VECTOROGRAPHIC ASSESSMENT OF THE EFFECT OF PSYCHOSTIMULANTS ON AVOIDANCE BEHAVIOR IN RATS

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The effect of psychostimulants on relearning of the avoidance direction by rats in a Y-maze was assessed. The effects were analyzed vectorographically with absolute and relative values for the main response indices. In both cases the behavior profile of the group of animals was traced. Sydnocarb (20 mg/kg) gave the optimal effect, for unlike caffeine (25 mg/kg) and amphetamine (0.5 mg/kg), it not only stimulated active avoidance but also improved relearning by the animals. An increase in the dose of sydnocarb to 50 mg/kg did not disturb the rats' behavior, whereas caffeine (50 mg/kg) and, in particular, amphetamine (5 mg/kg) disturbed behavior. The behavior profile after amphetamine went far beyond the bounds of the original level and was characterized by marked worsening of passive avoidance.

KEY WORDS: *conditioned-reflex avoidance; psychostimulants; vectorographic assessment of behavior.*

Vectorographic methods have been suggested in recent years for analysis of groups of changes in the emotional state of man and animals and also the effectiveness of neuroleptic therapy [1, 5].

In the investigation described below this method was used for the first time to study the action of psychostimulants. The writers' own modification of the vectorographic method was used, whereby quantitative changes in animal behavior produced by pharmacological agents can be demonstrated.

EXPERIMENTAL METHOD

Experiments were carried out on 114 noninbred albino rats weighing 180-300 g. The ability of the animals to form and adapt skill in avoidance was studied in a Y-maze. The experiment consisted of four successive training sessions with 10 transits in each. To avoid painful electric shocks the rats had to run 10 times into the right compartment of the maze. The left compartment was then made painless and the rats taught to run in the new direction. The direction of choice was then changed a further two times [3, 4]. Five basic indices of the avoidance response were analyzed: the latent period of the response, the number of mistakes when choosing the safe compartment, fluctuations in the number of mistakes between sessions (the mean difference between the number of mistakes in each session), the time taken to correct incorrect responses, and the number of spontaneous departures from the correctly chosen compartment.

Each index formed the axis of a complex vectorogram. Two methods were used to record the results. In the first case absolute values of one or another index were plotted along vectors starting from the center, on an arbitrary scale (Fig. 1, graph C, I). The mean values of the indices were determined in rats of the control group (30 animals, receiving physiological saline) and these were taken as the original reference point. The polygon formed by joining the corresponding points characterized the normal behavior profile of the avoidance re-

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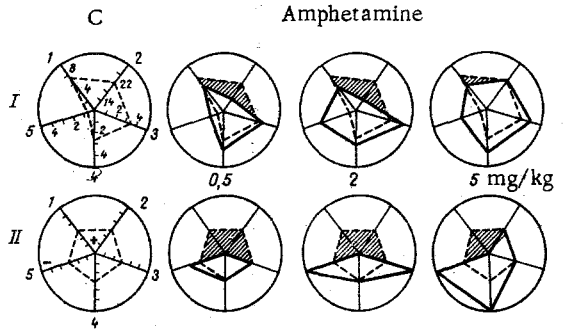

Fig. 1

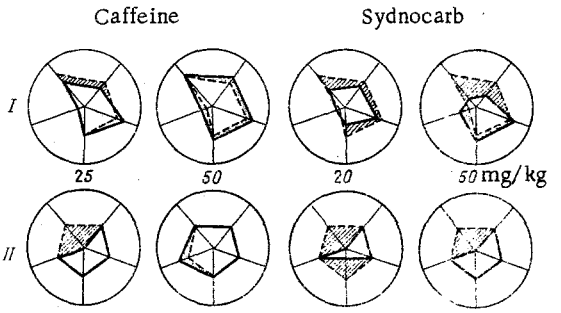

Fig. 2

Fig. 1. Vectorographic characteristics of action of various doses of amphetamine. Behavior profile of rats of control (C) and experimental groups. Arrangement of axes of vectorograms: 1) latent periods of responses (in sec); 2) time for correcting mistakes (in sec); 3) mean number of mistakes per session; 4) fluctuations in mistakes between sessions; 5) number of departures from safe compartment of maze. I) Vectorograms with absolute indices of avoidance response; II) vectorograms with relative (3-point) assessment of shifts in avoidance behavior. Broken line represents original configuration of behavior profile of control animals, continuous line profile after administration of increasing doses of amphetamine. Shaded zone conventionally characterizes optimization; dotted region characterizes worsening of avoidance behavior.

