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Memory effects of arginine vasopressin (AVP) and [7-9] fragment of its peptide chain in rats

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Abstract. The effect of arginine vasopressin (AVP) and [7-9]-vasopressin on different memory types was examined in tests of active avoidance, passive avoidance and water maze after both intraventricular and subcutaneous injections. Results were compared with AVP and [7-9]AVP effects in open field and holeboard tests. Significant latency time elongation was observed after both icv and sc injections of AVP but not [7-9]AVP in the passive avoidance test. This effect was blocked by [β-Mercapto-β, β-cyclopentanometyleno^{1}-propionylo^{1}-O-Et-Tyr^{2},Val^{4},Arg^{8}]-vasopressin, an antagonist of V_1 receptors. Injections of both peptides did not improve the performance in other performed tests including the open field test and the holeboard test. Therefore the results confirmed that AVP improves memory only in the passive avoidance test. This effect is probably mediated by central V_1 receptors and is not induced by exploratory and locomotor activity impairment. Considering the above results together with the literature data, it seems that the most important fragment of AVP is [4-6] AVP.

Key words: memory, vasopressin, [7-9]-vasopressin, active avoidance, passive avoidance, water maze test, locomotor activity, exploratory activity

INTRODUCTION

The study of de Wied et al. (1965) became the groundwork for interest in the role of AVP and other peptides in the mechanisms of memory (de Wied 1965, de Wied et al. 1975). It is proved that in rats AVP influences memory in a passive avoidance test, but results obtained in other tasks are strongly divergent (Kovacs et al. 1979, Le Moal et al. 1987, Engelmann et al. 1992a).

Influence on human memory also was investigated. It seems that voluntary selective attention and arousal do not appear to be primary targets of AVP in humans. Effects of vasopressin in humans are, in fact, compatibile with the new animal research showing that the mediation of behavioural effects of vasopressin relies primarily on hippocampal and related limbic structures. In humans AVP is able to improve declarative memory formation. The effect appears to center on the encoding processes for memory (Perras et al. 1997, Born et al. 1998).

On the other hand it is known that some fragments ([4-9] and [5-8] AVP) of the peptide chain of AVP show to be even more potent than the native hormone (Dietrich et al. 1997, Vawter et al. 1997, Tanabe et al. 1999, Nakayama et al. 2000). Fujiwara et al. (1997) proved that in a radial maze test [4-9]AVP appeared to be 10,000 times more potent than [1-9]AVP. Also [5-8]AVP showed high behavioural activity, while both [6-8]AVP and [5-7]AVP demonstrated no activity in the same test.

A great number of inconclusive data obtained in different experimental models prompted me to investigate and compare the memory effect of vasopressin and [7-9] fragment of vasopressin peptide chain in three different tests, evaluating different types of memory in rats: passive avoidance, active avoidance and water maze tests.

METHODS

Subjects

Male Wistar albino rats were used for all experiments. The animals were bred in The Animal Farm of The Medical University of Silesia. During the duration of the experiments they were kept in standard conditions: artificial dark to light cycle (12h:12h), constant temperature 21°C with free access to standard food and water.

One week before icv injections polyethylene cannulas (id 0.4 mm, od 0.7 mm, total length 35 mm) were implanted under thiopenthal anaesthesia (Thiopental, United Pharmaceutical Works, Praha, Czech Republic, 40 mg/kg ip) into the right brain ventricle using the following coordinates: a depth 4 mm from the surface of the skull, 2 mm to the right from sagittal suture and 2 mm caudal from the coronal suture (Plech et al. 1997). Cannulas were attached to the skull bone with Deltamed PM4 glue (Chemical Factory Oświęcim, Poland). Every dose of icv-injected peptide was dissolved in 5 µl of 0.9% NaCl solution. Directly after the injection of peptide solution a second injection of 5 µl of 0.9% NaCl was made to fill the cannula and ensure that the whole dose of peptide reached the brain. Subcutaneous injections did not require any special procedure. The volume of scinjected solution was always 0.1 ml per 100 g of body weight.

Experiments were always performed at the same time of the day (between 10 am and 2 pm).

Apparatus and procedure

For memory evaluation the following tests were used: passive avoidance test, active avoidance test and water maze test. For exploratory and locomotor activity evaluation the open field and holeboard tests were used.

