DEGENERATION AND REGENERATION IN THE CHRONIC SPINAL PREPARATION OF RANA ESCULENTA

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Degeneration and regeneration processes of the peripheral nervous system are basically identical in all vertebrates (Lubińska and Olekiewicz 1950). However, our knowledge of the course of regressive and progressive changes after lesions within the central nervous system of lower vertebrates is incomplete and controversial. Until recently, attention was centred on the longlasting course of degeneration in the spinal cord tracts. Armstrong (1950), and Gamble et al. (1957) pointed out the dependence of the rate of degeneration on the temperature.

It is generally accepted that functional and morphological regeneration of the nervous system in adult Urodela and fish is possible. Tuge and Hanzawa (1937) found regeneration after spinal cord transection of adult Teleosts, and Stefanelli and Cervi (1946), Drummond (1954), and Piatt (1955) had similar results with Urodela. Reviewing publications on regeneration in the spinal cord of Anoura, Piatt (1955) stated that the only positive results in adult Ranidae dated from 19-th century (Sandmayer 1892, Masius and Vanlair 1869) were insufficient due to the limited experimental material and poor histology.

As investigations have been carried out on the plasticity of spinal reflexes in chronic spinal preparations (which will be described elsewhere), it was found necessary to verify the preparations from the morphological point of view. At the same time, the material was evaluated as far as degeneration and regeneration processes are concerned.
MATERIAL AND METHODS

Investigations were carried out on 32 adult specimens of *Rana esc.* (L). Transection of the spinal cord at the level of spino-bulbar junction was made by Fränzisket's method (1951) without narcosis, under sterile conditions. A complete transection was made in 19 specimens, hemisection in 3. The remaining, normal frogs (10) were used as control.

Healthy animals lived up to 2 years after operation, and the post-operative (up to 3 months) mortality rate was no more than 20 per cent. Frogs with damage to the skin probably caused by *Pseudomonas hydrophila* (Reichenbach-Klinke 1961), survived up to a maximum of 4 to 5 months after operation, and the post-operative mortality rate in such cases was 90 per cent.

After the operation, animals were kept in a moist atmosphere, at first in a temperature of 15°C, and later, at 16 to 23°C. After 3 months, they were fed, depending on the temperature, every 2 to 3 days, or even daily.

The animals, histologically examined, survived from 1 to 18 months. Most animals died, probably as a result of changes in the autonomic nervous system. Disturbances were observed, for instance, in the water balance (considerable amounts of liquid appeared under the skin and in the epidermis of the tongue), and they exhibited a tendency to hemorrhage (bursting of vertebral artery, bleeding from a great number of skin capillaries, etc.). It also occurred that even after a year some frogs suddenly stopped breathing by mouth (which was accompanied by darkening of the skin) and died after several days. In the initial postoperative period, some other animals showed a tendency to backward peristalsis (a tendency „to throw” the stomach into the mouth). Under these conditions feeding the animals could be the cause of death. Furthermore, a great number of specimens died in a state of exhaustion. These frogs looked as if they starved. Three specimens with a complete transection, and 3 others with a hemisection, were sacrificed in a good physical condition.

The material was fixed in 10 per cent neutral formalin for not shorter than 10 days. Sections of various thickness (from 4 to 20 microns) were made from paraffin blocks. The brain was embedded *in toto*. Part of the material was embedded in paraffin together with the bone, previously decalcified by 5 per cent sulphuric acid and 5 per cent sodium sulphuride. This method had no appreciable influence on the colouring and morphological picture of the tissue. Serial sections were, as a rule, made in the frontal and horizontal planes. The preparations were stained with Crezyl-violet, or with hematoxylin according to Woelcke, and impregnated with ammonia silver. Sections were successively stained by one of the three methods, so as to obtain a more complete survey of the morphological picture of the whole tissue.

RESULTS

Macroscopic picture of the nervous system of the experimental animals did not differ from that of the control group. In particular, no decrease in the diagonal measurements of the spinal cord and brain stem was observed. There was no dissymmetry as a result of total or partial transection of the spinal cord. The processes of cicatization of
the injured site did not as a rule lead to any pronounced deformation of the nervous tissue. The injured stumps of the nervous system were either enclosed in a common sheath, formed by the meninges, or the cephalic and the caudal ends of the transected spinal cord remained separated (Figs. 1 and 2).

**Microscopic examination.** Nissl staining (crezyl-violet) of transverse sections showed pathological changes, consisting of slight but distinct glial proliferation, but only in the immediate vicinity of the injury (Fig. 3). The nerve cells remained completely intact, even in the neighbourhood of the operation site (Fig. 4). Occasionally, vacuolation of nerve cells appeared both in the experimental and control groups. Myelin exhibited considerable swelling, and fragmentation of fibres was observed almost exclusively in the immediate vicinity of the injury. Some fibres underwent fragmentation, leaving deposits of myelin, which stained intensively with hematoxylin (Figs. 5, 6 and 7). The existence of similar deposits inside the glia cells could not be detected. In places topographically corresponding to the areas of myelin changes, distortion and frag-
Fig. 3. Horizontal cross-section of the operation area
Slight glia and connective tissue reaction. Nissl X 30

Fig. 4. Horizontal cross-section of the operation site with the incomplete spinal cord transection
Nerve cells preserved, minimal glia proliferation in the immediate vicinity of the injury. Bielschowsky X 100
Fig. 5. Myelin changes in the immediate vicinity of operation site
Fragmentation, swelling, separate globules staining with hematoxylin. Woelcke × 400

Fig. 6. Horizontal cross-section of the spinal cord below the transection, 6 months after operation
Slight demyelination
mentation of axon fibres was observed after impregnation with ammonia silver. The above described changes in nerve fibres were, as a rule, local in character despite the long survival period of some of the animals. De-

![Image](http://rcin.org.pl)

**Fig. 7.** Cross section of the spinal cord several hundred microns below the transection, 18 months after operation

*Myelin picture absolutely normal. Woelcke × 30*

composition of fibres could be noticed as far as several hundred microns from the lesion in rostral and caudal sections of the spinal cord. Glial and connective tissue reaction in the areas of progressive degeneration was minimal.

**DISCUSSION**

**Degeneration.** The rather long survival period of the animals suggests that degeneration of the long tracts which pass through the injured area took place. Therefore, the above described slight degeneration changes seemed insignificant as compared with those observed in mammals.

