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Effects of Vasopressin on Spontaneous Black-White Choices in a T-Maze

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ALLIOT, J. *Effects of vasopressin on spontaneous black-white choices in a T-maze.* PHARMACOL BIOCHEM BEHAV **35**(4) 981–987, 1990.—The effects of subcutaneous administration of vasopressin on spontaneous black-white choice were investigated to determine whether they could account for modifications of performances during learning. First, pretrial injections of 0.2 μg of lysine-vasopressin (LVP) were given to rats fed ad lib submitted after the last injection to ten consecutive choices in the T-maze. Rats received one or five injections and were tested after either 30 minutes or 24 hours. Treatment with LVP reduced natural photophobia and modified the activity. A more striking effect was observed after one injection and with an injection-test interval of 30 min. Second, the influence of repeated injections of LVP on free choices was studied in food-motivated rats. The effect of repeated injections was marked, suggesting greater sensitivity to treatment in such rats. Third, we compared the action of posttrial administration of the peptide on the behavior of food-restricted rats submitted to appetitive learning in the T-maze, or to free choices. The treatment slightly disturbed the learning of the white arm and altered the preference for black in free choices condition. The two actions were different, showing that the effect on spontaneous behavior cannot account for the effect on learning.

Vasopressin Spontaneous behavior Learning and memory

NUMEROUS studies have demonstrated that vasopressin may have an effect on learned behavior. The most consistent effects have been found in aversively motivated tasks [see (16) and (37)]. The data obtained with positively reinforced tasks are more ambiguous. Studies using pretrial administration of vasopressin or fragments showed either a lack of effect in a runway (23) and in a radial maze (9), or an impairment in a bar-pressing task (6) or a facilitation of performance during a visual discrimination (1, 25, 34), in a bar pressing task (29) and in a spatial one (36).

Disruptive effects have often been shown after peripheral posttrial administration of this neurohypophyseal hormone (2–4, 8, 10, 32, 39). However, since the initial study of Ettenberg *et al.* who showed that vasopressin enhanced performance in a water-finding task (19), three workers have recently reported facilitatory effects of posttrial administration of either arginine-vasopressin (AVP) on memory for a juvenile conspecific for male rats (14), or lysine-vasopressin (LVP) on memory on brightness discrimination (39), or fragment AVP 4–9 on spatial memory in a radial maze (36). Several methodological differences (nature and dose of the peptide injected, strain and age of the animals, and experimental procedure) might account for the discrepancy between the results. It is also possible that memory processes were not directly affected, as several authors suggested. In a previous experiment using a DRL paradigm, we showed that the deleterious effect induced by posttrial LVP injections was due to impairment of some aspects of the animal's abilities to perform the task rather than of learning (4). In addition, poststimulus administration of vasopressin was shown to impair performance in a delayed matching to sample task (DMS) and, in the same apparatus, to modify spontaneous choice of control rats (2). Other experiments which attempted to assess the effects of vasopressin on spontaneous behavior have produced conflicting findings. Thus, in the open-field, Ettenberg *et al.* (19) and Andrews *et al.* (6) observed a reduction of locomotion, whereas Schulz *et al.* (35) and Krejci *et al.* (26) did not find any effect of LVP injections. Messing and Sparber (29) found an increase in the number of nose-poke responses after DGAVP. Other modifications of behavior have been noted: reduction of grooming and scratching, increased freezing (28), decreased agoraphobia (12), and decreased photophobia (20). While such results do not point to any consistent pattern of effects, due doubtlessly to varying doses and experimental procedures, they strongly support the notion that LVP does actually modify spontaneous behavior.

This paper reports about a series of experiments investigating the effects of subcutaneous administration of vasopressin on spontaneous behavior in systematically controlled paradigms. Furthermore, it was aimed at determining whether such modifications of unlearned behavior could explain the modifications of performances during learning.

GENERAL METHOD

Animals

In all, 173 Sprague-Dawley male rats were used. Rats were 7

weeks old at the start of each experiment (250 g). After their arrival in the laboratory (at 5 weeks), the rats were housed in groups of three and they were handled and weighed daily.

In Experiments 2 and 3, rats were food deprived for 23 hours: they had 1 hr of free-feeding between 1800 and 1900 hr. Water was available ad lib.

Apparatus

Animals were tested in a T-maze, 10 cm wide and 15 cm high, consisting of a 80 cm straight alley, two 55 cm arms and two 20 cm goal boxes. The maze was lit by a 75-W bulb placed 1 m above it. The arms and the goal-boxes differed visually; one was black and the other white. The latency to enter one of the arms was recorded. All the observations were made between 1300 and 1700 hr.