Passive avoidance test was performed in a dodge tester (COTM Białystok, Poland). The apparatus consisted of two chambers (22 x 26 x 28 cm) connected with a door (6.5 x 12 cm) that enables free crossing from one chamber to another but it was modified in such a way that all walls of one chamber were black, with no light source available. The other chamber was light-painted, with a light source (40 W) in the ceiling. Both chambers had a grid floor. The diameter of the rods was 1mm, with 5 mm distance between the rods. The experiment consisted of three sessions performed in three consecutive days. In the first day, after 2 min habituation for darkness in the dark part of the tester, the animal was moved directly into the bright compartment and allowed to cross back to the dark, preferred chamber. The rat was allowed to stay another 2 min in the dark compartment and the cycle was repeated. The latency time from placing the animal in the bright compartment to its escape into the dark one was measured in three consecutive trials. The second session, carried out after 24 hours, was identical, but after the third trial an electric shock was given (AC current, 50 Hz, 0.5 mA for 10 seconds). 10 s after the shock vasopressin (10 pmoles, 0.5, 1 and 5 nmoles icv; 5 or 50 nmoles/kg sc) or [7-9]AVP (5 or 10 nmoles icv; 5 or 50 nmoles/kg sc) was injected. The third day of the experiment consisted of one trial conducted in the same way as in two previous days. The latency time from placing the

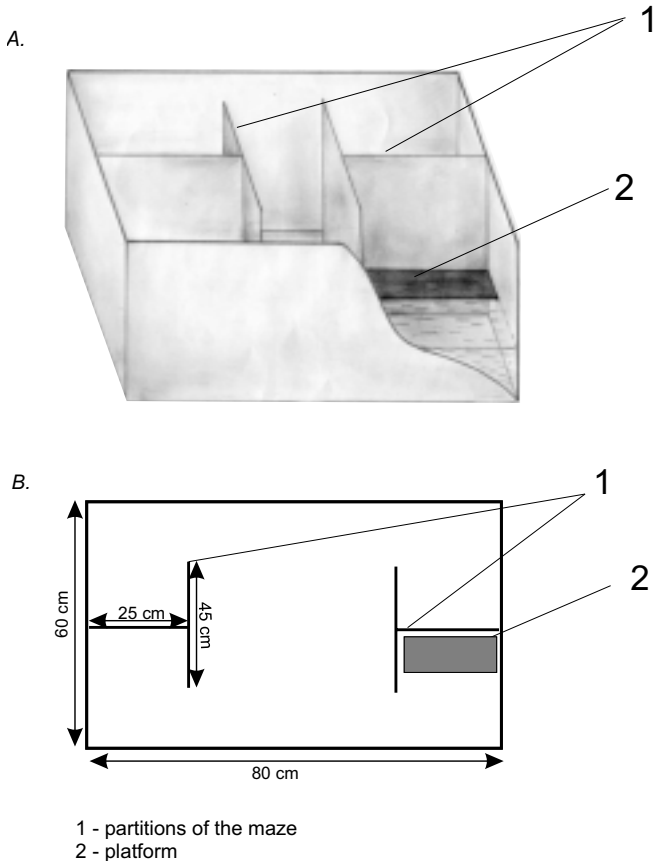

Fig.1. The diagram of the apparatus used in the water maze test. A, the three-dimensional draft; B, the schematic horizontal section.

animal in the bright compartment till its escape into the dark part of the apparatus was counted. Three hundred seconds was set as the maximum latency.

The active avoidance test was also performed in the same apparatus as the previous test (Tester uniku, COTM Białystok, Poland), but it was not modified as both its compartments were the same, i.e. bright. The peptide was injected every day 15 min (icv) or 30 min (sc) before the trial. The procedure of this test was the same as in Popieluch et al. (1995). After placing the animal in one of the compartments, the light in the ceiling was switched on for 5 seconds as a warning of approaching electric shock, and if the animal did not escape to the second chamber, AC current (0.5 mA) was automatically applied to the animal through the rods of the floor. The light was automatically switched off after the animal had moved to the safe compartment. After 20 seconds the cycle recurred. The test lasted 5 days, 5 min each day. Every day the mean number of errors (electric shocks that the animal managed to avoid) and the sum of response latencies (total duration of the light on period) were counted for each group. Vasopressin was injected every day 15 min (icv) or 30 min (sc) before the session.

