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Oxytocin-induced renin secretion by denervated kidney in anaesthetized rat

Cécile Loichot[a], Michèle Grima[a,b], Wybren De Jong[a,1], Jean-Jacques Helwig[c], Jean-Louis Imbs[a,b], Mariette Barthelmebs[a,c,*]

[a] *Institut de Pharmacologie, Faculté de Médecine, Université Louis Pasteur, 11 Rue Humann, 67085 Strasbourg Cedex, France*
[b] *Service d'Hypertension Artérielle, Maladies Vasculaires et Pharmacologie Clinique, Hôpital Civil, Strasbourg, France*
[c] *Laboratoire de Pharmacologie et de Physiologie Rénovasculaire (EMI-0015 INSERM-Université Louis Pasteur), Faculté de Médecine, Strasbourg, France*

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Abstract

The effects of oxytocin on renin secretion by denervated kidney were investigated in vivo, by infusing the peptide directly into the renal artery of anaesthetized rats. Renin secretion was calculated by the renal veno-arterial difference in plasma renin activity multiplied by renal plasma flow. The intra-renal arterial (i.r.a.) infusion of oxytocin (1.5 or 15 ng/kg/min, 10 min) induced a sixfold increase in renin secretion as compared to vehicle-treated controls, without effects on renal blood flow, mean arterial blood pressure, glomerular filtration rate or natriuresis. The effect of oxytocin (1.5 ng/kg/min) was prevented by pretreatment with an oxytocin receptor antagonist, desGly-NH_2,d$(CH_2)_5$[D-Tyr^2,Thr^4,Orn^8]vasotocin] (5.6 μg/kg bolus i.v. 20 min before oxytocin infusion, followed by 2.8 μg/kg/min i.r.a.). Nadolol (2.5 mg/kg i.v.), a β-adrenoceptor antagonist, also blocked the oxytocin-induced increase in renin secretion. These results show that oxytocin is able to stimulate renin release by activating oxytocin receptors but that β-adrenoceptors also seem to be involved.

Keywords: Oxytocin; Renin secretion; Oxytocin receptor; β-Adrenoceptor; Renal denervation; Pulsed infusion

1. Introduction

It has long been recognized that oxytocin is involved in lactation and parturition. However, similar levels of the peptide are present in the neurohypophysis and plasma of both sexes, which suggests that the hormone may have additional physiological roles. Renal effects of oxytocin have been reported such as an increase in glomerular filtration rate (Conrad et al., 1993) and in natriuresis (Verbalis et al., 1991; Soares et al., 1999). Oxytocin also has been shown to contribute to natriuresis under conditions of dehydration (Huang et al., 1996) or hypertonic overload (Huang et al., 1995). Furthermore, it has been observed that oxytocin is secreted in response to hypotension (Schiltz et al., 1997) but its action in this condition is not known.

Oxytocin receptors have been localized in the rat kidney exclusively in the macula densa (Stoeckel and Freund-Mercier, 1989). Macula densa is involved in the regulation of renin secretion (Harris, 1996). Since renin is a limiting factor in the renin–angiotensin system, its regulation is of importance in the control of the overall system. Oxytocin might be involved in this regulation. It has recently been shown that oxytocin enhances plasma renin activity in anaesthetized (Sjöquist et al., 1999) as well as in conscious rats (Huang et al., 2000). The mechanism involved in this enhancing effect was, however, not clearly established, in particular with respect to a possible contribution of renal sympathetic nerves.

The aim of our study was to evaluate the effects of oxytocin on renal renin secretion. We infused the peptide directly into the renal artery of the left kidney to assess its action. Perfusion was performed in anaesthetized rats with a recently developed method that allows a thorough mixing of the infused peptide with renal arterial blood (Parekh, 1995).

* Corresponding author. Institut de Pharmacologie, Faculté de Médecine, Université Louis Pasteur, 11 Rue Humann, 67085 Strasbourg Cedex, France. Tel.: +33-3-90-24-34-60; fax: +33-3-90-24-34-59.
E-mail address: mariette.barthelmebs@pharmaco-ulp.u-strabg.fr (M. Barthelmebs).
[1] Deceased.

