SENSORY AND MOTORIC COMPONENTS OF VARIOUS FORMS OF LEARNED MOVEMENT WITH CHANGE IN THE ACTIVITY OF THE CHOLINERGIC SYSTEM OF THE NEOSTRIATUM

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The participation of the cholinergic system of the neostriatum in the regulation of sensorily-monitored movements and the differentiation of sensory signals were investigated in 12 Wistar rats, 27 Sprague-Dawley rats, and 6 mongrel dogs, using the following models: 1) the maintenance of learned extension of the forelimb for a specified time (rats); 2) prolonged conditioned reflex flexion of the hind limb (dogs); and 3) active avoidance in a T-maze (rats). It was demonstrated that the injection of carbacholine (0.03 µg) into the dorsolateral division of the caudate nucleus of the rats does not bring about significant changes in the performance of movements associated with the maintenance of tonus of the forelimb, whereas the injection of carbacholine (0.05-0.1 µg) into the same division of the caudate nucleus of the dogs improves the realization of movement associated with the maintenance of tonus of the hind limbs. The injection of a blocker of the cholinergic system (scopolamine in the rats and atropine in the dogs) in both the first and the second instance disturbed the performance of the movement by the animals. Bilateral microinjections of carbacholine (0.03 µg) into the neostriatum of the rats significantly improves the development of a differentiated active avoidance conditioned reflex in a T-maze on the first three days of testing. The differentiation of acoustic signals by dogs also significantly improved against the background of the injection of carbacholine (0.05-0.1 µg) into the caudate nucleus. Thus, the data obtained in the various behavioral models and different animals suggest that the cholinergic system of the neostriatum participates in the regulation of both motor and sensory mechanisms in connection with the realization of learned movement.

The role of the cholinergic structures of the forebrain in the regulation of various forms of behavior has become the subject of study in recent years of a large number of investigators [13]. Special attention has been devoted to the role of the cholinergic depots of the nucleus of Meynert [11], which send cholinergic projections to all the structures of the forebrain, including the cerebral cortex [18, 22]. The data obtained have also made it possible to draw a conclusion regarding the existence of a whole series of cholinergic depots (no fewer than eight of these have been counted), both in the forebrain and lower-lying structures [25]. The neostriatum occupies a leading place in the brain with respect to the level of acetylcholine and of the enzymes of its synthesis and metabolism. However, the source (sources) of this activity in the neostriatum has (have) not been definitively established. It is assumed that the large cholinergic neurons located in the neostriatum itself are a principal source of cholinergic activity [14, 19]. The influence from the cholinergic structures of the pedunculopontine nucleus, the PPN [15], mediated in the CM-Pf complex of the thalamus, is one of the factors modifying the cholinergic activity of the neostriatum. At the same time, projections from the innominate substance (the nucleus of Meynert) to the neostriatum have not been definitively established, at least for the majority of vertebrates.
The organization of the efferent projections of the neostriatum makes it possible to hypothesize its participation in the triggering and correction of the functions of the subcortical sensory and motor systems. In this context, alteration in the cholinergic activity of the neostriatum, mediated by further change in the activity of its efferent outputs and above all of SII neurons, may be one of the pathways of the effect on these systems. The selection of appropriate models of motor behavior is of undoubted importance for the resolution of these questions. Taking note of the special significance of the neostriatum for the regulation of sensorily-monitored movements [2, 5, 20], we used two models of movements of this kind: 1) the maintenance of learned extension for a specified time (rats), and 2) prolonged conditioned reflex flexion (dogs). Another important feature of these motor reactions was the fact that they were associated with the maintenance of tonus, and further, that it was the tonic component of the learned movement in particular that was primary in the accomplishment of the set behavioral task. Finally, models of motor behavior associated with the differentiation of sensory signals were used both in the rat experiments and the dog experiments.

METHODS

Experiments on Rats. The series of experiments to study the role of the cholinergic system of the neostriatum in the realization of sensorily-monitored manipulatory movement was carried out in 12 white Wistar male rats, weighing 150-180 g. The animals were kept under vivarium conditions of normal illumination and free access to water. Those animals were selected preliminarily which obtained food spherules with one of the forelimbs from a horizontal tubular food dispenser (d = 11 mm) set up on the wall of the experimental box at a height of 60 mm. The training was carried out in a setup equipped with such a tube with a piston which at a depth of 17 mm could not be displaced by more than 1 mm. The rats were trained to press the piston with the paw for a certain length of time. The food reinforcement was delivered from an opening placed 15 mm below the tube containing the piston when the reflex was performed correctly. A detailed description of the methods and the training process has been given previously [3, 25]. The piston-pressing time was measured and the density of the distribution of the pressing times with respect to each of the training cycles (64 movements) and the number of erroneous movements per minute and per cycle were calculated on a DVK-3 computer. The statistical analysis of the results using the Student test was done on the same computer. A statistically significant change in the mean pressing time over the course of five to seven cycles was the criterion of a rat’s training level.

The operation for the stereotactic implantation of the cannulae through which the microinjectors were then introduced was carried out after training under nembutal anesthesia (40 mg/kg, intraperitoneally). The cannulae, with an external diameter of 0.9 mm, were introduced bilaterally (AP = 1.5; H = 4; L = 2.5 medially and L = 3.5 laterally) and fixed to the skull with protacryl. The control of the site of introduction was accomplished on the basis of the tracks in brain slices after the experiments were completed. The animals were brought into the experiment following the recovery of the preoperative level of training. The following were injected by means of a Hamilton syringe: 0.03 μg carbacholine and 0.3 μg scopolamine in 1 μl physiological solution. The solvent in the same volume was injected into the animals in the control experiments. The tip of the microinjector could protrude from the guide cannula by 0.5-1 mm. The introduction of the pharmacological agents into the brain took about 1 min. Monitoring of the performance of the motor task was done after 15, 30, 60, 90, and 120 min, as well as 24 hours after the injection, at the same duration of the reinforced movement in each cycle.

The experiments to study the role of the cholinergic system of the neostriatum in the differentiation of sensory signals were carried out in 27 male Sprague-Dawley rats, weighing 250-300 g. The animals were kept in a vivarium under standard conditions on the usual diet. The rats were trained to active avoidance of an electric current in a T-maze consisting of a darkened starting chamber (30 × 20 × 20 cm), and of two arms, the right and the left (30 × 20 × 50 cm). The unconditional stimulus was an electric current of 1-2 mA, delivered through the wire floor covering. The conditional signal was the light of an electric lamp (right and left). The isolated action of the conditional signal was 10 sec; the combined action of the unconditional and the conditional stimuli was also 10 sec. At the beginning of each experimental trial (before the conditional signal was turned on), the rat was placed in the starting chamber; the light was turned on after 2-3 sec, at 10 sec of the action of which the electric current was delivered to two sections of the maze: to the starting chamber and the left section of the maze when the left lamp was turned on, and to the starting chamber and the right section of the maze when the right lamp was turned on. Correspondingly, in the first instance, the animal had to run into the right section, and in the second instance, into the left section of the maze. The rats were trained over the course of five days, by presenting 16 combi-