latter is indicated when the pen drops below the baseline). The third gives the EKG and the fourth, the cardiotachographic transformation of the EKG.

For both dogs, there was little heart-rate responding to the CS on the last avoidance trial prior to curarization (Fig. 1 and 2, record A). Under curare where no avoidances could occur the dog in the „Reinforced EMG" group (where the CS was terminated when an EMG response occurred) also showed a very small heart-rate response (Fig. 1, records B and C). However, the dog in the „Reinforced No EMG" group (where the CS was prolonged until no EMG occurred) showed the full-blown heart-rate response (Fig. 2, records B and C). Thus it would seem that prevention of the avoidance response itself did not produce an increase in the heart-rate response provided the CS duration was brief. Only when CS duration was prolonged was there a marked heart-rate response. These two figures illustrate typical data. The next figures show that the same results are found when we consider the grouped data.

Fig. 3 shows data for the „Reinforced EMG" group and the control group. The last trial in the normal state before curarization, and the first extinction trial are shown. For the „Reinforced EMG" group the first extinction trial was under curare, while for the control group the first extinction trial occurred in the normal state following curarization. The heart-rate was sampled at 2 second intervals for 10 seconds immediately preceding and 10 seconds following CS onset[3]. The arrows show the mean time after CS onset at which the CS was terminated.

In these two groups CS termination occurred shortly after CS onset. In the control group, the avoidance response occurred at CS termination, while in the „Reinforced EMG" group it did not. Thus, if the avoidance response produces conditioned inhibition or a conditioned „relief" res-

[3] Heart-rates were measured in the following manner. The time for the first two beats after a given reference point (such as CS onset, or 2 sec. after CS onset) was measured. Then the reciprocal of this time was computed to give the rate per minute for these two beats.

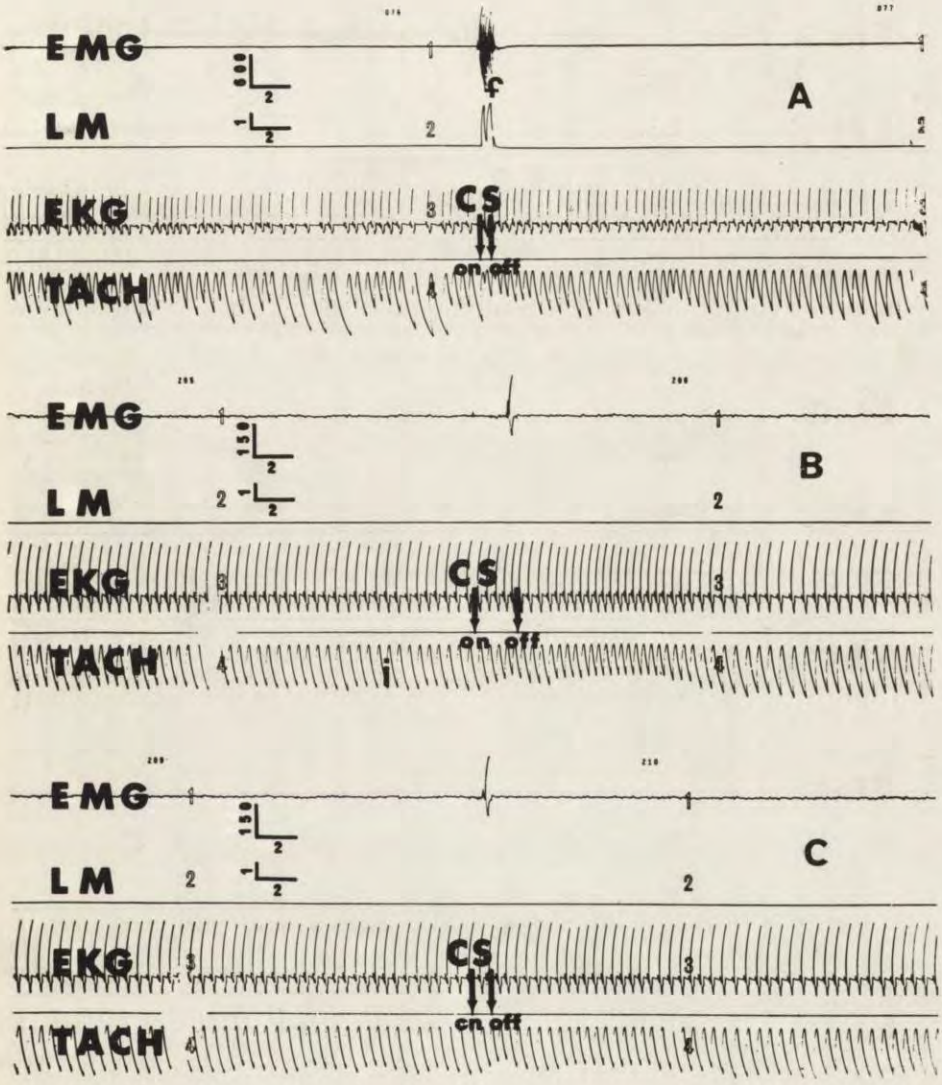

Fig. 1. Heart-rate (channels 3 and 4), muscle potentials (channel 1), and leg movements (channel 2) for a single dog during avoidance conditioning. Data are shown for 3 trials

Record A: the last avoidance trial in the normal state. Records B and C: the first and second trials in the curarized state. In channel 2, both vertical leg movements and pedal presses are presented; when a pedal press occurs the marker drops below the baseline and remains there until the pedal is released. CS termination was contingent on a pedal press in the normal state, and on an EMG response in the curarized state. Calibrations: time, 2 sec.; EMG amplitude (normal) 600 uv., (curarized) 150 uv.; vertical leg movements, 1 cm. (this scale is nonlinear)

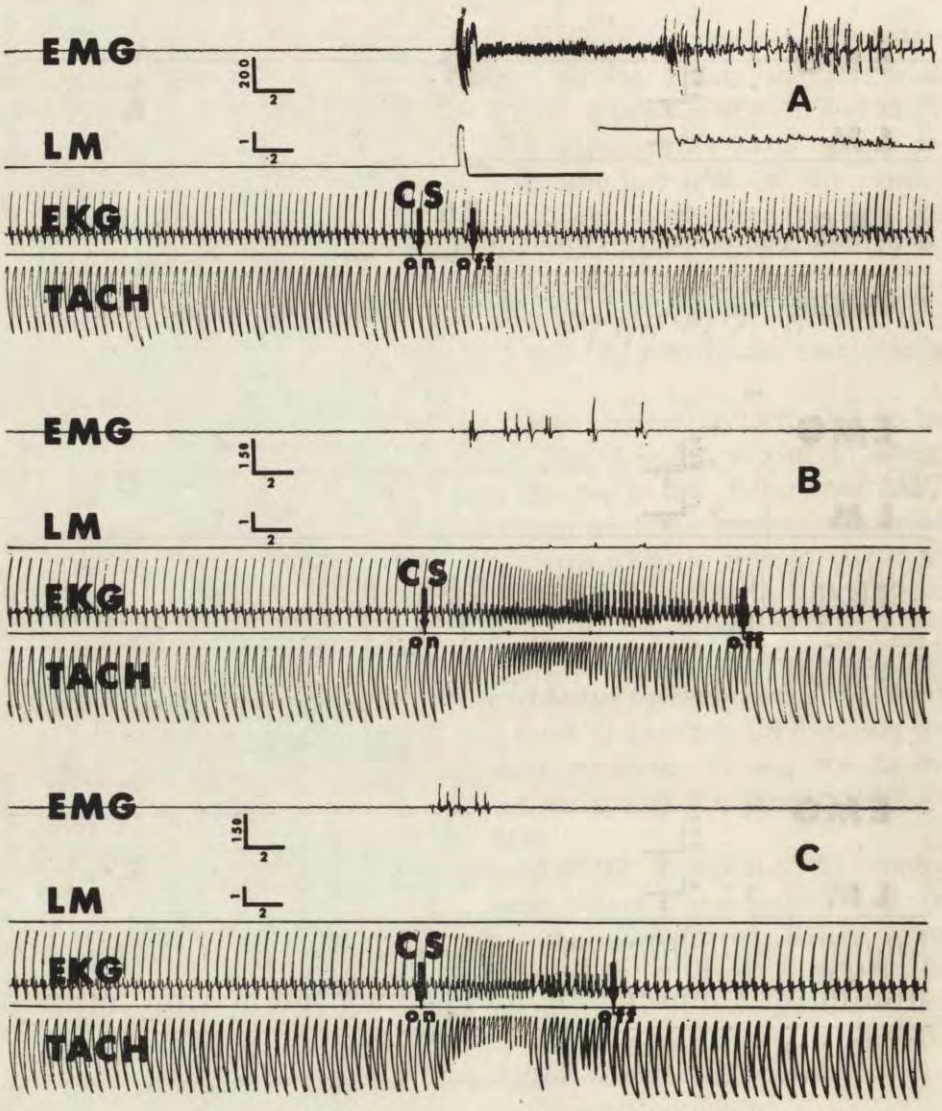

Fig. 2. Heart-rate (channels 3 and 4), muscle potentials (channel 1), and leg movements (channel 2) for a single dog during avoidance conditioning. Data are shown for 3 trials

Record A: the last avoidance trial in the normal state. Records B and C: the first and second trials in the curarized state. In channel 2, both vertical leg movements and pedal presses are presented; when a pedal press occurs the marker drops below the baseline and remains there until the pedals is released. CS termination was contingent on a pedal press in the normal state, and on a five-second period with no EMG response in the curarized state. Calibration: time, 2 sec. EMG amplitude, (normal) 200 uv., (curarized) 150 uv., vertical leg movements, 1 cm. (this scale is nonlinear)

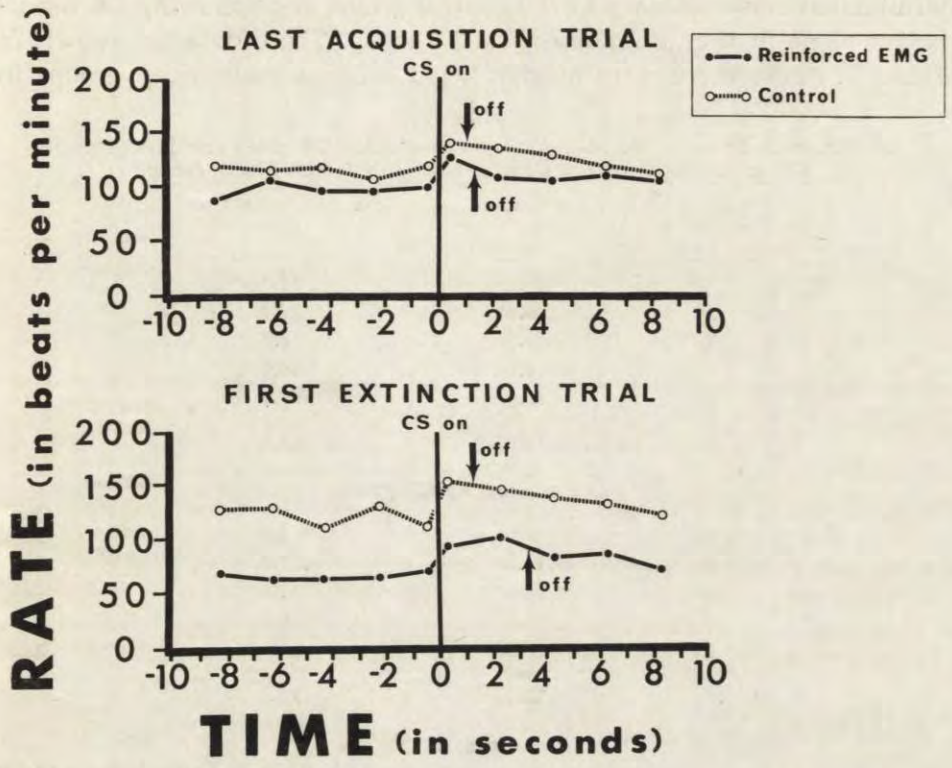

Fig. 3. Heart-rate as a function of time for dogs in the control and „Reinforced EMG" groups. Data are shown for the last acquisition trial in the normal state, and the first extinction trial. „Reinforced EMG" dogs received the first extinction trial while curarized and control dogs received the first extinction trial in the normal state. Heart-rate was sampled at 2 sec. intervals before and after CS onset

ponse, we would expect a higher heart-rate response under curare than in the normal state. An examination of Fig. 3 suggests that this did not happen. While there is a difference in overall level of heart-rate, there seemed to be little difference between the heart-rate responses during the CS or the responses following CS termination.

