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Vasopressin Receptors of the Vasopressor (V_1) Type in the Nucleus of the Solitary Tract of the Rat Mediate Direct Neuronal Excitation

Mario Raggenbass, Eliane Tribollet, Michel Dubois-Dauphin, and Jean Jacques Dreifuss

Department of Physiology, University Medical Center, Geneva, Switzerland

The existence of vasopressin-sensitive neurons in the nucleus of the solitary tract of the rat and the presence in this brain area of vasopressin binding sites were investigated using extracellular single-unit recordings from brain-stem slices and light microscopic autoradiography. About 45% of the recorded neurons responded to vasopressin at 5–2000 nM by a reversible, concentration-dependent increase in firing rate. The action of vasopressin was direct, was suppressed by a vasopressor antagonist, and was mimicked by a vasopressor agonist. Oxytocin was 10–100 times less efficient than vasopressin and a specific antidiuretic agonist was without effect. Using light microscopic autoradiography and ^{3}H-arginine vasopressin as a ligand, high-affinity vasopressin binding sites were found distributed over the whole rostrocaudal extent of the nucleus of the solitary tract. Binding was displaced by unlabeled vasopressor agonist but not by unlabeled antidiuretic agonist. Thus, the nucleus of the solitary tract contains V_1-type vasopressin receptors which are, at least in part, located on neuronal membranes and whose activation generates bioelectrical signals. Solitary tract vasopressin-sensitive neurons may be the target of a vasopressinergic innervation originating in the hypothalamic paraventricular nucleus and could be involved in the central regulation of cardiovascular functions.

The nonapeptides vasopressin and oxytocin may act as neurotransmitters in selected regions of the dorsal brain stem of the rat. Vasopressin immunoreactivity has been detected in the nucleus of the solitary tract and, although to a lesser extent, in the dorsal motor nucleus of the vagus nerve, and oxytocin-like immunoreactivity has been found in the latter nucleus (for references, see Buijs, 1987; Dubois-Dauphin and Zakarian, 1987; Raggenbass et al., 1987a). Using immunoelectron microscopy, vasopressin- and oxytocin-containing presynaptic terminals were shown to be present in the nucleus of the solitary tract (Voorn and Buijs, 1983) and calcium-dependent vasopressin and oxytocin release could be evoked *in vitro* from dorsal brain-stem tissue (Buijs and Van Heerikhuize, 1982). Binding sites for tritiated vasopressin and for a radioiodinated oxytocin antagonist have been detected in the nucleus of the solitary tract and in the dorsal motor nucleus of the vagus nerve, respectively (Dorsa et al., 1983; Dreifuss et al., 1988; Tribollet et al., 1988). Using brain-stem slices, we have shown that vagal motoneurons are directly depolarized by oxytocin and that this effect is mediated by oxytocin receptors (Charpak et al., 1984; Raggenbass et al., 1987a).

The nucleus of the solitary tract is involved in the regulation of cardiovascular functions. It contains second-order neurons of the baroreceptor reflex arc, and bilateral lesions of this nucleus cause hypertension in rats (for reviews, see Bystrzycka and Nail, 1985; Talman, 1985). Various compounds, such as excitatory or inhibitory amino acids, catecholamines, cholinergic agonists and neuropeptides, can alter blood pressure and heart rate when injected into the region of the nucleus of the solitary tract (for references, see Carter et al., 1985; Catelli et al., 1987; Gardiner and Bennett, 1989; Sundaram et al., 1989; Talman and Robertson, 1989). Vasopressin, by acting in or near this nucleus, is able to alter cardiovascular parameters (Matsuguchi et al., 1982; Vallejo et al., 1984; Pittman and Franklin, 1985; Vallejo and Lightman, 1987).

These data suggest that the nucleus of the solitary tract probably contains a subpopulation of cardiovascular-related neurons whose bioelectrical activity may be affected by exogenous vasopressin. In the present study, using electrophysiological recordings from brain-stem slices, we show that vasopressin indeed excites neurons in the nucleus of the solitary tract. The receptor specificity of this action was determined by testing the effect of various synthetic structural analogs which have selective affinities with respect to peripheral vasopressin and oxytocin receptors. In addition, we have used light microscopic autoradiography to map precisely the distribution of vasopressin binding sites in the dorsal brain stem. By carrying out displacement studies, we have determined the pharmacological profile of these sites. The data gathered from the electrophysiological study and those obtained using the morphological approach were found to be in good agreement.

Materials and Methods

The study was performed on male adult rats (200–300 gm) of the Sivz strain, which is derived from the Sprague-Dawley strain. The animals were decapitated, the brain was removed from the skull, and the brain stem was dissected out.

Electrophysiology. Coronal or parasagittal slices (300–400 μm thick) containing the dorsal medulla were cut using a vibrating microtome. The slices were incubated in a thermoregulated (34–35°C) interface-type chamber. The perifusion solution had the following composition (in mM): NaCl, 135; KCl, 5; $NaHCO_3$, 15; KH_2PO_4, 1.25; $MgSO_4$, 1; $CaCl_2$, 1; and glucose, 10. It flowed at 2–3 ml/sec and was saturated with 95% O_2–5% CO_2 (pH 7.35–7.45). Compounds tested were dissolved in the

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Correspondence should be addressed to J. J. Dreifuss, M.D., Ph.D., Département de Physiologie, Centre Médical Universitaire, 9 Av. de Champel, CH-1211 Geneva 4, Switzerland.