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Renin secretion was evaluated by measuring the renal veno-arterial difference in plasma renin activity and renal blood flow. To exclude the influence of renal sympathetic nerve activity, experiments were performed in rats with denervated kidney.

2. Materials and methods

2.1. Animals

Male Sprague–Dawley rats (8 weeks of age, 250–300 g, Iffa-Credo, L'Arbresle, France) were used. Animals were housed in a room at 20 °C with a 12-h light/dark cycle (light on at 6:00 a.m.) and allowed free access to tap water and standard food (AO4 pellets, UAR, Villemoisson/Orge, France). The rats stayed in our animal facility for at least 1 week before experiments. Experiments were performed in accordance with guidelines of the European Community and the French Government concerning the use of animals.

2.2. Surgical preparation

Rats were anaesthetized by i.p. injection of thiobutabarbitone sodium (Inactin®, 100 mg/kg), placed on a temperature-controlled table to maintain a body temperature of 37 °C and prepared for experiment. Briefly, following cannulation of the trachea, a catheter was inserted into the left femoral artery for mean arterial blood pressure monitoring via a strain-gauge transducer (Statham P23 Db), and for blood sampling. Another catheter was inserted into the jugular vein for i.v. infusions. A third catheter was inserted into the left renal artery via the right femoral artery and abdominal aorta for intra-renal arterial (i.r.a.) infusions. The tip of this catheter was advanced about 0.5 cm past the orifice of the renal artery. Drugs were infused intrarenally via a pulsed infusion using a mixing pump. The catheter consisted of a multiple catheter system with an intrarenal Teflon cannula as developed by Parekh (1995). During infusion, a pulsed pump aspirated about 4-μl blood from the renal artery into the Teflon cannula over 1000 ms and reinjected it within 100 ms. Turbulence at the cannula orifice ensures thorough mixing of the infusate with renal arterial blood.

To denervate the kidney, a subcostal abdominal incision was made and the left renal artery and vein were carefully stripped of connective tissues. All visible nerves along the renal artery and vein were removed and the vessels were then swabbed with 10% phenol in absolute ethanol (Pelayo et al., 1983). Acute renal denervation was performed in all rats, except for a group of three rats in which a chronic renal denervation was realized. In this group, denervation of the left kidney was performed, 1 week before experiment, under pentobarbital anaesthesia (45 mg/kg i.p.) as described above. At the end of the experiment, both kidneys of these three rats were removed for measurement of noradrenaline content by high-performance liquid chromatography coupled with an electrochemical detector (Ichihara et al., 1997). Denervation was considered effective when the left renal content of noradrenaline was $<10\%$ of the content of the controlateral intact kidney.

For measurement of renal blood flow, an electromagnetic flow probe (internal diameter 0.5 mm; Skalar electromagnetic blood flowmeter, Delft, The Netherlands) was placed around the left renal artery. Renal blood flow was continuously monitored together with mean arterial blood pressure (Philips Recorder, Philips, Bobigny, France). A curved 26-gauge needle connected to a polyethylene tubing was inserted into the left renal vein for renal venous blood sampling. To compensate for fluid loss, rats were supplemented i.v. with 2 ml 6% bovine serum albumin in Tyrode's solution at the end of surgery. At the end of the experiments, animals were killed by anaesthetic overdose.

2.3. Experimental protocol

Following a 60-min resting period, renin secretion was first evaluated at the end of a basal period, i.e. a 10-min i.r.a. infusion of vehicle (NaCl 0.9%). To compensate for fluid loss, rats were then again supplemented i.v. with 1 ml 6% bovine serum albumin in Tyrode's solution. Following another 30-min recovery period, the effects of hormone or drugs on renin secretion were evaluated a second time, at the end of the experimental period, i.e. the 10-min i.r.a. infusion of oxytocin (1.5 or 15 ng/kg/min), or isoproterenol (0.1 μg/kg/min) used as positive control. In the time-control group, vehicle continued to be perfused during the experimental period. The effects of the low-dose oxytocin (1.5 ng/kg/min) were also analysed in chronically denervated rats.

In order to investigate the contribution of oxytocin receptors in the renin response to oxytocin, the effects of the hormone were also analyzed in the presence of the selective oxytocin receptor antagonist, desGly-NH_2,d$(CH_2)_5$[D-Tyr^2, Thr^4,Orn^8]vasotocin (Manning et al., 1995). The antagonist was administered 20 min before oxytocin infusion as an i.v. bolus (5.6 μg/kg), immediately followed by a continuous i.r.a. infusion (2.8 μg/kg/min) up to the end of the experiment.