Drugs

Sixty-two international milliunits of LVP [0.2 μg of lysine-vasopressin (LVP), Sandoz, biological activity = 270 UI/mg] were dissolved in 0.25 ml of standard buffered solution (pH = 4). Injections were administered subcutaneously. Control rats were given 0.25 ml of standard solution.

This dose of LVP was chosen because it was the effective dose in our previous experiments using appetitive learning procedure. The same dose was also effective in defensive tasks (16) and on spontaneous behavior of yoked controls in DMS task.

EXPERIMENT 1

Experiment 1 investigated the effect of pretrial LVP administration on the black-white free choice of rats. The effects of a single injection were compared with those of repeated injections of 0.2 μg of LVP. The time interval between the injection and the test was also varied.

PROCEDURE

Treatment

Sixty-one male rats were split into seven groups. Rats in groups 1 (n = 7) and 4 (n = 7) were controls. For five days, they received 0.25 ml of standard buffered solution. Groups 2 (n = 10) and 5 (n = 10) were injected for four days with the standard solution and were given one injection of 0.2 μg of LVP on the fifth day. Groups 3 (n = 10) and 6 (n = 10) were injected for the five days with 0.2 μg of LVP. Group 7 (n = 7) was put in the T-maze without any injection.

Test

Rats of groups 1, 2 and 3 were tested in the T-maze 30 minutes after the last injection, while rats of the other groups (groups 4, 5 and 6) were tested on the sixth day, 24 hours after the last injection. Animals underwent ten successive trials in the T-maze. For each trial, the arm chosen and the latency to enter it were recorded. The rat was then taken out and placed immediately (20 sec) at the entrance to the maze for a new trial. If the rat did not enter either arm within 180 sec, the trial was stopped, the animal was taken from the apparatus and replaced for a new trial.

Statistical Analysis

The distribution of first choices was compared by chi-square analysis.

A two-way analysis of variance [factor 1: treatment (0, 1 or 5 injections), factor 2: interval injection-test (30 minutes or 24 hours)] was used for the total number of choices (white, black, neither) and for the response latencies.

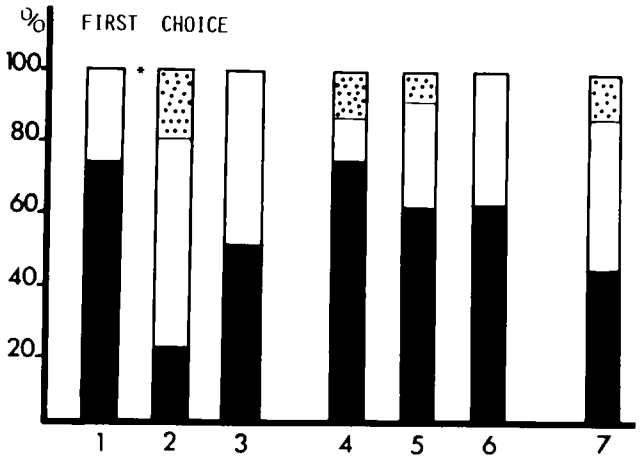

FIG. 1. Percent of choice of the black arm (black columns), the white arm (open columns), or refusal to choose (dotted columns) in the first trial. Pretrial injection of LVP decreases the preference for the black arm. *$p<0.05$ relative to controls of group 1. Group 1: five injections of vehicle. Test 30 min after the last injection. Group 2: one injection of LVP. Test 30 min after the injection. Group 3: five injections of LVP. Test 30 min after the last injection. Group 4: five injections of vehicle. Test 24 hr after the last injection. Group 5: one injection of LVP. Test 24 hr after the injection. Group 6: five injections of LVP. Test 24 hr after the last injection. Group 7: noninjected.

RESULTS

Study of the First Choice

Control rats showed a clear-cut preference (71%) for the dark arm of the T-maze (photophobia). Treatment with LVP decreased this natural preference ($\chi^2 = 2.9$, $0.10 > p > 0.05$). A more marked effect was seen in group 2 (one injection of LVP, interval 30 min) where the natural free-choice was inverted ($\chi^2 = 5.14$, $p<0.05$) (Fig. 1). The choice latencies on the first choice were not modified by the LVP injections.

Study of the Ten Successive Choices (Table 1)

The tendency (because of the absence of any reinforcement) to choose neither arm increased as trials proceeded. Analysis of variance performed on the data showed an overall effect of the interval between the test and the last injection on the number of trials with no choice, $F(1,54) = 4.8$, $p<0.05$, and on the total number of white arm choices, $F(1,54) = 4.1$, $p<0.05$. A pair comparison showed that it was only significant for control groups ($t = 2.7$, $p<0.05$). As the behavior of rats was identical in groups 4 and 7, the difference between the animals tested at 24 hours and those tested at 30 minutes could perhaps be attributed to the lack of injection on the sixth day.