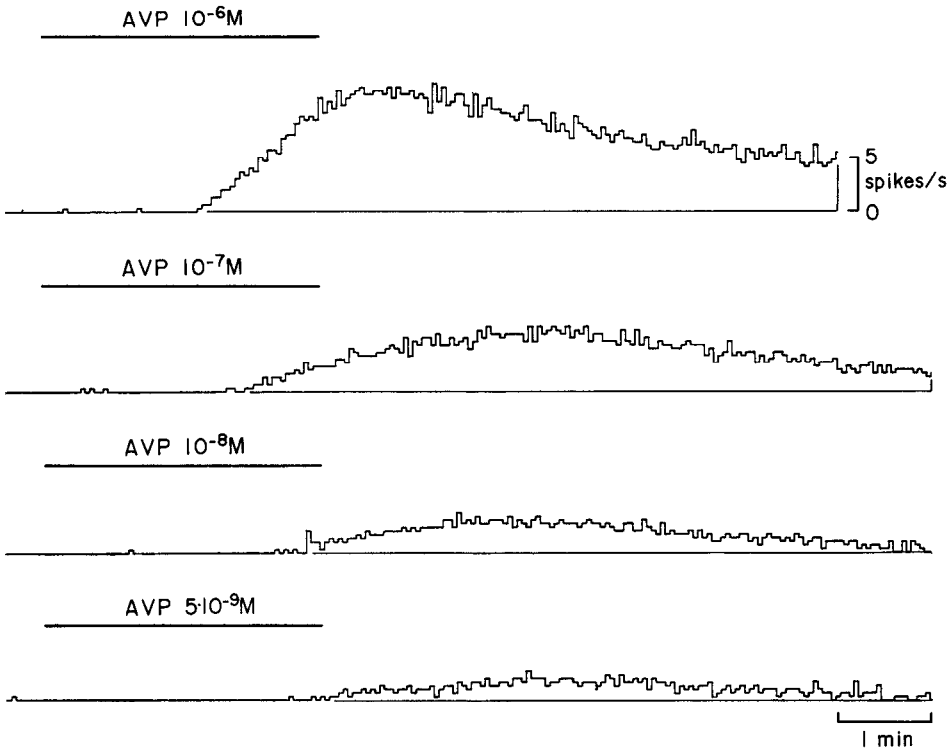

Figure 1. Vasopressin (AVP) effect on a solitary tract neuron. The traces represent frequency histograms of neuronal firing as a function of time. The peptide was added to the perifusion solution for the time indicated by the *solid bar* above each trace. Different concentrations of the peptide were tested in a random order. Note that the increase in firing induced by vasopressin was reversible and concentration dependent.

perifusion solution. In order to block synaptic transmission, the slices were perifused with a modified solution, in which the $CaCl_2$ concentration was lowered to 0.2 mM and the $MgSO_4$ concentration was raised to 6 mM (Raggenbass et al., 1987a).

Extracellular single-unit recordings were obtained from the nucleus of the solitary tract. Micropipettes were filled with 4 M NaCl and had tip DC resistances of 5–25 MΩ. Bioelectrical signals were amplified, displayed on an oscilloscope under AC conditions (band width, 0.1–3 kHz), and stored on magnetic tape. Ratemeter records of neuronal firing were plotted on paper with an oscillograph.

Part of the recordings were carried out using micropipettes containing 2% (wt/vol) Niagara Sky Blue in 0.5 M Na-acetate. At the end of the recording session the dye was ejected by applying a negative voltage (50–80 V) to the micropipette for 2–3 min. The slices were fixed in 4% paraformaldehyde solution in PBS for 2–3 min and immersed in 30% sucrose in PBS. Sixty-μm-thick sections were cut in a cryostat. Following counterstaining of the sections with Neutral Red, the blue spots marking the recording sites could be localized within the boundaries of the nucleus of the solitary tract.

Autoradiography. Following removal, brain tissue was rapidly frozen in isopentane (2-methylbutane) at −25°C. Series of 10- to 15-μm-thick sections were cut, mounted on chromalun gelatin-coated slides, and stored at −80°C in closed boxes until use.

For the binding procedure, the sections were preincubated for 20 min by dipping the slides in 50 mM Tris-HCl (pH 7.4). Incubation was carried out for 1 hr in a humid chamber by covering each section with 100–200 μl of the incubation medium (50 mM Tris-HCl, 0.1 mM Bacitracin, 5 mM $MgCl_2$, 0.1% BSA) containing 1.5 nM ^{3}H-arginine vasopressin (AVP) alone or in the presence of various unlabeled peptides. Specificity of binding was assessed in adjacent sections incubated with the same concentration of ^{3}H-AVP in the presence of 1–10 μM unlabeled AVP.

Incubation was followed by two 5 min washes in ice-cold incubation medium and a quick rinse in distilled water. The slides were then dried in a stream of cold air, put for 2 hr in a desiccator containing paraformaldehyde powder preheated at 80°C and then placed in an X-ray cassette in contact with tritium-sensitive LKB ultrofilm during 4 months. Films were developed for 5 min in Kodak D19 and the sections stained with cresyl violet.

Differentiation of receptor subtype was assessed in competitive binding experiments using series of brain-stem sections of 5 animals. For each series, one section was incubated with 1.5 nM ^{3}H-AVP alone; adjacent sections were incubated with the same concentration of ^{3}H-AVP and in addition with 10, 20, 100, or 150 nM of [Phe^2,Orn^8]VT or of dDAVP. The latter is a selective V_2 agonist, the former a V_1 agonist (see below).