Analysis of variance of these data further substantiate this conclusion. First of all, the difference between the heart-rate just before CS onset and just before CS termination was analyzed. This difference measures the magnitude of the response to the CS. These data are shown in Table I. There were no significant differences.

Secondly, the differences between the heart-rate just before CS termination and the heart-rate 0, 2, 4, and 6 sec. after CS termination were analyzed. These give a measure of the heart-rate response following CS

termination and avoidance in the control group, and following CS termination alone in the „Reinforced EMG" group. These data are shown in Table II. Again there were no significant differences between groups in

Table I

The difference between the heart-rate just preceding CS onset and just preceding CS termination for the Control and „Reinforced EMG" groups

Dog	Last Acquisition Trial	First Extinction Trial
Control group		
1	36.0	36.0
2	5.0	18.0
3	− 4.0	6.0
4	4.0	38.0
5	10.0	64.0
$\bar{x}$	10.2	32.4
„Reinforced EMG" group		
1	9.6	1.1
2	− 19.0	27.2
3	28.0	67.4
4	34.0	0.0
5	15.0	20.1
$\bar{x}$	13.5	23.2

Table II

The difference between the heart-rate just preceding CS termination and 0, 2, 4, and 6 sec following CS termination for the Control and "Reinforced EMG" groups

Dog	Last Acquisition Trial				First Extinction Trial			
Control group								
	0″	2″	4″	6″	0″	2″	4″	6″
1	− 29.0	− 9.0	− 56.0	− 64.0	− 12.0	28.0	− 4.0	− 61.0
2	− 11.0	− 6.0	7.0	22.0	1 0	11.0	− 23.1	− 19.0
3	− 6.0	16.0	0.0	− 19.0	− 5.0	− 25.0	− 44.0	− 44.0
4	43.0	8.0	− 6.4	− 5.2	5.0	− 3.0	11.0	7.0
5	20.0	15.0	− 13.8	− 22 4	17.0	0.0	8.0	13.0
$\bar{x}$	3.4	4.8	− 13.8	− 17.7	1.2	2.2	− 10.4	− 20.8
„Reinforced EMG" Group								
1	39.5	46.5	8.5	2.9	22.4	6.5	13.8	2.0
2	− 4 0	0.0	− 12.0	− 14.0	− 16.9	− 19.8	− 12 5	− 9.9
3	15.0	33.0	− 10.0	− 26.0	− 18.0	− 36.0	− 56 8	− 64.6
4	23.0	− 22.0	− 34.0	− 10 0	24.1	62.1	25.1	− 22.6
5	6.0	− 22.0	− 28.0	− 17.0	− 12.0	7.0	14.0	17.0
$\bar{x}$	15.9	7.1	− 15.1	− 12.8	− .08	4.0	− 3.3	− 15.6

the heart-rate response following CS termination. Thus, the occurrence or non-occurrence of the avoidance response did not seem to make any difference in the magnitude of the heart-rate response to the CS or in the magnitude of the heart-rate response following CS termination.

Fig. 4 shows data comparing the „Reinforced No EMG" and the „Reinforced EMG" groups. Data on the last trial in the normal state and the first extinction trial under curare are shown for both groups. The heart-rate was sampled at two second intervals for 10 sec. immediately preceding and 10 seconds following CS onset. The arrows show the mean time of CS termination. (In the „Reinforced No EMG" group no arrow appears since the CS did not terminate until after 10 sec.).

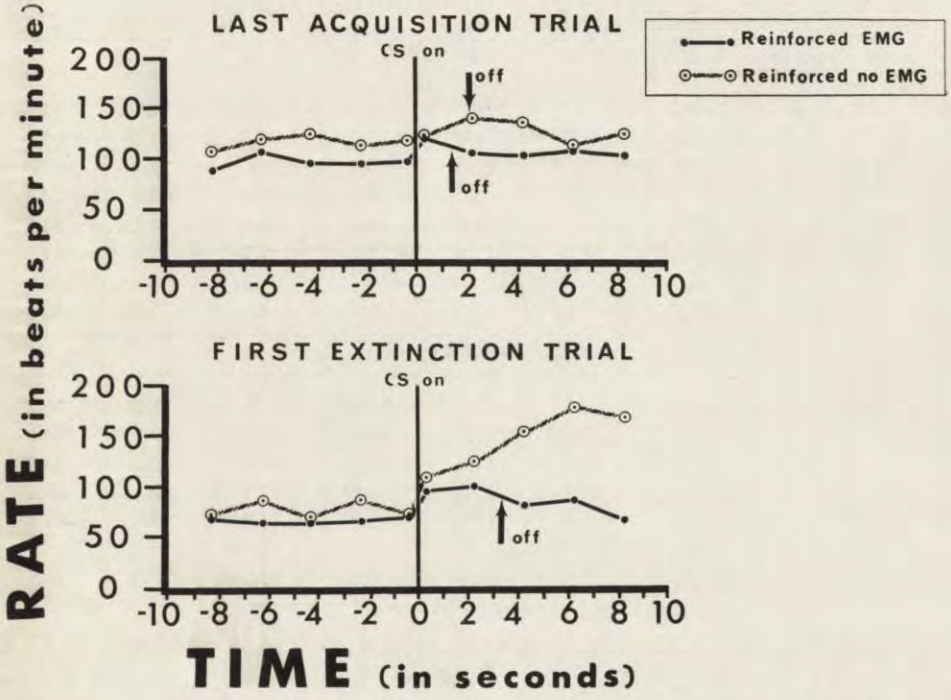

Fig. 4. Heart-rate as a function of time for dogs in the „Reinforced EMG" and „Reinforced No EMG" groups. Data are shown for the last acquisition trial in the normal state and the first extinction trial under curare. Heart-rate was sampled at 2 second intervals before and after CS onset

The avoidance response could occur in neither of these groups. For one, CS termination occurred shortly after CS onset while in the other CS termination was delayed. If CS termination were important in producing a decrement in the heart-rate response we would expect that delaying CS termination would produce an increase in the magnitude of the heart-

rate response. The expected results occurred; there was a full-blown heart-rate response when CS termination was delayed. This is further substantiated by an analysis of variance of the data. In this analysis the reference point was the occurrence of an EMG response. The heart-rate was measured just before the first EMG response after CS onset and then 0, 2, 4, and 6 sec. after the response. The difference between these measures of heart-rate are shown in Table III. While there was a drop in

Table III

The difference between the heart-rate just preceding the response and 0, 2, 4 and 6 sec following the response for the "Reinforced EMG" and the "Reinforced No EMG" groups

Dog	Last Acquisition Trial				First Extinction Trial			
	„Reinforced EMG" Group							
	0″	2″	4″	6″	0″	2″	4″	6″
1	39.5	46.5	8.5	2.9	22.4	6.5	13.8	2.0
2	− 4.0	0.0	− 12.0	− 14.0	− 16.9	− 19.8	− 12.5	− 9.9
3	15.0	33.0	− 10.0	− 26.0	− 18.0	− 36.0	− 56.8	− 64.6
4	23.0	− 22:0	− 34.0	− 10.0	24.1	62.1	25.1	− 22.6
5	6.0	− 22.0	− 28.0	− 17.0	− 12.0	7.1	14.0	17.0
$\bar{x}$	15.9	7.1	− 15.1	− 12.8	− .08	4.0	− 3.3	− 15.6
	„Reinforced No EMG" Group							
1	29.0	− 18.0	− 13.0	5.0	21.0	41.0	13.0	10.0
2	41.0	33.0	21.0	− 27.0	20.0	61.0	99.0	108.0
3	9.0	− 23.6	− 19.0	− 14.0	41.0	75.0	109.0	143.0
4	2.0	15.0	− 15.0	− 64.0	2.9	32.1	52.1	29.1
5	5.0	3.0	− 7.0	11.0	8.0	75.0	90.0	107.0
$\bar{x}$	17.2	1.9	− 6.6	− 17.8	18.6	51.2	78.2	79.4

heart-rate for the groups in which either the avoidance response and CS termination, or the EMG response and CS termination occurred simultaneously, there was a marked increase in the heart-rate response for the one group in which the CS was prolonged after the EMG response occurred. This effect is shown in analyses of variance where there was a significant interaction among the groups for the heart-rate scores 4 and 6 seconds after the response.

DISCUSSION

First of all the comparison between the two curarized groups showed that CS termination was effective in preventing or reducing the heart-rate response. When CS termination was delayed a full-blown heart-rate

response occurred. Secondly, the comparison between the control and „Reinforced EMG" groups showed that the occurrence or non-occurrence of the avoidance response seemed to be irrelevant when CS termination occurred shortly after CS onset, (and simultaneously with avoidance responses when they could be made). These data suggest that it is CS termination and not feedback from avoidance behavior which controls the subsequent heart-rate response. Thus, they support the theories of Mowrer (1947) and Solomon and Wynne (1954) rather than those of Mowrer (1960) and Sołtysik (1960, 1963).

One could, of course, criticize this conclusion. First of all, the comparison between the control and „Reinforced EMG" groups showed that the occurrence of the avoidance response made no difference for the condition where CS termination occurred soon after CS onset. It might be, however, that a different result would be obtained if CS termination were delayed. That is, if a normal group was compared with a curarized group, and the CS termination was delayed for 10 or more sec. it might be that the heart-rate response would be less for the group that could make the avoidance response. This does not seem likely. While we have no formal data on this point, three dogs were subjected to delay of CS termination in the normal state where an avoidance could occur. In each case, there was a marked heart-rate response accompanied by violent struggling; the struggling was so intense at times that it often prevented the recording of the heart-rate. It would seem that the response would be greater for normal dogs as compared to curarized dogs rather than less.