Two mutually excluding hypotheses are possible to explain these observations: 1) There is no degeneration of the long tracts; 2) The apparent lack of degeneration may be due to: a) a lack of ascending and descending long tracts passing through the severed section of the spinal cord, or, b) that long spinal tracts constitute only a small fraction of the fibres which pass in random order through the junction between the brain and spinal cord, thus making their identification (at least by means of histological methods used) impossible. The degeneration of fibres observed in the vicinity of the transection would then apply only to the short intersegmental spinal tracts.
Little is known about the spinal-brain stem coordinating system in Urodela (Herrick 1948). It is, however, certain that Müller’s fibres descending from the metencephalon into the spinal cord and ending at the motor cells are already found in fish. Some authors (Hsiang Tung Chang and Ruch 1954) deny the existence of long afferent tracts in lower vertebrates, considering them as a part of the more complex sensory and behavioural systems. Goldby and Robinson (1962), however, describe long afferent fibres in the dorsal tract of Lacerta viridis (as to the existence of which there are similar doubts), as homologous with the corresponding nerve tracts of higher vertebrates. The above mentioned authors made their observations while examining degeneration of nerve fibres in the central nervous system after dorsal root section in animals kept during the postoperative period at the temperature of over 30°C. It was almost impossible to obtain degeneration of the long tracts at a lower temperature. Taking into consideration the results of Goldby and Robinson it could be stated that the failure of finding degeneration in our material could have resulted from the fact that degeneration did not occur in spite of the existence of the long spinal tracts. The 18-month postoperative period could have been too short to observe the degenerating processes at the temperature in which our experiments were carried out (see also Armstrong 1950, and Gamble et al. 1957).

Regeneration. The majority of authors explains the basic differences between regeneration in lower and higher vertebrates by the fact that in mammals a glial reaction constitutes a mechanical obstacle for the regenerating fibres, thus making renewal of the continuity of the spinal cord impossible. This phenomenon does not appear, or is considerably less marked in poikilothermic animals and in the embryonal stage. It was supposed that removal of the glial barrier (for instance by the administration of pyromen, ACTH, etc.) in the postoperative and recovery periods would advantageously influence the course of regeneration in mammals. However, the results obtained by this method are not encouraging (Wohlfart 1961, McMasters 1962). Investigations of several authors as well as our own observations preclude attributing any particular role to the glial barrier in the prevention of regeneration in the central nervous system. For example, Tuge and Hanzawa (1937), in fish, and Piatt (1955) in Urodela found that regeneration of nerve fibres across the scar sporadically appeared at the operation site. On the other hand, Hess (1954) did not observe regeneration in guinea-pig embryos despite failure of the scar. We did not find any signs of regeneration in spite of a minimal glial and mesenchymal reaction
either. We did not observe the formation of neuromas, a phenomenon typical for the regeneration of nerve fibres under conditions of impeded growth. Since part of the material was embedded in paraffin together with the bone, and serial sections were cut across the injured site, we excluded the presence of thin unmyelinated fibres. It seems that the same basic differences in the course of regeneration can appear not only between the distant animal species (amphibia-mammals), but also between comparatively close related species (Urodela-Anoura).

The histological observations (fragmentation of the fibres only in the vicinity of the transection, lack of retrograde changes in the nerve cells, lack of glial proliferation and regeneration of nerve fibres), and our limited knowledge of the normal anatomic relations of the myelencephalon of the frog together with the observed longlasting motor efficiency of the operated animals rather calls for great caution in the interpretation of the results and indicates the needs for further investigations in this direction.

**SUMMARY**

Regeneration and degeneration in the spinal cord of _Rana esc._ was studied after a complete or partial section at the spino-bulbar junction level. The survival period of animals was from 1 to 18 months.

No symptoms of regeneration of the nerve fibres were observed even though there was an absence of glial barrier.

Degenerative changes in the nerve fibres were observed only in the immediate vicinity of the injured area. The nerve cells were as a rule very well preserved.

Possible explanations of the scarcity of degenerative changes are discussed.

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INHIBITION OF THE PERSEVERATIVE TENDENCY IN RATS

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Our previous studies have demonstrated that rats are able to solve correctly the task of returning to the starting place by the same route which leads to the food (Łukaszewska 1961). However, if the starting place is changed during the experimental session, the animals have a tendency to commit perseverative errors, i.e., to choose the route used in the preceding trial (Łukaszewska 1962).

There is an experimental evidence to show that perseverative errors committed in certain tasks are gradually eliminated. Therefore the problem arose whether in our experimental conditions these errors would also tend to decrease in the course of training. The present investigation is an attempt to solve this problem.

MATERIAL AND METHODS

Nine albino rats were used. They were 5 months old at the beginning of the experiment.

The elevated T maze was employed (Fig. 1). The animals were required to leave the cage which was placed on one of two starting platforms, reach the cup on the maze stem, grasp the food from it and return to the cage where they were allowed to eat.

Experiments were preceded by the preliminary training in which the animals became accustomed to the experimental situation. A full description of the method is given elsewhere (Łukaszewska 1961). Each experimental session consisted of 5 trials. In trials I and II, the animal started from one platform (e.g. S1), and, then, the cage with the rat was transferred to the second platform (e.g. S2) from which the animal started in trials III, IV and V. On the next day, the cage was
situated on the same platform as in the last trials of the preceding day. The whole experimental series consisted of 50 sessions which were divided into 5 blocks, of 10 sessions. Correction method was applied, i.e., the animals were permitted to correct an error in the same trial.

RESULTS

The course of each experimental session was, in general, the same in all 5 blocks (Fig. 2). In trials I and II, the percentage of correct responses was rather high. In trial III, following the change of the starting place, it became much lower. The number of errors diminished again in trials IV and V, in which the starting place was the same as in trial III.
In consecutive blocks a gradual improvement in nearly all trials occurred. However, it was most conspicuous in trial III (Fig. 3). In the first block, the rats reacted correctly only in 40 per cent of cases in trial III, while in the next block the number of correct response increased to 66 per cent, and, then, gradually, to the level of 86 per cent in the fifth block.

After each block, control experiments were carried out consisting of a sham change of starting place in trial III, or in changing the starting place in trial II instead of trial III. Both these procedures did not influence the performance of rats.

The improvement in performance in trial III was not quite symmetrical on both sides of the maze (Fig. 4). When the rats started from the cage situated on the left platform they made less errors in their return route than when the cage was on the opposite platform. In the second block, correct choices on the left path suddenly reached the ultimate level of 80 per cent, while the improvement on right path was more gradual.

Great individual differences were noticed in the behaviour of animals (Fig. 5). Rats Nos. 1 and 2 did not show perseverative tendency at all. Rat No. 5 committed 5 errors in trial III of the first block; rat No. 3, 6 errors; rats Nos. 4, 7 and 9, 8 errors; and rats Nos. 6 and 8, 9 errors. In spite of a marked tendency to repeat the last reinforced response almost all animals succeeded eventually in inhibiting it completely, or, at least, reached a considerable improvement. Only one rat (No. 9) remained at the same level of performance in all blocks (7 to 9 errors in each block).
Fig. 4. Increase of correct responses after the change of starting platform on both paths of the maze
L, trials on the left path of the maze; R, trials on the right path of the maze; 1—10, 41—50, consecutive blocks of experimental sessions. Each column represents the percentage of correct return reactions in trial III.

Fig. 5. Correct and incorrect responses in trial III during consecutive experimental sessions in each rat
1,2,3... 9, Nos. of rats. The marks above the horizontal line denote correct responses; marks below, incorrect responses.
As seen in Fig. 5, the perseverative tendency disappeared at various times in different animals: rat No. 3 reacted correctly from the 13th day, No. 4 from the 24th day, No. 5 from the 36th day, and No. 6 from 39th day on. It should be emphasized that suppression of this tendency was permanent, and when it occurred no more errors were observed in the given animal.