Chemicals. AVP and oxytocin were purchased from Bachem Fine Chemicals (Bubendorf, Switzerland) and from Novabiochem (Läufelfingen, Switzerland). The following synthetic structural analogs were kindly provided by M. M. Manning (Department of Biochemistry, Medical College of Ohio, Toledo, OH) : dEt_2Tyr(Me)dAVP, [1-(β-mercapto-β, β-diethylpropionic acid),2-*O*-methyltyrosine,8-D-arginine]vasopressin (Manning et al., 1985); HO[Thr^4,Gly^7]OT, [1-(L-2-hydroxy-3-mercapto-propionic acid),4-threonine,7-glycine]oxytocin (Lowbridge et al., 1977); dDAVP, 1-deamino-[8-D-arginine]vasopressin (Vávra et al., 1968); [Phe^2,Orn^8]VT, [2-phenylalanine,8-ornithine]vasotocin (Berde et al., 1964; for a recent review on synthetic structural analogs of vasopressin, see Manning et al., 1987).

^{3}H-AVP (specific activity, 60–87 Ci/mmol) was purchased from Du Pont New England Nuclear (Boston, MA) and purified before use by HPLC followed by affinity chromatography on neurophysin bound to Sepharose-4B.

Results

Electrophysiological study

Single-unit extracellular recordings were obtained from 121 neurons located in the nucleus of the solitary tract in parasagittal or coronal slices of the rat brain stem. They were silent or fired spontaneously at frequencies of 1–15 spikes/sec. All these neurons were tested for sensitivity to vasopressin, dissolved in the perifusion solution at concentrations ranging from 1 to 2000 nM. Fifty-six neurons, i.e., 46%, responded to the peptide by a reversible increase in firing rate. The remaining neurons were unaffected. Vasopressin-sensitive neurons were apparently distributed over the whole rostrocaudal extent of the nucleus of the solitary tract.

The effect of vasopressin on the sensitive neurons was concentration dependent (Fig. 1). The lowest vasopressin concentration still effective in evoking an excitation was 5 nM, which caused a peak increase in firing rate, above the resting firing

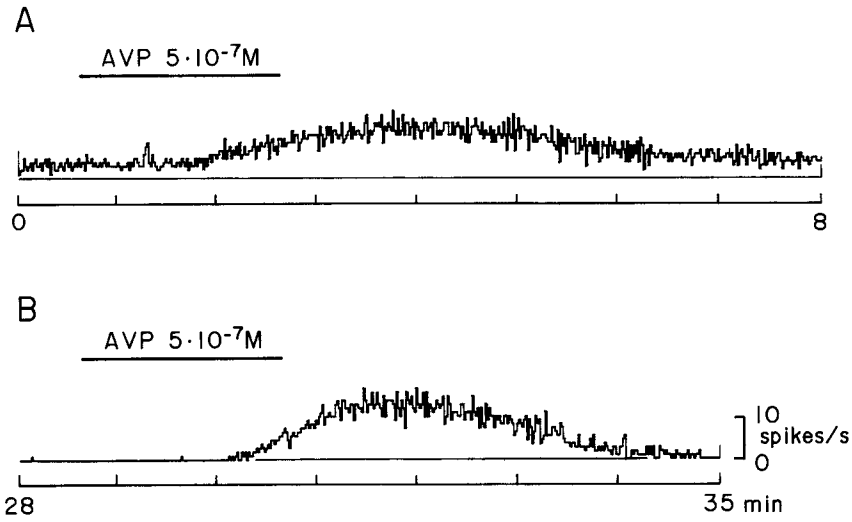

Figure 2. Effect of vasopressin (AVP) on a solitary tract neuron during perifusion with the normal solution (*A*) and with a low-calcium, high-magnesium solution (*B*). In the normal solution, the neuron, which fired spontaneously at low frequency, was excited by vasopressin at 500 nM. During perifusion with the modified solution, which started at the 17th min, the neuron became silent, but vasopressin still excited it. The traces are in chronological succession but are not continuous.

level, of 2.1 ± 0.2 spikes/sec (mean ± SEM; $n = 5$). At 10 nM the increase was 3.5 ± 0.3 spikes/sec ($n = 6$), and at 100 nM it was 7.9 ± 0.5 spikes/sec ($n = 13$); at 1000 nM it was 11.3 ± 0.6 ($n = 11$), and at 2000 nM it amounted to 11.2 ± 0.9 ($n = 4$). In all 4 neurons tested, raising the vasopressin concentration from 1000 to 2000 nM caused no net increase in the peptide-induced excitation, indicating that micromolar concentrations of vasopressin evoked maximal or nearly maximal effects. The quantitative data concerning the concentration dependency of the vasopressin action were gathered from 13 neurons. Each was tested for at least 3 different vasopressin concentrations, and in all cases the peptide was added to the perifusion solution for a fixed period of 3 min.

The effect of vasopressin was postsynaptic, rather than presynaptic, since it persisted when the preparation was perifused in a low-calcium, high-magnesium solution (Fig. 2; tested on 8 neurons). Using brain-stem slices of the rat, we have previously shown that in the latter solution synaptic transmission in the dorsal medulla is reversibly blocked (Raggenbass et al., 1987a).