Secondly, one could argue that the EMG response was a component of the avoidance response, and as such provided enough feedback to elicit the „relief" response, or to act as a conditioned inhibitor[4]. This hypothesis cannot be tested directly using the present data; we would need an additional group where CS termination occurred before an EMG response could be made. If the EMG response were equivalent to the avoidance response we would expect that dogs in the „Reinforced EMG" group would show a smaller heart-rate response than dogs in the new group described above. This should occur because the response and CS termination occur in the „Reinforced EMG" group and provide two sources of

[4] Buchwald et al. (1964) have emphasized the role of the gamma efferents and proprioceptive feedback in motor conditioning. They argue that motor conditioning can occur even when there is loss of movement as long as proprioceptive feedback takes place. In the present experiment the gamma motoneurons and associated proprioceptive feedback were presumably intact since EMG activity occurred under curare. If their arguments are correct, then, one of the most crucial components of the avoidance response was present under curare.

decrement in the CFR, while only CS termination occurs in the new group and provides only one stimulus controlling the decrement. If the EMG response were not equivalent to the avoidance response we would predict, of course, no differences between the groups, because only one stimulus control of the decrement in heart-rate — CS termination — would occur in each of the two groups.

The present data do, however, show that CS termination is more important as a controller of the heart-rate than the EMG. The EMG response occurred in both the „Reinforced EMG" and the „Reinforced No EMG" groups, and we would, therefore, have expected the heart-rate response to be similar in both groups if the EMG were the most important controlling variable. This expectation was not fulfilled; rather, the heart-rate response was correlated with delay of CS termination.

On the basis of the present experiment, it would seem that the concept of inhibition is not necessary to account for the decrease in heart-rate following CS termination. One could argue simply that the CS produces an increase in conditioned fear and its termination produces a decrement in conditioned fear. If CS termination occurs very shortly after CS onset no response would be apparent; if CS termination is prolonged then the response increases in magnitude to an asymptote. Thus, the present data indicate that the concepts of the relief response or conditioned inhibitor are not necessary in explaining avoidance conditioning using a delayed procedure. They do not preclude, however, the possibility that feedback from avoidance results in conditioned inhibition or relief in other avoidance situations. For example, if acquisition were carried out for very long periods[5] the avoidance response might become a conditioned inhibitor. Also, we might find some evidence for conditioned inhibition in trace avoidance conditioning or in S i d m a n avoidance where CS termination does not occur simultaneously with the avoidance response.

SUMMARY

The role of CS termination and feedback from an avoidance response as controllers of subsequent changes in conditioned fear responses, were compared. Following acquisition of a pedal-press avoidance response, three groups of dogs were paralyzed with d-tubocurarine chloride, and given extinction trials under the following conditions: one group was presented with a contingency between CS termination and the occurrence of an EMG response and a second group with a contingency between CS termi-

[5] The mean number of trials to the acquisition criterion was 55 and the range was 20 to 120 (The data do not include the 30 criterion avoidances).

nation and an absence of the EMG response. A third group received CS presentations in the normal state after recovering from curarization. Heart-rate responses on the last trial before curarization and the first extinction trial were examined.

Results indicated that the occurrence or non-occurrence of the avoidance response did not make any difference in the magnitude of the heart-rate response to the CS or in the magnitude of the heart-rate response following CS termination. Rather, the magnitude of the heart-rate response was correlated with CS duration. It was concluded that it is CS termination rather than feedback from avoidance behavior which controls the subsequent heart-rate response.

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THE EFFECT OF INTRAVENOUS INJECTION OF GLUCOSE ON FOOD INTAKE AND CONDITIONED REFLEX ACTIVITY IN RABBITS WITH LESIONS OF THE HYPOTHALAMIC „FEEDING CENTERS"

Halina BALIŃSKA

Laboratory of Animal Physiology, University of Łódź, Łódź, Poland

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It has been shown by numerous investigations that animals with lesions of the medial hypothalamus prefer such food as fats and carbohydrates, while proteins or the food containing much water is eaten less readily (Marshall and Mayer 1954, Teitelbaum and Campbell 1954, Larsson 1957, Soulairac 1958, Balińska 1963 a). On the other hand, lesions of the lateral hypothalamus cause an aversion to standard types of food and to the water. At the same time, a specially prepared liquid food is eagerly drunk by those animals which become voracious and obese.

It has also been shown by our previous experiments, in which rabbits were presented with a choice of two types of food, that, in addition to the increased food intake, a preference for oats or potatoes over carrot was caused by the lesion of the hypothalamic „satiety center". Since being given food was a reward for animals' performance of an instrumental response, different for each type of food, an increase was simultaneously recorded in the food conditioned response in relation to oats or, in another group of animals, to potatoes (Balińska 1963 a). Lesions of the lateral hypothalamus resulted in stopping the food intake which, however, was recovered after a subcutaneous injection of the Ringer liquid with glucose. Despite the hypophagia, thus produced, a preference for carrots was observed while oats were eaten unwillingly and it was not till a few weeks after the operation. In animals with the lateral lesion of the hypothalamus, a decline of the conditioned instrumental response (CR), previously

trained, occurred immediately after operation and persisted after the restoration of the food intake. Over a period of a few weeks, this response was gradually reproduced and the movement, related with feeding carrot (Balińska 1963 b), was in all cases, restored as the first one. In rabbits in a dynamic stage of hyperphagia, we tended to ascribe the results, presented above, to an increased demand for types of food with the low water content and, in former aphagic animals, to an increased demand for a food, containing more water. It seemed interesting to investigate what effect, if any, will be caused by glucose, intravenously injected, on the food preference in rabbits with lesions of either the lateral or medial hypothalamus.

MATERIAL AND METHOD

Subjects and procedure. Experiments were performed on 12 rabbits, male and female, up to 3 years old, weighing 2 to 3 kg. When not experimented on, these animals lived in separate cages where they were fed fixed amounts of a standard food. During the preoperative period, their weight was taken once a week, while after the surgery — every day. Each animal was trained two different Type II CR's, reinforced by two different types of food. The experimental cage was a box with two revolving food trays, placed in corners. A small board was attached near one of the food trays and a bakelite ring near the other. Both the board and the ring were connected to the kymograph recorder (Balińska 1963 a).

The first CR consisted in placing the fore paw on the board of the food tray and it was reinforced by a few grains of oats or, in other rabbits, by some purée-type potatoes. In addition, another CR, consisting of grasping and pulling a bakelite ring, was produced according to the Malinovskii technique (1952). The method of forming the CR reaction has been described elsewhere (Balińska 1963 a). Pulling the ring was rewarded by a piece of carrot. During the experiment, animals ate *ad libitum*, that is, as long as they performed the trained movements, thus controlling the quantity and quality of the food presented. The situation of the experiment was a joint conditioned stimulus (CS). Sixty, 45, 30, 15 and 5 minutes prior to the experiment, rabbits were injected intravenously 10 ml. of a 5 per cent glucose. Injections were given daily over a period of a few days changing the time of administering glucose, that is,

on the 1st day — 5 per cent glucose, 5 min. before the experiment,
on the 2nd day — 5 per cent glucose, 15 min. before the experiment,
on the 3rd day — 5 per cent glucose, 30 min. before the experiment,
on the 4th day — 5 per cent glucose, 45 min. before the experiment,
on the 5th day — 5 per cent glucose, 60 min. before the experiment.

After the series of experimental intravenous injections of glucose, given at various times before the experiment, were completed, lesions of the hypothalamus were carried out. Depending on the location of the hypothalamic lesions, animals were divided into the following two groups:

Group M, consisting of 6 rabbits with lesions of the medial hypothalamus and,

Group L, also with 6 animals whose lesions were located in the lateral hypothalamic region.

Surgery. Hypothalamic lesions were made stereotaxically in the Horsley-Clark stereotaxic apparatus with a head holder for rabbits, described by Sawyer, Everett and Green (1954). The animals were anesthetized by means of Nembutal (37 to 40 mg per 1 kg. of the body weight), injected intravenously. The operation was performed under aseptic conditions. Bilateral lesions, reaching 1 mm. posteriorly to the bregma, were located 0,8 mm. in the case of the medial, and 2 mm. — in the case of the lateral lesion, laterally from the crossing of the sagittal and coronal sutures. Electrodes were implanted to the depth of 14 to 16 mm below the surface of the dura. The coagulation was effected by passing 3 mA DC through the electrodes for 20 sec. Afterwards, the wound was sewn up and dressed.

On the next day after the surgery, distinct differences, depending on the location of the hypothalamic lesions, occurred as a rule in animals' behavior. The electrocoagulation of the medial hypothalamus resulted in the hyperphagia and preference for oats or potatoes over carrots (Balińska 1963 a). The rabbits with lateral hypothalamic lesions displayed aphagia, considerably decreased motility and lower degree of reactivity to external stimuli. The stage of complete aphagia was not long and it was already after a few days (Balińska 1963 b) that the spontaneous food intake was restored by daily subcutaneous injections of the isotonic saline solution with glucose (10 ml. of a 40 per cent glucose, dissolved in 100 ml. of the isotonic saline solution).

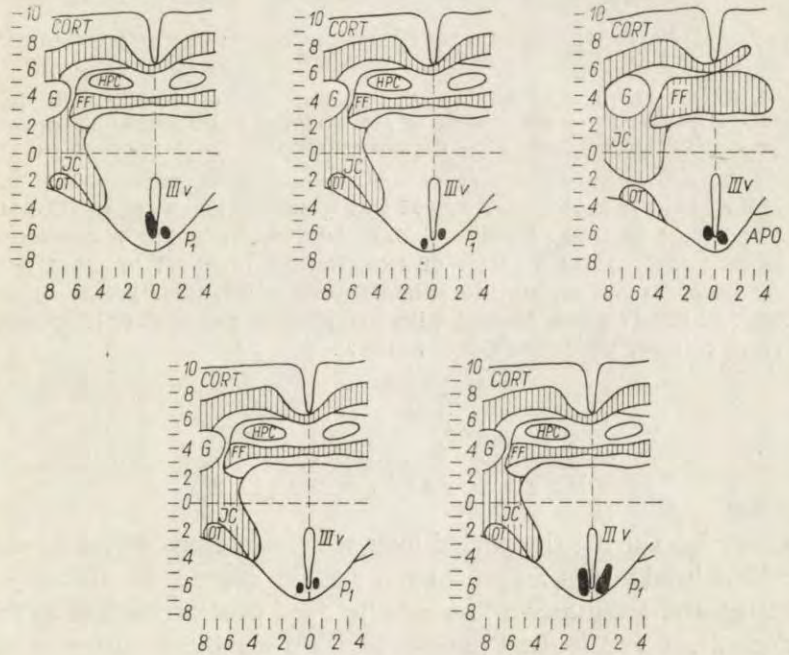

Fig. 1. Reconstructions of ventromedial hypothalamic lesions described in the text (the brain of the sixth animal was unintendently damaged and the lesions could not be identified)