There was no main effect of treatment, but an interaction between treatment and interval, $F(2,54) = 3.73$, $p<0.05$, on the refusal to choose was found. When animals were tested after 30 min, the administration of LVP increased the number of no choices, whereas a decrease was noted after an interval of 24 hours. For paired comparisons, the effect was significant only in single-injected groups ($t = 3.67$, $p<0.05$)

TABLE 1

ANALYSIS OF THE TEN TRIALS: PERCENT OF CHOICES AND TOTAL RUNNING TIME (IN SEC)

Groups	Injections	Interval	Choice % Black	% White	% Neither	Total Running Time
1	Vehicle (5)		37 ± 14.8	31.5 ± 9.9	31.5 ± 17	311 ± 106
2	Vehicle (4) + LVP (1)	30 minutes	28 ± 17	28 ± 19	44† ± 29	380 ± 135
3	LVP (5)		39 ± 24	25 ± 14.3	36 ± 31	351 ± 156
4	Vehicle (5)		22 ± 19.5	13* ± 7.4	65* ± 24	433 ± 105
5	Vehicle (4) + LVP (1)	24 hours	37 ± 26	29 ± 6.4	34† ± 29	354 ± 127
6	LVP (5)		27 ± 13	19 ± 14	54 ± 23.5	445 ± 141
7	—	—	21 ± 14.6	20 ± 11.9	59* ± 23.6	472 ± 91

Mean ± S.D.
*$p<0.05$ relative to group 1.
†$p<0.05$ relative to vehicle group in the same condition.

CONCLUSION

Vasopression decreased the spontaneous photophobia when it appeared in the controls in the first trial. Over the ten consecutive trials, only the choice/no choice number ratio was modified, which might be interpreted as a modification of activity. A more striking effect was observed after one injection of LVP. This observation suggests a tolerance to LVP.

EXPERIMENT 2

Experiment 1 showed that pretest administration of LVP was able to modify spontaneous black-white choices, even when the injection to test interval was of 24 hours. However, the effect was reduced with daily injections which were the usual conditions of administration of the peptide during our previous learning tests. However, in these previous experiments, the rats were food-deprived. Accordingly, the aim of the next experiment was to study the influence of repeated injections of LVP on free-choice test in food-motivated rats.

PROCEDURE

This experiment proceeded in two stages:

Experiment 2a: Twenty-seven food-deprived rats were divided into 3 groups: one (group 1, n = 7) without any injection served as control for the effect of the injections, another control group (group 2, n = 10) was injected daily with 0.25 ml of vehicle, and an experimental group (group 3, n = 10) injected daily with 0.2 μg of LVP for five days. All the rats were tested in the T-maze in the same conditions as in the first experiment. The test was given 30 minutes after the last injection for the animals in groups 2 and 3.

Experiment 2b: Using the same procedure, 21 food-restricted rats were divided into two groups: a control group (n = 10) injected with 0.25 ml of vehicle, and a treated group (n = 11) injected with 0.2 μg of LVP. The test in the T-maze was performed 24 hours after the last injection.

RESULTS

Experiment a (30 Minutes)

Vehicle-injected rats showed greater activity (96% of choices) compared with noninjected rats and had no marked preference for the black arm of the T-maze. Injection of LVP did not modify the relative number of the black and white choices. However, the treatment decreased the total number of choices ($t = 2.8$, $p<0.05$). Activity and choices became analogous to those of noninjected rats (Table 2).

Experiment b (24 Hours)

Control rats showed a preference for black on the first choice (60–40%) and a weaker overall activity (decrease of the total number of choices) than control rats in Experiment a (61% of choices versus 98%).

A decrease of a) the total number of choices and b) black choices ($t = 2.6$, $p<0.05$) was observed after LVP. In the first choice, the preference for black also decreased, but it was not significant ($\chi^2 = 1.7$, ns) (Table 3).

CONCLUSION

Experiment 1 suggested a tolerance to treatment with LVP. Nevertheless, repeated injections of LVP induced modifications of black-white free choices in Experiment 2. This result suggests a greater sensitivity of food-restricted rats to LVP.

Photophobia is less marked in food-motivated rats. In these conditions, LVP did not modify the black-white choice frequency on the first choice.

EXPERIMENT 3

In Experiment 2b described above, an influence of vasopressin

TABLE 2

EFFECT OF PRETRIAL INJECTION OF LVP ON FREE-CHOICE BEHAVIOR IN FOOD-MOTIVATED RATS WHEN THE TEST WAS PERFORMED 30 MINUTES AFTER THE LAST INJECTION

Groups	All Choices Black	White	Neither	Total Running Time
Vehicle	56%	40%	4%	187 ± 84
LVP	55%	22%	23%*	268 ± 141
Controls	53%	24%	23%*	282 ± 195

*$p<0.05$ relative to vehicle-injected group.