The excitatory effect of vasopressin was receptor-mediated. Indeed, a vasopressor antagonist, $dEt_2Tyr(Me)DAVP$, at 500 nM, partially (in 1 of 5 neurons) or fully (in 4 of 5 neurons)

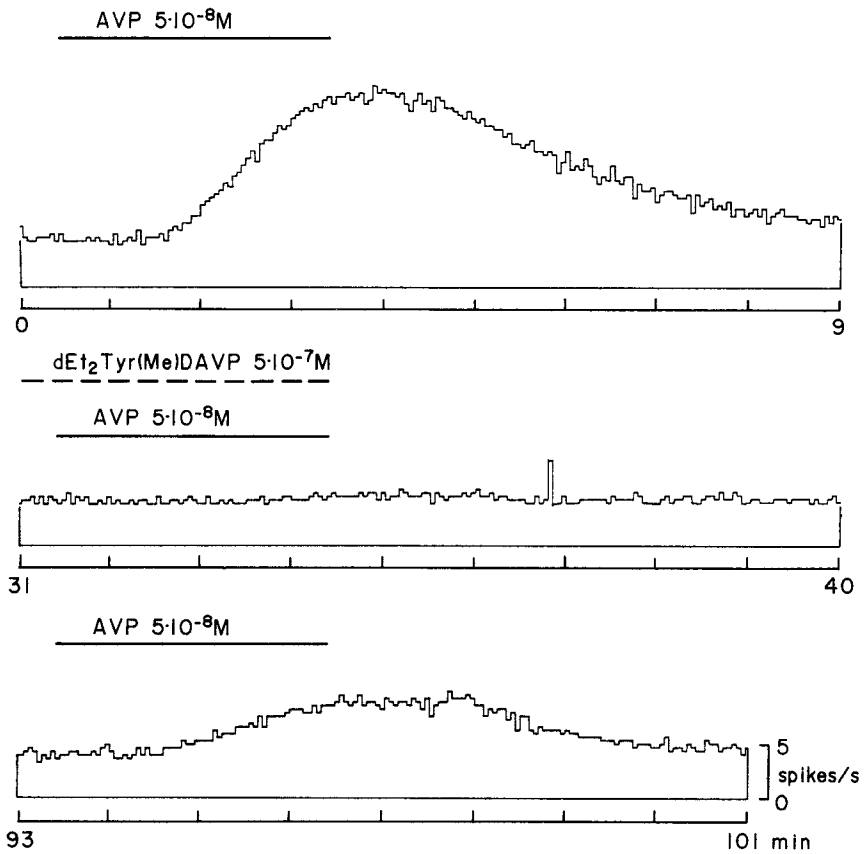

Figure 3. Effect of vasopressin (AVP) and its blockade by a vasopressor antagonist, $dEt_2Tyr(Me)DAVP$. The latter compound was present in the perifusion solution for 11.5 min, from the 23rd min. It did not affect the spontaneous firing of the neuron, but suppressed the vasopressin-induced excitation (cf. *first* and *second traces*). Following wash-out, the neuron recovered, although incompletely, its sensitivity to vasopressin (*third trace*).

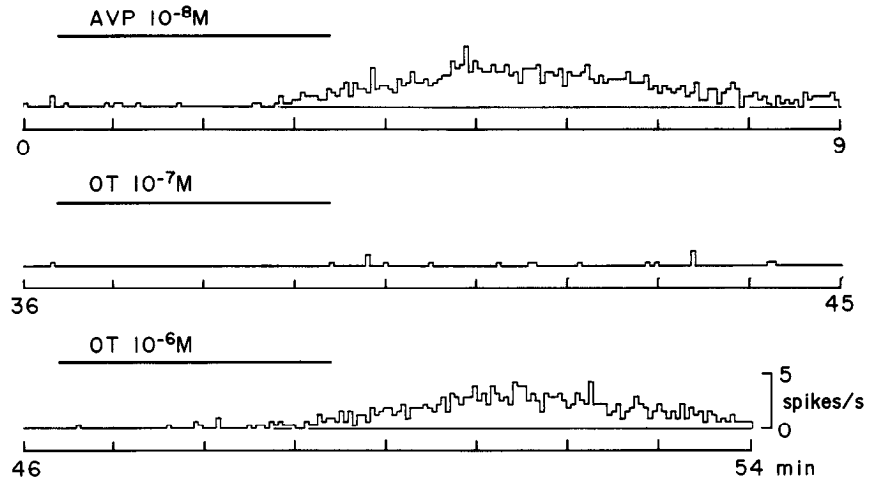

Figure 4. Effect of vasopressin (AVP) and oxytocin (OT) on a solitary tract neuron. Note that in order to evoke an increase in firing comparable to that induced by 10 nM vasopressin, oxytocin had to be added to the perifusion solution at 1000 nM (*first* and *third traces*).

suppressed the excitation induced by vasopressin at 50–1000 nM (Fig. 3).

In order to determine the type of receptor which mediates the effects of vasopressin in the nucleus of the solitary tract, the efficiency of this peptide in evoking a neuronal excitation was compared with that of oxytocin and of various synthetic structural analogs having selective oxytocic, vasopressor, or antidiuretic effects on peripheral neurohypophysial hormone receptors.

Thirty-two vasopressin-responsive neurons were also tested for their responses to oxytocin at 10–1000 nM. In all cases, oxytocin was either without effect or 10–100 times less potent than vasopressin (Fig. 4). The selective oxytocic agonist, HO[Thr^4,Gly^7]OT, at 1000 nM did not affect any of 6 vasopressin-sensitive neurons. This indicates that the excitatory action of vasopressin was not mediated by oxytocin receptors.

