EFFECT OF SYDNOCARB* ON LEARNING AND MEMORY

M. M. Ganiev, A. N. Kharlamov,
K. S. Raevskii, and D. Ya. Guseinov

UDC 615.214.31.015.4:612.821.2

KEY WORDS: sydnocarb*; learning; memory.

Sydnocarb* is an original Soviet psychostimulant [10], which differs significantly from other psychomotor stimulants and, in particular, from amphetamine, in a number of parameters of its psychopharmacological action [4, 5]. The compound facilitates conditioned-reflex activity [3] and stimulates mental functions moderately in man [1, 10].

However, no special study has yet been made on the effect of sydnocarb on different stages of memory formation, and the investigation described below was accordingly undertaken for this purpose.

EXPERIMENTAL METHOD

Experiments were carried out on 108 noninbred male albino rats weighing 180-220 g. A conditioned passive avoidance reflex (CPAR), based on single electrodermal reinforcement, was used as the model [9]. The technique was based on realization of an inborn cortical reflex. The experimental chamber consisted of two compartments: a large, illuminated and a small, darkened compartment, connected by an opening. To form the CPAR the rat was placed in the middle of the illuminated compartment with its tail toward the opening. By investigating the illuminated compartment the animal discovered the opening and entered the dark part of the chamber, where it preferred to spend most of its time. The learning time was 3 min. At the end of the learning session, when the animal as a rule was in the dark compartment, an alternating current with a strength of 2 mA was applied to the electrode floor of the chamber for periods of 1 sec, separated by an interval of 2 sec. Preservation of CPAR was assessed after 24 h by measuring the total time spent by the rat in the dark compartment out of a stay of 3 min in the experimental situation. Another criterion of learning was the time spent by the rats in the dark compartment under 60 sec when the animals were tested 24 h after training. In the first case the number of trained animals reached 86%, but only 30% in the second case (Fig. 1). Preliminary experiments showed that with this technique CPAR could be preserved to a varied degree depending on the intensity of reinforcement. In accordance with the aims of the investigation, and to achieve different degrees of CPAR, two versions of reinforcement were used: in the first case, when the rat was in the dark compartment of the chamber, for a few seconds before electrical stimulation was applied, the passage from the dark into the illuminated compartment of the chamber was closed and, for 15 sec, the animal was subjected to aversive stimulation 5 times. In the second version of the experiment, during electrical stimulation the animal was able to leave the dark compartment.

The threshold of nociceptive stimulation was determined from the animals' vocalization response.

Sydnocarb was injected into the stomach through a tube in a dose of 15 mg/kg, which, as the results of previous investigations [4] showed, is effective. The schedule of administration of sydnocarb (before or immediately after the first training session or before retesting) was such that the effect of the drug could be assessed on different stages of CPAR formation, namely on the formation, consolidation, and recall of the memory trace. Control animals received 0.9% NaCl solution.

The results were subjected to statical analysis [6].

*Western equivalent: mesocarb.

Department of Pharmacology, N. Narimanov Azerbaijan Medical Institute, Baku. Laboratory of Neurochemical Pharmacology, Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 10, pp. 453-454, October, 1987. Original article submitted June 20, 1986.

0007-4888/87/0010-1413$12.50

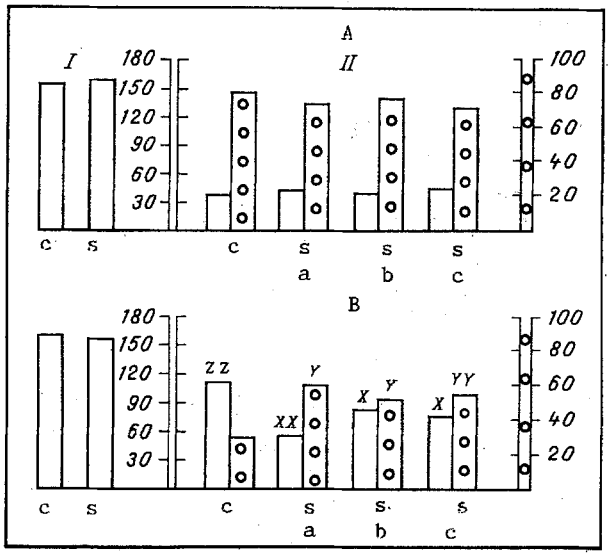

Fig. 1. Effect of sydnocarb on different stages of memory trace formation. On left: time spent by animals in dark compartment (in sec); on right: number of animals trained in CPAR (in %). Abscissa: c) control, s) sydnocarb. a, b, and c) Administration of sydnocarb on 1st day 15 min before training and immediately after training, and on 2nd day, 15 min before retesting. Significance of difference: A) Willcoxon–Mann–Whitney test; B) Fisher's exact method; ZZ) difference between parameters for control group of animals on 2nd day and on 1st day (a), $P < 0.01$; X, Y) comparison of experimental groups with control group, in accordance with the following scales: X) $P < 0.05$, XX) $P < 0.01$, Y) $P < 0.05$, YY) $P < 0.01$.

EXPERIMENTAL RESULTS

The study of the effect of sydnocarb on different stages of CPAR formation showed (Fig. 1A) that in the group of well trained rats (receiving prolonged aversive reinforcement), the drug caused no marked improvement of the parameters of CPAR. Meanwhile, after receiving the drug, the animals' performance of passive avoidance was not impaired, which is characteristically found with other psychomotor stimulants and, in particular, with amphetamine [2].