In another group, the effects of oxytocin on renin secretion were evaluated in the presence of nadolol, a β-adrenoceptor antagonist. Nadolol was injected 20 min before oxytocin infusion (2.5 μg/kg bolus i.v.). In a pilot study in anaesthetized rats, we controlled that this dose completely abolished isoproterenol-induced hypotension for more than an hour.

2.4. Renin secretion

Systemic arterial and renal venous blood samples (0.6 ml each) were simultaneously withdrawn at the end of both the basal and experimental periods. Blood was collected in ice-chilled tubes containing sodium ethylenediaminetetraacetic acid, rapidly centrifuged and the plasma stored at −20 °C

until plasma renin activity was determined by radioimmunoassay as previously described (Michel et al., 1994). Plasma renin activity was expressed as nanograms of angiotensin I generated per milliliter of plasma per hour incubation (ng angiotensin I/ml plasma/h). Systemic arterial hematocrit was determined in glass capillaries. Renal plasma flow was calculated by: renal blood flow × (1 − hematocrit). Renin secretion (arbitrary units) was calculated as: renal plasma flow × (renal venous plasma renin activity − arterial plasma renin activity). Because there occurred some variation in the values of basal renin secretion over the different experimental groups, although not statistically significant (Table 1), we calculated the relative renin secretion during the experimental period for each animal (experimental − basal renin secretion) and expressed results as absolute increase over basal renin secretion.

2.5. Clairance studies

In another group of rats, glomerular filtration rate and renal plasma flow were determined from the clearance of polyfructosan, an inulin analog, and *p*-aminohippuric acid, respectively, as previously described (Barthelmebs et al., 1991). Rats were prepared as described above, with thiobutabarbital anesthesia, left kidney denervation and surgical preparation for i.r.a. infusion. Polyfructosan and *p*-aminohippuric acid were infused through jugular vein as a bolus (2 ml/kg, 3.75% w/v *p*-aminohippuric acid and 25% w/v polyfructosan), followed by a constant infusion (2.8 ml/h, 2% *p*-aminohippuric acid and 8% polyfructosan). Blood was sampled from femoral artery. The left kidney ureter was cannulated to collect urine. After an equilibration period of 1 h, the experimental protocol comprised five 10-min periods, two control periods preceding and following the i.r.a. infusion of oxytocin (1.5 ng/kg/min). In two animals, the protocol was extended to seven 10-min periods, so that oxytocin could also be tested at the higher dose (15 ng/kg/min). Finally, one time-control animal only received NaCl 0.9% infusion. Animals were killed by anaesthetic overdose. The left kidney was excised, blotted and weighed, in order to normalize results per gram kidney weight.

Polyfructosan was measured by an enzymatic method (D-glucose/D-fructose kit, Boehringer Mannheim, Germany) after hydrolysis by inulinase (Société Realco, Louvain-la-Neuve, Belgium). *Para*-aminohippuric acid was measured by a colorimetric method on microplate. Sodium was measured on urine with ion-selective electrodes (EL-Ise, Beckman, Gagny, France).

2.6. Plasma oxytocin measurements

In vehicle and oxytocin-perfused (1.5 or 15 ng/kg/min) rats, systemic arterial blood (0.8 ml) was withdrawn from the femoral artery at the end of the experimental period for plasma oxytocin measurement. Blood was collected on sodium heparinate, rapidly centrifuged and stored at −20 °C until the plasma oxytocin was assayed by radioimmunoassay (Lutz-Bucher et al., 1977).

2.7. Drugs

The following drugs were used: bovine serum albumin, fraction V (Euromedex, Souffelweyersheim, France); isoproterenol hydrochloride, nadolol (Sigma, St. Quentin Fallavier, France); *p*-aminohippuric acid (PAH 20%, Laboratoires Pharmaceutiques SERB, Paris, France); polyfructosan (Inutest®, Laevosan-Gesellschaft, Linz, Austria); oxytocin (Biogenesis, Stinsford, United Kingdom); sodium pentobarbital (Nembutal®, Sanofi Santé Animale, Libourne, France); sodium thiobutabarbitone (Inactin®; Byk Gulden, Constance, Germany). All other chemicals were of pro-analysis quality from Merck (Darmstadt, Germany). The oxytocin receptor antagonist, desGly-NH_2,d$(CH_2)_5$[D-Tyr^2,Thr^4,Orn^8]vasotocin, was a gift from Dr. Manning (Medical College of Ohio, Toledo, USA).