Cort — cerebral cortex, FF — the fimbria of the fornix, G — the mammillotegmental tract, HPC — the hippocampus, IC — the internal capsule, OT — the optic tract, III V — the third ventricle

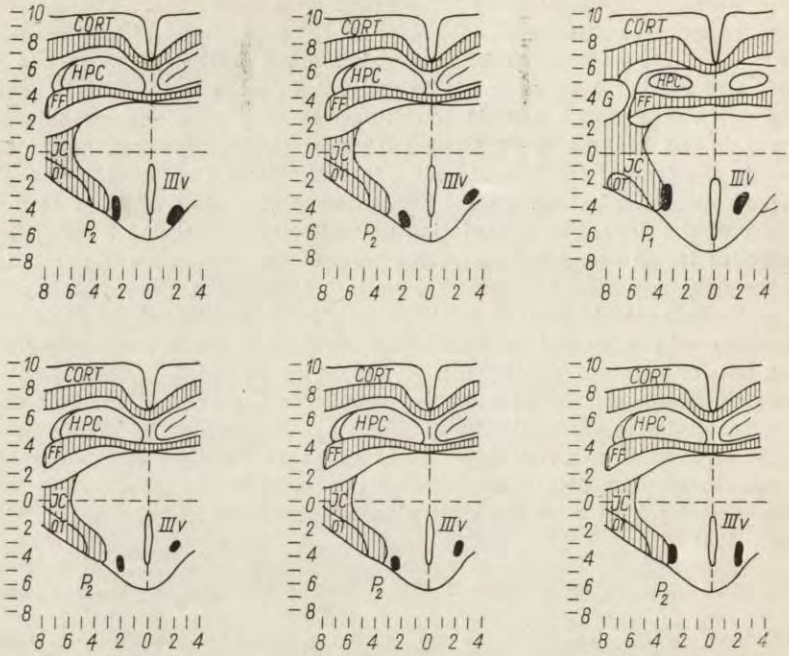

Fig. 2. Reconstructions of lateral hypothalamic lesions described in the text
Cort — cerebral cortex, FF — the fimbria of the fornix, G — the mammillotegmental tract, HPC — the hippocampus, IC — the internal capsule, OT — the optic tract

After the surgery, testing in group M was resumed on the 3rd to 5th postoperative day and, that in group L, several days later when animals recovered their ability to take food. After a series of experiments, identical to those performed during the preoperative period, the animals were killed, their brains subjected to the histological analysis and stained with hematoxilin and eosine, or cresyle violet for the verification of the lesion (Figs. 1 and 2).

RESULTS

Preoperative period

Food intake. During the period over which no glucose was administered, the food intake was marked by a certain degree of stability, both quantitative and qualitative. The rabbits' food preference was as follows: carrots, potatoes and oats. Changes in the food intake were caused by the intravenous glucose injections. The time lapse between the injection and the starting moment of the experiment appeared important. It was found that, under the conditions of a free choice between carrots and oats, as well as between carrots and potatoes, after the intravenous injections of glucose, an increase occurred in the ingestion of both types of food.

However, there was a decrease in the food intake, concerning both oats and potatoes, observed during an experiment, carried out after 15 and 45 min. (Table I).

Type II food CR. During the preoperative period, no effect of the glucose injections on the instrumental CR was found.

Table I

The effect of glucose injection on food intake in normal rabbits

Time of glucose injection before measurement (in min.)	Food intake after glucose injection			
	Carrots	Oats	Carrots	Potatoes
5	142 ± 21	130 ± 16	135 ± 10	146 ± 16
15	134 ± 16	66 ± 8	130 ± 8	90 ± 12
30	139 ± 8	150 ± 8	131 ± 10	131 ± 7
45	141 ± 9	29 ± 4	146 ± 16	68 ± 10
60	170 ± 11	123 ± 9	120 ± 13	144 ± 11

The results are calculated in relation to food intake before glucose injection, taken as 100. Means from 6 animals.

Note an obvious decrease of intake of oats and potatoes 15 and 45 min. after glucose injections.

Postoperative period

Lesions of the medial hypothalamus

Food intake. Lesions of the medial hypothalamus caused an increased food intake and the preference for oats or potatoes (B a l i ń s k a 1963 a). After the application of the intravenous glucose injections, a decrease was found in the intake of both types of food. Under the conditions of the free choice between carrots and oats, as well as between carrots and potatoes, the intake of carrots was slightly decreased. A considerable drop in the carrot intake 45 min. after the glucose injection was a characteristic symptom, while, during the preoperative period, a drop in the ingestion of oats and potatoes was observed in the identical time (Table II).

Type II food CR. The hyperphagic animals, intravenously injected with glucose, displayed a drop in their instrumental CR performance. This was particularly distinct in conditioning, rewarded by the presentation of oats and potatoes. It should be emphasized that, under the conditions when no glucose injections were given, a remarkable increase was found in the instrumental CR performance. It was manifested in both the increase in the number of movements and in a more violent form

Table II

The effect of glucose injection on food intake in rabbits with lesions of the medial hypothalamus

Time of glucose injection before measurement (in min.)	Food intake after glucose injection			
	Carrots	Oats	Carrots	Potatoes
5	91 ± 7	90 ± 11	100 ± 9	88 ± 7
15	90 ± 9	75 ± 7	86 ± 4	67 ± 5
30	102 ± 6	56 ± 6	93 ± 6	50 ± 8
45	67 ± 8	60 ± 4	61 ± 8	61 ± 7
60	111 ± 8	63 ± 6	105 ± 9	70 ± 6

The results are calculated in relation to food intake before glucose injection, taken as 100. Means from 6 animals.

Note that, under conditions of glucose injection, the rabbits with medial hypothalamic lesions show a tendency to accept less oats and potatoes than carrots.

of their performance (Balińska 1963a). The manner of performing the CR resembled the behavior of rabbits with lesions of the lateral hypothalamus in the initial stage of the restoration of the instrumental CR (Balińska 1963b).

Lesions of the lateral hypothalamus

Food intake. After the coagulation of the lateral hypothalamus, a brief aphagia and, afterwards, a considerable decrease in the intake of both types of food, were found. The decrease in the food intake was accompanied by the abolition of the instrumental CR. This continued for several days and, afterwards, was followed by the recovery of the instrumental CR performance which occurred first for the CR, rewarded by the presentation of carrots, regardless if it was pulling the ring with teeth, or placing the paw on the board. After several days, the second CR, rewarded by oats or potatoes, was restored. The intravenous glucose injections were given only when the food intake was recovered and when both CRs were already resumed.

The glucose injections, given to the rabbits with lesions of the lateral region of the hypothalamus caused a considerable raise in the intake of oats and potatoes as compared to the stage during which no glucose was administered. Data, depicting the food intake by rabbits with lesions of lateral hypothalamus after the injections of glucose are shown in Table III as a percentage in the relation to the period during which no glucose was given. A sudden postoperative increase in the ingestion of oats caused by the glucose injection, is noteworthy because such an increase was never observed before.

In animals with lateral hypothalamic lesions, the glucose injection did not affect markedly the intake of carrots (Table III). However, comparing to analogous conditions of the preoperative period, a distinct drop was occasionally noticed in the ingestion of carrot.

Table III

The effect of glucose injection on food intake in rabbits with lesions of the lateral hypothalamus

Time of glucose injection before measurement (in min.)	Food intake after glucose injection			
	Carrots	Oats	Carrots	Potatoes
5	91 ± 8	133 ± 6	116 ± 15	190 ± 11
15	117 ± 9	250 ± 16	119 ± 20	124 ± 12
30	83 ± 5	137 ± 10	84 ± 13	106 ± 11
45	68 ± 4	193 ± 4	70 ± 8	102 ± 8
60	95 ± 12	252 ± 11	115 ± 7	120 ± 7

The results are calculated in relation to food intake before glucose injection, taken as 100. Means from 6 animals.

Note that, under conditions of glucose injection, the rabbits with lateral hypothalamic lesions accept more oats and potatoes than carrots.

Type II food CR. The increase in the intake of oats after the glucose injection, in rabbits with lesions of the lateral hypothalamus, was associated with the intensification of the instrumental CR. The increased numbers of CR performances, conditioning the presentation of oats, as well as the raise of their amplitude were found. In individual cases, single performances were transformed into short series. The increase in the instrumental CR was correlated with the type of the food, applied as a reinforcement, regardless if the CR consisted in pressing the board or in pulling the ring. When the glucose injections were discontinued the former stage, that is, the hypophagia and a considerable impairment of the type II food CR was restored.

DISCUSSION

In unoperated animals, an increase in the intake of the food used was caused by intravenous injections of glucose, with the exception that in the 15th and 45th min after the injection, a considerable drop was found in the intake of oats and potatoes.

A considerable decrease in the intake of the food was caused by the glucose injections, given to rabbits with medial hypothalamic lesions. This decrease was particularly distinct in the relation to oats and potatoes which, prior to the injection, were a preferred food of the operated ani-

mals. The impairment of the type II food CR was associated with the decrease in the food intake. An increase in the ingestion of oats and potatoes as compared to the period when no glucose was administered was caused by the glucose injections given to the animals with the lesions of the lateral hypothalamus. At the same time, a considerable increase was found in these animals in the CR associated with the presentations of oats and potatoes.

The control of the blood sugar level is a complex neurohumoral process which aroused much interest (Mayer 1953, Anand and Dua 1955, and others). The participation of the hypothalamic „satiety center" in the neuro-control of the carbohydrate metabolism was indicated by the results of numerous investigations. A decisive role in this process is ascribed to the hypothalamic glucoreceptors, particularly sensitive to changes in the level of the metabolic glucose (Mayer, Vitale and Bates 1951, Mayer and Bates 1952, Mayer 1953). A drop in a given level of the metabolic glucose is associated with the activation of the autonomic system which, in turn, sets in operation the hepatic glycogen store. The enrichment of the blood in sugar, effected by the intra-arterial glucose injection, brings about the state of hyperglycemia and the decrease in the food intake. The electrical stimulation of the „satiety center" in the state of hyperglycemia is accompanied by the inhibition of the contractions of the stomach muscular wall and the drop in the feeling of hunger (Anand, Dua and Chhina 1958, Mayer and Sudsanek 1959, Anand, Dua and Singh 1961, Sharma, Anand, Dua and Singh 1961). Frequent glucose injections may stop the food intake and result in the starvation and death (Mayer and Bates 1952). It has been shown by Sakata, Hayano and Sloviter (1963) that the hyperglycemia is caused only by a slow intra-arterial glucose injection. Very slight changes can be caused by a sudden glucose injection, given intra-arterially or by an intravenous injection. In such cases, the symptoms of the hyperglycemia are visible only in the 10th to the 15th and in the 40th minute after the injection (Janowitz, Hanson and Grossman 1949).

