PHARMACOLOGICAL ANALYSIS OF DISTURBANCES OF GOAL-DIRECTED BEHAVIOR IN INTACT AND LOBECTOMIZED DOGS

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Small doses of chlorpromazine compensate the effect of frontal lobectomy and restore goal-directed behavior in lobectomized dogs, while administration of small doses of amphetamine induces disturbances of behavior similar in many features with those observed after extirpation of the frontal cortex. This indicates that the frontal lobes have an inhibitory effect on adrenergic (primarily reticular) subcortical structures involved in the formation of goal-directed behavior.

The main feature of injury to the frontal lobes is a disturbance of the goal-directed quality of behavior because of the absence of effective integration [2, 4, 9]. It is assumed that such integration is carried out by the frontal cortex [2, 3, 5, 8], which modifies the activity of other cortical areas through modulation of the ascending influences of the mesencephalic reticular formation, the hypothalamus, and the limbic structures [7, 13].

The activity of these subcortical structures can be selectively modified by administration of chemical substances. Chlorpromazine and amphetamine, for instance, affect principally the adrenergic structures of the reticular formation and hypothalamus [1, 10, 11].

Comparison of behavioral changes after administration of chlorpromazine or amphetamine to intact and lobectomized dogs would help to elucidate the way in which the frontal cortex controls other brain structures during the formation of goal-directed behavior. The present investigation was carried out for this purpose.

EXPERIMENTAL METHOD

Stable instrumental conditioned reflexes in a situation providing for the choice of one or two different reinforcements were produced in five dogs by the method developed by N. V. Asmayan and G. A. Golitsyn. The experiment was carried out as follows. When the experimenter switched on a metronome (M_{60}) the dog was able to obtain a lump of sugar from a feeding bowl on one side by pressing on one pedal, and water from a bowl on the opposite side by pressing another pedal. The dog's behavior in the experimental chamber was directed at a definite goal: obtaining water or sugar. At each period of the experiment one of two motivations – hunger or thirst – predominated alternately. Depending on the dominant motivation, in response to the signal the dog carried out the movements in one order or the other. At the end of the experiment, when both hunger and thirst were completely satisfied, in response to the metronome the dog jumped down from the apparatus or lay quietly on the bench.

Ten months before the experiment the frontal cortex (areas F and FL in the terminology of O. S. Andrianov and T. A. Mering) was extirpated as far as the anterior sigmoid gyrus in two dogs (Tom, Pegii). Immediately after the operation the dogs showed typical symptoms of lobectomy (fixed gaze, stepping movements, chewing inedible objects, and so on).

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TABLE 1. Changes in some Parameters of Goal-Directed Behavior or Intact (A) and Lobectomized (B) Dogs after Administration of Chlorpromazine and Amphetamine (results for one experiment)

	A								B					
	Trishka			Dzheka			Vais		Pegii			Tom		
	Background	Chlorpromazine	Amphetamine	Background	Chlorpromazine	Amphetamine	Background	Chlorpromazine	Background	Chlorpromazine	Amphetamine	Background	Chlorpromazine	Amphetamine
Reinforcement:														
water	18	0	20	16	21	36	18	1	13	4	5	55	13	8
sugar	43	5	9	7	12	3	19	4	8	24	-	45	64	8
Number of crossings over (switches of motivations) . .	6	0	4	5	5	1	11	2	5	7	0	8	18	2
Number of wrong responses	0	2	0	1	4	0	1	0	1	0	0	0	0	0
Number of "blank" responses	0	0	0	0	2	3	0	0	5	0	0	1	0	37
Mean number of intertrial instrumental responses	0	2	7.2	0.73	1.16	1.07	2.8	1.08	0.69	0.14	5.17	0.45	0.40	3.56
Mean number of intertrial locomotor responses	0	2.5	0.31	0.94	0.45	0.1	1.07	0.35	1.21	0.35	6.67	1.42	0.78	7.60
Mean latent period of instrumental conditioned responses (in sec)	1	101.4	2.3	4.7	16.9	3.8	1.5	2.3	8.65	3.85	7.75	1.95	8.39	2.00

Note. The term "blank" describes movements when, in response to the stimulus, the dog presses on the pedal and runs to the feeding bowl but does not take the reinforcement. The term "wrong" applies to those movements when, in response to the metronome the dog presses one pedal but immediately crosses over to the other or, having pressed one pedal, runs to the feeding bowl on the opposite side of the bench.