Table 1
Haemodynamic parameters and renin secretion in thiobutabarbitone-anesthetized rats

Treatment	*n*	Plasma renin activity (ng angiotensin I/ml plasma/h)		Renin secretion (arbitrary units)	Renal blood flow (ml/min)		Mean arterial pressure (mm Hg)	
		Basal	Basal	Basal	Basal	Experimental	Basal	Experimental
		Arterial	Renal venous					
Vehicle (0.9% NaCl)	7	68 ± 11	94 ± 17	96 ± 33	7.6 ± 0.2	7.7 ± 0.3	104 ± 2	105 ± 3
Oxytocin (1.5 ng/kg/min)	9	78 ± 13	105 ± 16	122 ± 32	7.7 ± 0.5	8.2 ± 0.5	110 ± 3	106 ± 3
Oxytocin (15 ng/kg/min)	6	87 ± 10	130 ± 16	166 ± 41	6.8 ± 0.6	6.9 ± 0.4	98 ± 4	93 ± 5
Isoproterenol (0.1 μg/kg/min)	5	47 ± 8	78 ± 12	121 ± 43	7.2 ± 0.6	7.9 ± 0.8	108 ± 4	109 ± 4
Oxytocin (1.5 ng/kg/min) + oxytocin receptor antagonist	6	67 ± 6	84 ± 11	60 ± 21	6.7 ± 0.3	7.5 ± 0.4	101 ± 2	96 ± 2
Oxytocin (1.5 ng/kg/min) + nadolol	5	49 ± 10	71 ± 13	103 ± 28	8.5 ± 0.6	8.6 ± 0.5	106 ± 4	103 ± 2

Basal measurements were made at the end of the basal period, after a 10-min i.r.a. infusion of vehicle (0.9% NaCl) in all groups. Experimental data of the different groups were obtained after a 10-min i.r.a. infusion as indicated by treatment.
Data are expressed as means ± S.E.M. for *n* individual values. Statistical analysis was performed by one-way analysis of variance or two-way analysis of variance for repeated measurements. No statistical difference was observed.

2.8. Statistical analysis

Results are expressed as means ± S.E.M. Results were analyzed by paired *t*-test, one-way analysis of variance or two-way analysis of variance for repeated measurements when appropriate. Student–Newman–Keuls test was used for multiple paired comparisons of treatments. A logarithmic transformation of data was used to equalize variances when necessary. A P value less than 0.05 was considered significant. All statistical calculations were made using SigmaStat (SPSS, Chicago, USA).

3. Results

3.1. Effect of oxytocin on renin secretion

The experimental groups did not differ in their basal values of renal blood flow, mean arterial blood pressure or renin secretion (Table 1). Arterial plasma renin activity remained relatively stable throughout the experiment, reaching for instance a value of 68 ± 11 and 91 ± 15 ng angiotensin I/ml plasma/h in vehicle-treated group, at the end of the basal and experimental period, respectively ($n = 7$, paired *t*-test, nonsignificant). Relative renin secretion (experimental − basal) was moderate in the vehicle-treated group (Fig. 1).

The 10-min i.r.a. infusion of oxytocin at 1.5 ng/kg/min induced a significant increase in relative renin secretion when compared with vehicle infusion ($P < 0.05$, Fig. 1). Renin secretion was increased sixfold as compared to vehicle-treated controls. The higher dose of oxytocin (15 ng/kg/min i.r.a. for 10 min) induced an increase in relative renin secretion similar to that of the lower dose of the hormone (Fig. 1). The i.r.a. infusion of oxytocin did not elicit changes in renal blood flow or mean arterial blood pressure, whatever the dose (Table 1). In comparison, relative renin secretion was increased 25-fold by the 10-min i.r.a. infusion of isoproterenol (0.1 μg/kg/min), the β-adrenoceptor agonist ($P < 0.001$ versus vehicle-treated controls, Fig. 1). Isoproterenol also was devoid of effect on renal blood flow or mean arterial blood pressure (Table 1).