Conversely, in animals with a low level of training (30% in the control) sydnocarb significantly improved avoidance performance at all stages of its formation. The drug had the strongest facilitating effect when given before the training session, i.e., when training took place against the background of the psychostimulant. In the group of animals with a low level of learning, the number of rats trained against the background of the drug was doubled, to reach 60% (Fig. 1). The absolute duration of the rats' stay in the dark compartment of the chamber on the 2nd day of the experiment under these conditions was appreciably reduced (to 57 sec). Characteristically, the facilitatory effect of the drug was manifested at all stages of development and formation of CPAR (Fig. 1: a-c). Meanwhile, amphetamine is known to have a facilitatory effect only on the early stages of formation of the memory trace [13]. Under the influences of sydnocarb the length of stay in the animals in the illuminated compartment during the testing session was significantly increased (122 sec compared with 70 sec in the control), evidence that sydnocarb may have a favorable influence on learning in rats.

It was interesting to discover whether the improvement in the parameters of CPAR against the background of sydnocarb was connected with its direct influence on this process or whether it was due to loss of sensitivity to painful electrical stimulation. Dependence of this kind has been described for amphetamine [11].

A special series of experiments showed that sydnocarb has no significant effect on the threshold of painful electrical stimulation, but merely causes this parameter to rise a little 90 min after its injection into animals [7]. In the light of these data it can be postulated that the improvement in preservation of CPAR after administration of sydnocarb is most

probably connected with its direct stimulating effect on memory processes. This view is supported by the effectiveness of sydnocarb on all three stages of memory tract formation.

After analysis of data in the literature on the possible neurochemical mechanisms of action of sydnocarb [12] and also of the results of the writers' recent investigation [5], it is logical to suggest that the stimulating effect of sydnocarb on CPAR may be based on its activating effect on monoaminergic (and, in particular, catecholaminergic) systems of the brain, which have an important functional role in the mechanisms of memory formation [8]. Our hypothesis on the mechanisms of the facilitatory effect of sydnocarb on CPAR in poorly trained animals is in agreement with the results of investigations [14] which shows that amphetamine has a similar effect, due to its action on the activating monoaminergic systems of the brain. However, this interpretation of the mechanism of action of sydnocarb on CPAR does not rule out the possibility that other mechanisms may be involved and, in particular, weakening of GABA-ergic control [4].

LITERATURE CITED

1. R. A. Al'tshuler, M. D. Mashkovskii, and L. F. Roshchina, Farmakol. Toksikol., No. 1, 18 (1973).
2. V. A. Baturin, Farmakol. Toksikol., No. 6, 691 (1977).
3. Yu. A. Belozertsev, Byull. Éksp. Biol. Med., No. 1, 53 (1984).
4. M. M. Ganiev, A. N. Kharlamov, and O. V. Shumkova, Farmakol. Toksikol., No. 3, 30 (1984).
5. M. M. Ganiev, V. S. Kudrin, and K. S. Raevskii, Farmakol. Toksikol., No. 2, 27 (1985).
6. E. V. Gubler, Computerized Methods of Analysis and Diagnosis of Pathological Processes [in Russian], Leningrad (1978), pp. 68-91.
7. E. B. Katkova, R. S. Bystritskii, and A. R. Martynikhin, The Psychopharmacology of Emotional Stress and of Zoosocial Interaction [in Russian], Leningrad (1975), pp. 91-97.
8. R. I. Kruglikov, Neurochemical Mechanisms of Learning and Memory [in Russian], Moscow (1981).
9. B. I. Lyubimov, Farmakol. Toksikol., No. 4, 399 (1985).
10. M. D. Mashkovskii, R. A. Al'tshuler, G. Ya. Avrutskii, et al., Zh. Nevropatol. Psikhi. im. S. S. Korsakova, No. 11, 1704 (1971).
11. J. V. Brady, Science, 123, 1033 (1956).
12. S. L. Erdö, B. Kiss, and B. Rosdy, Pol. J. Pharmacol. Pharm., 33, 141 (1981).
13. J. A. Krivanek and L. L. McGaugh, Agents and Actions, 1, 36 (1969).
14. D. Quaterman and M. E. Judge, Physiol. Psychol., 11, 166 (1983).

EFFECT OF BEMITIL ON PERCEPTION OF VISUAL STIMULI

Yu. G. Bobkov, A. I. Machula, and É. G. Dvalishvili

UDC 615.232:547.781.1/015.4:612.833.843.7

KEY WORDS: bemitil; visual stimuli; conditioned defensive reflex.

The effect of bemitil on various aspects of activity of man and animals has now been investigated. In particular, its effect has been studied on physical working capacity [5], processes of mental fatigue [4], and actinoprotector activity [3].

Meanwhile a comprehensive analysis of the action of drugs affecting the CNS cannot be undertaken without a study of their effect on the components of organization of behavioral responses and, in particular, on visual perception of the surrounding world. This enunciation of the problem is determined by the fact that there is no single mental manifestation which can be independent of information processes [8].

Research Institute of Pharmacology, Academy of Medical Sciences of the USSR. All-Union Research Center for Medico-biological Problems of the Prevention of Drunkenness and Alcoholism.

(Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 10, pp. 455-456, October, 1987. Original article submitted February 20, 1987.