In consecutive blocks, improvement was noticed also in other trials. Thus, in addition to a high performance in trials I and IV of block I, the number of correct responses in the last block increased to about 100 per cent. Due to the fact that the rats were doing well in trials II and V at all times, improvement in these trials was not observed.

DISCUSSION

Although perseverative symptoms are most often observed in pathological states, either functional (neuroses) or organic (brain lesions), they are also noticed in normal animals. Thus during the course of discrimination learning perseverative errors commonly occur in monkeys (Harlow 1950, Braun, Patton and Barnes 1952, Davis, McDowell and Thorson 1953), and rats (Mac-Gillivary and Stone 1930, Spence 1936). Ławicka (1959) observed perseverative errors in normal cats during delayed response training. As a rule, perseverative tendency in normal animals is only transitory and is suppressed in the course of training. In Harlow's experiments, perseveration in monkeys (called by him differential cue factor) was seen in the first 200 problems but, then, it significantly decreased. The same is seen in our experimental material. As indicated in a previous paper (Łukaszewska 1962), rats while returning to the starting place, after having seized food on the maze stem, show a competition between two reactions. One of them is guided by the traces of the run towards food (proper return reaction), the other one is guided by the traces of the return run in the previous trials (perseverative reaction). According to our present data, the second tendency may become gradually suppressed, and it ceases to occur after a long training.

SUMMARY

It has been found that, in rats, the perseverative tendency observed in the return reaction after the change of the starting platform tends to decrease in the course of training.

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REVERSAL LEARNING IN FRONTAL RATS

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In the first paper of this series (Dąbrowska 1959), it was shown that in a four-unit-quadruple-choice-apparatus the rate of mastering the habit of running through the apparatus for food changes considerably in successive tasks. On the average, the first task requires about 50 trials to reach the criterion of 6 errorless runs. However, in the second task, with a different set of doors unlocked, training is much more rapid, requiring only about 28 trials. In each subsequent task, the animals master the problem more and more promptly until they are able to reach the criterion in a few trials.

This spectacular improvement in the performance of the rats has been explained by assuming that the animals gradually learn to synthesise the whole run through the apparatus, so that it ultimately represents not a complex but a single motor act which can probably be solved even in one trial. This conclusion is supported by the fact that even if the change in doors is restricted to the final partition, the whole habit is destroyed and must be learnt afresh (Dąbrowska 1963).

There is both experimental (Stępień et al. 1960) and clinical (Lurić 1963) evidence that both animals and humans with lesions in the premotor cortex have difficulty in performing chains of motor acts. It would therefore be interesting to see if similar lesions in our experimental animals would have a disturbing effect on the formation of habits in the four-unit-quadruple-choice-apparatus.

The elucidation of this problem was the aim of this paper.
MATERIAL AND EXPERIMENTAL PROCEDURE

Experiments were performed on 25 white rats, 2.5 month old. During the training period the animals were deprived of food for 22 hours before testing.

The apparatus was the same as that used in our previous study (Dąbrowska 1959, 1963), (Fig. 1). It was composed of four units, A.B.C.D., with the transverse partitions. Each unit had four doors, 1.2.3.4. In the preliminary training, which lasted 6 days, all the doors were unlocked, so that the animals could pass from the starting platform to the goal-box by any route.

After the preliminary training had been terminated the animals were divided into three groups: Group I (normal group) consisted of 10 animals. They were subjected to a sham operation consisting of removal of the bone covering the frontal area. Group II (frontal group) consisted of 10 animals. Each of them was subjected to an operation in which the rostro-dorsal parts of the cortex in front of the motor area were bilaterally removed (Fig. 2, Nos. 1 to 10). Group III (motor group) consisted of 5 animals with lesions in the motor area (Fig. 2, Nos. 11 to 15).

Each type of operation had been performed one month before the proper experiment. Localisation of the frontal and motor areas was defined according to Zubek (1951). The cortex was removed by suction under nembutal anesthesia. The recovery of the animals was uneventful.

The first task was the same for all the animals. In this task only one door in each partition was unlocked, so that the animals had to learn the route required to reach the goal. 6 trials were given in each experimental session.

In the first task, the route which the animals had to pass was A-4, B-2, C-3, D-1. When the rats reached the criterion (6 errorless trials in succession) the route of the maze was changed to A-2, B-4, C-1, D-3. After this task had been mastered, the frontal animals were subjected to the third task in which the doors A-3, B-1, C-4, D-2 were unlocked.

After the termination of the whole series of experiments, the animals were sacrificed, the brains removed, fixed in 10 per cent formalin, embedded in paraffin and cut serially. The sections were stained with Nissl technique and reconstructions

Fig. 1. Four-unit-quadruple-choice-apparatus
A, B, C, D, Partitions; 1, 2, 3, 4, Doors in each partition

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of the cortical lesions were done as described by Lashley (1931). The black areas in Fig. 2 denote the parts of brains in which both grey and white matter were removed. Striped parts show the parts in which grey matter was removed. Striped parts show the parts in which grey matter was removed with or without a slight damage to the white matter.

RESULTS

In Fig. 3, the course of training in the first task in each group is represented. As seen from the figure, there are no significant differences between groups in the rate of acquisition of the habit. This is also seen in Table I in which the numbers of trials to criterion are shown for each rat. The number of trials required to reach criterion varied between 48 and 56 (mean 51.7), in normal animals; between 53 and 66 (mean 57.6), in frontal animals; and between 54 and 58 (mean 55.6), in the motor group.
Fig. 3. Average number of errors made by rats with lesions of the frontal or motor cortex, and by normal rats in the first task (original learning). 1, normal rats; 2, rats with lesions of the frontal region; 3, rats with lesions of the motor cortex.

Table I
Number of trials to criterion in successive tasks in rats with lesions of the frontal or motor cortex and in normal rats

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<tr>
<th>No. of rat</th>
<th>Frontal Group</th>
<th>Motor Group</th>
<th>Normal Group</th>
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<td>57.6</td>
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The course of the second task for all groups is given in Fig. 4. It may be seen that in normal and motor groups the training goes much more rapidly than in the frontal group. For the normal group the number of trials required to reach criterion was 22 to 32 (mean 26), in the motor group it was 24 to 30 (mean 26), while in the frontal group as many as 55 to 63 trial (mean 58.2) were necessary (Table I).

As indicated in the previous section, the frontal animals were also submitted to a third task. Both from Fig. 5 and from Table I, we see that the course of acquisition of this task is very similar to that of the first and second ones, each of them requiring nearly the same number of trials to criterion. The only difference between the first, the second and the third tasks occurred in the first two experimental sessions (12 trials). While the average number of errors in the first task was 8.7, in the second task it was 6.4, and in the third, 5.2.