The potent, selective antidiuretic agonist, dDAVP, at 1000 nM was without effect on 8 of 8 vasopressin-responsive neurons (Fig. 5, second trace). By contrast, the selective vasopressor agonist, [Phe^2,Orn^8]VT, at 100–1000 nM was nearly as potent as vasopressin on all 9 neurons tested (Fig. 5, first and third traces). Thus, the excitatory action brought about by vasopressin on solitary tract neurons is probably mediated by vasopressin receptors of the V_1 type.

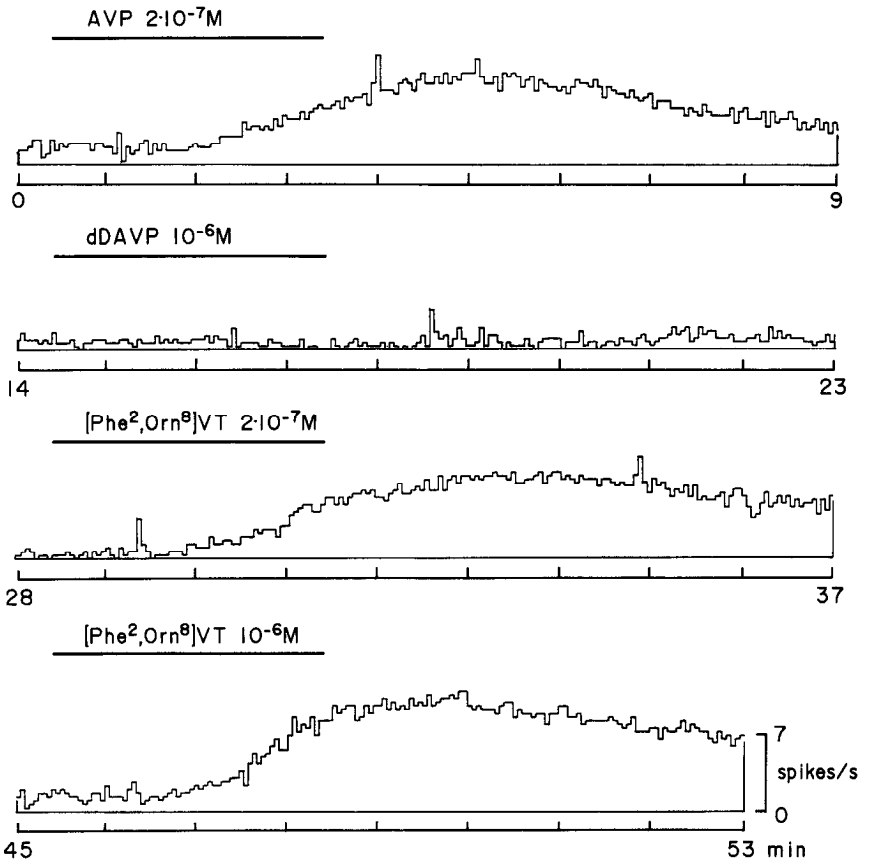

Figure 5. Effect of vasopressin (AVP), of a selective antidiuretic agonist, dDAVP, and of a selective vasopressor agonist, [Phe^2,Orn^8]VT, on a solitary tract neuron. Note that vasopressin and the vasopressor agonist, both added to the perifusion solution at 200 nM, caused a comparable increase in neuronal firing (*first* and *third traces*). At 1000 nM, the antidiuretic agonist had no effect (*second trace*), while at the same concentration the vasopressor agonist evoked a vigorous neuronal excitation (*fourth trace*).

