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BRIEF COMMUNICATION

Vasopressin Antagonizes Retrograde Amnesia in Rats Following Electroconvulsive Shock

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PFEIFER, W. D. AND H. B. BOOKIN. *Vasopressin antagonizes retrograde amnesia in rats following electroconvulsive shock*. PHARMAC. BIOCHEM. BEHAV. 9(2) 261–263, 1978.—Rats given an electroconvulsive shock immediately following training in a passive avoidance task showed amnesia when tested 24 hr after training. This amnesia was prevented if lysine vasopressin was injected either one hr before the training trial or one hr before the first test trial. The results indicate that it is unlikely that either electroconvulsive shock or lysine vasopressin affect memory storage.

Lysine vasopressin Electroconvulsive shock Retrograde amnesia

RETROGRADE amnesia can be produced experimentally in animals by electroconvulsive shock (ECS), and it is often a side effect of clinical electroconvulsive therapy. The dominant hypothesis has been that ECS administered immediately following a learning experience disrupts memory consolidation processes, and thus, prevents long-term memory storage [5,6]. If, following ECS memories are not consolidated, they should be permanently lost. However, several experiments suggest that the ECS induced amnesia can be overcome by administering a reminder of the training trial, a noncontingent aversive stimulus [4, 7, 8, 11, 12]. The results of these reminder studies question the hypothesis that ECS interferes with consolidation and suggest that retrograde amnesia is due to a blocking of retrieval processes.

Memory losses following treatment with other amnesic agents have also been reinstated or prevented. For example, administration of desglycinamide lysine vasopressin (DGLVP) prevents puromycin induced amnesia if it is injected between 20 hr prior to training and 12 hr after training [3]. DGLVP also attenuates the amnesia induced by CO_2 administration when it is given either 1 hr prior to training, or 1 hr prior to the test trial [13]. We have recently found that lysine vasopressin (LVP) can effectively antagonize the amnesic action of pentylenetetrazol when given either prior to the training trial or prior to the test trial [1]. We now report that the effectiveness of LVP as an amnesia antagonist is not limited to CO_2, puromycin and pentylenetetrazol, but that it is also effective in antagonizing the amnesia produced by electroconvulsive shock.

METHOD

Sixty male Sprague Dawley rats were obtained from Charles River Breeding Laboratories. The animals were housed two to a cage in a room with a 12 hr light/dark cycle, with food and water available *ad lib*, for 2 weeks before the start of the experiment. Body weight at the beginning of the experiment was between 200 and 255 g.

The passive avoidance apparatus was a standard two compartment chamber with a large darkened compartment 40 cm square with a grid floor for the delivery of footshock. The smaller compartment was 6×25×13 cm and was lighted by a 25 W lamp 40 cm above the center. The compartments were separated by a 6 cm square guillotine door. On the day of training, each animal was placed in the small chamber, and after 1 min, the guillotine door was opened. Latency to enter the large compartment was recorded to a maximum of 30 sec. If animals did not enter in 30 sec, they were dropped from the experiment and replaced by other animals. A constant current power supply delivered a footshock of 0.3 mA for 3 sec and after an additional 7 sec animals were removed from the large compartment. ECS was administered through ear clips immediately after removal from the large compartment, with a current of 100 mA for 3 sec. Animals receiving sham ECS had ear clips attached but never experienced the current. Seizures were observed in all animals receiving ECS.

Animals were randomly assigned to one of six treatment groups on the day of training. They received either an injection of LVP (10 μg/rat) or saline 1 hr prior to training, ECS or sham ECS immediately following training, and an injection of either saline or LVP 1 hr prior to the 24 hr retention test. These combinations resulted in the following six groups: Group 1) LVP-Train-ECS-SAL-Test; Group 2) SAL-Train-ECS-LVP-Test; Group 3) SAL-Train-ECS-SAL-Test; Group 4) LVP-Train-Sham ECS-SAL-Test; Group 5) SAL-Train-Sham ECS-LVP-Test; Group 6) SAL-Train-Sham ECS-SAL-Test. All groups were retested 4, 8 and 12 days after training. On all test trials, animals not entering the large

TABLE 1
MEDIAN STEP-THROUGH LATENCIES IN SECONDS DURING TEST TRIALS

Group	Treatment	N	Hours 24	96	192	288
1	LVP-ECS-SAL	10	102.2	300.0	300.0	278.2
2	SAL-ECS-LVP	10	300.0	300.0	300.0	300.0
3	SAL-ECS-SAL	10	15.7	18.9	13.8	14.1
4	LVP-Sham ECS-SAL	10	300.0	300.0	300.0	300.0
5	SAL-Sham ECS-LVP	10	300.0	300.0	300.0	300.0
6	SAL-Sham ECS-Sal	10	149.6	110.5	58.9	55.1

compartment within 300 sec were placed in the compartment for 10 sec and assigned a latency of 300 sec.