Fig. 4. Average number of errors in rats with lesions of the frontal or motor cortex, and in normal rats in the second task
1, normal rats; 2, rats with lesions in frontal region; 3, rats with lesions in motor cortex
Fig. 5. Average number of errors in rats with lesions of the frontal region in the first, second, and third tasks
1, the first task; 2, the second task; 3, the third task

DISCUSSION

The results of our experiments clearly show that, in the original task, the rats with frontal and motor lesions did not differ significantly from normal rats. In subsequent tasks, the rate of acquisition in both normal and motor groups was much reduced. In contrast, learning of the frontal group in successive tasks was nearly the same as in the first task. The third task, which was mastered by normal animals even more rapidly than the second task (about 18 trials to criterion according to the previous data, Dąbrowska 1959), was solved by animals with frontal lesions at the performance level of the first and second tasks. In other words, the frontal animals did not appear to utilize the experience acquired in the earlier tasks. The fact that this deficit was observed only in animals with frontal lesions suggests that it is specific for this type of lesion.

In the region situated in front of the motor area on the dorsal surface
of the rat's brain, the premotor and prefrontal areas have not been differentiated so far. It is very likely that our frontal ablations included both areas.

In view of the present results, our hypothesis put forward in the beginning of this paper seems to be substantiated. Thus, while the normal animals in the course of successive tasks learn to synthesise the chain of motor acts of a given habit, the frontal animals are not able to do so. For frontal animals, each task appears to be composed of four separate tasks, one in each unit of the maze, and this remains in the subsequent tasks. In other words, frontal animals are not able to integrate the components of the task.

The only difference between the first, the second, and the third tasks in the frontal group was found during the performance on the first 12 trials, in which the number of errors became smaller in each series. An analysis of errors showed that this was due to some general practice acquired by the animals in dealing with the task, namely that the rats learnt not to approach the door in each partition more than once at a time.

A few investigations have recently been reported on the behaviour of rats with frontal lesions (Epstein and Morgan 1943, Carpenter 1952, Maher 1955, Maher and McIntire 1960). However, different methods from ours as well as different factors, such as goal gradient, anticipation, and perseverative errors, have been used. Analysis of errors committed by the rats in our apparatus did not show any evidence of an increase in perseveration in frontal animals as compared with normal ones, or with those with lesions of the motor cortex. It seems that this discrepancy is due to different tasks used in different studies.

SUMMARY

1. The rate of acquisition of successive tasks in the four-unit-quadruple-choice-apparatus in normal rats and in rats with frontal or motor lesions was studied.

2. It was found that the rate of acquisition of the first task was nearly the same for all three groups.

3. The rate of acquisition of the second task was considerably reduced in normal animals and in animals with motor lesions. Contrastly, animals with frontal lesions performed at the level of the first task. Furthermore, while, in the third task, the rate of acquisition of normal animals was even more reduced, animals with frontal lesions remained at the original level of performance.

4. The mechanism of the deficit in learning ability of frontal rats is discussed.
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FUNCTION OF CINGULATE AND PREFRONTAL CORTEX IN FRUSTRATIVE BEHAVIOR

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Ever since Papez (1937) proposal for a neural mechanism of emotion investigations have been conducted to clarify the behavioral functions of neural structures within the rhinencephalic system. Supporting evidence for Papez thesis has been derived from behavioral changes following amygdalectomy in monkeys, especially with regard to aggressive behavior (Klüver and Bucy 1939) and dominance status (Rosvold et al. 1954). Ablations of cingulate cortex, however, has not been found to affect aggressive or dominant behavior in monkeys (Pribram and Fulton 1954; Mirsky et al. 1957) and, as stated in a recent review article "...as regards the anterior cingulate region, renewed studies find as yet no conclusive evidence to substantiate the earlier claims of the importance of this area in emotion" (Kaaada 1960, p. 1368). A clue to the possible implications of cingulate cortex in behavior has been reported by Pribram and Fulton (1954) who observed shortened duration of avoidance behavior in a "frustrating" situation after cingulectomy. These authors observed similar reactions in a monkey after ablation of dorsolateral frontal cortex.

The present experiment was designed to investigate more systematically the role of cingulate cortex with regard to frustrative responses. Frustration has been conceptualized (Amsel 1958) as an implicit reaction elicited by non-reward after a number of prior rewards. In the normal animal the withholding of a reward after training which leads to...

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1 This investigation was conducted at the Institute of Living, Hartford, Connecticut, U.S.A. with support from Grant G-9688, National Science Foundation. The author gratefully acknowledges the advice and assistance of Dr. Karl Pribram, Donald Chambers, and Marcia Knight.
the expectation of rewards results in a frustrative behavior. The experimental requirements for eliciting frustrative responses might be met by the operant schedule of reinforcement, labelled DRL (differential reinforcement at low rates, Wilson and Keller 1953). On this schedule an animal receives a reward for pressing a lever, provided it has refrained from responding for a predetermined delay period. If it presses too soon, the reward will be further delayed. By first training monkeys on the DRL schedule with a short delay setting, so they obtain a high ratio of rewarded responses, and then suddenly lengthening the delay, frustrative responses might be elicited following lever presses which had previously been rewarded.

This experimental design has been followed in the present experiment with cingulectomized and normal control monkeys. Because of the observations by Pribram and Fulton (1954) and the clinical interest in prefrontal lobe functions, monkeys with ablated dorsolateral prefrontal cortex were also tested.

MATERIAL AND METHODS

Subjects. Three groups of immature monkeys were used-four monkeys (Group C) that had been subjected to bilateral ablations of cingulate cortex, six monkeys (Group F) that had had bilateral ablations of dorsolateral prefrontal cortex, and six normal controls (Group N). All of these subjects had been used in a previous experiment on timing behavior (Stamm 1963).

Apparatus. The subject was tested in a portable cage (16” × 13” × 22” high), that was placed in a sound-absorbing converted icebox. The front of the cage faced a white lucite panel, from which a lever protruded one inch into the cage. A food cup was beneath the lever. A dimooverhead light provided constant illumination, and blower provided air circulation and a masking noise.

Control and recording panels were located in an adjacent room. The subjects were trained on the DRL schedule of reinforcement. For this schedule the first lever press in each session was rewarded with a 48 mg. dextrose pellet, and subsequent presses were rewarded only if they occurred after a predetermined delay period. If the monkey pressed during the delay, the timer reset so the subject had to wait until the delay terminated before it could receive a reward. Concomitant with each reward a white light behind the lucite panel was turned on for two seconds. Responses and rewards were recorded on counters, a cumulative recorder, and an Esterline Operation Recorder.

Procedure

Prior Training. In the previous experiment (Stamm 1963) the subjects had been trained on the DRL schedule with gradual delay increments. They were first tested on 10 sec. delay settings until they met the criterion of 50% rewarded responses during each of three consecutive sessions or during the first, second, and
fourth of four consecutive sessions. On the following day the delay was increased to 15 sec. and training continued to criterion. This procedure of step-wise increments by 5 sec. was continued to the maximum setting of 70 sec. delay or until a subject failed to meet criterion. If a subject did not meet criterion performance after 25 sessions on a delay setting, that delay was increased by 5 sec. and testing continued for a maximum of 15 sessions. Monkeys which did not meet criterion on that delay were considered to have failed. In that experiment all subjects met criterion on the 25 sec. delay setting, but on longer delay settings subjects in each group failed. On the 70 sec. delay criterion was met by only two normal and three prefrontal monkeys.