Spatial memory was determined by means of latency in the water maze test which was developed in our laboratory (Plech et al. 2000). The maze consisted of a rectangular pool filled with water (27°C) to the depth of 18 cm and equipped with divisions forming four identical compartments in the corners of the pool and leaving its central part free (Fig. 1). One of the compartments (always the same) contained an escape platform. The platform was visible for the animal only after entering the proper compartment because it was placed 0.5 cm above the water surface. Every day of the experiment consisted of three subsequently performed trials. During the 30 s intertrial interval the animal was allowed to stay on the platform. Fifteen minutes after icv, or thirty minutes after sc AVP injections, respectively, the rat was placed in the free, central part of the maze and the time for reaching the platform was measured. The mean time of three subsequently performed trials was calculated. The next day the experiment was repeated, but without injections of the peptide. The mean of three trials was calculated and compared with the results obtained from the same experiment in the control group treated with saline.

Moreover, the open field test on a circular black painted board of 100 cm diameter (Janseen et al. 1960) and the holeboard test (File 1973, File and Pope 1974) were performed on other groups in order to evaluate the effect of the same doses of vasopressin on their locomotor and exploratory activity. The holeboard apparatus dimensions were: wooden square box 100 x 100 x 40 cm with 16 holes (the diameter of each hole was 6.5 cm). Both tests were performed 15 min, 30 min, and 24 hours after the injection. Observation time in both these tests was always 3 min.

The positive effect of vasopressin in the passive avoidance test was blocked by pretreatment with [β-Mercapto-β,β-cyclopentanometyleno^{1}-propionylo^{1}-O-Et--Tyr^{2},Val^{4},Arg^{8}]-vasopressin (BV_1) injected 10 s after electric shock. The vasopressin injection was performed 15 min after the blocker administration. The dose of BV_1 was twice that of vasopressin for sc injections. Equimolar dose was used for icv injections.

After the experiments, the animals were sacrificed by injections of lethal doses of chloral hydrate (3 g/kg ip) and then marker dye solution (1% crystal violet) was injected icv. The brains were isolated and visual inspection of accuracy of implantation was made.

The means of each group were statistically evaluated by analyses of variance (one-way ANOVA) followed by Dunnett's test at $P<0.05$ (Tallarida and Murray 1987).

RESULTS

A single AVP dose injected intracerebroventriculary (in the doses 10 pmoles, 0.5, 1 and 5 nmoles) significantly prolonged the latency time of rats in the passive avoidance test (Fig. 2). The above-mentioned effect was completely blocked by an equimolar dose of [β-Mercapto-β,β-cyclopentanometyleno^{1}-propionylo^{1}-O-Et-Tyr^{2},Val^{4},Arg^{8}]-vasopressin, an antagonist of V_1 receptors, administered icv 15 min before the AVP injection (Fig. 3).

Subcutaneous injections of AVP in the doses of 5 and 50 nmoles/kg also significantly prolonged the latency time (Fig. 4). This effect was blocked by a double dose of [β-Mercapto-β,β-cyclopentanometyleno^{1}-propionylo^{1}-O-Et-Tyr^{2},Val^{4},Arg^{8}]-vasopressin, but to a smaller extent in comparison to icv injections (Fig. 5).

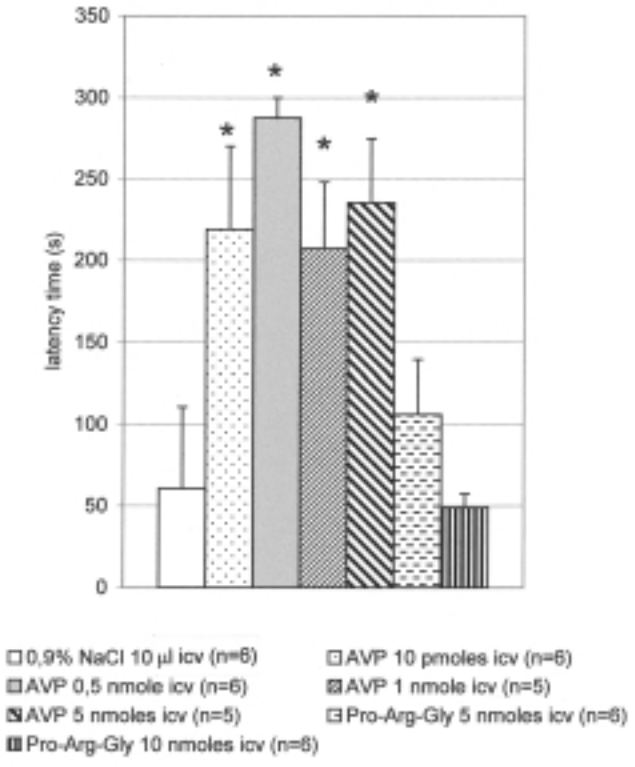

Fig. 2. Effect of vasopressin (AVP) and [7-9]AVP (Pro-Arg--Gly) injected intracerebroventriculary (icv) on latency time in passive avoidance test. Means of groups (± SEM). * significance *versus* saline group $P<0.05$ (Dunnett's test preceded by one-way ANOVA)

Subcutaneous injections of the vasopressin V_1 receptor antagonist, [β-Mercapto-β,β-cyclopentanometyleno^{1}-propionylo^{1}-O-Et-Tyr^{2},Val^{4},Arg^{8}]-vasopressin alone caused a similar effect as the injections of an equimolar dose of native AVP itself (Fig. 5).