The increase in the food intake, obtained in our experiments after the intravenous glucose injections, given to the unoperated rabbits can be explained by the activation of a hormonal mechanism which controls the blood sugar level. This process takes place with the coöperation of the glucoreceptors of the hypothalamic „satiety center" which — through the excitation of the vagus pathways — starts the hepatic glycogenolysis and causes the drop in a given level of the metabolic glucose, potassium and high-energy phosphoric bonds (Mayer and Bates 1952, Mayer

and Sudsanek 1959). This is related with the intensification of the contractions of the muscular wall of the stomach and the feeling of hunger (Wall, Glees and Fulton 1951, Mayer and Sudsanek 1959). According to the experiments, described by many authors, a food, containing fats and carbohydrates (Marshall and Meyer 1954, Larsson 1957) is particularly preferred by hyperphagic animals which are not so eager to eat a food with higher water content (Balińska 1963a). The decrease in the ingestion of oats and potatoes, observed in the 15th and 45th min. after the intravenous glucose injection may be ascribed to the state of hyperglycemia which occurred as a result of the formation of the metabolic glucose surplus. The transformation of the cerebral hypoglycemia into the hyperglycemia is suggested by Santiago and Solohaga (1957) and, Altszuler, Dunn, Stecle, Bishop and De Bodo (1963).

The neurohumoral control of the carbohydrate metabolism is abolished or at least considerably reduced by the lesion of the hypothalamic „satiety center" and its glucoreceptors. This results, after the intravenous glucose injection, in a considerable raise of the level of the metabolic glucose, contained in the blood which produces such symptoms as, the inhibition of the contractions of the stomach muscular wall and the decrease in the food intake, both of them typical of the hyperglycemia (Mayer and Sudsanek 1959, Sharma, Anand, Dua and Singh 1961). Under such conditions, the intake of the types of food with a high calorific value such as, oats and potatoes, is particularly impaired. The decrease in the drive for food causes a drop in the performance of the CR activity rewarded by the food presentation. This phenomenon, occurring in obese hyperphagic rats, was described by Miller, Bailey and Stevenson (1950).

The lesion of the lateral hypothalamus results in the abolition or strong reduction of the functioning of the „feeding center" and in the distinct supremacy of the medial „satiety center". The food intake is then stopped and the food CR abolished (Anand and Brobeck 1951, Anand, Dua and Shoenberg 1955, Teitelbaum and Stellar 1954, Morrison and Mayer 1957, Morgane 1960, Balińska 1963b). Under such conditions, an excessive activation of the neurohumoral emergency system would be caused by the glucose injections which, in turn, might lead to the decrease in the metabolic blood sugar level, to the intensification of the hunger feeling and to the increased intake of the food with high calorific value. The increase in the type II CR activity, observed after the glucose injection given to the rabbits with lateral hypothalamic lesions, might be ascribed to the intensification of the food motivation.

SUMMARY

An increase in the food intake was caused by the glucose injection, given to rabbits, trained in two food CRs, reinforced by two types of food. In the 15th and the 45th minute after the injection, a drop was recorded in the rate of eating, probably caused by hyperglycemia. The glucose, injected to animals with lesions of the medial hypothalamus, produced a decrease in the ingestion of food with both high and low calorific value. It is suggested that as a result of the destruction of the hypothalamic „satiety center" glucoreceptors, the metabolic blood sugar level was raised which produced symptoms, typical of the hyperglycemia. Following lesions of the lateral hypothalamus, the glucose injection is likely to cause an excessive activation of the neurohumoral control system which results in the drop of the metabolic blood sugar level and classical symptoms of hypoglycemia. On the basis of the experiments, described above, the role of glucose in passing of the state of the hypophagia into the hyperphagia and *vice-versa* has been proved.

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EVOKED POTENTIALS IN THE HYPOTHALAMUS DURING PERIPHERAL STIMULATION[1]

Andrzej ROMANIUK[2]

Institute of Physiology, Georgian Academy of Sciences, Tbilisi, USSR

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It has been shown that potentials, evoked in response to peripheral stimulation, were recorded in the hypothalamus. Thus, potentials evoked to the nociceptive stimulation were recorded by Gellhorn and Ballin (1946), Dell (1952), as well as by Feldman, Van der Heide and Porter (1959). Starzl, Taylor and Magoun (1951), as well as Ingvar and Hunter (1953) recorded potentials from the posterior hypothalamus, evoked in response to optical, acoustic and cutaneous stimuli. It has been indicated by the most recent investigations (Abrahams, Hilton and Malcolm 1962, and Abrahams and Langworth 1963) that, as a result of peripheral stimulation, evoked potentials occurred on the entire area of the hypothalamus, that is, in both the posterior and anterior parts of it.

In our previous papers (Romaniuk 1962, 1963), the aggression and flight reactions have been localized in the medial hypothalamus, as well as the functional and morphological separation of these reactions has been demonstrated. On the basis of these results, we took up the investigations on the influence, exerted by sensory peripheral stimuli on the electrical activity of the hypothalamic aggression and flight „centers". It seemed to be interesting to investigate the character of potentials evoked in these „centers" which are responsible for two reactions, each of them marked by different motor and autonomic characteristics. To obtain as accurate and many-sided results as possible, these investigations were carried out under the conditions of acute and chronic experiments.

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[1] This research was conducted in the Institute of Physiology, Tbilisi, while the author was a Poland's Ministry of Higher Education Research Fellow.

[2] Now at the Laboratory of Animal Physiology, University of Łódź, Łódź, Poland.

MATERIAL AND METHOD

Investigations were performed on 9 adult cats, male and female, 2.0 to 2.5 kg in weight. These animals were divided into the following three experimental groups: Group I: acute experiments made under the Nembutal narcosis (cats Nos. N-1, N-2, N-3, N-4 and N-5); Group II: acute experiments with curarized preparations (cats Nos. K-1 and K-2); Group III: chronic experiments (cats Nos. C-1 and C-2).

Group I. Under the Nembutal narcosis (40 to 80 mg per 1 kg of body weight), injected intraperitonealy, cats were fixed in the Horsley-Clark stereotaxic apparatus. After cutting the skin and drilling holes in the skull, bipolar electrodes (poles being set 0.5 mm apart) were introduced to the medial parts of the anterior and posterior hypothalamus. The implantation of the electrodes was effected according to the slightly modified Delgado technique (1955). Each cat was implanted with two electrodes in each hemisphere. Stainless steel electrodes 0.15 mm in diameter and Teflon coated over their entire length except for 0.5 mm tips were used. The electrodes were distributed in the hypothalamus according to the following stereotaxic coordinates of the Jasper and Ajmone-Marsan (1954) atlas: A = 10.0 and 13.0, L = 1.5, H = −2.0 to −7.0. Owing to the micromanipulators used. the positions of electrodes in the vertical plane could be changed during the experiment. After the implantation of the electrodes, potentials, evoked in the hypothalamus in response to the peripheral stimulation were recorded. Potentials were led in a mono- and bipolar manner and, at the same time, recorded by the 8-channel electroencephalograph (Alvar, Paris) and by the double-beam cathode oscillograph (VEB Messgerätewerk, Zwönitz, type 2KO-1). In the case of the monopolar lead, the role of the „indifferent" electrode was played by the stereotaxic apparatus. The stimulation was obtained by optic, acoustic and electrocutaneous stimuli. Flashes of light produced optic stimuli and single clicks of a duration of 1 msec and a frequency of 1—50 Hz, emitted by the Alvar generator at its maximum reinforcement, constituted acoustic stimuli. Both the lamp and the loudspeaker were located at the height of the animal's head, 30 cm in front of its muzzle. In addition, electrical stimulation of the right fore paw was applied. The stimulation of the paw was effected by flat, metal electrodes, stuck to the shaved skin by means of an electrolytic paste. Square current pulses of a duration of 0.05 to 0.5 msec., a frequency of 1—50 Hz and an intensity of 10—30 V were used. Experiments were carried out in a sound-proofed and shielded chamber.

Group II. In contradistinction to the former group, the implantation of electrodes were made under the ether narcosis. Subsequently, a tracheotomy was made. The preparation was switched over to the artificial respiration and a solution of the d-tubocurarine was intravenously introduced. If necessary, it could be steadily added. After awakening from the narcosis, thus prepared animal constituted a non-dormant but immobilized preparation. All parameters and the remaining parts of the procedure were identical with those in Group I.

Group III. The cats of this group were implanted with chronic electrodes, inserted into the hypothalamus under a slight Nembutal narcosis (30 mg per 1 kg of body weight). The ends of electrodes, protruding over the skull surface, were fastened by the Styracryle to the skull bone and then, the skin was sutured around the socket. Experiments were started 5 days after the surgery. During the experiments, cats were placed in a wire-mesh cage which in turn was put into a sound-proofed and shielded chamber. A complete freedom of movements within the cage was allowed to cats. The remaining experimental procedure was identical with

that in former groups. After the completion of the experiments, to examine the place where electrodes were implanted, the brains of all cats were subjected to a histological control.

RESULTS

In response to the peripheral stimulation, fairly stable and typical evoked potentials were recorded in the investigated areas of the hypothalamus. They were observed in all the animals experimented on with only slight differences in amplitudes, durations and latencies. On the other hand, the nature of the potentials did not display any changes dependable on the position of the leading-off electrodes in the horizontal and vertical planes and, therefore, these potentials were identical in both the anterior and posterior hypothalamus, as well as in its ventral and dorsal areas. No difference was observed between experimental groups of animals, and the character of the potentials recorded was the same for the narcotized and curarized preparations, as well as for the chronic animals.

