Pharmacology Biochemistry & Behavior, Vol. 9, pp. 269–271. Printed in the U.S.A.

BRIEF COMMUNICATION

Effect of n-Dipropylacetate on the Consolidation of a Brightness Discrimination[1]

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(Received 12 June 1978)

GRECKSCH, G., W. WETZEL AND H. MATTHIES. *Effect of n-dipropylacetate on the consolidation of a brightness discrimination.* PHARMAC. BIOCHEM. BEHAV. 9(2) 269–271, 1978.—The posttraining intrahippocampal injection of the GABA level enhancing substance n-dipropylacetate revealed an improvement of the retention performance in a brightness discrimination task in rats.

n-Dipropylacetate GABA Memory consolidation Brightness discrimination Hippocampus

NEUROPHYSIOLOGICAL studies have demonstrated a postsynaptic inhibitory mechanism in pyramidal neurons of the hippocampus [1]. Gamma-aminobutyric acid (GABA) was shown to be the inhibitory transmitter of the basket cells, mediating the inhibition of hippocampal pyramids [3, 11, 12, 13, 16]. The importance of the hippocampus in consolidation processes was evidenced by many findings [14]. In previous investigations we have studied the effects of cholinergic and cholinolytic substances injected intrahippocampally on memory consolidation [5,6]. In the present experiment the role of GABA-ergic hippocampal systems was investigated, using the same learning method, a brightness-discrimination in a Y-chamber. Posttraining injections were used in order to have a specific influence of the treatment on consolidation processes [8]. The GABA-influencing substance n-dipropylacetate (n-DPA) was injected intrahippocampally. n-DPA blocks the metabolization of GABA resulting in an increase of GABA level, probably by a competitive inhibition of the 4-aminobutyric: 2-oxoglutarate transaminase (GABAT), that converts GABA into succinic semialdehyde [2, 4, 17].

METHOD

Animals

Thirty-five adult male Wistar rats of our own breeding stock were used.

Procedures

One week before the learning experiment, chronic microcannulae were implanted into the dorsal hippocampus of both sides using the following coordinates: AP=−3.1 mm, lateral=3.1 mm and 3.1 deep according to Skinner [18]. The learning task was a foot-shock motivated brightness discrimination in a semi-automatic Y-chamber [15]. Rats had learned to run in the illuminated alley of the chamber in order to avoid an electric foot-shock (1 mA), given in the dark alley. The training session consisted of 31 runs. Retention was tested 24 hours later, using a relearning procedure performed in the same way as the training procedure. Number of training errors and number of relearning errors were used for calculation of percent savings:

$$\%\text{Savings} = \frac{\text{training errors} - \text{relearning errors}}{\text{training errors}} \times 100$$

One hundred μg n-DPA in a volume of 1 μl was injected intrahippocampally immediately after the training. Control rats received artificial cerebrospinal fluid (ACF), 1 μl per hippocampus. According to the number of training errors, each animal was assigned to the n-DPA group or the control group, in order to have the same mean value of training errors for both groups.

RESULTS AND DISCUSSION

Number of training errors, number of relearning errors and % savings of n-DPA group and of control group, respectively, are shown in Fig. 1. The n-DPA treated rats exhibited significant fewer relearning errors than controls, resulting in significant higher % savings ($p<0.01$). Since n-DPA was injected after training and, on the other hand, according to biochemical findings [17], the substance effect is no longer present 24 hours after injection (i.e. during relearning), we can conclude that the n-DPA effect was an effect on consolidation of long-term memory. If we suppose that the n-DPA treatment was followed by an increase of GABA level in hippocampus, the present findings suggest that hippocampal

[1]This work was supported by the Ministry of Science and Technology of the G. D. R.

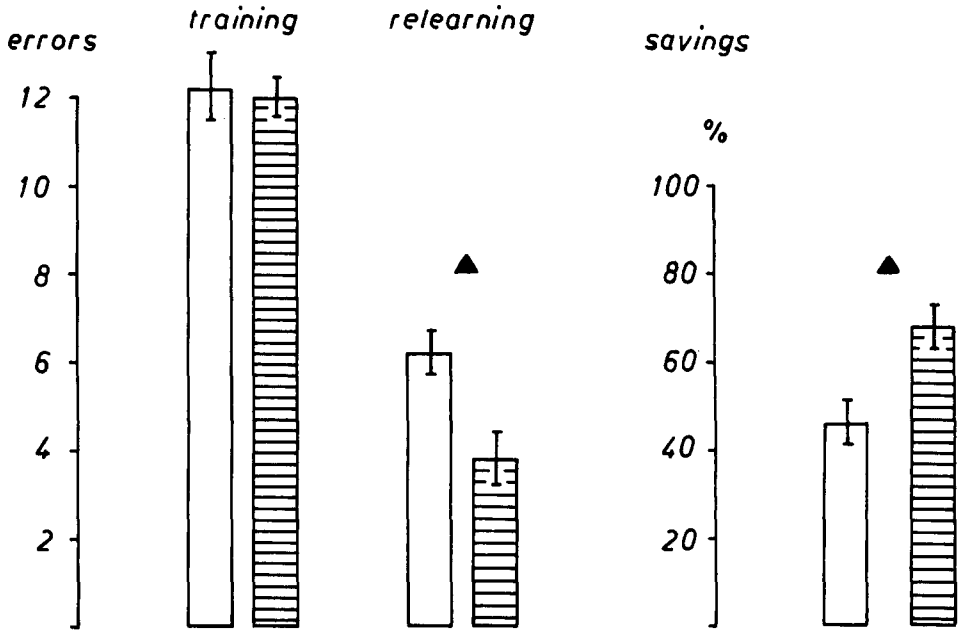

FIG. 1. Effect of posttraining intrahippocampal injection of n-dipropylacetate on the retention of a brightness discrimination; Open bars = control group, n=18, Shaded bars = n-DPA group, n=17, ▲ $p<0.01$, (Mann-Whitney U test).

GABA-ergic neurons would play an important role in memory consolidation, at least in the consolidation of a brightness discrimination.

If the literature only few data exist about the involvement of GABA in consolidation processes. Ishikawa and Saito [7] found an increase of correct responses in a brightness discrimination in rats, posttraining injected intraventricularly with 100 μg of GABA. A facilitation of the acquisition of a conditioned reaction was found using n-DPA [9] and 2-propyl 2-pentenoic acid [10] that increased the GABA level in the brain too. However, further experiments using direct GABA agonists and antagonists might be necessary to verify the role of GABA in memory processes.

ACKNOWLEDGEMENT

We wish to express our appreciation to Professor P. Mandel (Strasbourg) for his generous gift of n-dipropylacetate.

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