Neither the icv injections of [7-9]AVP in a dose of 5 and 10 nmoles (Fig. 2) nor the sc administration in a dose of 5 or 50 nmoles (Fig. 4) influenced the latency time in this test.

In the active avoidance test AVP administrated for 6 successive days in a dose of 10 pmoles icv changed neither the latency time nor the number of errors made by rats (Tab. I, II). Higher doses could not be examined for they caused the death of the majority of animals in the second or third day of the experiment. For two doses used: 10 pmoles and 0.5 nmole, mortality in accordance to dose was 60 or 100% respectively.

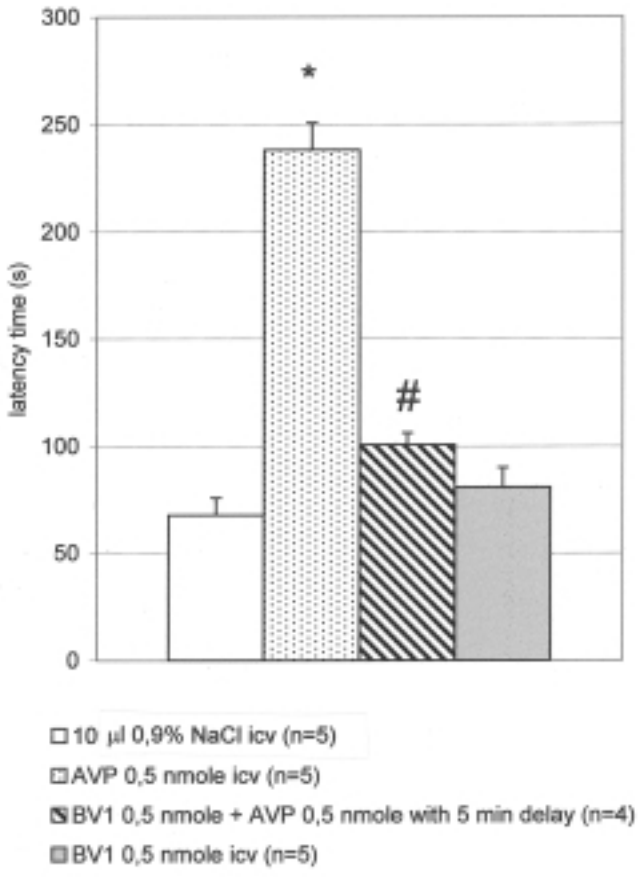

Fig. 3. Effect of [β-Merkapto-β,β-cyclometyleno^{1}-propionylo^{1}-O-Et-Tyr^{2},Val^{4},Arg^{8}]-vasopressin (BV1) on latency time in passive avoidance test after intracerebroven- tricular (icv) injection of AVP. (Means of groups ± SEM). * significance *versus* saline group $P<0.05$; # significance *versus* AVP group $P<0.05$ (Dunnett's test preceded by one-way ANOVA)