Three intact dogs (Dzheka, Vais, Trishka) were used as the control. Chlorpromazine was injected intramuscularly in a dose of 1.5-2 mg/kg intramuscularly 15-20 min before the experiment, while amphetamine was injected subcutaneously in a dose of 0.3-5 mg/kg 5 min before the experiment.

EXPERIMENTAL RESULTS

Injection of chlorpromazine in the intact dogs led to disintegration of behavior through suppression of the motor component of the conditioned reflex: the dog did not immediately approach the pedal, pressed it so weakly that the feeding bowl did not turn, and in some cases it made no effort whatever to approach the pedal. The primary motivations of hunger and thirst were strong enough: if the experimenter gave the animal the feeding bowl, turned it and tapped on its side the dog immediately ran toward it and swallowed the sugar or water; if after the metronome was started and the dog did not respond to it, water or sugar was offered to it in a basin, and the animal swallowed it eagerly.

Administration of chlorpromazine to the intact dogs did not disturb their primary motivation but it did disturb the accuracy of assessment of the dominant motivation. When the metronome was switched on the dog pressed one pedal, but despite a tap on the corresponding feeding bowl, it ran to the opposite side of the frame (wrong response, see Table 1A).

Administration of chlorpromazine had a completely different effect on the behavior of the lobectomized animals. On the whole, the behavior of these dogs in the experimental situation became more organized and goal-directed. Together with some increase in the latent period of the instrumental motor response, the hyperactivity disappeared and there was a decrease in the number of crossings over from one feeding bowl to the other during the intertrial interval, in the number of intertrial instrumental movements during the experiment, and in the number of instrumental responses and movements toward the feeding bowl

at the end of the experiment, when the motivations of hunger and thirst were no longer present. Since the number of reinforcements used in the course of the experiment was not significantly changed in these cases it can be postulated that the "improvement" in the dogs' behavior after administration of chlorpromazine was not due to a decrease in the primary motivations of hunger and thirst. The behavior of the lobectomized dogs after administration of chlorpromazine can be regarded as more goal-directed in character also because of the increase in the number of switches from one type of reinforcement to the other. In other words, the animals were able to assess their internal need more accurately, and they modified their behavior when the dominance of one need over the other was still only slight in degree.

Whereas administration of chlorpromazine to the lobectomized dogs made their behavior more goal-directed in character, administration of the drug to the intact animals had almost the opposite effect.

Since chlorpromazine has an inhibitory action on the adrenergic structures of the reticular formation [1, 10, 11] it can be postulated that lobectomy results in some form of "liberation" from cortical control. This is confirmed by the fact that chloral hydrate [6] and luminal [12] have no significant effect on the behavior of lobectomized dogs, whereas pentobarbital improves the performance of deferred responses [14]. To test this hypothesis experiments were carried out in which the adrenergic brain structures, especially the reticular formation, were subjected to artificial pharmacological stimulation by amphetamine [11].

The behavior of the intact animals after administration of this substance became basically similar to that of the dogs after lobectomy (see Table 1A). Throughout the experiment the dogs pressed on the pedal almost without interruption, but when the feeding bowl was presented they did not go up to it. The primary motivations of hunger and thirst were of considerable strength, for if the experimenter presented the feeding bowl with lumps of sugar or water to the animal it rushed to the dish and swallowed the reinforcement.

The symptoms described above were all observed in their sharpest form after administration of amphetamine to the lobectomized dogs (see Table 1B). Stereotyped perseverative purposeless movements were very conspicuous in these animals. Now, however, the whole program of the animal's behavior was not aimed at obtaining the reinforcement. The goal of behavior was apparently limited to the performance of the instrumental movement only.

It can be concluded from the results of these experiments as a whole that after removal of the frontal lobe of the cortex there is "liberation," of the adrenergic (predominantly reticular) structures of the brain stem and limbic formation. It seems most probable that the formation of the goal and the taking of decisions, the central processes of integration of goal-directed behavior, take place on account of suppression of the activity of these structures by the frontal cortex at the stage of afferent synthesis [2, 3].

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