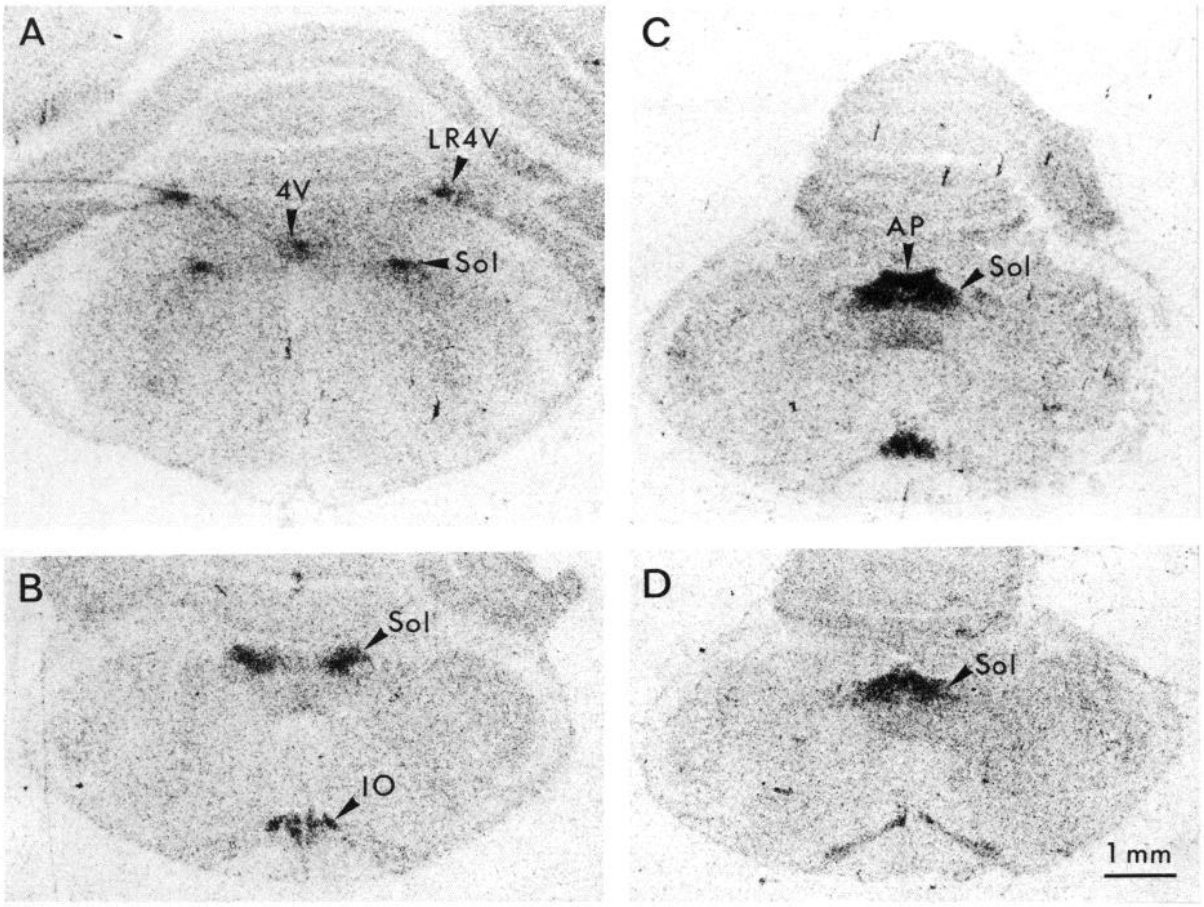

Figure 6. Vasopressin binding in the brain stem. Autoradiography showing ^{3}H-AVP binding in coronal sections arranged from rostral (*A*) to caudal (*D*) levels of the rat brain stem. All sections show ^{3}H-AVP bound to the nucleus of the solitary tract (*Sol*). Other labeled sites include the choroid plexus of the fourth ventricle (*4V*, including its lateral recess, *LR4V*), the inferior olive (*IO*), and area postrema (*AP*). Binding to all these sites was displaced by cold AVP (data not shown).

Autoradiography

Sites which bind tritiated vasopressin (^{3}H-AVP) were detected in the rat brain stem, in particular, in the nucleus of the solitary tract over its whole extent. Rostrally, the left and right nuclei of the solitary tract are small and located at a distance from the midline (Fig. 6*A*). Approximately 2 mm more caudally, the nuclei have enlarged and moved closer to the midline (Fig. 6*B*). At one point, the left and right nuclei fuse, the most medially located cells forming the so-called commissural nucleus. The nucleus of the solitary tract lies immediately ventrally to the area postrema, which is also labeled (Fig. 6*C*), and more caudally ventral to the unlabeled gracile nuclei (Fig. 6*D*). It is noteworthy that at these caudal levels a strong labeling was noted, particularly in the dorsal part of the nucleus of the solitary tract. Binding of ^{3}H-AVP was absent from the dorsal motor nuclei of the vagus and was light in the hypoglossal nuclei (see Fig. 7, *A, B*).

Intense binding was also detected on the choroid plexus present in the ventricular spaces (Fig. 6*A*), in area postrema (Fig. 6*C*), as well as in the inferior olivary complex (Figs. 6, *B–D*; 7, *B, D*).

In order to assess the ligand specificity of the vasopressin binding sites, competition experiments were performed to discriminate between V_1 and V_2 receptor subtypes. Toward this end we used the same synthetic structural analogs as in the electrophysiological study. Typical results are illustrated in Figure 7. They show that the selective V_2 receptor agonist, dDAVP, did not interfere with ^{3}H-AVP binding (Fig. 7*C*). In contrast, the V_1 agonist [Phe^2,Orn^8]VT competed for binding (Fig. 7*E*), as did unlabeled AVP (Fig. 7*F*), in area postrema, nucleus of the solitary tract, and inferior olive.

Discussion

When acting as a hormone, vasopressin can interact with 2 classes of peripheral receptors: (1) V_1, or phospholipase C-coupled receptors, which are located on vascular smooth muscle and on hepatocytes, where they mediate the vasoconstrictor and glycogenolytic effects of vasopressin, respectively; (2) V_2, or adenylate cyclase-coupled receptors, present in the kidney and responsible for the antidiuretic effect of vasopressin (for a review, see Jard and Barberis, 1989). In the present study, we have investigated the effect of exogenous vasopressin in a selected area of the rat brain, the nucleus of the solitary tract, and found that this peptide can induce neuronal excitation by acting on receptors which are pharmacologically indistinguishable from V_1 vasopressin receptors (Figs. 1, 3–5). Moreover, these receptors are probably located on the postsynaptic neuronal membrane, since the vasopressin-induced excitation persisted in the absence of synaptic transmission (Fig. 2).