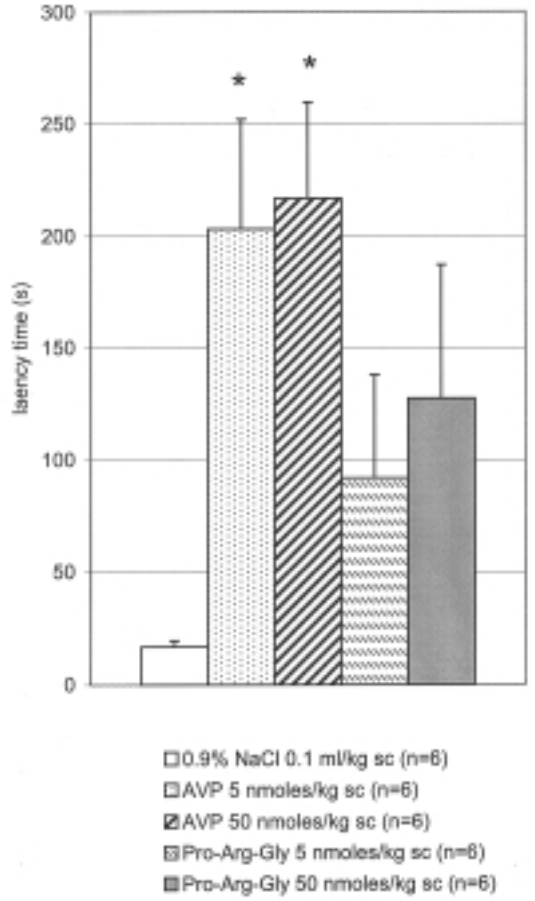

Fig. 4. Effect of vasopressin (AVP) and [7-9]AVP injected subcutaneously (sc) on latency time in passive avoidance test. (Means of groups ± SEM). * significance *versus* saline group $P<0.05$ (Dunnett's test preceded by one-way ANOVA)

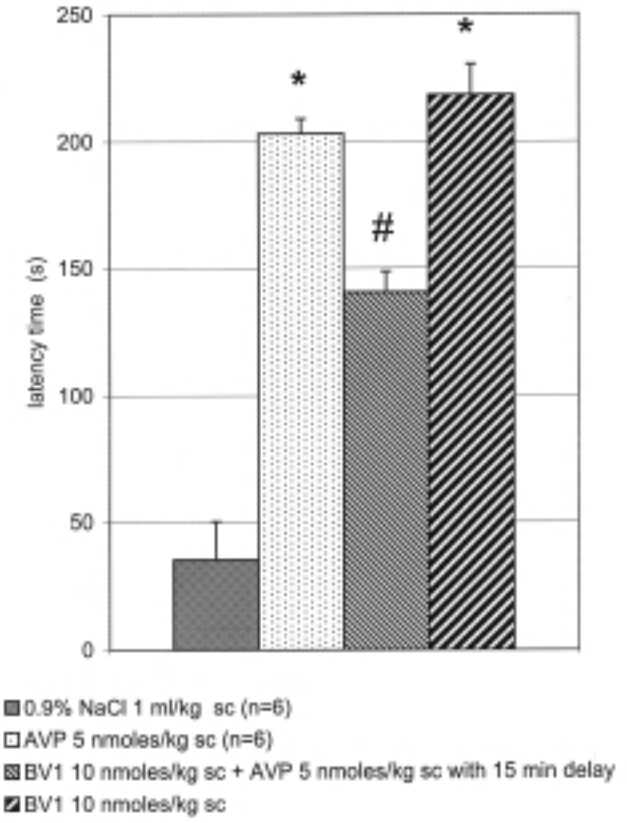

Fig. 5. Effect of [β-Merkapto-β,β-cyclometyleno[1]-propionylo[1]--O-Et-Tyr[2],Val[4],Arg[8]]-vasopressin (BV_1) on latency time in passive avoidance test after subcutaneous (sc) injection of AVP. (Means of groups ± SEM). * significance *versus* saline group $P<0.05$; # significance *versus* AVP group $P<0.05$ (Dunnett's test preceded by one-way ANOVA)

Subcutaneous injections of AVP in a dose of 1 and 10 nmoles/kg of body weight had no effect on performance in the active avoidance test except for a significant increase in the number of errors made by rats in the fifth day of the experiment after the dose of 1 nmole sc. Subcutaneous doses of AVP did not exert a lethal effect after repeated injections (Tab I, II).

AVP injected icv in the same range of doses as in passive avoidance (10 pmoles to 5 nmoles) did not influence spatial memory in the water maze test. Subcutaneous injection of this hormone in a dose of 50 nmoles/kg of body weight caused significant elongation of latency time (Tab. III).

[7-9]AVP injected in two doses: 1 and 10 nmoles/kg in fact did not influence memory in rats in any of the examined types of memory. The lower dose of this peptide caused only transient but significant improvement of the active avoidance test performance in the sixth day of the experiment (Tab. II).

Neither the icv nor the sc injections of AVP and [7-9]AVP influenced exploratory and locomotor activity in open field test and holeboard test evaluated 24 hours after icv injection (Tab. IV).