In response to the flashes of light and cutaneous stimulation, evoked potentials were produced in all the experimental animals, while — in response to the clicks — these potentials were recorded only in chronic animals. At the same time, potentials, evoked as a response to clicks were, weaker than those, caused by the remaining stimuli (Fig. 1) which con-

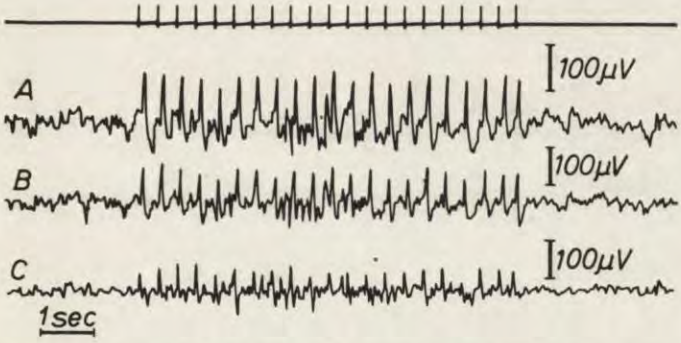

Fig. 1. Potentials evoked in the hypothalamus by different peripheral stimuli

A, potentials evoked by cutaneous stimulation; B, potentials evoked by flashes of light; C, potentials evoked by clicks. Monopolar recording from the anterior hypothalamus. Frequency of stimulation 3/sec

stituted a characteristic feature of these experiments, performed with different, that is, between 1 and 50 Hz, frequencies of stimulation. It has been found that, when stimuli with a frequency within limits of 1 and 10 per sec. were used, regular responses occurred to each stimulus according to the rhythm of stimulation (Fig. 2). In general, at first, a certain elevation was observed of the potential amplitude and, afterwards,

with the prolongation of the time of the stimulation, a gradual decrease in potentials was recorded. A complete disappearance of evoked potentials might even be caused by a long-lasting stimulation. When the sti-

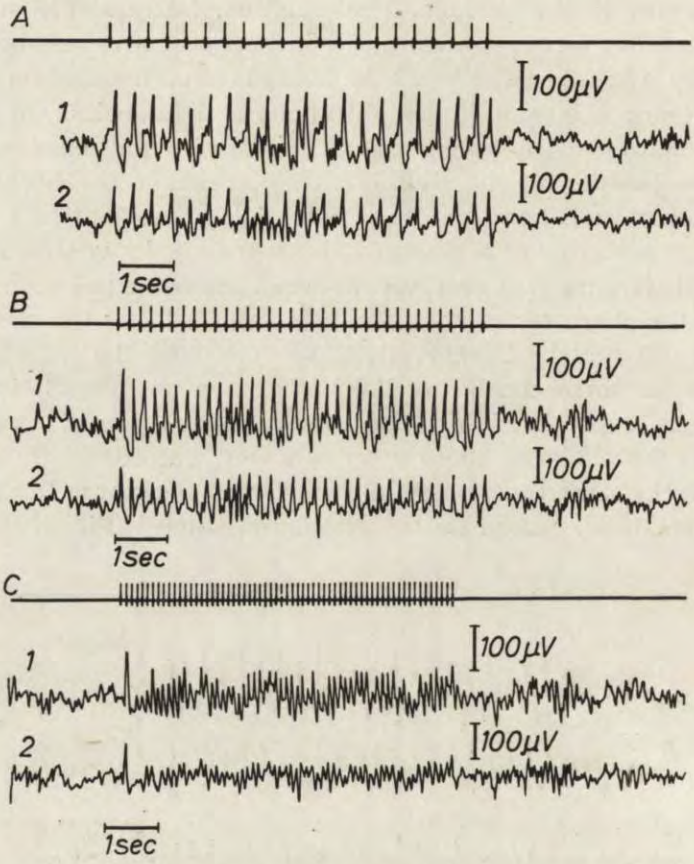

Fig. 2. Potentials evoked in the hypothalamus by variable frequency of stimulation
A, 3/sec; B, 5/sec; C, 10/sec. Monopolar recording from the anterior (1) and posterior (2) hypothalamus

mulation of a frequency of 20 to 50 stimuli per sec. was applied, no evoked potentials were recorded, certain damping of the spontaneous electrical activity (Fig. 3) being observed instead.

In experimenting on preparations under Nembutal anesthesia, different doses of the narcosis were given. With a narcosis of 40 mg/kg (cats Nos. N-1 and N-2), evoked potentials with a negative-positive double — peaked wave occurred regularly as a response to the peripheral stimuli applied. while with a dose of 60 mg/kg (the cat No. N-3), these potentials

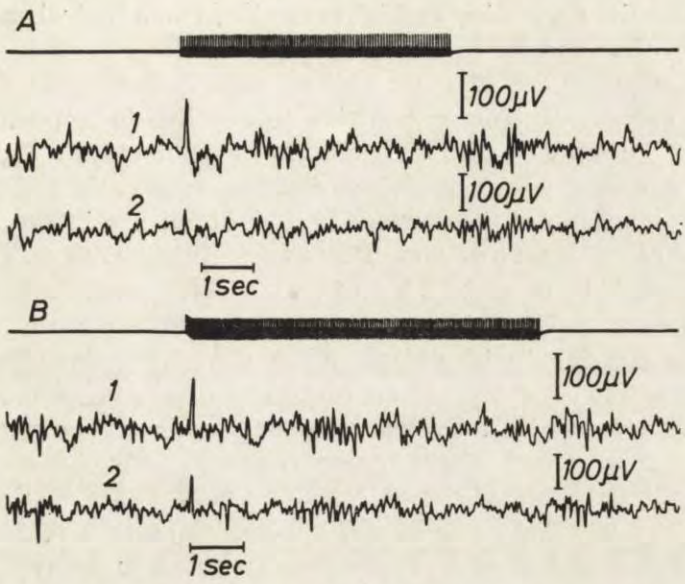

Fig. 3. Electrical activity of the hypothalamus caused by the high frequency cutaneous stimulation
A, 20/sec.; B, 50/sec. Monopolar recording from the anterior (1) and posterior (2) hypothalamus

occurred less regularly and had a negative phase only. In cats Nos. N-4 and N-5, which were given a deep narcosis (80 mg/kg), regardless of the stimulation parameters, no evoked potentials, as a response to the stimuli applied, were recorded in the structures investigated.

Potential characteristics. Evoked potentials, recorded in medial regions of the anterior and posterior hypothalamus, appearing as a response to the excitation by the optic, acoustic and cutaneous stimuli, were complex and long-lasting. They were formed by the double-peaked wave with a negative-positive phase in which a predominating role was played by the negative phase, while the positive phase, which followed it, was barely outlined at all. The duration of the potential amounted to from 150 to 200 msec. The latency period of these potentials was fairly long and averaged to about 30 msec. The amplitude of the negative phase equalled 100 μV.

DISCUSSION

It has been shown by the results obtained that in both the „aggression center" and „flight center" identical evoked potentials were produced as a response to the optic, acoustic and cutaneous stimuli. Clearly, then, the peripheral sensory stimuli which, under natural conditions,

may produce the aggression or flight reaction, reach both these „centers" at the same time and act to the same extent. These results are in conformity with observations of other authors who indicate that the sensory system is extensively connected with the entire diencephalon (Dell 1952, French, Verzeano and Magoun 1953). They are also in a good agreement with the view that the autonomic and motor reactions, characteristic of the aggression and flight, are integrated by the hypothalamus (Cannon and Britton 1925, Bard 1928). Abrahams, Hilton and Zbrożyna (1960) consider the hypothalamus to be not only an integrating area, but also a center, mediating the reflexes associated with defensive behavior. We believe the hypothalamic „aggression" and the „flight centers" to form together a hypothalamic „defensive center". Evoked potentials which we recorded in the „aggression center" and „flight center" were, in their characteristics, similar to potentials, recorded by Abrahams, Hilton and Malcolm (1962) in other parts of the hypothalamus as a response to peripheral stimuli and considered by these authors to be typical of this structure.

In our investigations, it has been found that evoked potentials occurred in response to the acoustic stimuli only in chronic animals which, during the experiments, freely moved within the cage. The absence of these potentials, in response to acoustic stimuli, in the narcotized and curarized animals should probably be explained by a fact that, due to an animal's head being fixed and immobilized in the stereotaxic apparatus, acoustic stimuli do not reach the ears because auditory canals are blocked by ear bars. It has been also observed that in response to acoustic stimuli, evoked potentials were weaker as compared to those, recorded as a response to the optic and cutaneous stimuli. These differences in the potentials recorded seemed to be caused by a partial injury, done to the tympanic membrane during the surgery.

In experimenting on narcotized preparations, a change was observed up to a complete disappearance of the evoked potentials, recorded with different doses of the narcosis. A high degree of sensitivity of these potentials to the barbiturates is indicated by the latter result which is in full conformity with the observations of other authors (Abrahams, Hilton and Malcolm 1962).

SUMMARY

The aim of this paper was to investigate the effect of peripheral stimuli (cutaneous, acoustic and optic) on the electrical activity of the hypothalamic „centers" of aggression and flight. Experiments were carried

out on narcotized and curarized preparations, as well as on chronic animals.

The following issues resulted from the experiments carried out:

(1) Evoked potentials, consisting of a double-peaked wave with a negative-positive phase, a duration of 150 to 200 msec, a latency period of 30 msec and an amplitude of 150 μV, appeared in the investigated structures of the hypothalamus in response to the peripheral stimuli.

(2) Identical evoked potentials were recorded in all the animals and in response to all stimuli, except for acoustic ones.

(3) Evoked potentials in response to acoustic stimuli were recorded only in chronic animals. The absence of such potentials in the curarized and narcotized preparations was probably caused by fixing an animal's head in the stereotaxic apparatus.

(4) The potentials recorded were marked by a considerable sensitivity to the barbiturates since, with larger doses of the Nembutal narcosis, they disappeared completely.

(5) The peripheral sensory stimuli reached the hypothalamic „aggression" and „flight centers" at the same time and to the same extent.

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Book Reviews

Neiro-gumoralnye regulatsii u pozvonochnykh zhivotnykh (Neuro-humoral control processes in vertebrates) by S. I. GALPERIN. Gosudarstvennoe Izdatelstvo „Vysshaia Shkola", Moskva, 1960, 342 pp., 23 tables, 57 figures.

Professor Semen Ilich Galperin, the author of this valuable monograph, is an eminent scientist who devoted nearly 40 years to the studies of the physiology of the nervous system. He has been interested in various fields of neuro-physiology and the physiology of higher nervous activity. Recently, however, all his attention and efforts were focused on functions of the autonomic system and neuro-humoral control. Professor Galperin's scientific activities were started in L. A. Orbeli's and A. D. Speranskii's laboratories of the Institute of Experimental Medicine whose Department of Physiology was headed by Ivan Petrovich Pavlov. The results of his work were published in numerous journals and periodicals, both Soviet and foreign, such as, the well-known Leningrad yearbooks, entitled, „Trudy fiziologicheskikh laboratorii im. akad. I. P. Pavlova" („Papers of the I. P. Pavlov Departments of Physiology"). He also spent some years at the Sukhumi biomedical station on the Black Sea, famous the world over, where he conducted interesting observations on apes and monkeys. These observations were, in a certain sense, pioneer in character. His long and fruitful scientific cooperation with Professor G. V. Skipin, also Pavlov's student, and with his first wife and close collaborator, the late K. P. Golysheva, deserves particular attention.

Professor Galperin is also an outstanding pedagogue and an author of a popular textbook of physiology, prepared jointly with K. P. Golysheva. A new edition of this textbook is now in press.

In his monograph, *„Neuro-humoral control processes in vertebrates"*, the following four problems are discussed: (1) motor functions associated with the alimentary „center"; (2) higher nervous activity and the subcortical structures; (3) correlation of somatic and autonomic functions; (4) neurohumoral mechanisms of the higher nervous activity.

The author precedes his monograph by an extensive introduction, discussing former and current views on the role of autonomic and neuro-humoral processes, as well as changes that have occurred in these processes in the course of the evolution. It is a well-known fact that much interest in this problem was shown even as early as in the mid-19th century and many invaluable discoveries in this field were achieved by such Russian investigators as, Danilevskii, Mislavskii, Bekhterev, Pavlov and others. It is with much pietism that Professor Galperin treats the pioneers of this physiological trend, while he sceptically evaluates some views of E. S. Airapetiants and the recently deceased K. M Bykov

who treated the controlling role of neural and humoral processes in the same way as the information stimuli, coming from the environment and from the internal organs.