RESULTS

During the training trial, all animals entered the large compartment within 30 sec. Median acquisition latencies for the six groups ranged from 6.9 sec to 12.9 sec. There were no statistically significant differences between the groups using a Mann Whitney U Test, indicating that LVP did not affect latency on the acquisition trial. Also, LVP did not affect seizures, as there were no observable differences in overt seizures between animals receiving saline or the hormone.

Median step-through latencies for all groups on the retention tests are presented in Table 1. Group 6, the control group, had a significantly higher step-through latency on the 24 hr retention test than on the acquisition trial (Friedman Test, $\chi^2=10.0$, $p<0.005$), indicating retention of the passive avoidance learning. All four groups receiving LVP also had higher step-through latencies at 24 hr ($p<0.005$ for all groups) than on the acquisition trial. Group 3 which received only saline and the ECS treatment had a significantly lower median step-through latency at the 24 hr retention test ($p<0.02$) than Group 6, confirming the amnesic action of ECS. Groups 1 and 2 which received LVP along with the amnesic treatment demonstrated retention. Group 1 which received LVP 1 hr before acquisition was significantly different from Group 3, the amnesic group ($p<0.02$). When LVP was administered 1 hr before the 24 hr retention test (Group 2), retention was also evident ($p<0.002$ compared to Group 3). Group 3, the amnesic group did not show any recovery from the amnesia with repeated testing. In Group 6 there was evidence of extinction with repeated testing, as the median step-through latency decreased from 149.6 sec on the 24 hr test to 55.1 sec when tested on Day 12. There was no evidence of extinction in any of the groups that received LVP. Thus, when the hormone was administered prior to either training or testing, and alone or in conjunction with amnesic treatment, it still was able to inhibit extinction.

DISCUSSION

Several studies have been reported in which there was a spontaneous recovery from ECS induced amnesia [10,14], and it has been said that the recovery indicates that ECS interferes with retrieval processes rather than with consolidation processes. There was no evidence of recovery from amnesia in the present study up to 12 days after the ECS treatment. It is possible that the method of testing used in this study is not conducive to recovery. It has been argued that the daily testing procedure usually employed is a variation of the reminder studies and that reminders actually provide additional information to the animal and do not overcome a block of the retrieval mechanisms [2].

The results of the present study, as well as several other reports, offer firm evidence that LVP is an effective antagonist of amnesia. As the neuropeptide is capable of antagonizing ECS induced amnesia, pentylenetetrazol induced amnesia [1] and CO_2 induced amnesia [13] when administered 23 hr after the training trial, it is unlikely that either the hormone or the amnesics affect consolidation processes. It appears that the storage of information occurs rapidly and is rather insensitive to disruption [9].

LVP, as has been repeatedly shown, was effective in inhibiting extinction in the present study and the effects of the hormone were not weakened by ECS. The inhibition of extinction when the hormone is injected prior to training is consistent with the suggestion of other investigators that LVP facilitates consolidation. However, the inhibition of extinction when the hormone is injected just prior to the first test trial would seem to be due to its effects on retrieval, or perhaps activity. It is unlikely that it affects activity in the passive avoidance apparatus. A group of rats that did not receive footshock during the training trial were injected with LVP 23 hr later, 1 hr before the first test trial. There was no increase in latency to enter the large chamber (Mdn 8.4 vs. Mdn 7.1 sec). It is conceivable that LVP may effect both processes, consolidation when given prior to the training trial and retrieval when given prior to the first test trial.

The consolidation-retrieval dichotomy, as well as the short-term and long-term memory dichotomy, may be artificial ones that are due to the insensitiveness of the experimental testing situation, and neither are likely to be resolved with the behavioral testing paradigms currently used [9]. Appropriate performance in the passive avoidance situation necessitates both consolidation and retrieval, while failure to perform appropriately cannot indicate which of the processes has been disrupted. If these concepts are going to continue to guide research in this area, new behavioral tests must be developed in order to resolve the issue. It is difficult, however, to conceive of a behavioral test that will be able to separate these processes. At present, the continued use of these terms implies a better understanding of the phenomenon of memory than we really have.

For the most part, investigations are currently designed with preconceived notions of underlying processes, such as consolidation, retrieval, short-term memory and long-term memory. It may prove to be more beneficial to enter experiments without these preconceived notions, and to look for neurobiological endpoints that may be qualified, quantified

and correlated with behavioral changes observed in the passive avoidance situation. The judicious use of combinations of agents that disrupt and facilitate the passive avoidance behavior would be an aid in investigating such neurobiological correlates.

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