DISCUSSION

The existence of vasopressinergic tracts in CNS (Buijs 1983, Goldsmith et al. 1991) as well as binding sites for AVP (Pearlmutter et al. 1983, Tribollet et al. 1988) suggest that this hormone can modulate activity of the brain. There is also evidence that AVP causes excitatory (Mizuno et al. 1984) and inhibitory (Mühlethaler et al. 1984, Burnard et al. 1987) effects on neurons of hippocampus in rats. Albeck and Smock (1988) suggest

Table I

Active avoidance test

Peptides and doses	Days of the experiment						
	1	2	3	4	5	6	7
0.9% NaCl 10 µl icv	8.3 (± 0.4)	8.0 (± 0.2)	4.7 (± 0.8)	4.2 (± 0.9)	4.2 (± 5.9)	2.6 (± 1.1)	X
AVP 10 pmoles icv	7.2 (± 0.5)	7.2 (± 0.7)	5.2 (± 0.8)	5.7 (± 0.6)	4.2 (± 1.4)	5.2 (± 1.7)	X
0.9% NaCl 0.1 ml/kg sc	7.5 (± 0.5)	7.3 (± 0.4)	6.0 (± 0.9)	5.2 (± 1.0)	3.7 (± 0.6)	5.3 (± 1.2)	4.2 (± 0.6)
AVP 1 nmol/kg sc	7,3 (± 0.2)	7.0 (± 0.2)	5.3 (± 0.6)	3.8 (± 1.4)	1.3 (± 0.5)*	4.0 (± 1.0)	2.7 (± 0.8)
0.9% NaCl 0.1 ml/kg sc	8.3 (± 0.5)	7.4 (± 0.5)	6.0 (± 1.3)	3.0 (± 0.8)	3.1 (± 1.1)	3.1 (± 1.3)	2.0 (± 0.6)
AVP 10 nmol/kg sc	6.7 (± 1.0)	8.1 (± 0.3)	5.6 (± 1.0)	3.7 (± 1.0)	4.1 (± 1.3)	3.8 (± 0.9)	3.3 (± 0.9)
0.9% NaCl 0.1 ml/kg sc	7.2 (± 0.5)	7.2 (± 0.5)	7.5 (± 1.3)	5.5 (± 1.2)	4.2 (± 1.5)	3.7 (± 1.4)	3.7 (± 1.3)
Pro-Arg-Gly 1 nmol/kg sc	8.0 (0.1)	7.8 (± 0.5)	5.2 (± 1.4)	3.3 (± 0.8)	3.3 (± 1.1)	1.2 (± 0.4)	1.8 (± 1.1)
0.9% NaCl 0.1 ml/kg sc	8.0 (± 0.6)	5.8 (± 1.2)	5.2 (± 1.3)	6.3 (± 1.4)	4.5 (± 1.5)	2.8 (± 1.0)	1.7 (± 0.5)
Pro-Arg-Gly 10 nmol/kg sc	8.8 (± 0.2)	8.8 (± 0.5)	7.0 (± 0.9)	5.8 (± 0.5)	4.3 (± 0.9)	4.2 (± 1.0)	2.7 (± 1.1)

Data are the means of the error number (SEM); *, significance at $P<0.05$ (Dunnett's test). X-not performed

Table II

Active avoidance test

Peptides and doses	Days of the experiment						
	1	2	3	4	5	6	7
0.9% NaCl 10 µl icv	76.2 (± 15.3)	53.5 (± 3.0)	42.0 (± 3.5)	42.0 (± 3.3)	37.8 (± 4.2)	34.4 (± 2.8)	X
AVP 10 pmoles icv	72.5 (± 8.1)	52.5 (± 3.7)	47.7 (± 6.3)	59.0 (± 12.8)	40.7 (± 5.6)	42.2 (± 4.1)	X
0.9% NaCl 0.1 ml/kg sc	77.2 (± 8.5)	55.7 (± 1.7)	52.8 (± 3.2)	44.2 (± 5.3)	38.3 (± 4.0)	50.3 (± 8.9)	39.5 (± 4.1)
AVP 1 nmol/kg sc	65.5 (± 9.3)	53.7 (± 2.8)	53.2 (±4.1)	38.8 (± 5.5)	27.8* (± 2.2)	37.7 (± 3.8)	34 (3.7)
0.9% NaCl 0.1 ml/kg sc	97.7 (± 12.3)	85 (± 17.5)	54.8 (± 7.7)	37.1 (± 5.1)	37.1 (± 5.0)	32.4 (± 6.4)	31.8 (± 2.9)
AVP 10 nmol/kg sc	115.4 (± 29.4)	72.4 (± 11.1)	49.6 (± 5.7)	35.1 (± 4.1)	39.8 (6.1)	38.1 (± 4.2)	38.8 (± 5.9)
0.9% NaCl 0.1 ml/kg sc	82.7 (± 11.5)	58.2 (± 5.5)	59.5 (± 5,3)	47.5 (± 8.2)	39.2 (± 5.3)	37.2 (± 4.0)	36.8 (± 4.9)
Pro-Arg-Gly 1 nmol/kg sc	68.2 (± 3.4)	63.7 (± 9.3)	50 (± 9.8)	35.2 (± 3.9)	36.3 (± 5.2)	27.2 (± 1.5)	32.3 (4.0)
0.9% NaCl 0.1 ml/kg sc	61.7 (± 7.4)	72.8 (± 23.0)	46.8 (± 7.0)	49.2 (± 6.5)	42.7 (± 5.2)	35.2 (± 2.7)	28.3 (± 2.1)
Pro-Arg-Gly 10 nmol/kg sc	77.5 (± 5.4)	54.7 (± 4.7)	53.7 (± 5.0)	55.8 (± 6.4)	43.2 (± 11.0)	49.8 (± 11.9)	34.5 (± 6.5)