Very interesting are the author's remarks on the functions of the alimentary center and particularly on its association with the motor functions of the alimentary tract which, among other things, was a subject of his own experiments. As is well-known, many valuable papers on the functions of the alimentary center and especially this part of it which is located in the hypothalamus have been published during the last 20-year period. Papers by Brobeck, Anand, Larsson, Mayer, Wyrwicka and many others have thrown much light on the functions of this center, on the mechanism of the food intake, hunger, etc. The problem of the alimentary center is approached by Professor Galperin in a quite different manner. He is interested in the reactivity of the receptors of various parts of the alimentary tract to mechanical and chemical stimuli and, in this connection, he discusses Bulygin's, Chernigovskii's, Mogendovich's and his own investigations. Much space is devoted to the mechanism of passing the food from the stomach fundus to the pylorus as a result of the excitation of the oral cavity mucosa, of the action of different components of the food on the processes of chewing, swallowing, contractions of the muscles of the stomach, intestines, etc. Particularly interesting data are presented by the author on the influence, exerted by the excitation of the receptors of the stomach, intestines or of the gall and urinary bladder on conditioned reflexes and — *vice-versa* — on the influence of the conditioned food and defensive stimuli, both exciting and inhibiting, on the secretion of saliva, as well as on the motor activity of the stomach and other parts of the alimentary tract. Applying surgery within the peripheral and central nervous system, or anesthetizing the nerve fibers and recording of the reactions observed, the author and his associates have found that the impulses, coming from different parts of the alimentary tract, that is, from the oral cavity mucosa, from the stomach and intestine mucosa and muscles and from the gall bladder are received selectively by brain centers. A part of these investigations was carried out in Bykov's laboratory, and, as is clear from the above description, it is closely associated with the relationship between „the cerebral cortex and internal organs" dealt with at that laboratory.

Referring to the now already classical work of Asratian, as well as to his own results, indicating that after the bilateral removal of upper cervical sympathetic ganglia, changes occur in salivary conditioned reflexes, Galperin has recently dealt with a detailed analysis of this operation and with the effect of the stimulation of these sympathetic ganglia on a variety of functions.

This part of Professor Galperin's monograph is also devoted to valuable observations on dogs and cats, as well as to the considerations of the location of the so-called (according to the Pavlovian terminology) analyzer of the internal organs. He recalls that already in 1875, Danilevskii found the control center of the heart action in the frontal cortex. It was somewhat later that centers, influencing the control of the blood pressure, movements of the urinary bladder, micturition, secretion of sweat and saliva have been also found by Bekhterev and Mislavskii in the frontal cortex. In the Thirties, it was shown by J. F. Fulton and his group that the premotor region (field 6) of the cortex is related to several autonomic, including visceral, functions. Recently, an experimental evidence has been provided by a team of workers of the Nencki Institute of Experimental Biology in Poland and by N. A. Shustin in the U.S.S.R. that, as a result of the

lesion of the prefrontal regions of the brain, a disinhibition of the food and defense conditioned reflexes and a temporary increase in unconditioned reflexes occur in dogs which indicates that normally, frontal parts of the brain exert an inhibitory influence on certain emotional and affective states. By the application of the methods of electrical stimulation, neuronography and surgical treatment, it was shown that the ventral and medial parts of the frontal cortex, viz. the cortex orbitalis, are here primarily concerned. Admittedly, these regions are linked up with the hypothalamus and limbic system structures which are associated with the autonomic functions, emotions and unconditioned behavior patterns. No conclusions are drawn, however, by Professor Galperin from these anatomical and physiological data, so numerous nowadays, but he states that the bilateral lesion of area 6 in dogs (Bulygin), carried out under his guidance, did not affect the conditioned reflexes elicited by the excitation of stomach receptors and that, after such an operation, it was possible to establish new food conditioned reflexes to the interoceptive stimuli. On the basis of this material, the author concludes that the interoceptive reflexes depend mainly on the subcortical centers and that the premotor cortex is concerned with the regulation and control of the subcortical center functions and, in particular, of the functions of the midbrain reticular formation.

To explain the role of neural and humoral factors in the formation of motor activities, resulting from the excitation of interoceptors, several ingenious and original experiments were carried out on frogs by the author and his close associates. Many observations were made dealing with the effect of the interoceptor excitation on the Sechenov inhibition against the background of acting with various pharmacological substances, such as, adrenalin, acetylcholine and atropine or, without the use of these substances. Mechanical, electrical and chemical stimuli were applied and the fluctuations in the latent period and chronaxy were indexes of changes in motor reactions. The author's conclusion that a decisive role in motor reflex actions, caused by the interoceptor excitation, is played in frogs by cerebral hemispheres, is very interesting from the physiological point of view. The importance of the midbrain and of the medulla oblongata for these functions is clearly lesser. Thus, for instance, in spinal frogs, no motor responses can be evoked even by an intensive interoceptor excitation. A part of the experiments was made on frogs, deprived of anterior parts of the telencephalon and the author concluded that, in cold-blooded animals, these regions are associated with the same functions as the premotor cortex in warm-blooded animals.

The evidence that the chronaxy of the skeletal muscles is influenced by the excitation of the receptors of internal organs, makes up one of the most original results, obtained by the author. This shows that the physiological state of somatic systems and organs is changed by the impulses, coming from the interoceptors. This important physiological fact was established by M. P. Mogendovich who, in Professor Galperin's laboratory, made experiments on both cold-blooded and warm-blooded animals (frog, white rat, rabbit, cat, dog). It has thus been shown that, in passing from animals with a less complex body organization to those of a higher degree of the evolutionary development, the influence of the internal organs on somatic activity decreases and, in higher systems, according to Orbeli's views, becomes adaptive-trophic in character. Similar correlations are also found in the ontogenetic development and, as is well-known, in early stages of the ontogenesis in higher organisms, the impulsation, coming from internal organs, results in a yet more distinct motor response. A baby' cry and movements, caused by the interoceptive stimulation, may serve as an example in this respect.

G. N. Kuzmenko's valuable experiments, carried out in Professor Galperin's laboratory, also deserve attention. They constitute an attempt to explain the part of humoral factors in the Sechenov inhibition. For this purpose, an original method has been worked out by the author who perfused the telencephalon of a frog, in which a stage of inhibiting motor responses was at the same time produced by placing a small crystal of natrium chloride on its corpora bigemina in the midbrain. A perfusate, thus obtained, contained a substance, approaching or even identical with the acetylcholine. It caused a decrease in the action of heart or even stopped it at all and — in another preparation — produced the Sechenov type inhibition. A perfusate, collected prior to the Sechenov inhibition, did not produce such effects. These experiments were successfully repeated on rabbits, cats and puppets. In these animals, Sechenov inhibition was caused by an electric current, transmitted to electrodes, planted in the midbrain. The results of these experiments show that the acetylcholine is present in the brains of both the cold-blooded and warm-blooded animals which confirms data, reported by Feldberg and other authors. In certain cases, also adrenalin derivatives are produced by the brain. As a sidenote for this rich and valuable experimental material, a supposition is expressed by Professor Galperin that the mechanism of Sechenov inhibition is related with the elimination of the function of the midbrain reticular formation and that the perfusate, obtained during the experiments he described, contained chemical substances, developed in the formatio reticularis.

The problems of the effect of mediators, hormones, vitamins, enzymes and metabollites on neural and nervous functions and particularly on conditioned reflexes are dealt with in the last chapter of Professor Galperin's book. The literature on this subject has been fairly rich, but no systematic investigations have been available thus far. The author and his associates devoted their efforts to the investigation of only some of these substances. They found that different effects may be obtained by means of identical chemical compounds, depending on the dose, on a place in which a reagent is introduced, on the type of an animal's nervous system, etc. Thus, for instance, small doses of the thyroxine, administered to the dog, at first, cause a brief drop and, afterwards, a raise of the level of the salivary conditioned reflexes. After the removal of upper cervical sympathetic ganglia, these changes become more remarkable. On the other hand, large doses of thyroxine cause a considerable drop in salivary reflexes in normal animals, while, after the sympathectomy, this drop is not so distinct. Large doses of adrenalin decrease the salivary conditioned reflexes and produce a disinhibition of the differentiation, medium doses slightly raise the salivary reflexes and small doses produce a very large increase in the secretion of saliva. After the sympathectomy, the effect of the action of adrenalin was, in all the three cases, more clearly marked and, therefore, a considerable drop in reflexes was recorded with large doses, a slight raise — with medium doses, and a slightly more marked raise — with small doses.

It has also been found that, for instance, a secretion of saliva from the parotid gland was caused by the hypodermic injection of acetylcholine, while the intravenous injection set in operation all the remaining salivary glands, although the secretion from the parotids continued to be the most profuse. On the whole, however, the secretion of saliva, caused by acetylcholine, introduced hypodermically, is larger than after the intravenous injection. The largest salivation is observed after small doses of acetylcholine. The secretion can be increased several times by the addition of eserine. On the other hand, acetylcholine, administered intravenously, results in a temporary (a few days) drop in conditioned reflexes and the smaller

the doses of acetylcholine, the larger is this drop. A more distinct effect is obtained after the injection of a small amount of eserine.

In addition, it has been found that the introduction of a large dose of acetylcholine to the blood considerably decreases a profuse salivation, caused by pilocarpine, while small doses of acetylcholine produce, under such circumstances, an increased salivation, particularly after the sympathectomy.

An important conclusion is drawn by Professor G a l p e r i n from these investigations that acetylcholine and probably also other mediators, hormones, metabollites and enzymes which are present in the nervous tissue, as well as the metabollites of the organ innervated are transmitters of the nerve impulse, passing along the paths of reflex arcs which are mediated by the brain and involved in the formation of a classical salivary conditioned reflex. According to the author, serotonin is also of a great importance for these reactions. A leading role, however, is probably played by acetylcholine which participates in the processes of excitation and inhibition at all levels of the nervous system.

Professor G a l p e r i n's book, presenting his own and his associates' achievements, is a constructive contribution to neurophysiology, a work which suggests ideas of further investigations and indicates the possibilities to solve the problems discussed by means of modern neurophysiological methods, the latter being its greatest advantage. In addition, it is an excellent guide to problems, related with neuro-humoral mechanisms in the vertebrates. Nowadays, the attention of neurophysiologists and biochemists is focused precisely on these problems and, therefore, year by year, new facts, new ideas and new durable conquests of science are recorded in this field. Under such circumstances, it is no wonder that, although a vast number of about a 1,000 items of Soviet and foreign literature have been discussed by the author, certain papers, particularly those, published in the most recent years, are not considered in his book.

To conclude my remarks, I would like to express my admiration for the author's great effort, as well as my appreciation of his profound knowledge and reliability of his work.

Since the neuro-humoral mechanisms are discussed in Professor G a l p e r i n's book in a comparative manner his book should interest biologists who work in different fields.