Present Experiment. On the day following completion of the prior training, each subject was tested on the DRL schedule, with a delay setting 60 sec. longer than that on which it had previously met criterion performance. Consequently, delay settings for individual subjects were from 85 sec. to 130 sec. Fifteen consecutive daily sessions were given, each of 80 or 100 min. duration, depending upon the length of the delay setting.

RESULTS

Anatomy. The surgical procedure and landmarks for cingulate ablations were similar to those previously described (Pribram and Fulton 1954), except that resection of cingulate cortex continued posteriorly, approximately to the level of the splenium of corpus callosum. Reconstructions of these ablations (Fig. 1) show nearly complete destructions of cingulate cortex, with occasional damage to adjacent cortical structures and to corpus callosum. The intended limits for dorsolateral prefrontal ablations were from frontal pole to anterior bank of arcuate sulcus, and from midline to orbital surface, including the banks and depth of principal sulcus. Reconstructions of the brains indicate complete ablations within these limits for all subjects, except for one where the tip of one frontal pole was spared.

Behavior. The two normal and four prefrontal monkeys, which in the previous experiment (Stamm 1963) had met criterion on the 70-sec. delay, were tested on 130-sec. delay. For the other subjects, delay settings were between 85 and 120 sec. Because of the procedural requirements in the previous experiment differing numbers of training sessions had been given to individual subjects before the 60 sec. delay increment. There were, however, no systematic differences among the experimental groups in the amount of prior training, as seen by median scores (Table 1), or in the ranges of scores for subjects within each group, which were from 80 to 160 sessions (except for one normal monkey, 71 sessions). Also, there were no systematic differences in the amount of prior training between the groups of monkeys tested on 130 sec. delay and on shorter delay set-
tings. The response patterns for each subject stabilized during the course of testing, so quantitative analyses were based on the subjects' performance during the final four testing days.

The records of responses frequently revealed episodes of two or more lever presses in rapid succession. Responses which occurred after inter-response intervals of two seconds or less were scored as multiple presses, while responses after longer intervals were considered timing responses.

Fig. 1. Reconstructions of cingulate ablations. Ablated areas are indicated in black. For each brain the cross-sections correspond to the levels indicated for #389.
The proportion of multiple presses to total number of responses was appreciably higher for the normal than for the brain-lesioned monkeys. Group medians of these proportions are indicated in Table I and represented by Fig. 2. For individual subjects scores ranged from 10.8 to 23.8 for Group N, 1.7 to 10.0 for Group C, and 1.1 to 9.2 for Group F. The higher incidence of multiple presses for normal monkeys is statistically highly significant (Mann-Whitney U-test, p < .001).

### Table I

<table>
<thead>
<tr>
<th>Group</th>
<th>No. Sessions - Prior Training</th>
<th>Multiple Press</th>
<th>Reward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cingulate</td>
<td>113</td>
<td>4.1</td>
<td>13.6</td>
</tr>
<tr>
<td>Prefrontal</td>
<td>111</td>
<td>5.6</td>
<td>18.4</td>
</tr>
<tr>
<td>Normal</td>
<td>128</td>
<td>16.1</td>
<td>9.2</td>
</tr>
</tbody>
</table>

1 percent multiple presses of total responses
2 percent rewards of timing responses

Multiple presses occurred, moreover, predominantly after nonrewarded lever presses, as seen by the following analyses. Each subject's response records were examined for multiple press episodes on the eight alternate sessions during the 15 session period. For responses following rewards the median incidence of these episodes was 2.5 per cent of rewarded responses for Group N, 0.4 per cent for Group C and 1.5 per cent for Group F, whereas the medians of multiple press episodes were 15. per cent of nonrewarded timing responses for Group N, 5. per cent for Group C, and 6. per cent for Group F.

The rates of rewarded responses, as percentages of timed responses, resulted in higher median values for the cingulate and prefrontal groups

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Fig. 2. Percent of group medians for. (I) multiple presses to total number of responses; (II) rewards to timing responses; and (III) responses after interresponse times longer than twice the means. N, normal group, F, prefrontally ablated group, and C, cingulectomized group.
than for the normal group (Table I and Fig. 2). There was considerable overlap, however, among reward scores for subjects in these groups, so group differences were statistically not significant.

The distributions of interresponse times (of timing responses) are presented in Fig. 3. The distributions in the left column are means for two subjects in each group on delays of 85 or 90 sec., those in the middle column are for two normal and two cingulate monkeys on delays near 105 sec., and the graphs in the right column are for the two normal and three prefrontal subjects tested on 130 sec. delay. The distributions for the normal monkeys express marked disruptions of timing behavior, with high proportions of very short and very long (more than 130 sec.) interresponse times. By contrast, the prefrontal and cingulate groups obtained

![Fig. 3. Interresponse time distributions (of timing responses) during last four sessions. Means for subgroups on delay settings (D) indicated. Arrows indicate mean interresponse times. Units of interresponse times are 12.8 sec. for left hand column and 25.6 sec. for other distributions](http://rcin.org.pl)
relatively adequate timing distributions. Although the normal and prefrontal subgroups tested on 85 or 90 sec. obtained the same mean interresponse time (32 sec.), the shapes of the two distributions differ markedly.

The degree of positive skewing of the distributions may be expressed by the proportion of timing responses longer than twice the median interresponse time for each subject. Medians of these indices for the three groups, as represented in Fig. 2, indicated no marked differences among the groups. However, the three prefrontal subjects that were tested on the 130-sec. delay obtained lower indices (1.3 per cent to 3.4 per cent) than did any of the normal monkeys.

On the 130-sec. delay setting marked differences were obtained in the IRT distributions between the normal and prefrontal subgroups (Fig. 3). The mean IRT (67 sec.) for the two normal monkeys on this setting was shorter than the mean IRT (76 sec.) which these subjects had obtained on the previous 70-sec. delay setting. By contrast, the three prefrontal monkeys, whose mean IRT on the 70-sec. delay was 72 sec., were able to adapt their responses on the final 130 sec. delay, so that they obtained a mean IRT of 112 sec. The shift in mean IRT by the prefrontal monkeys from 72 to 112 sec. is statistically significant (t-ratio = = 17.7; p (.01).

DISCUSSION

The outstanding finding in the present experiment is the higher incidence of multiple presses by normal than by the brain-damaged monkeys. High proportions of short interresponse times (below two seconds) seem to be characteristic for interresponse time distributions on the DRL schedule for rats (Sidman 1956) and for monkeys (Brady 1960). But the incidence of these short interresponse times is also dependent upon the experimental procedure, as has been discussed in a previous communication (Stamm 1963), because they occur only rarely under the procedure of gradual delay increments.

The finding that multiple presses were emitted predominantly after nonrewarded responses satisfies Amsel's (1958) requirements for the conditions eliciting frustrative responses. We observed, furthermore: (a) that multiple presses generally did not occur after the first nonrewarded response following a reward; (b) that multiple presses were frequently succeeded by short interresponse times or by bursts of lever presses in rapid succession; and (c) that the subjects during multiple press episodes exhibited gross "emotional" behavior patterns, as expressed by hyperac-
tivity, yelling, or banging on cage and apparatus. Consequently, the rate of multiple presses may be considered as an index of frustrative behavior.