Data are the means of the error number (SEM); *, significance at $P<0.05$ (Dunnett's test). X-not performed

Table III

Influence of AVP and [7-9]AVP on rats' spatial memory in water maze test

Investigated peptide: dose and way of administration	Means of latency time (± SEM)	Means of adequate control group (± SEM)
AVP 10 pmoles icv (n=6)	16.6 (± 2.64)	13.9 (± 2.54)
AVP 1 nmol icv (n=5)	65.8 (±10.5)	49.1 (± 11.0)
AVP 5 nmoles icv (n=5)	14.6 (± 1.85)	13.9 (± 2.54)
AVP 5 nmoles/kg sc (n=6)	23.2 (± 4.7)	20.0 (± 4.7)
AVP 50 nmoles/kg sc (n=6)	78.1 (± 10.7)*	39.9 (± 2.2)
Pro-Arg-Gly 5 nmoles/kg sc (n=5)	32.8 (± 3.3)	20.0 (± 4.7)

Data are the means of the latency time (SEM); *, significance at $P<0.05$ (Dunnett's test)

Table IV

Influence of AVP and [7-9]AVP on locomotor and exploratory activity in rats 24 hours after icv or sc injection

Substance and dose	Open field test Form of rat behaviour expressed as a mean number of episodes/3 min (± SEM)					Holeboard test Number of episodes/3 min (± SEM)
	Ambulations	Peeping	Rearing	Grooming	defecations	
0.9% NaCl 10 µl icv	14.7 (± 4.21)	4.1 (± 1.48)	0.9 (± 0.96)	0.3 (± 0.12)	1.8 (± 0.65)	5 (± 0.7)
AVP 10 pmoles icv	20.5 (± 2.01)	4.3 (± 1.4)	0.16 (± 0.16)	0.6 (± 0.49)	0.16 (± 0.16)	3.16 (± 1.01)
AVP 0.5 nmole icv	12 (± 3.48)	6.16 (± 2.57)	0	0	4.16 (± 1.01)	4.5 (± 1.68)
AVP 5 nmoles icv	20.8 (± 5.37)	6.4 (± 1.9)	2.6 (± 0.81)	0.8 (± 0.2)	1.6 (± 1.02)	4.2 (± 1.31)
Pro-Arg-Gly 5 nmoles icv	7 (± 2.17	1.6 (± 1.1)	0	1 (± 0.63)	0	2.83 (± 0.47)
0.9% NaCl 0.1 ml/kg sc	8.2 (± 3.44)	3.2 (± 0.86)	0	0	8.6 (± 0.97)	1.8 (± 0.37)
AVP 5 nmoles/kg sc	11.2 (± 3.96)	6.4 (± 2.15)	0.2 (± 0.2)	0.8* (± 0.2)	7.2 (± 1.15)	3.8 (± 2.38)
AVP 50 nmoles/kg sc	13.8 (± 1.65)	4 (± 1.09)	0	0.2 (± 0.2)	4.8 (± 1.35)*	Not performed

Data are the means of episode number/3 min (SEM); *, significance at $P<0.05$ (Dunnett's test)

that AVP stimulates spontaneous activity of hippocampal interneurons causing depression of this structure. There are also papers showing that the Brattelboro strain of rats with congenital vasopressin deficiency show significantly worse performance in the passive avoidance test (de Wied et al. 1975). All these data, taken with some results of the current study suggest that vasopressin influences memory processes. All doses used were the same in each test to give the opportunity to compare the effects of both native AVP and [7-9]AVP.