Fig. 2. Comparative vectorographic assessment of effects of caffeine and sydnocarb. Legend as in Fig. 1.

sponse studied. A reduction in the indices closer to the center of the vectorogram and a reduction in the area of the figure as a whole were evidence of improvement or optimization of behavior. Since fluctuations in the absolute indices could not be used to judge the degree of reliability of the changes recorded, in the second variant relative units were plotted along the axes of the vectorogram, on a point system. The zero reference point corresponding to the mean values of the index in the control group was placed at the center of each axis. The area of the regular pentagon formed by joining them also conventionally demonstrates the original behavior profile of the animals of the control group (Fig. 1, graph C, II). Three equal segments toward the center (with a plus sign) and outward (with a minus sign) were plotted from the zero point. They corresponded to the rating, in points, of the index of significance (P), determined with the aid of Student's criterion [6]. Significant shifts from the original level toward a decrease (+) or increase (—) of the difference indices at the $P < 0.05$ level were taken as 1, at the $P < 0.01$ level as 2, and at the $P < 0.001$ level as 3 points. In this method of analysis, only significant shifts of the indices fell outside the limits of the original figure.

The pharmacological part of the investigation was carried out on animals of seven groups (6-20 rats in each group). During the 30 min before the experiment they were given an intraperitoneal injection of one of the doses of amphetamine (0.5, 2.0, and 5.0 mg/kg), caffeine (25 and 50 mg/kg), or sydnocarb (20 and 50 mg/kg).

EXPERIMENTAL RESULTS

The axes of the vectorograms were ascribed an interdependent ranking position (see Figs. 1 and 2). The latencies of the responses were closely connected with the time of correction of mistakes, which was also determined largely by the state of the animals' locomotor activity. Usually, the higher this activity the faster the rat corrected its mistakes. That is why these two parameters lie side by side and demonstrate the animal's ability to carry out active avoidance. Meanwhile the parallel between them was not complete. At times they changed differently. This is because the time taken to correct an incorrect response also depends on the animal's ability to orient itself in the maze and the speed of modifying a previous skill; it is therefore connected with the number of mistakes made.

On the other hand, the last index itself is not very informative. With consistent perseveration of the motor program, when the animal ran invariably into the same compartment of

the maze and, consequently, when behavior was inadequate, the total number of mistakes for all four sessions could be small. Evidence of the adequacy and flexibility of the program and of the animal's ability to relearn is given by the magnitude of fluctuations in the number of mistakes between sessions. This criterion, in conjunction with the mean number of incorrect responses and the number of spontaneous departures from the correctly chosen compartment, characterizes to some degree the state of passive avoidance — refraining from performing purposeless actions. From this point of view each of the three indices is mutually complementary. It can be said conventionally that the top part of the vectorogram, with a given arrangement of the axes, reflects the state of active, and the lower part the state of passive avoidance.

A small dose of amphetamine (0.5 mg/kg), conventionally described as a "psychostimulant" dose, led to changes in the two processes in different directions. However, analysis of the degree of significance of the shifts showed that active avoidance underwent the greatest changes, evidently because of primary potentiation by amphetamine of the animals' locomotor activity. Administration of the drug in a larger dose (2 mg/kg) was accompanied by disturbances of the rats' purposive behavior: Besides shortening of the response latencies, the number of mistakes and the number of spontaneous departures from the safe compartment increased appreciably. Deformation of the behavior profile on the vectorogram took place, although without any gross disorders in ability to modify the motor skill (the number of fluctuations in mistakes between sessions showed only a tendency to increase).

The more marked shifts of passive avoidance corresponded to the development of an amphetamine behavioral stereotype (from 5 mg/kg). The figure formed on the vectorogram went considerably beyond the boundaries of the original behavior profile. It is interesting to note that the mean error was close to the control values because of the appearance of consistent perseveration of running into one (more often the right) compartment of the maze, leading to an increase in the number of fluctuations of mistakes between sessions. Collapse of the restraining mechanisms was accompanied by an increase in the number of departures from the safe compartment.