No systematic behavioral differences were obtained in the present experiment between the cingulectomized and prefrontal lobectomized groups of monkeys. This finding agrees with the report by Pribram and Fulton (1954). The anatomical connections between these two cortical structures might be responsible for the lack of differential results between the two experimental groups.

The present findings of lower rates of frustrative responses by the cingulectomized and prefrontal lobectomized monkeys are in agreement with the earlier observations by Pribram and Fulton (1954). These results, point to relatively subtle behavioral differences between normal and brain damaged monkeys, since the latter subjects showed no marked impairment in meeting the experimental requirements and exhibited no gross emotional disturbance, such as excessive fear or aggressiveness toward the experimenter. Similar findings by Miskye et al. (1957) lead to the conclusion that cingulectomy in monkey does not necessarily result in disturbed emotional behavior. In contrast to these reports, cingulectomy has been found to greatly increase the dog's savageness and aggressiveness toward man (Brutkowski et al. 1961) and to markedly impair hoarding (Stamm 1954) and disrupt maternal behavior (Stamm 1955) in rats. The differing consequences of cingulectomy may of course be related to species differences. However, consideration should also be given to the environmental conditions which may affect the behavioral consequences of brain damage. The monkeys in the present and the previous investigations had had a great deal of experience in the experimental situation before they were tested for emotional responses and in the social experiment a stable dominance hierarchy had been established prior to cingulectomy. In the hoarding experiment, the cats also had a certain amount of preoperative testing, whereas in the maternal experiment the rats had only limited prior experience, by having given birth to one litter each before cingulectomy.

The increased threshold for frustrative responses found in the present experiment would implicate cingulate and prefrontal cortex in the neuronal control of emotional behavior. Primary motivation by the brain damaged subjects, however, was not markedly impaired, since their rates of timed lever presses were not below the rates by normal controls and they actually obtained more rewards than did the normal monkeys. The function of cingulate cortex may be related to the functions of other rhinencephalic structures, because of the extensive anatomical interconnections in this neuronal system. Gloor (1960) assigns to the rhinence-
phalic system functions of modulating primary motivational activities which are integrated in subcortical structures. With regard to the amygdaloid structures Gloor (1960) concludes that the basic defect resulting from amygdaloid lesions „could be described as a disturbance in those motivational mechanisms which normally allow the selection of behavior appropriate to a given situation” (p. 1416). He therefore considers these structures to be implicated in „motivational selection”. It is then conceivable that cingulate cortex and related structures function in a second motivational modulating system, which serves to maintain a high state of drive. This hypothesis might explain the present paradoxical finding of superior performance by the brain-damaged subjects. The higher drive state in the normal subjects under the conditions of motivational conflict resulted in frustrative responses, which in turn interfered with efficient performance. The more precise functions of this motivational modulating system in relation to frustrative situations need to be examined by further experimentation. Of particular relevance will be the interactions between the experimental conditions and motivational variables in evaluating the consequences of cingulectomy.

SUMMARY

Three groups of monkeys — 4 subjects with ablated cingulate cortex, 6 subjects with ablated prefrontal cortex, and 6 normal controls — were tested on the operant DRL schedule. On this schedule a food reward is given for a lever press, provided no response had been given for a predetermined delay period. If the lever is pressed during the delay, the subject has to wait again for the period of the delay in order to receive a reward. All subjects had prior training with the DRL schedule, under conditions of gradual delay increments (Stamm 1963). The experimental testing was with a delay setting 60 seconds longer than the last setting on which the subjects had prior training. Fifteen daily sessions were given.

The response records revealed episodes of multiple presses, i.e. responses which occurred within 2 second intervals. The normal monkeys responded at significantly higher rates of multiple presses than did either of the brain-damaged groups. No significant differences were obtained between the cingulectomized and prefrontal lobectomized groups. Interresponse time distributions revealed clearer timing responses by the ablated than by normal subjects.

Analyses of the results indicate that multiple presses were expressions
of frustrative behavior. The paradoxical finding of superior performance by the brain-damaged monkeys is interpreted in terms of motivational function of cingulate cortex. It is proposed that this neuronal system serves to maintain a high drive state in the organism.

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CONDITIONING AND TRANQUILIZING ACTION.
I. THE EFFECT OF TRANQUILIZING DRUGS ON CONDITIONED REFLEX TYPE II ACTIVITY FOLLOWING TRANSFORMATION OF AN ALIMENTARY CS INTO A DEFENSE CS*

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There is a general agreement that tranquilizing drugs like chlorpromazine, reserpine or hydroxyzine are very effective in decreasing or abolishing a defense (avoidance-type) conditioned reflex activity. It has however been indicated that the dosages of tranquilizers which are capable of interfering with defense behavior in animals exceed by far those used in human patients. For instance, the dosages of hydroxyzine which exert an inhibitory effect upon an avoidance response amount up to several dozens of miligrams per one kilogram of body weight (Desce 1961, Levis et al. 1961, Maffii 1959). A logical implication of this finding is that the efficacy of the tranquilizing drugs (or at least some of them) in medical treatment has no or little relation to the depressant effect of those drugs on defensive conditioning. This is not altogether a surprise since the beneficial effect of this class of pharmacological agents upon a variety of behavior disorders can hardly be interpreted in terms of reducing or blocking the conditioned reflex performance, i.e. a kind of activity which permits the organism to fit to its environment. One possible explanation is that the tranquilizing drugs are most efficacious in producing differences in behavior response patterns. To verify this hypothesis it was attempted to device a method which would permit to watch an animal reacting to the presentation of a conditioned sti-

mulus (CS) associated with responses based on two antagonistic reinforcements.

The method of CS-transformation developed by Pavlov and his students (Frideman 1951, Rikman 1949, Jakovleva 1944, Vatsuro 1948), and recently adopted by Konorski and Szejkowska (1952, 1956), and the author (Wojtczak-Jaroszowa 1962 a, b), was expected to be particularly reliable to carry out such experiments. It consists either of formation of an alimentary response to a CS which was originally paired with punishment by means of an electric shock, or, vice versa, of formation of a defense response to a CS previously associated with food reinforcement. It further was anticipated that this method would reveal its usefulness in reflecting the role of tranquilizing drugs in certain types of behavioral inhibition. This expectation was based on the evidence that the CS-transformation procedure is associated with suppressing the previously acquired behavior patterns.

In view of the above considerations, the present investigation was undertaken to study the effects of chlorpromazine, reserpine and hydroxyzine on conditioned reflex activity type II following transformation of an alimentary CS to a defense CS.

MATERIAL AND METHODS

Animals and experimental situation. Experiments were carried out on 5 adult male mongrel dogs, weighing from 7 to 15 kgms. The experimental situation was a regular sound-proof conditioned reflex chamber equipped with a small window placed so that all parts of the chamber could be seen. Within the chamber, a Pavlovian frame was mounted in which the experimental animal was placed in harness during the testing session. The animal faced and had access to a food box situated in the anterior portion of the frame. The food box contained a round tray equipped with 10 food cups covered by the top lid, except the front cup which was empty and visible through a small opening; the remaining cups were filled out with the experimental food. A small board holding conditioned signals was attached to the chamber side in front of the animal. Both the food tray and the signals were activated by the experimenter from outside the chamber. By turning on a switch the experimenter caused a restricted rotation of the food tray, whereby the food cup containing the food reward was placed in the position of the empty cup, being accessible to the animal. The animal's responses and the presentation of CSI were recorded on a kymograph.