TABLE 3

EFFECT OF PRETRIAL INJECTION OF LVP ON FREE-CHOICE BEHAVIOR IN FOOD-MOTIVATED RATS WHEN THE TEST WAS PERFORMED 24 HOURS AFTER THE LAST INJECTION

Groups	All Choices			Total Running Time
	Black	White	Neither	
Vehicle	41%	20%	39%	390 ± 145
LVP	18%*	23%	59%*	441 ± 111

*$p<0.05$ relative to vehicle injected group.

on free-choice was observed for an injection to test interval of 24 hours. In Experiment 3, we set out to determine if this effect of vasopressin on spontaneous behavior could account for the effect of posttrial injections of LVP on performance during learning. Thus, we compared the action of posttrial administration of vasopressin on behavior of rats submitted either to appetitive learning or to free choices. In addition, in the DMS experiment (2), a differential effect related to the color (white or black) of the boxes has been seen in DMS group, not in yoked controls. Hence, in the free-choice group, we administered vasopressin either after white choice or after black choice. Finally, this experiment was designed to assess reinforcing properties of vasopressin.

PROCEDURE

Sixty food-restricted rats were used. During the habituation to the apparatus, natural preference for black or white was noted. Sixty percent of the animals preferred the black arm and 40% preferred the white one. Animals were split onto five groups. They were submitted to one daily trial for twelve days in the following conditions:

a) Groups 1 (n = 12) and 2 (n = 12) learned to choose the white arm of the T-maze (a pellet of food was placed in the white goal-box).