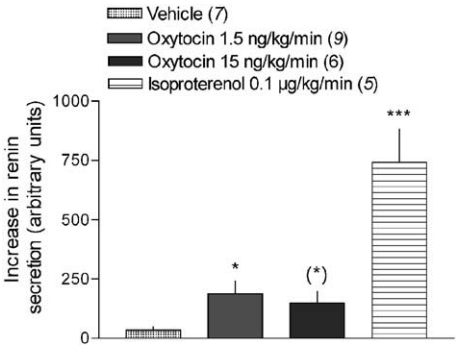

Fig. 1. Increase in renin secretion by acutely denervated kidneys, following 10-min i.r.a. infusion of vehicle (0.9% NaCl), oxytocin or isoproterenol. For each rat, the relative change in renin secretion during the experimental period (drug or hormone infusion) was calculated by subtracting basal renin secretion (see Section 2). Data are expressed as means ± S.E.M. Statistical analysis was performed by one-way analysis of variance; Student–Newman–Keuls test was used for multiple paired comparisons with the vehicle-treated group. *$P < 0.05$; ***$P < 0.001$, (*) $P < 0.05$ one-tailed.

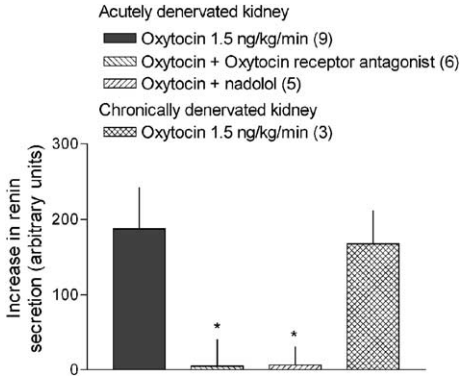

Fig. 2. Inhibition of oxytocin-induced increase in renin secretion by denervated kidneys, following treatment with an oxytocin receptor antagonist (desGly-NH_2,d$(CH_2)_5$[D-Tyr^2,Thr^4,Orn^8]vasotocin) or a β-adrenoceptor antagonist (nadolol). For each rat, the relative change in renin secretion during the experimental period (drug or hormone infusion) was calculated by subtracting basal renin secretion (see Section 2). Data are expressed as means ± S.E.M. Statistical analysis was performed by one-way analysis of variance; Student–Newman–Keuls test was used for multiple paired comparisons with the oxytocin group. *$P < 0.05$.

The infusion of oxytocin directly into the renal artery dose-dependently enhanced systemic arterial plasma level of the hormone. It averaged 77 ± 22 and 316 ± 20 pg/ml, respectively, after the low and the high dose oxytocin, while a level of 25 ± 4 pg/ml was measured at the end of the experiment in vehicle-treated controls ($P < 0.001$).

3.2. Effect of oxytocin receptor antagonist on oxytocin-induced renin secretion

Pretreatment with the oxytocin receptor antagonist, desGly-NH_2,d$(CH_2)_5$[D-Tyr^2,Thr^4,Orn^8]vasotocin, completely prevented oxytocin-induced increase in renin secretion (Fig. 2). The oxytocin receptor antagonist had no effect on renal blood flow (respectively, 7.3 ± 0.4 and 7.5 ± 0.4 ml/min, before and after a 20-min infusion of the antagonist, $n = 6$), or on mean arterial blood pressure (respectively, 98 ± 1 and 96 ± 2 mm Hg).

3.3. Effect of β-adrenoceptor antagonist on oxytocin-induced renin secretion

Pretreatment with the β-adrenoceptor antagonist, nadolol (2.5 mg/kg, i.v.), also completely prevented oxytocin-induced increase in renin secretion (Fig. 2). Nadolol per se, however, was devoid of effects on renal blood flow (respectively, 8.7 ± 0.7 and 8.5 ± 0.4 ml/min, before and 20 min after injection of nadolol, $n = 5$), or on mean arterial

blood pressure (106 ± 2 and 103 ± 2 ml/min). As expected, nadolol reduced heart rate (respectively, 370 ± 10 and 345 ± 15 beats/min, $P < 0.01$).