Procedure

Training of an alimentary CR. The CSI were an intermittent flashing a lamp in dog No. 1, the sound of a buzzer in dogs Nos. 2, 3 and 4, and a tactile excitation of the skin on the animal's back in dog No. 5. The instrumental (or type II) CR consisted of the animal placing its right foreleg on the food tray, trained by passi-
ve placing the leg during the pre-testing period (Końorski and Miller 1933). Each trial was started by the presentation of a CS, followed by the CR. After the response had been made the food reward was delivered.

Each day, 8 to 10 trials separated by intervals, ranging from 30 sec. to 1 min., were used. Training was continued until a criterion of a fully correct responding pattern within 10 consecutive days was attained. The animals were then allowed a week of no testing which was followed by training of a defense CR.

Training of a defense CR. All testing was conducted in the previous experimental situation. The CSi (hereinafter called „regular defense CSI, RCSi“) were: the sound of a whistle in dog No. 1, intermittent flashing a lamp in dogs Nos. 2, 3 and 4, and the sound of a buzzer in dog No. 5. Each animal was trained to avoid electric shock, ranging from 40 to 60 volts, applied to the animal’s right hind leg. In dogs Nos. 2, 3 and 4, the avoidance response was a flexion of the leg in response to the presentation of a CS, trained by passive flexing the leg prior to regular testing. The conditioned avoidance response in dogs Nos. 1 and 5 was barking, which was taught by not reinforcing a contingent vocalization response accompanying noxious reinforcement during the pretesting period. The CS remained on for 5 sec. permitted for response. If the prescribed response did not occur, the shock was delivered, and an intertrial interval lasting randomly between 30 sec. and 1 min. was begun. Eight to 10 trials were used daily.

CS-transformation and drug administration. Dogs Nos 1, 2, 3, 4, and 5 then were given drugs prior to testing session to see the effect of drug administration on regular avoidance behavior (Experiment 1). This was followed by CS-transformation experiments. On half the trials the avoidance CS occurred, and on half the trials the alimentary CS, each presentation of the alimentary CS being followed by shock until the animal made an avoidance response. The sequence of CS presentations was randomized. If the animal succeeded in making the appropriate response before shock was given, the alimentary CS (hereinafter called „a transformed defense CS, TCS“) was terminated and shock postponed.

Training was discontinued when the animal made 11 avoidance CRs to the presentation of the defense TCS within a series of 12 consecutive trials. Hereafter dogs Nos. 1, 2, and 5 were submitted to drug administration (Experiment 2). During drug experiments no shock was ever administered, no matter whether or not a CR was elicited.

Chlorpromazine (Largactil-Specia) was injected intravenously in a dosage of 0.5 mg/kg of body weight; reserpine (Sedaraupin-„Boehringer“) was given intramuscularly in a dosage of 0.04 mg/kg; hydroxyzine (Atarax-Union Chimique Belge S.A.) was given intramuscularly in a dosage of 4.5 mg/kg. Testing the animal was started 30 min after administration of chlorpromazine, 3 hrs. after reserpine, or 2 hrs. after injection of hydroxyzine. The drugs were given periodically, on every 10th day.

RESULTS

Generally, the tranquilizing drugs at the dosage level used in this experiment were without any marked effect on gross motor behavior, except for some sluggishness and narrowing the eyes 1/2 hrs. after chlorpromazine administration, which was reminiscent of a sleep condition.
Experiment 1

As seen in Table I, chlorpromazine was very effective in decreasing or delaying the avoidance performance. Contrastly, neither hydroxizine nor reserpine were capable of altering the avoidance response. The only effect noted was a slight extension of latency after reserpine administration.

Table I

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Percentage of conditioned avoidance responses after administration of</th>
<th>Chlorpromazine</th>
<th>Reserpine</th>
<th>Hydroxizine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog No.</td>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>100</td>
<td>10</td>
<td>100</td>
<td>100</td>
</tr>
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<td>2</td>
<td>100</td>
<td>10</td>
<td>100</td>
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<tr>
<td>3</td>
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</tr>
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</tr>
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<tr>
<td>9</td>
<td>100</td>
<td>0</td>
<td></td>
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</tr>
</tbody>
</table>

-, not tested.

Experiment 2

Chlorpromazine. That chlorpromazine has marked reducing effect on avoidance behavior under CS-transformation conditions is well borne out by the data in Table II. It is seen that the TCS was persistently follo-

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Fig. 1. Dog No. 5. Fragment of a record from an experiment carried out prior to drug administration

RCS, regular conditioned stimulus; TCS, transformed conditioned stimulus; I, avoidance response (barking); II, alimentary conditioned response (fleing the right foreleg); III, conditioned stimulus; IV, time (5 secs.)
CONDITIONING AND TRANQUILIZING ACTION

Fig. 2. Dog No. 5. Fragment of a record from an experiment carried out after chlorpromazine administration

Explanations as in Fig. 1

wed by no avoidance response, and the RCS elicited a response only occasionally. It is of interest, however, that, on half the trials with TCS the alimentary CR occurred. Figs. 1 and 2 are records of experiments in dog No. 5 before and after chlorpromazine administration.

Fig. 3. Dog No. 5. Fragment of a record from an experiment carried out after reserpine administration

Explanations as in Fig. 1

Reserpine. The administration of reserpine also effectively reduced the avoidance responses both to the presentation of RCSi and TCSi with a greater deficit in the second situation. In 18 trials with TCS, the response was elicited only 6 times. In general, a considerable variability in responsiveness from day to day was found. Thus sessions with fully correct

Fig. 4. Dog No. 5. Fragment of a record from an experiment carried out after hydroxyzine administration

Explanations as in Fig. 1

reflex activity were followed by poor performance, and vice versa. It should be noted, however, that in the case of a failure of an avoidance response no alimentary CR was produced either. The results are given in Table II. Figs. 1 and 3 illustrate segments of records in dog No. 5 obtained before and after reserpine administration.
### Table II

**Experiment 2 (CS-transformation)**

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Number of RCS presented in each experiment</th>
<th>Number of avoidance responses after administration of chlorpromazine</th>
<th>Number of avoidance responses after administration of reserpine</th>
<th>Number of avoidance responses after administration of hydroxyzine</th>
<th>Number of TCS presented in each experiment</th>
<th>Number of avoidance responses after administration of chlorpromazine</th>
<th>Number of avoidance responses after administration of reserpine</th>
<th>Number of avoidance responses after administration of hydroxyzine</th>
<th>Number of alimentary responses administration of chlorpromazine</th>
<th>Number of alimentary responses administration of reserpine</th>
<th>Number of alimentary responses administration of hydroxyzine</th>
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<td>5</td>
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<td>18-22</td>
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<td>6</td>
<td>19</td>
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</table>

—, not tested.