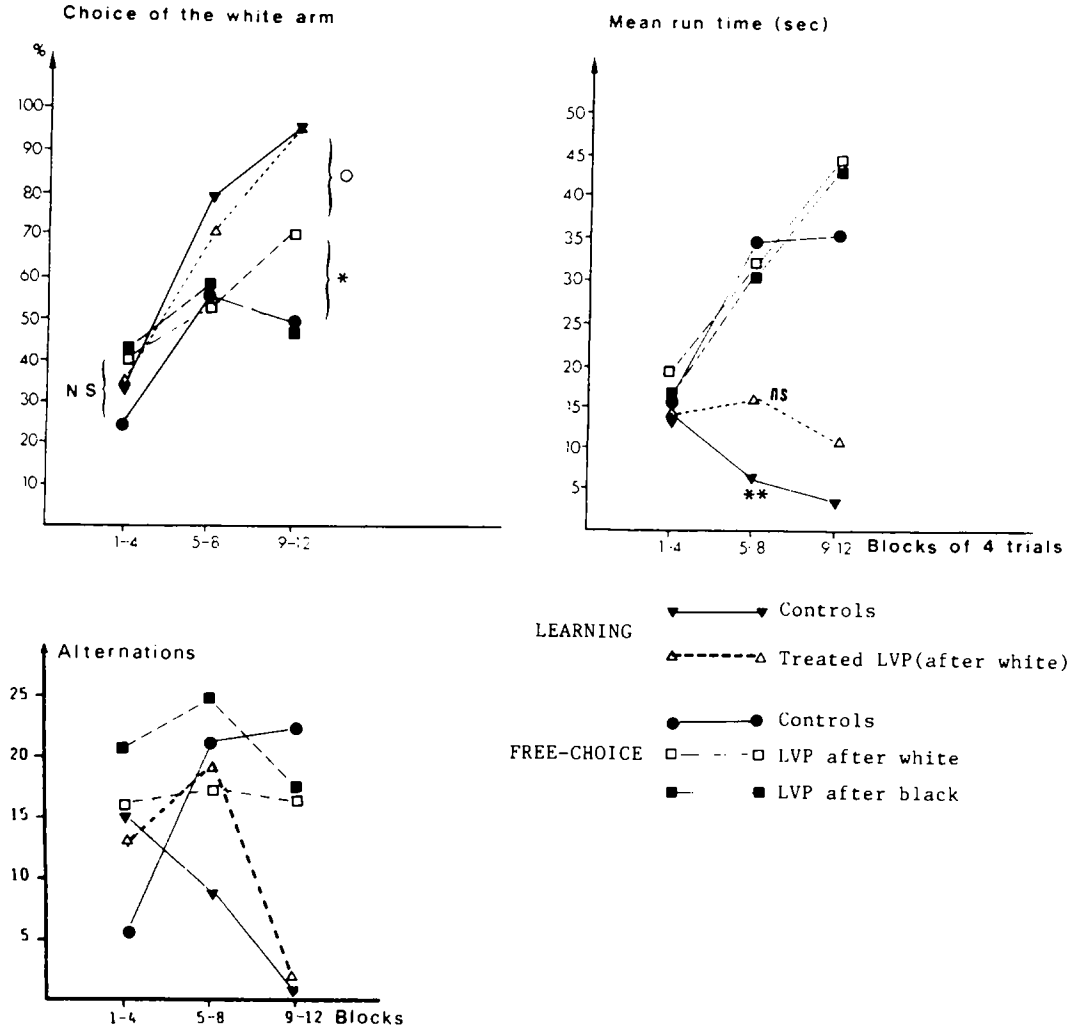

FIG. 2. Effect of LVP on the performances of rats submitted to one daily trial for twelve days in learning or free-choice conditions in the T-maze. Vasopressin perturbs learning, decreasing total number of correct choices and increasing running time. The effect on the number of alternations and the number of white choices was at opposite sign in learning and free-choice conditions. O $p<0.05$ relative to the treated group in learning condition. *$p<0.05$ relative to the control group in free-choice condition. **Significant decrease ($p<0.01$) of running time during trials. ns: not significant.

b) Groups 3 (n = 12), 4 (n = 12) and 5 (n = 12) were given free-choice trials: no food was put in either white goal-box or the black one. We note the latency to enter one arm, the running time and the number of alternated responses (alternations).

Treatment

Injections were given immediately after each trial, before the rat was put back to its home-cage. Groups 1 and 3 received vehicle whatever arm was chosen (Control groups). Groups 2 and 4 were injected with vehicle after the black choices and with 0.2 μg of LVP after white ones. Group 5 was injected with vehicle after the white choices and with LVP after black ones.

RESULTS

The Effect of Vasopressin on Learning Versus Spontaneous Choice

The effect of reinforcement and of treatment on the data presented in Fig. 2 was evaluated using a two-factor analysis of variance on repeated measures. The presence of reinforcement induced a rapid increase of white arm choices which reached 98% at the end of training, a simultaneous decrease of alternations and a shortening of the running time, whereas in the nonreinforced group, the percentage of white arm choices increased, but was stabilized at around 50%. The number of alternations remained high and the running time was markedly increased.

There was no overall effect of treatment but an interaction was shown by statistical analysis, $F(2,49) = 2.5, 0.10 > p > 0.05$. Whereas the correct choices were not significantly changed by treatment in learning group, vasopressin injections increased white choices in nonreinforced group. A clear preference for the white arm was seen in group 4 compared to group 3 (72%/50%, $t = 2.6$, $p < 0.05$). The same result was observed when alternations were studied, $F(2,49) = 6.6$, $p < 0.01$. No significant effect of vasopressin on running time was found. There were wide intragroup variations. However, it is noteworthy that during learning the treated group did not show a significant enhancement of the running time (13.2–10.6 sec, $t = 0.55$, ns), whereas the control group showed a clear-cut improvement (13.8–3.7 sec, $t = 3.4$, $p < 0.01$).

The Effect of Vasopressin on Free-Choice According to the Brightness of the Arm

The treatment did not modify the behavior of rats injected after the black arm choice (Fig. 2), but further analysis of the data (Fig. 3) revealed that the natural preference for the dark arm observed in the controls disappeared in the two treated groups. However, whereas white-injected rats preferred the white arm, black-injected animals showed no preference.

CONCLUSION

Treatment with vasopressin slightly disturbed T-maze learning. This deleterious action mainly affects choice latencies and may reflect a nonspecific action of LVP such as, e.g., an altered incentive value of the reinforced stimulus. This confirmed the results which we had obtained in other food-reinforced tasks, such as lever pressing and delayed matching-to-sample tasks.

Posttrial administration of the peptide also modified white-black free-choices as pretrial injections in Experiments 1 and 2. However, this effect cannot explain the effect of LVP on learning: effects on the number of alternations, on the number of white choices and on the latencies appeared to be different in learning and free-choice conditions. In addition, the behavior of injected

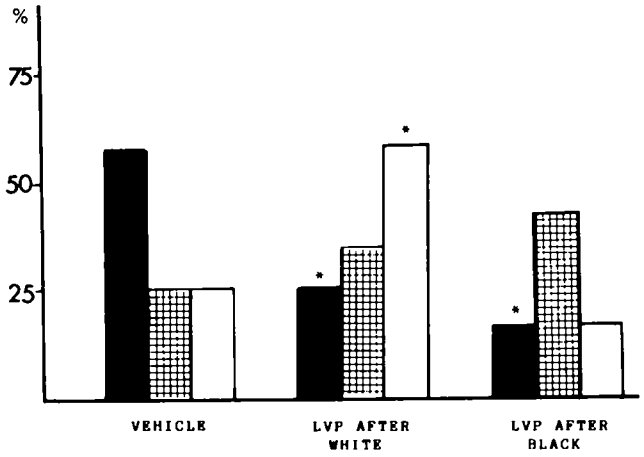

FIG. 3. Percent of animals trained in free-choice conditions showing on the 12 trials a preference for the black arm (black columns), a preference for the white arm (open columns) or showing no preference (checkered columns). LVP decreases the natural preference for the black whatever the arm associated with the injection. *$p < 0.05$ relative to the vehicle group.