3.4. Effect of chronic denervation on oxytocin-induced renin secretion

In chronically denervated kidney, oxytocin (1.5 ng/kg/min, i.r.a. 10 min) increased relative renin secretion to a similar degree as observed in acutely denervated kidneys (Fig. 2). The relative increase in renin secretion during the experimental period (oxytocin infusion) amounted to, respectively, 167 ± 44 and 187 ± 54 (arbitrary units) for chronically and acutely denervated kidneys. Chronic denervation was associated with a marked decrease (>90%) in noradrenaline content of the kidney. A mean noradrenaline content of 0.023 ± 0.005 μg/g kidney weight ($n = 3$) was measured in the left chronically denervated kidneys whereas the noradrenaline content was of 0.27 ± 0.05 μg/g kidney weight in the controlateral intact kidneys ($n = 3$, $P < 0.001$).

3.5. Effect of oxytocin on renal functions

The 10-min i.r.a. infusion of oxytocin at 1.5 ng/kg/min elicited no change in renal hemodynamics, glomerular filtration rate or urinary excretion of sodium and water (Fig. 3).

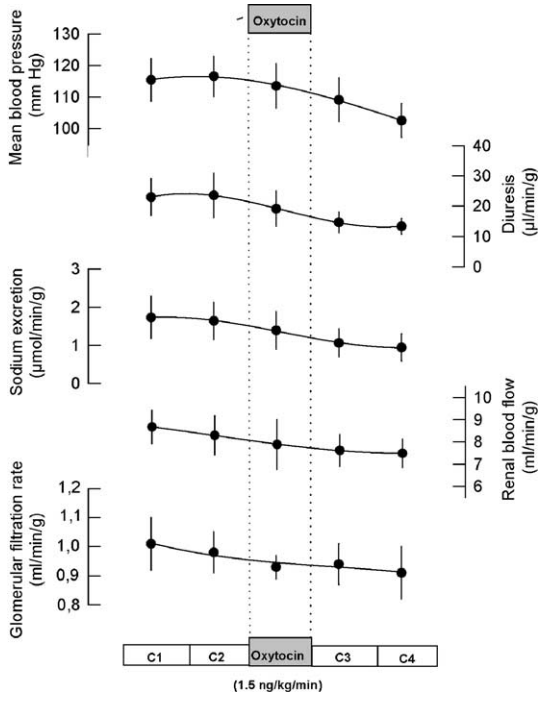

Fig. 3. Effects of oxytocin on renal hemodynamics and urinary water or sodium excretion. The 10-min i.r.a. infusion of oxytocin was preceded and followed by two control periods. Polyfructosan and *p*-aminohippuric acid clearances were used to evaluate glomerular filtration rate and renal plasma flow respectively (see Section 2). Data are expressed as means ± S.E.M. for $n = 6$ individual values.

Similar results were obtained with oxytocin at 15 ng/kg/min and in the time-control experiment (data not shown).

4. Discussion

The effects of oxytocin on renin secretion were investigated in rats by infusing the peptide directly into the renal artery of the left denervated kidney. Our results show that oxytocin enhances renin secretion via oxytocin receptor but that a β-adrenoceptor-dependent mechanism also seems to be involved. Oxytocin-elicited renin secretion occurred without concomitant change in renal hemodynamics, glomerular filtration rate and sodium excretion, thus excluding an indirect signal for macula densa mediated renin secretion. Oxytocin was infused into the renal artery at a dose of 1.5 ng/kg/min for 10 min, which might achieve a plasma concentration of the peptide of about 0.1 nM (100 pg/ml) in the renal artery. This plasma level is similar to the concentration reported during hypotension (Schiltz et al., 1997). A 10 times higher dose of oxytocin elicited the same increase in renin secretion. This limitation in oxytocin response was not due to a limitation of the denervated kidney to increase renin secretion since isoproterenol was able to elicit a more pronounced stimulation. Present results rather show that the maximum stimulation in renin release by oxytocin already was obtained at the lowest dose of the peptide tested.