A widely used criterion of assessment of the action of psychostimulants on avoidance behavior is the shortening of the latent periods of conditioned responses produced by them [7]. Using this index, the effect of 25 mg/kg caffeine is comparable with that of the small dose of amphetamine. However, the entire vectorographic pattern after injection of 25 mg/kg caffeine differs by the lesser degree of its deviations from the initial level (Fig. 2). With the exception of latency, the changes do not exceed the limits of fluctuations in the control animals. Only in the case of a higher, subtoxic, dose of caffeine (50 mg/kg) was a tendency observed for the behavior profile to worsen on account of the very small increase in all the parameters studied. The only significant change was an increase in the number of departures from the safe compartment, produced by the action of amphetamine in a dose of 0.5 mg/kg. Comparison of the vectorographic profiles of the action of different doses of the psychostimulants showed that amphetamine is less effective.

The action of sydnocarb differs appreciably (favorably) from the effect of the other two psychostimulants mentioned above. The range of its psychostimulant action is considered to be much wider than that of amphetamine [2]. Our observations showed that sydnocarb, in a dose of 20 mg/kg, i.e., 4-5 times greater than the threshold for stimulation of motor activity, was more effective according to several criteria than 0.5 mg/kg amphetamine. Comparison of the absolute shifts showed that this psychostimulant characteristically produced a tendency for nearly all the avoidance indices to shorten (Fig. 2). Not only the latency of the responses, but also fluctuations of mistakes between sessions changed significantly. Under the influence of sydnocarb the animals modified the program of their motor skill faster and, what is particularly important, more successfully. Meanwhile, unlike with the small dose of amphetamine, purposeless spontaneous departures from the safe compartment did not take place. Consequently sydnocarb optimizes the retraining of rats more effectively than the other two psychostimulants and improves the indices of both active and passive avoidance.

With an increase in the dose of sydnocarb to 50 mg/kg the animals developed stereotyped behavior resembling motor automatisms after the use of 5 mg/kg amphetamine. Strange as it may seem, under these circumstances the performance of the behavioral task suffered very little. Compared with the gross defects of behavior arising under the influence of amphetamine, sydnocarb did not lead to any sharp deterioration of passive avoidance. The mean values of the mistakes, their fluctuations between sessions, and the number of

spontaneous departures did not significantly exceed the control figures, whereas the vectorogram allowing for the significance of the shifts had the same configuration as after 25 mg/kg caffeine. The situation can be summed up by saying that the behavior of the rats appeared to be even more purposive than after administration of 0.5 mg/kg or, more especially, of 2 mg/kg amphetamine.

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EFFECT OF BENACTYZINE AND ARECOLINE ON Mg^{2+}-ATPase ACTIVITY AND CONTENT OF Ca^{2+} AND Mg^{2+} IONS IN THE RAT BRAIN

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The effect of the central cholinolytic benactyzine (40 mg/kg) and of the cholinomimetic arecoline (2.5 mg/kg) on activity of Mg^{2+}-dependent ATPase was studied and the content of Ca^{2+} and Mg^{2+} ions determined in rat brain. Benactyzine and arecoline caused biphasic changes in the activity of the enzyme and content of the electrolytes. It is concluded that inhibition of the enzyme is linked with the accumulation of Ca^{2+} ions and its activation with an increase in the concentration of Mg^{2+} ions in brain tissue. It is suggested that benactyzine and arecoline exert their influence on the liberation and retention of neuromediators in the tissue depots through these effects.

KEY WORDS: *brain; benactyzine; arecoline; Mg^{2+}-dependent ATPase; electrolytes.*

The action of the central cholinolytic benactyzine is accompanied by an increase in liberation of neuromediators from the brain of several animals [1, 3, 4]. The cholinomimetic arecoline causes acetylcholine to accumulate in the rat brain [9]. The mechanism of these effects remains unexplained. A leading role in the regulation of neuromediator liberation is ascribed to Ca^{2+} and Mg^{2+} ions [6, 11]. Both liberation and storage of neuromediators in the tissue depots are dependent on the presence of ATP, which is utilized in various ATPase reactions. A change in ATPase activity should lead to liberation or accumulation of neuromediators. In the investigation described below the effect of benactyzine and arecoline on the activity of Mg^{2+}-dependent ATPase was studied and the concentrations of Mg^{2+} and Ca^{2+} ions were determined in rat brain.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 150-250 g which were given intraperitoneal injections of benactyzine (40 mg/kg) and arecoline (2.5 mg/kg) (in solution,

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