The conditioned reflex to time (CR) is often used in experimental investigations as a model of trace processes [3, 5, 16]. On the basis of published and our own data we have devised a hypothesis [19, 11] in the form of a general block scheme concerning the structural-functional prerequisites of the system organization of the CR to time as an independent neurophysiological formation, reflecting one of the most important mechanisms of the behavioral act — the perception of temporal parameters. This hypothesis later gained theoretical support [6, 7, 10-14].

The question as to what activity, how and when it should be actualized or restrained, is decided by a cortical-subcortical system of interaction, at the level of which the neocortical projection zones ensure first of all the creation of a complex of trace processes from the excitations present. All reactions, including the CR to time, are formed on the basis of these excitations. The anatomical substrate of the actual complex, i.e., the engrams, is unknown. The associative structures of the brain (parietal cortex) are preferentially involved in the afferent synthesis necessary for the current moment (present excitations), while the prefrontal cortex is involved in the temporal programming of actions.

Integrative-release formations [1] time the developed reactions to a strictly fixed period, regulating behavior and dependent, in particular, upon the activity of the septo-hippocampal component as a pacemaker mechanism (of an endogenous or exogenous character), a unique internal timer, a reference scale producing temporal markers of events [6, 7, 11, 13, 14].

Consequently, the CR to time is complicated by mechanisms predicting activity in a temporal perspective, which makes the structure of the reaction more complete, for the organism must decide not only how but also when to react.

Thus, the functional structure of the CR to time as a specific prognostic function consists of various neurodynamic processes: the present excitations, trace phenomena, and rhythmic oscillations [9, 12].

With the aim of extending the understanding of the relationship of these processes we attempted their neurochemical analysis by means of pharmacologic action on certain mediator systems of the brain.

To solve the problem we used three experimental situations where the traces, rhythm, and prognosis were represented relatively independently: deferred behavior, the CR to time, and the test reaction to temporal prognosis.

METHODS

The experiments were conducted using unrestrained cats with food reinforcement by three methods. In the first method the CR to time was developed on the basis of the timed restraint of the animal in a cage positioned 2.5 m from a screen (2 m length and 1 m height), on either side of which were feeders: 30 sec were required to circumvent the barrier on the right and 10 sec on the left. In the second method, intervals during temporal prognosis of less than 30 sec (20, 15, 10, and 5 sec) were indicators for a run from the starting point and subsequent screen circumvention on the left, while 30 sec and more (40, 45, 50, and 60 sec), on the right. The given extrapolation was conditionally denoted as a minute "fan." In the
third method, the well-known direct variant of postponement was employed to study deferred reactions (delay time of 1 min) to two feeders under the former experimental conditions.

Ten tests of the alternative selection of the feeder side were presented in random order during an experiment.

The frontal associative cortex (proreal gyrus) was extirpated bilaterally, and the head of the caudate nucleus lesioned electrolytically in a variable sequence (Fig. 1). The frontal cortex was almost completely removed; the caudate nucleus head had destruction in all segments.

The effects of the systemic injection (intraperitoneal and subcutaneous) of drugs were investigated. Depending upon the characteristics of the dopaminergic, cholinergic, and GABAergic preparations, the experiments were conducted 30-90 min and two days after the injections of intact and operated cats. The doses were selected individually as physiologically effective; they are indicated in Tables 1-4. The conditions of the analysis of each drug were identical for all experimental models, making it possible to speak of the preferential influence of the studied drugs on particular mediator systems of the brain.

The significance of the differences in the compared group of observations and the number of correct and incorrect reactions was determined by the nonparametric Wilcoxon-Mann-Whitney criterion.

RESULTS

Deferred Behavior, CR to Time, and Temporal Prognostication during Neuropharmacologic Manipulations in Intact Cats. The main results of the statistical analysis of experimental material with respect to groups with a CR to time, temporal prognostication, and deferred behavior prior to injection and under the action of various psychotropic drugs of the dopaminergic, cholinergic, and GABAergic series are presented in Tables 1 and 2. As follows from Table 1, neurochemical manipulations of cerebral cholinoreactive structures significantly altered the occurrence of the CR to time. The central cholinolitics, atropine and scopolamine, blocked cerebral cholinoreceptors and sharply disrupted the realization of the temporal reaction; the percentage of correct responses declined compared with the control (before drug injection) by more than 1.5-2 times. By contrast, the stimulation of cholinergic neurons by inhibiting cerebral acetylcholinesterase with galantamine markedly improved the reactions to time and increased the percentage of correct responses from 71 to 91 (p < 0.05).

Parenteral injections of blockers or activators of dopaminergic and GABAergic transmission proved ineffective with respect to the assessment of long intervals of time (Table 1).

An analysis of the behavior associated with temporal prognostication in intact cats in