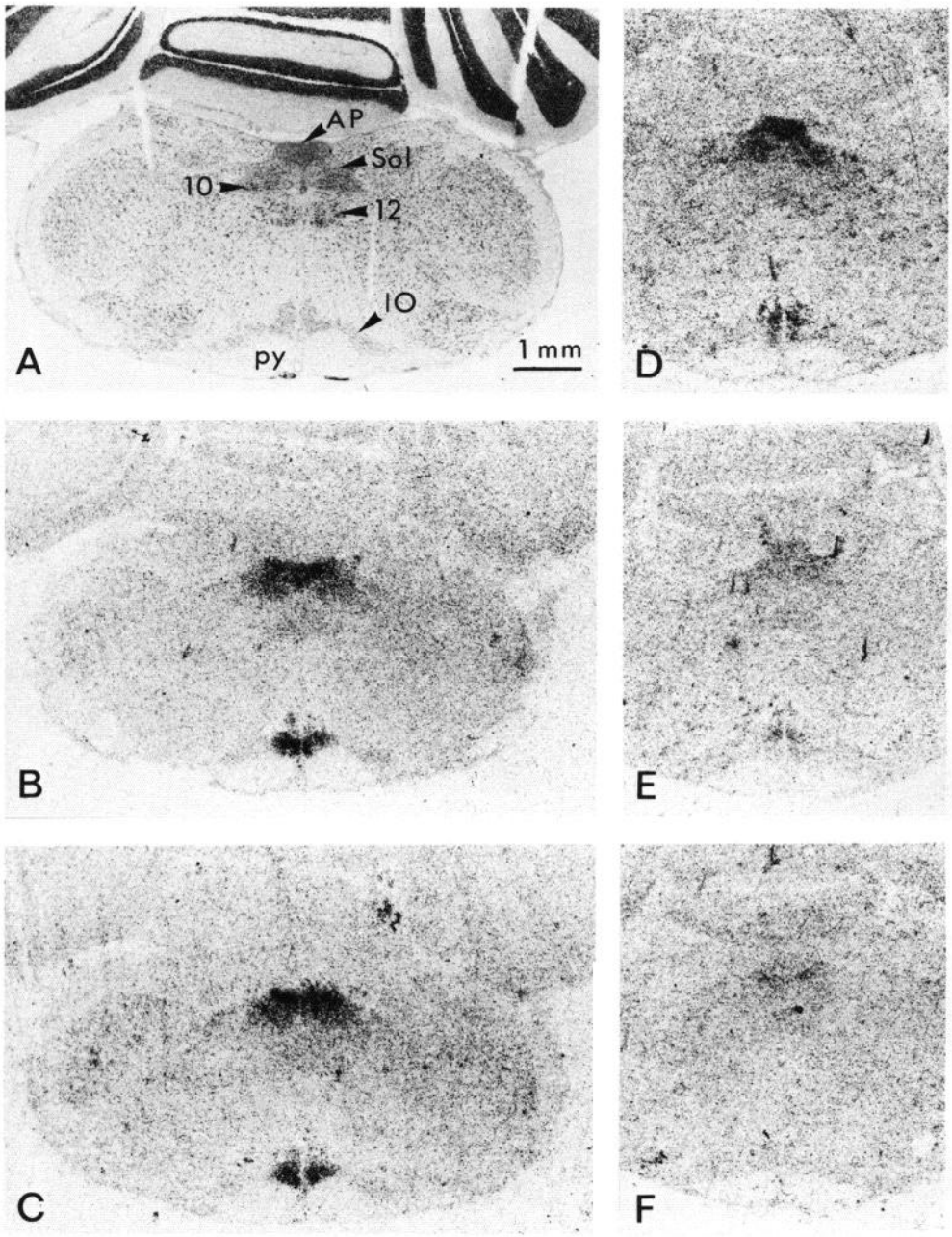

Figure 7. Pharmacological characterization of vasopressin binding sites. *A–C* are from one animal, *D–F* from another. *A* was stained with cresyl violet; *B* is the autoradiograph of binding obtained from section *A* after incubation with 1.5 nM ^{3}H-AVP alone; *C* is the autoradiograph of an adjacent section incubated with the same amount of ^{3}H-AVP in association with 100 nM dDAVP. Note that the latter compound, a specific V_2 receptor agonist, did not displace ^{3}H-AVP in either area postrema (*AP*) or nucleus of the solitary tract (*Sol*) or inferior olive (*IO*). Other abbreviations: *py,* pyramidal tract; *10,* dorsal motor nucleus of the vagus; *12,* hypoglossal nucleus. *D–F* were incubated with 1.5 nM ^{3}H-AVP alone (*D*) or in association with either 150 nM [Phe^2,Orn^8]VT (*E*) or 10,000 nM AVP. At the concentrations used, the former, a V_1 receptor agonist, displaced most, and the latter virtually all, of the ^{3}H-AVP bound.

Using brain slices, other regions of the CNS have been shown to contain neuronal populations whose bioelectrical activity can be affected by exogenous vasopressin acting via V_1-type receptors: the suprachiasmatic nucleus of the hamster (Liu and Albers, 1989), the lateral septum (Raggenbass et al., 1987b, 1988), the hypothalamic paraventricular nucleus (Inenaga and Yamashita, 1986), and the lateral horn of the spinal cord of the rat (Ma and Dun, 1985). By contrast, Abe et al. (1983) suggested that vasopressin could depolarize hypothalamic supraoptic neurons in the guinea pig through activation of adenylate cyclase, i.e., possibly by interacting with V_2- rather than V_1-type receptors. Although intriguing, this finding has not been confirmed, to our knowledge, by other groups.

Our electrophysiological results are in agreement with data gathered using autoradiography. Indeed, high-affinity binding sites for tritiated vasopressin are present in the nucleus of the solitary tract (Fig. 6) and their pharmacological profile, as determined by displacement studies, corresponds to that of V_1 vasopressin receptors (Fig. 7). This is in accordance with the notion that vasopressin receptors present in the brain of rats of various strains are of the V_1 rather than of the V_2 type (Horn and Lightman, 1987; Van Leeuwen et al., 1987; Lawrence et al., 1988; Moratalla et al., 1988; Phillips et al., 1988; Shewey and Dorsa, 1988; Tribollet et al., 1988).