Stefan Brutkowski
Warsaw, Poland

Vliianie ioniziruiushchikh izluchenii na tsentralnuiu sistemu (The effect of ionizing radiation on the central nervous system) by P. F. MINAEV. Izdat. Akad. Nauk SSSR, Moskva, 1962, 130 pp., illust.

This monograph by Pavel Fedorovich M i n a e v contains a rich and versatile material, both experimental and theoretical, concerning the effects of ionizing radiation on the central nervous system. It presents the results of 10 years of investigations, carried out by the author and his associates from the Institute of Biological Physics, Academy of Sciences of the USSR, on different animals and by the use of various investigation methods. Experiments were performed, in different functional stages and by the use of the local and general irradiation, on a vast material of 6,000 animals, such as, dogs, cats, rabbits, rats, mice, guinea-pigs, hens. ducks and

Siberian marmots. The effect of ionizing radiation on the central nervous system as a whole and on its particular structures was investigated by the use of physiological, biochemical, histological and clinical tests.

The contents of the book are divided into 9 chapters, preceded by the author's introduction and closed by the list of the literature cited. The list of literature contains 225 items by the Soviet and 105 by foreign authors. It gives an exhaustive review of the present state of knowledge of the problems under study.

A brief historical outline of the investigations, concerning the effect of the ionizing radiation on the nervous system and views of different authors who explain the mechanism of the action of this radiation on the nervous system, are presented in chapter 1. It is also in this chapter that the author expresses his own opinion that contradictory results, obtained by different investigators, are probably caused by insufficiently accurate methods of irradiation. According to M i n a e v, the application of the method of the general irradiation of an animal's entire body is one of the main causes of inaccuracies.

Chapter 2 contains an outline of various methods of examining the functions of the central nervous system, that is, the conditioned reflex technique, the ablation, the electrical stimulation and recording biopotentials. The methods of the general and local irradiation, their advantages and drawbacks are also discussed in this chapter. Most part of it contains a detailed description of the method of the local irradiating the brain, worked out by the author, the doses and time applied, the course of particular experiments, methods of irradiating the superficial layers of the brain and the subcortical structures, the pharmacological drugs used and several other details of the technique.

Chapter 3 is devoted to clinical observations after the irradiation of the cerebellum, brain hemispheres, bulbar area and spinal cord. Symptoms similar to those which occur after the extirpation of the cerebellum, that is, astasia, ataxia and asthenia were observed after the irradiation of this part of the brain. The irradiation of the brain hemispheres was as a rule followed by the decrease in the motor activity. A typical bulbar ataxia appeared after the irradiation of the bulbar area and a spinal ataxia — after the irradiation of the spinal cord. Particular stages of disorders, their duration and a time lapse after which they occurred are specified by the author.

Physiological observations are presented in chapter 4. Several experiments on different animals and with the use of different doses of radiation, given to various brain structures are in this chapter. An effect was also investigated of the ionizing radiation on unconditioned and conditioned reflexes, as well as on the EEG patterns. Different disorders in the reflex activity, the order of their appearance, their character and duration are described. On the basis of these experiments, the author stated that the central nervous system is very sensitive to the ionizing radiation but, at the same time, that it proves to be highly resistant to this action.

Chapter 5 presents the results of the changes in biochemical processes together with the physiological changes which occur as an effect of radiation. The transformations in the metabolism and in the energy output of the nervous tissue, subjected to the ionizing radiation, were the main subject of the investigations. The results of the studies on the processes of the phosporylation, changes in the contents of glucose, of lactic, pyruvic and glutamic acids, of nucleic acids and other compounds, occurring in the nervous system as an effect of the local and general irradiation are extensively presented. These investigations were made on many animals and with the use of different methods. This chapter, most extensive of all, contains a consi-

derable number of tables and diagrams which make up a good illustration of the results obtained.

Miscellaneous morphological changes in particular layers of the cortex and cerebellum, in nerve cells, synapses and cellular organella, which occur as an effect of the irradiation are discussed in chapter 6. The results of experiments are illustrated by very good microphotographs.

Chapter 7 contains descriptions of experiments, performed on animals which, prior to irradiation, were subject to surgical lesions, or extirpation of certain brain areas, or were given a narcosis. It was found that the character of changes, occurring as an effect of irradiation, became different, depending on the changes in functional stages of the nervous system.

An extensive interpretation of the results obtained, their critical evaluation, a dispute with other authors' work and various interpretative suggestions, concerning the mechanism of the effect of the ionizing radiation on the nervous system, are presented in chapter 8.

In the last chapter, the results obtained are briefly summarized by the author who also explains the reasons of failures in certain experiments, draws conclusions and presents his suggestions as to the continuation of these studies.

In general, it should be emphasized that the book reviewed is very valuable because it contains several original and new methodical solutions, as well as throws much light on the action of the ionizing radiation on the nervous system, discussed by the author in an extensive and versatile manner. The results are very carefully elaborated in the form of tables, diagrams, figures and microphotographs which constitute an excellent illustration of experiments and greatly facilitate understanding the text. The application of modern investigation methods to the biochemical, physiological and histological experiments makes the results obtained fully reliable and trustworthy. The book is written in a clear and concise style which allows the readers to easily understand many rather complex problems. Brief conclusions, put at the end of each chapter, give an excellent synthesis of the questions presented.

Andrzej Romaniuk
Łódź, Poland

Olfaction and taste. Proceedings of the First International Symposium held at the Wenner-Gren Center, Stockholm, September, 1962. Edited by Y. ZOTTERMAN. Symposium Publications Division, Pergamon Press, Oxford-London-New York-Paris, 1963, LX + 396 pp. illust.

Papers, collected in this volume, make up a review of modern research achievements in the field of the physiology of olfaction and taste which, thus far, were examined together with the problems of sensory communications and neural control of food intake.

The book, provided with an introduction by Lord A d r i a n, contains 30 publications by outstanding specialists, a quarter of this number being devoted to the olfactory system only and the rest — mostly to the gustatory system. These papers cover a broad range of both the subjects dealt with and methods and experimental materials made use of. They are illustrated by numerous diagrams, oscillograph records, photographs and tables. Experiments were performed on man, squirrel monkeys and many other mammals, as well as on birds, reptiles, amphibians,

fishes and insects. Electrophysiological methods were mostly used and a correlation between the electrical activity, recorded from nerve cells and fibers, and physico-chemical properties of stimuli was a most frequent subject of investigation. In experimenting on man, in addition to comparing the stimulus with the sensory experience, conditioning tests were used and, in the case of animals, experiments were carried out under conditions of preference and free choice. The use of an electronic microscope and the Bodian silver method has enriched the knowledge of morphology in many new details, concerning the structure of the olfactory and gustatory receptors. Our present knowledge of a manner in which olfactory and gustatory stimuli are manifested is based on hypotheses. As to the organ of taste, it is reckoned by Lord Adrian, together with organs of hearing and vision, among the most „elaborate structures". Examining processes which, according to the mechanical effect of the sound wave, take place in the ear, an assumption can be made that there occur spatial and temporal analyses. „The vibration frequencies in the sequence of sounds cause distinctive patterns of deformation in the basilar membrane and that pattern and its temporal fluctuation contain all the information needed to specify the sound"... Depending on their lengths, light waves may have different photochemical effects and, therefore, in addition to spatial and temporal analyses, due to the existence of specific receptors, an analysis of colors takes place in the eye. On the other hand, discerning the quality of a smell seems to depend mostly on specific receptors for particular smells since the particles of smells may have an immense extent of chemical effects although they may be aided by characteristic patterns, justifying a vast number of smells which we are capable to distinguish. Thereafter, this very interesting hypothesis is confronted with facts, described by Lorenz in a paper, dealing with the ultrastructure and histophysiology of the cellular membrane, nerve fibers and synaptic connections in the olfactory and gustatory receptors of the rabbit. Although the rabbit olfactory receptors are believed to develop a high degree of physiological specificity to substances with different smells, the author did not record any considerable differences in their structures. Two types of receptors have been morphologically distinguished. This classification is based on the presence or paucity of mitochondria in the olfactory rods. The author's suppositions as to the fine structural differences in receptor cells pertain rather to the number and orientation of the cilia constitute. This view is interestingly concurrent with a fact, described by Ottoson, that the cell body does not participate in the production of impulses and that these phenomena occur rather in the hairs of the cell. According to other authors (Gesteland and others), one cell can differ from the next in having different ratios of the receptor sites. In such a case, a receptor response depends on the relative occupation of different sites, or on occupation of a minimum number of sites of more than one type. A problem of the structure and functions of gustatory receptors is also discussed. Since there are four fundamental tastes, it is supposed that there are also four gustatory receptors, each of them represented by a separate group of identically functioning taste buds. Some authors declare for the existence of special receptors, specifically distinctly differentiated, some others consider this problem not from the viewpoint of the existence of many receptor types but — many types of fibers. Maybe, it is more than one type of the taste receptor that are innervated by single fibers. According to these authors, a neural message for gustatory quality is a pattern made up of the amount of neural activity across many neural elements. The division into the four gustatory qualities is not based on the subjective analysis in man only. The four identical groups of stimuli have been

behaviorally established in a vast number of animal species from the invertebrates to man and, in addition, it was proved that, in some species, the water constitutes a separate gustatory stimulus. The existence of an accurate similarity of the gustatory sense in man and animal does not, however, seem to be justified. Although the history of the studies on the taste is fairly long, really comparative investigations were taken up relatively not long ago. On the basis of their experiments, Kare and Ficken believe that each species has its own separate range of tastes and, in addition, their individual differences. On the one hand, therefore, comparative investigations point out the commonness of many phenomena and, on the other, warn against the generalization of the results, obtained in the experiments on a given species. It is even within the same group of animals (mammals) that there are considerable differences in both the reaction to the same chemical compound and anatomical structure of the olfactory and gustatory systems (for instance, in the structure and ramifications of the chorda tympani, Kitschell; in the structure of the thalamus in rats of different varieties, Benjamin; in the structure of gustatory receptors, Beidler and others, etc.).

Due to a considerable versatility and manysidedness of the investigations, it is difficult to summarize, in a brief review, all the papers, published in this volume. In addition to the questions, mentioned above, such problems were investigated as, physico-chemical changes, occurring in receptors as a result of various stimuli, generation and transmission of signals, localization of the functions of taste and olfaction in the central nervous system, „life-time" and sensitivity of receptors in response to anesthesia and to the temperature, correlation between the taste and the control of the food and water intake and between the sensation of taste and various types of organic deficiencies, as well as physiological stages. The problems of the specificity of receptors and nerve fibers, the cooperation of the senses of the olfaction and taste, etc. were examined as well.

Several problems, mentioned above, are still in the early stage of investigation. There is, however, a number of papers whose authors' attention is focused on particular questions, investigated by means of most modern methods and which promise a successful development of this relatively less-known branch of the neurophysiology. A broad range of the subjects, dealt with, can interest the neurophysiologists, neurologists and psychologists. Besides, many questions, still open to discussion and studies (among other things, the localization of the function of taste in the central nervous system), should induce scientists to take up new investigations.

M. Krystyna Lewińska
Łódź, Poland