rats did not reflect a conditioned aversion, as suggested by Ettenberg *et al.* (19). A conditioned aversion would be seen as a reduction of the choice of the arm paired with injection, which was never seen in this work. According to the present data, Ebenezer (18) has recently shown that only high doses of vasopressin could act as an aversive stimulus.

A role of positive reinforcement by vasopressin (13) can also be rejected since, although a preference for the white arm was seen after pairing white and LVP administration, no preference for black was observed after pairing black and LVP. As in Experiments 1 and 2, vasopressin reduced photophobia and this effect was stronger when the injection was paired with white. This last result shows that the potentiation of the action of vasopressin by association with white appears also in spontaneous behavior.

GENERAL DISCUSSION

These results are evidence that pretest subcutaneous administration of 0.2 μg of lysine vasopressin specifically modifies black-white free-choice behavior. Our findings suggest that the food-motivated rats showed a greater sensitivity to treatment. This result had also been found in a study of spontaneous behavior in a hole-board (5). As Carrol *et al.* have suggested (11), "feeding conditions or deprivational state appears to represent a major class of variables controlling drug-reinforced behavior in laboratory animals."

It was found also that one injection was more effective than five which may suggest a gradual tolerance to the treatment. Although the effects on behavior were greater after an interval of an hour, modifications were found when an injection-test interval of 24 hours was introduced. Thus, a proactive action of vasopressin on behavior for long injection-test intervals can be observed.

It is noteworthy that the most constant effect of vasopressin was a reduction of the natural photophobia. There are other reports of vasopressin altered species-specific phobia. In the previous experiment of DMS (2), vasopressin reduced the spontaneous avoidance for white in the yoked control rats. Frucht-Celaru and Sterescu-Volanschi (20) found an increase in the preference for light after treatment with LVP. Crine (12) and Gaffori and De Wied (21) observed a reduction of centrophobia. The same result

was found in the hole-board apparatus (5).

It may be that the action of vasopressin on phobia is linked to an enhancement of arousal, as postulated by Sahgal (33). In Experiments 1 and 2, events known to enhance arousal such as food-deprivation or a vehicle injection reduced phobia. However, food-deprivation or injection increase activity, resulting here in a greater frequency of choice. Injection of vasopressin generally reduced the activity except in Experiment 1 for the group tested after an injection-test interval of 24 hr. Hence, enhanced arousal apparently does not account for all the effects of vasopressin for which other mechanisms are responsible.

Vasopressin has a positive effect on the number of choices made by the groups tested after an interval of 24 hr (Experiment 1). It is noteworthy that this group differs significantly from the other groups as the number of choices made (35%) by the control rats was particularly low. Thus, it was suggested that LVP has a differential effect according to the natural behavior (of nontreated animals). Such an observation had already been made in a brightness discrimination (3) where vasopressin injection increased the bar pressing rate in "good learners" that have a low basal response rate and decreased bar pressing rate in "bad learners" that have a high basal response rate. Sahgal (33) noted also that vasopressin decreased the activity of Brattleboro rats when the responding rate was high and increased the activity when this level was low. This differential action of vasopressin depending on the basal behavior was also reported by Strupp (36) in learning.

In Experiment 3, LVP administration associated with the choice of one arm (without reinforcement) also showed the alteration of natural photophobia. The action was greater when injection was paired with white, as in DMS task (when reward was contingent upon matching). The association with white generally potentiated the effect of the peptide on behavior.

The present findings also demonstrate that behavioral changes induced by low doses of LVP do not reflect an aversive effect. However, an increase in the level of arousal certainly occurs, which accounts for some of the results, particularly the modification of phobia. As in the delayed matching-to-sample task, the modifications of behavior in free-choice conditions cannot account for impaired performance in appetitive learning. No reduction of photophobia ever occurs in learning conditions, for which reduction of white box or reduction of white arm choice is generally observed. It may be that in certain tasks the effect of vasopressin on nonreinforced behavior counteracts the effect on performance during learning.