**Hydroxyzine.** Following hydroxyzine administration no detectable change in regular avoidance response was observed, and drug was also relatively ineffective in diminishing the defense TCR. Only in a single experimental session in dog No. 1 was the defense TCR found to be impaired on 3 trials out of 5. The only contamination noted was that on ca. half the trials the TCS elicited both the defense and alimentary CRs. Table II summarizes the main results, and Figs. 1 and 4 are records of experiments in dog No. 5 before and after hydroxyzine administration.

**DISCUSSION**

The present findings indicate that, except for chlorpromazine, the tranquilizing drugs like reserpine and hydroxyzine in dosages used in this experiment do not affect the avoidance response trained under regular circumstances. At the same time, all three drugs are found to interfere with an avoidance response elicited after transforming an alimentary CS to a defense CS.

The abolition of an avoidance response under chlorpromazine administration is interpreted in terms of the drug blocking the synaptic transmission from the afferent pathways to the neural centers involved in the
defense conditioned-reflex arc (Anokhin 1961, Rutledge and Doty 1957, Shumilina 1961, Wojtczak-Jaroszowa 1962c). This accounts for the opposite effects of chlorpromazine on alimentary and defense types of behavior in the CS-transformation experiment: a general decrease in avoidance conditioning associated with the recovery of the alimentary response. According to our earlier results (Wojtczak-Jaroszowa 1962a, b) and those of Konorski and Szwiejkowska (1952, 1956) the kind of conditioned response to be elicited under transformation conditions is largely dependant upon the emotionality level. It thus was found that a decrease in anxiety obtained by means of extinguishing the avoidance response was associated with the reacquisition of the alimentary response (Wojtczak-Jaroszowa 1962b). The data of this study indicate that this is also true for chlorpromazine condition.

One of the principal differences in the effect of chlorpromazine as compared with reserpine upon the defense behavior is the depressant action of reserpine upon avoidance response after CS-transformation (Experiment 2) with no sign of success before it (Experiment 1). It is interesting to note that under conditions of Experiment 2, the avoidance response to the RCS was also affected occasionally. Another striking difference in the effects of these two drugs upon avoidance conditioning is that reserpine impairs the performance on avoidance response without indication to a restitution of the alimentary performance. In other words, a decrease in anxiety produced by reserpine administration is not associated with an increase in the alimentary behavior. In fact, a diminution of alimentary functions can be expected after the administration of reserpine since, in most instances, the drug appears to produce disorders of the digestive system. To escape intestinal disturbances testing the animals was conducted 3 hrs. after injecting the drug. It is quite likely though that some kind of nausea was then present, with interfered with the alimentary CR.

The positive effect of hydroxizine was that in the CS-transformation experiment both the defense and alimentary response often were elicited to the presentation of the TCS. It is interesting that in the majority of instances the avoidance occurred first and it was immediately followed by the alimentary response. This suggests that action of hydroxizine consist in an abrupt interrupting the fear reaction to the defense CS. At the same time, the alimentary drive appears to increase and an alimentary CR occurs. This is generally in line with our most recent observation (Romaniuk and Wojtczak-Jaroszowa 1963) that autonomic manifestations which normally persist long beyond aggressive or defense (fear) behavior patterns produced while stimulating the medial hypo-
thalamus, disappear with the termination of hypothalamic stimulation if hydroxizine is administered prior to the stimulation. It thus may be speculated that the positive results with hydroxizine in the treatment of obsessive states in human patients are explained in terms of suppressing some of the affective and autonomic components associated with obsession.

The conclusions to be drawn from the present findings are: a) the CS-transformation technique is very effective in revealing changes of the conditioned-reflex behavior under tranquilizing drug administration; thus, even though drugs in the dose used have no depressing effect on regular conditioning performance, the fact remains that they influence an avoidance response under CS-transformation conditions; b) each of the three tranquilizing drugs used in this experiment has a specific suppressor or facilitatory effect on conditioned reflexes.

SUMMARY

Conditioning technique, described by Pavlov as „CS-transformation” was employed for studying the effects of three tranquilizers on the higher nervous activity in dogs. The following drugs were used: chlorpromazine in dosages of 0.5 mg/kg, reserpine 0.04 mg/kg, or hydroxizine 4.5 mg/kg. The animals were given drugs after the transformation of an instrumental alimentary CS into a defense CS, eliciting an avoidance response. For control, prior to the transformation experiments the effect of the tranquilizing drugs on regular defense conditioning was tested.

It was found that, in control experiments, only chlorpromazine decreased the defense CRs. Contrastly, in transformation experiments, the defense CRs were decreased following injections of chlorpromazine and reserpine, while dogs treated with hydroxizine performed both defense and alimentary CRs within a trial.

The results demonstrate that the CS-transformation technique is very fruitful for measuring the efficacy of some of the tranquilizing drugs since marked alterations in conditioned-reflex activity follow injections of doses, not exceeding those used in human patients.

REFERENCES


RIKMAN V. V. — in Pavlovian Wednesdays, 1949, Moskva, p. 313.


Book Review


This monograph cannot fail to impress with its authoritative presentation of a subject about which much has been written. The authors examined the function of the visual system after cerebral lesions. Two main problems are discussed: 1) the characteristic features of field defects after missile wounds, and 2) the question as to what extent these changes conform to the known anatomic arrangements in higher visual pathways.

Out of a total of 232 men with penetrating gunshot wounds of the brain, 46 were found to have visual field defects in repeated test extending over a period of ten years after their original wounding. For the purpose of comparison and contrast, 9 additional cases from earlier studies involving the acute after-effects of wounds of the visual pathways have been discussed, and 8 of these are illustrated.

The results were analyzed with reference to the classic principle of retinotopical projection. The authors believe that the varied shapes of field defects after penetrating wounds of the optic radiation may require a revision of current views regarding the intrinsic organization of the central visual pathways. They suggest that the macular fibers cannot form a distinct bundle coursing at intermediate height between ventral and dorsal bundles of the optic radiation. They showed that the homonymous field defects are not identical and they have not confirmed Hen- shen's notion of an "almost mathematical congruence" of homonymous field defects. The most probable interpretation of this incongruence is that, contrary to current anatomic conceptions, corresponding elements in the visual system are not perfectly aligned, even at the level of the striate cortex.

The study summarizes the results of experiments showing the completion of apparent movement across blind areas. Also, other ways are discussed in which completion of contours makes the patients functioning fields seemingly wider than the perimetric fields. These all results seem to indicate that while different areas of the visual field are projected to approximately corresponding loci in the higher visual pathway, the various levels of visual function are not so represented.

The various circumscribed scotomata are essentially compatible with the principle of point-for-point projection of retina into cortex. However, we know that various aspects of visual performance are affected in the presence of circumscribed lesions and that their alteration extends over the entire field and to either side of the midline. These effects may mean either that the lesions are more diffuse than the circumscribed scotomata indicate or that the functions in all parts of the field...
depend on the integrity of every individual part. We cannot decide between these two views, diffuseness of lesions, or diffuse representation”.

This work stands out as one of the most carefully prepared, complete, comprehensive and convincind books on visual performance after cerebral lesions and will be equally useful to the students, neurologists and neurophysiologists, in fact to all who are interested in the functional organization in defective visual fields and in the theories of vision.

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