Oxytocin appears to evoke renin secretion via the activation of oxytocin receptors, since the response was prevented by pretreatment with a specific oxytocin receptor antagonist. DesGly-NH_2,d$(CH_2)_5$[D-Tyr^2,Thr^4,Orn^8]vasotocin, the oxytocin receptor antagonist used in the present study, is selective for oxytocin receptor. It interacts with the oxytocin receptor in isolated uteri at a pA_2 of 7.7, while its pA_2 for the vasopressin V_{1A} receptor amounts 5.39 (Manning et al., 1995). The oxytocin-elicited increase in renin secretion does not seem to be linked to activation of vasopressin receptor. Oxytocin is able to interact with vasopressin receptor but only at high concentration (μM), and inhibition of renin release by vasopressin has been documented (Bunag et al., 1967). Vasopressin was shown to inhibit renin release both in vivo (Malayan et al., 1980; Schwartz and Reid, 1986) and in vitro, in the isolated perfused kidney (Konrads et al., 1978). The inhibition of renin release by vasopressin was mediated by vasopressin V_1 receptor activation (Schwartz and Reid, 1986).

The inhibitory effect of nadolol on oxytocin-elicited renin secretion indicates the involvement of β-adrenoceptors in the oxytocin response. These receptors are present on the juxtaglomerular apparatus where the afferent arterioles receive a particular rich supply of sympathetic nerve fibers. The activation of renal β-adrenoceptors is a well-known stimulus for renin release, as was also found in our study with isoproterenol. As expected, the i.r.a. infusion of isoproterenol markedly enhanced renin secretion.

The inhibition of oxytocin-induced renin secretion by both an antagonist of oxytocin receptor and an antagonist of β-adrenoceptors is difficult to concile. The two receptors seem to act in series, since the separate inhibition of each receptor completely prevented oxytocin response on renin secretion. Oxytocin receptors are present on the macula densa cells of the rat kidney (Stoeckel and Freund-Mercier, 1989). However, the stimulation of renin secretion via a macula densa mechanism usually occurs independently of β-adrenoceptor activation (Lorenz et al., 1991). Present results therefore seem difficult to be explained by the activation of oxytocin receptors on macula densa cells. Moreover, although the peptide was infused directly into the renal artery, renal venous overflow occurred with a subsequent increase in systemic arterial level of the hormone. Systemic effects of oxytocin can therefore not be excluded. It should be noticed that the hormone level (25 ± 4 pg/ml) measured in our experimental setting in control rats was previously shown to be insufficient for the activation of renin release (Huang et al., 2000).

Oxytocin-induced increase in renin secretion could be mediated by a central effect of the hormone. In a previous study, infusion of oxytocin into the vertebral artery of anaesthetized dogs was shown to enhance renin secretion (Brooks et al., 1984). The brain therefore could be a potential site of action of the peptide to affect renin release, although oxytocin does not readily cross the blood brain barrier.

Since our experiments were performed in denervated kidneys, a contribution of renal sympathetic innervation in oxytocin-induced renin secretion was improbable. The effectiveness of renal denervation was checked in chronically denervated kidneys, where depletion in kidney noradrenaline content was higher than 90%. We cannot exclude that a very low residual renal innervation was responsible for oxytocin effect on renin secretion, in as much as the effect of oxytocin was rather limited and not dose-dependent. Huang et al. (2000), however, recently reported a similar low degree of stimulation of renin release by oxytocin in intact kidneys, when oxytocin was i.v. infused to achieve a plasma concentration similar to that reached in our study. Although we did not test oxytocin in our experimental setting on innervated kidneys, it seems likely that renal innervation is not a prerequisite for the stimulation of renin secretion by oxytocin.

Oxytocin could also enhance renin secretion via the stimulation of catecholamine release by the adrenal medulla. Indeed, oxytocin has been reported to increase catecholamine content in rat adrenal medulla (Plecas et al., 1989), an effect which occurred slowly and was associated with a mitogenic effect of the hormone. The link between this observation, circulating catecholamines and oxytocin-induced renin secretion needs, however, further experiments to be established.

In conclusion, oxytocin infused into the renal artery induces an increase in renin secretion. This effect appears to be the result of activation of oxytocin receptors while β-adrenoceptors also seem to be involved in this response. Since oxytocin is secreted in response to hypotension (Schiltz et al., 1997), the peptide may contribute to support blood pressure via the activation of the renin–angiotensin system.

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