Area postrema contains a high density of ^{3}H-AVP binding sites (Fig. 6*C*). Although we cannot exclude that occasionally electrophysiological recordings could have been carried out from this area, most of them were undoubtedly obtained from the nucleus of the solitary tract. Indeed, Niagara Sky Blue spots marking the recording sites were never located outside the

boundaries of this nucleus (see Material and Methods). In addition, area postrema was present only on a minority of coronal brain-stem slices and was virtually absent from parasagittal slices.

The nucleus of the solitary tract has efferent connections with the hypothalamic paraventricular and supraoptic nuclei. Noradrenergic solitary tract neurons in the A2 region project to the parvocellular and, although less consistently, to the magnocellular division of the paraventricular nucleus (Cunningham and Sawchenko, 1988). Also, a group of noncatecholaminergic solitary tract neurons, which can be stained with antisera against inhibin *beta,* a gonadal peptide hormone, send axons toward oxytocin magnocellular neurons in the paraventricular and supraoptic nuclei (Sawchenko et al., 1988). In addition, the nucleus of the solitary tract is probably also indirectly connected to the paraventricular nucleus via a disynaptic pathway involving the A1 noradrenergic cell group in the caudal ventrolateral medulla (Ross et al., 1985; Cunningham and Sawchenko, 1988).

The paraventricular nucleus, in turn, sends efferents toward the nucleus of the solitary tract. Indeed, vasopressin and oxytocin neurons in the paraventricular nucleus, and primarily in its lateral parvocellular part, have been shown to project toward both the nucleus of the solitary tract and the dorsal motor nucleus of the vagus nerve (Sofroniew and Schrell, 1981; Sawchenko and Swanson, 1982; for a review, see Swanson and Sawchenko, 1983). Following ^{35}S-cysteine injection into the paraventricular nucleus, vasopressin and oxytocin synthesized in this nucleus have been shown to reach the nucleus of the solitary tract by axonal transport (White et al, 1984). Also, lesioning the paraventricular nucleus resulted in a substantial decrease of the vasopressin and oxytocin content in the brain stem, as measured by radioimmunoassay (Lang et al., 1983).

Our results suggest, though do not prove, that endogenous vasopressin may be a neurotransmitter in the nucleus of the solitary tract. On the basis of the evidence summarized above, we are led to speculate that vasopressin-sensitive solitary tract neurons are the target of vasopressinergic parvocellular neurons located in the autonomic-related subdivision of the paraventricular nucleus. This would imply that vasopressin-sensitive neurons in the nucleus of the solitary tract may participate in the feedback regulation of gustatory and visceral sensory information conveyed by the 5th, 7th, 9th, and 10th cranial nerves (Norgren, 1985) and ascending, via this nucleus, toward the paraventricular and supraoptic nuclei of the hypothalamus, whereby they may modulate the release of vasopressin from the neurohypophysis (for a review, see Bisset and Chowdrey, 1988).

The caudal part of the nucleus of the solitary tract projects to the dorsal motor nucleus of the vagus nerve (Norgren, 1978; Ross et al., 1985). In the present work, some of the neurons which responded to vasopressin were found in coronal brainstem slices containing the caudal end of the nucleus of the solitary tract. Thus, part of the vasopressin-sensitive solitary tract neurons may have connections with vagal preganglionic neurons and could therefore indirectly modulate the parasympathetic outflow toward thoracic and abdominal viscera. To corroborate this conjecture, however, a more precise mapping of the distribution of vasopressin-responsive neurons within the nucleus of the solitary tract is needed.

Working on rats, Matsuguchi et al. (1982) and Vallejo et al. (1984) reported that vasopressin—but neither oxytocin nor the antidiuretic agonist dDAVP—injected into the nucleus of the solitary tract *in situ* increased blood pressure and heart rate; these hemodynamic changes were prevented by local pretreatment with d(CH$_2$)$_5$Tyr(Me)AVP, a vasopressor antagonist, or by ganglionic blockade. Injection into the nucleus of the solitary tract/vagal area of this same antagonist reduced the pressor and tachycardic response elicited by electrical stimulation of the paraventricular nucleus of the hypothalamus (Pittman and Franklin, 1985). Also, coinjection of subthreshold doses of vasopressin and noradrenaline in the nucleus of the solitary tract resulted in a pressor response (Vallejo and Lightman, 1987). The vasopressin-sensitive solitary tract neurons characterized in the present work, or at least part of them, probably mediate the vasopressin-induced pressor and tachycardic effects described above. By acting on these neurons, endogenous vasopressin may play a role in the central regulation of cardiovascular functions. One possibility, although not the sole, is that this neuropeptide could affect cardiovascular parameters by modulating the sensitivity of the baroreceptor reflex. Circulating vasopressin has been reported to specifically enhance the gain of the baroreceptor reflex in dogs, sheep, and rabbits but not in rats (for a review, see Share, 1988). One may speculate that in the latter species vasopressin, acting as a neurotransmitter/neuromodulator in the dorsal brain stem, may exert some cardiovascular regulatory functions that in other species are partially or totally performed by circulating vasopressin, probably acting at circumventricular organs lacking a blood–brain barrier, like area postrema (Undesser et al., 1985).

In conclusion, the positive correlation between electrophysiological and autoradiographic data obtained in the present as well as in a previous study, performed in the lateral septal area, suggests that at least part of the high-affinity vasopressin binding sites present in the rat brain represent function neuronal V_1-type vasopressin receptors involved in bioelectrical signaling.

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