Concerning the behavioral effect of vasopressin, three main theoretical viewpoints have been held to date: specific central theory (17), arousal theory (33) and aversive theory (19). The major result of this series of experiments was to clearly show that the effect of vasporessin on behavior is both general and subtle. Indeed, it depends on the testing situation, the motivational state and the baseline behavior. It can be assumed that the mechanism by which vasopressin acts on behavior is probably subtle also. It may explain why it has so far proved difficult to account for the various effects on behavior obtained after injection of vasopressin in terms of a single mechanism. Thus, the action of peripheral and central injections may not be mediated by similar mechanisms and through the same site of action as shown by Alescio-Lautier *et al.* (1) and suggested by Le Moal *et al.* (27).

As regards the peripheral administration of the natural peptide (AVP or LVP), it is probable that the behavioral action is linked, at least in part, to peripheral endocrine modifications. Although the results reported here cannot be ascribed to an aversive action, other mechanisms may be involved. We have shown in the laboratory that the injection of 0.2 μg of LVP significantly increased the blood level of corticosteroids. This specific internal state could consequently modify the performance during testing, besides any central specific effect.

The use of fragments, virtually devoid of AVP's endocrine properties [as, e.g., in the studies of Strupp (36) and De Wied *et al.* (16)] is, therefore, crucial for determining if the behavioral effect that has been observed in learning tasks should be interpreted as an effect on memory function. The problem that remains is that the endocrine effects of vasopressin are manifold and that it is very difficult to be certain that the fragments studied have none.

REFERENCES

1. Alescio-Lautier, B.; Devigne, C.; Soumireu-Mourat, B. Hippocampal lesions block behavioral effects of central but not of peripheral pre-test injection of arginine vasopressin in an appetitive learning task. Behav. Brain Res. 26:159–169; 1987.
2. Alexinsky, T.; Alliot, J. Vaospressin injections impair working memory in a delayed matching-to-sample task in rats. Behav. Neural Biol. 48:167–182; 1987.
3. Alliot, J.; Alexinsky, T. Effects of post-trial vasopressin injections on appetitively motivated learning in rats. Physiol. Behav. 28:525–530; 1982.
4. Alliot, J.; Alexinsky, T. Repeated post-trial administration of vasopressin impairs subsequent differential reinforcement of low rates (DRL) performance. Behav. Proc. 8:345–362; 1983.
5. Alliot, J.; Alexinsky, T. Behavioral dose-related effects of subcutaneous administration of vasopressin. Relationships with experimental procedure. Behav. Brain Res. 26:202–203; 1987.
6. Andrews, J. S.; Newton, B. A.; Shagal, A. The effects of vasopressin on positively rewarded responding and on locomotor activity in rats. Neuropeptides 4:17–29; 1983.
7. Bohus, B. Effect of hypophyseal peptides on memory functions in rats. In: Adam, G., ed. Biology of memory. New York: Plenum Press; 1971:93–100.
8. Boulanger, B.; Crine, A. F.; Sulon, J.; Carlier, P. Effects of daily post-trial AVP injections on lever-pressing conditioning in rats. 4th Conference of the European Society for Comp. Physiol. Biochem., Bielefeld, FRG; 1982:219.
9. Buresova, O.; Skopkova, J. Vaospressin analogues and spatial short-term memory in rats. Peptides 1:261–263; 1980.
10. Buresova, O.; Skopkova, J. Vasopressin analogues and spatial working memory in the 24-arm radial maze. Peptides 3:725–730; 1982.
11. Carroll, M. E.; France, C. P.; Meisch, R. A. Food deprivation increases oral and intravenous drug intake in rats. Science 205: 319–321; 1979.
12. Crine, A. Effects of vasopressin on open-field behavior in rats. Physiol. Psychol. 9:109–113; 1981.
13. Crine, A. Vaospressin effects on food-rewarded learning tasks might be due to its action on carbohydrate/lipid metabolism, not memory. Appetite 5:233–238; 1984.
14. Dantzer, R.; Bluthe, R.-M.; Koob, G. F.; Le Moal, M. Modulation of social memory in male rats by neurohypophyseal peptides. Psychopharmacology (Berlin) 91:363–368; 1987.
15. De Wied, D. Effects of peptide hormone on behavior. In: Ganong, W. F.; Martini, L., eds. Frontiers in neuro-endocrinology. Oxford: Oxford University Press; 1969:97–140.
16. De Wied, D. Neurohypophyseal hormone influences on learning and memory processes. In: Linch, G.; McGaugh, J. L.; Weinberger, N. M., eds. Neurobiology of learning and memory. New York: The Guilford Press; 1984:289–312.
17. De Wied, D.; Gaffori, O.; Burbach, J. P.; Kovacs, G. L.; VanRee, J. M. Structure activity relationship studies with c-terminal fragments of vasopressin and oxytocin on avoidance behaviors of rats. J. Pharmacol. Exp. Ther. 241:268–274; 1987.
18. Ebenezer, I. S. Can vasopressin alone act as an unconditioned stimulus to produce passive avoidance behavior in rats in a typical