This paper confirms previous results (de Wied et al. 1984) of significant memory effects of vasopressin in rats in a comparable range of doses. The AVP effect was significant after use of much lower doses: 10 pmoles and 0.5 nmole, and it was mediated through central V_1 receptors, because it was blocked by [β-Merkapto-β,β-cyklopentanometyleno^1-propionylo^1-O-Et-Tyr^2,Val^4,Arg^8]-vasopressin, the specific V_1 receptor antagonist. Inhibition of locomotor activity could interfere with the results obtained in a passive avoidance test, so open field and holeboard tests were performed to detect probable changes of this form of rats' behaviour. The results showed that this effect is not connected with locomotor and exploratory activity inhibition, because both investigated peptides do not influence these forms of rats' behaviour.

There are many papers describing experiments with the different fragments of vasopressin chain (Dietrich et al. 1997, Fujiwara et al. 1997, Vawter et al. 1997, Tanabe et al. 1999, Nakayama et al. 2000). Some frag-

ments, e.g. [4-9]AVP (Nakayama et al. 2000) or [5-8]AVP (Fujiwara et al. 1997) show more potent memory activity than the native peptide, while [6-8]AVP and [5-7]AVP are inactive in the radial arm maze (Fujiwara et al. 1997). The results presented here indicate that the fragment [7-9]AVP also appears to be inactive. Considering these data it seems that the most important fragment for behavioural activity should be [4-6]AVP, but this conclusion needs further investigation.

On the other hand there are data suggesting that the memory-modulating effect of [pGlu^4,Cyt^6]AVP-(4-8) (DGAVP) is connected rather with the aminoacid sequence being similar to [4-8]AVP than with the presence or absence of concrete aminoacid in the peptide chain (Vawler et al. 1997).

The results presented above showed that AVP influences memory in the passive avoidance test, while in two other tests - active avoidance and water maze - it did not improve the rats' performance. The other observed influence was the impairment of the performance in the water maze test when a relatively high vasopressin dose was applied subcutaneously (50 nmols/kg). It is not possible to exclude that this phenomenon could be caused by peripheral effects of AVP, but this mechanism should be confirmed by proper investigation. For easier comparison of the effect of native hormone and its [7-9] fragment, all administered doses were shown in moles, not micrograms. Equimolar doses of [7-9] vasopressin in contrast to native peptide did not influence rats' performance in the passive avoidance test. It was also without any significant effect in two other performed tests.

Some authors suggest that a positive response in the passive avoidance test is caused by vasopressin itself being an aversive stimulus (Dantzer et al. 1982, Ettenberg et al. 1983, Ebenezer 1988). It has also been shown that vasopressin injected immediately after the stimulus is able to enhance arousal causing better consolidation of information (Yehuda 1987).

However, enhancing arousal should improve different types of memory, including spatial memory, while results obtained in the present experiments from different experimental models indicate that AVP administration shows no positive influence on rats' performance in different tasks evaluating this type of memory (Engelmann et al. 1992a). It has been found in the course of active avoidance study that daily repeated administration of AVP had lethal effect in the second or third day of experiment. On the other hand repeated subcutaneous doses of this peptide did not exert such effect. It is difficult to suggest at present the mechanism of this phenomenon and further investigations are necessary.

Negative results in the active avoidance test agree with the results of Baranowska et al. (1983), who proved that AVP injected icv in a dose of 1 μg does not influence rats' memory, though it significantly prolongs the extinction of active avoidance behaviour. On the other hand, it is known that microdialysis administration of V_1 receptor antagonist into the septum significantly impairs pole-jumping behaviour, while injections of AVP remains without any significant effect (Engelmann et al. 1992 b). In contrast, Fujiwara et al. (1997) proved that both AVP and [4-9]AVP markedly improved the disruption of spatial cognition by treatment with scopolamine in a radial maze test.

The lack of effect in the water maze test after icv injection seems to correlate with the results obtained by other authors in different tests. It is also known that microdialysis of AVP in the septum significantly impaired performance in the Morris test, while blocking of V_1 receptors in this area did not influence behavioural performance (Engelmann et al. 1992 a).

Conclusions:

1. AVP-induced improvement of rats' memory was confirmed in the passive avoidance test, while no effect was found in active avoidance and water maze tests.

2. This memory effect of AVP is mediated by central V_1 receptors.

4. Synthetic tripeptide Pro-Arg-Gly, [7-9] fragment of vasopressin peptide chain does not influence rats' memory.

5. Taking into account the results of the present study and results previously obtained by other authors, it seems that fragment [4-6] of vasopressin peptide chain may be the most important for the memory effect of this hormone.

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