memory experiment? Neuropharmacology 27:903–907; 1988.
19. Ettenberg, A.; Van der Koy, D.; Le Moal, M.; Koob, G. F.; Bloom, F. E. Can aversive properties of (peripherally-injected) vasopressin account for its putative role in memory? Brain Res. 7:331–350; 1983.
20. Frutch-Celaru, M.; Sterescu-Volanschi, M. The effect of lysine-vasopressin on short-term recall of noxious significance. Rev. Roum. Morphol. Embryol. Physiol. 12:285–287; 1975.
21. Gaffori, O. J. W.; Van Ree, J. M.; De Wied, D. Effect of desglycinamide (Arg^8) vasopressin (DGAVP) and ACTH 4–10 on memory and attentional processes as assessed with food search behavior in rats. Neurosci. Lett. (Suppl.) 22:S494; 1985.
22. Garrud, P. Effects of lysine-8-vasopressin on punishment-induced suppression of a lever-holding response. Prog. Brain Res. 42:173–186; 1975.
23. Garrud, P.; Gray, J. A.; De Wied, D. Pituitary-adrenal hormones and extinction of rewarded behavior in the rat. Physiol. Behav. 12: 109–119; 1974.
24. Hoglund, A. U.; Meyerson, B. J. Effects of lysine-vasopressin in an exploratory behaviour test situation. Physiol. Behav. 29:189–193; 1982.
25. Hostetter, G.; Jubb, S. L.; Kozlowsky, G. P. Vasopressin affects the behavior of rats in a positively-rewarded discrimination task. Life Sci. 21:1323–1328; 1977.
26. Krejci, Y. B.; Kupkova, B.; Metys, J.; Barth, T.; Jost, K. Vasopressin analogs: Sedative properties and passive avoidance behavior in rats. Eur. J. Pharmacol. 56:347–353; 1979.
27. Le Moal, M.; Dantzer, R.; Michaud, B.; Koob, G. F. Centrally injected arginine vasopressin (AVP) facilitates social memory in rats. Neurosci. Lett. 77:353–359; 1987.
28. Meisenberg, G. Short-term behavioral effects of posterior pituitary peptides in mice. Peptides 2:1–8; 1981.
29. Messing, R. B.; Sparber, S. B. Facilitation of appetitively motivated learning and memory by desglycinamide arginine vasopressin (DG-AVP). Eur. J. Pharmacol. 89:43–51; 1983.
30. Mulvey, D. J.; Watt, J. M.; McEwen, B. B.; Flannelly, L. M. Effect of lysine-8-vasopressin on retention and retrieval of a discrimination reward task in the rat. Behav. Neurosci. 102:580–585; 1988.
31. Packard, M. G.; Ettenberg, A. Effects of peripheally injected vasopressin and des-glycinamide vasopressin on the extinction of a spatial learning task in the rats. Regul. Pept. 11:51–63; 1985.
32. Sagales, T. Vasopressin retards the acquisition of positively reinforced lever pressing in homozygous Brattleboro rats. Regul. Pept. 4:317–326; 1983.
33. Sahgal, A. Vasopressin and behavior, some arguments for an arousal hypothesis. In: Endroczi, A., ed. Neuropeptides and psychosomatic processes. Budapest: Hung. Acad. Sci.; 1983:55–62.
34. Sara, S. J.; Barnett, J.; Toussaint, P. Vasopressin accelerates appetitive discrimination learning and impairs its reversal. Behav. Proc. 7:157–167; 1982.
35. Schulz, H.; Kovacs, G. L.; Telegdy, G. Effects of physiological doses of vasopressin and oxytocin on avoidance and exploratory behaviour in rats. Acta Physiol. Acad. Sci. Hung. 45:211–215; 1974.
36. Strupp, B. J. Improvement of memory by a vasopressin fragment: Importance of individual differences in mnemonic function. Behav. Neurosci. 103:743–754; 1989.
37. Strupp, B. J.; Levitsky, D. A. A mnemonic role for vasopressin: The evidence for and against. Neurosci. Biobehav. Rev. 9:399–411; 1985.
38. Van Haaren, F.; Heinsbroek, R. P. W.; Lowerse, A.; Van de Poll, N. E. Vasopressin has general rate-decreasing effects on schedules maintaining either high or low response rates. Psychopharmacology (Berlin) 89:69–72; 1986.
39. Van Haaren, F.; Van Zanten, S.; Van de Poll, N. E. Vasopressin disrupts radial maze performance in rats. Behav. Neural Biol. 45: 350–357; 1986.
40. Williams, A. R.; Carey, R. J.; Miller, M. Behavioral differences between vasopressin-deficient (Brattleboro) and normal long-Evans rats. Peptides 4:711–716; 1983.