Massage-like stroking of the abdomen lowers blood pressure in anesthetized rats: influence of oxytocin

Mieko Kurosawa *, Thomas Lundeberg, Greta Ågren, Irene Lund, Kerstin Uvnäs-Moberg
Department of Physiology and Pharmacology, Karolinska Institutet, S-171 77 Stockholm, Sweden

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Abstract

The aim of this study was to determine how massage-like stroking of the abdomen in rats influences arterial blood pressure. The participation of oxytocinergic mechanisms in this effect was also investigated. The ventral and/or lateral sides of the abdomen were stroked at a speed of 20 cm/s with a frequency of 0.017–0.67 Hz in pentobarbital anesthetized, artificially ventilated rats. Arterial blood pressure was recorded with a pressure transducer via a catheter in the carotid artery. Stroking of the ventral, or both ventral and lateral sides of the abdomen for 1 min with a frequency of 0.67 Hz caused a marked decrease in arterial blood pressure (approx. 50 mmHg). After cessation of the stimulation blood pressure returned to the control level within 1 min. The maximum decrease in blood pressure was achieved at frequencies of 0.083 Hz or more. Stroking only the lateral sides of the abdomen elicited a significantly smaller decrease in blood pressure (approx. 30 mmHg decrease) than stroking the ventral side. The decrease in blood pressure caused by stroking was not altered by s.c. administration of an oxytocin antagonist (1-deamino-2-o-Tyr-(Oet)-4-Thr-8-Orn-oxytocin, 1 mg/kg) directed against the uterine receptor. In contrast, the administration of 0.1 mg/kg of oxytocin diminished the effect, which was antagonized by a simultaneous injection of the oxytocin antagonist. These results indicate that the massage-like stroking of the abdomen decreases blood pressure in anesthetized rats. This effect does not involve intrinsic oxytocinergic transmission. However, since exogenously applied oxytocin was found to diminish the effect of stroking, oxytocin may exert an inhibitory modulatory effect on this reflex arc.

Keywords: Massage; Stroking; Blood pressure; Oxytocin; Oxytocin antagonist; Abdomen; Rat

1. Introduction

Somatic afferent stimulation can modify various autonomic functions, including blood pressure [15], heart rate [9,15], adrenal catecholamine secretion [2,11], gastrointestinal motility [7,10] and vesical contractility [16,17], by means of a reflex action. Studies on these somato-autonomic reflex responses have emphasized that the responses depend on both the type of somatic afferent stimulation (e.g., noxious or innocuous mechanical stimulation) and the segments of the skin stimulated in the respective autonomic functions.

Kanetake has shown that rhythmic massage-like stroking of the abdominal area elicits a sedative response in conscious rats [8]. Recently, we have reported that the same type of stroking increases the withdrawal latency to heat and to mechanical stimuli. The increase in withdrawal latency to heat could be blocked by an oxytocin antagonist directed against the uterine receptor, indicating that this effect involves oxytocinergic mechanisms [1].

In the present study we have investigated the influence on blood pressure by the stroking of the abdomen in anesthetized rats. We also investigated the role of oxytocinergic mechanisms in this response.

2. Materials and methods

2.1. Animals and general preparation

Experiments were performed on 28 male Sprague-Dawley rats (280–430 g) anesthetized with pentobarbital (60–70 mg/kg, i.p.). The trachea was catheterized, and the
respiration of the animals was artificially maintained with a respirator (Model 683, Harvard, MA, USA). Arterial blood pressure was continuously recorded with a pressure transducer via a catheter in the right carotid artery. In some experiments, the number of pulse waves was calculated from the blood pressure determination as a measure of pulse rate. Another catheter was inserted into a jugular vein for necessary infusions of additional pentobarbital, glucose and Ficoll 70 (Pharmacia, Uppsala, Sweden) solution. The animals' body temperature was maintained at 37.0–37.5°C with a thermostatically regulated heating pad.

All surgical procedures mentioned above were usually finished 1 h after the initial injection of anesthesia, then additional pentobarbital was administered intravenously at the rate of 10–20 mg/kg per h by an infusion pump (model STC-527, Terumo, Japan). During the experiment, the depth of anesthesia was routinely judged by observing the immobility and blood pressure of the animal.

2.2. Drug treatment

The rats were subcutaneously injected with saline, oxytocin (0.01, 0.1 and 1 mg/kg), oxytocin antagonist (1 mg/kg, 1-deamino-2-α-Tyr-(Oet)-4-Thr-8-Orn-oxytocin, Ferring, Malmö, Sweden) and a combination of oxytocin and the oxytocin antagonist (both 1 mg/kg) at the volume of 1 ml/kg.

2.3. Sensory stimulation

The ventral (approx. 10 cm²) and/or lateral (approx. 10 cm²) side of the abdomen was stroked at a pressure of 100–150 mmHg and at a speed of 20 cm/s for 1 min. In some experiments the stimuli were applied for 5 min. The stimulus frequency varied between 0.017 Hz and 0.67 Hz, i.e., stroking from every 60 to every 1.5 s. The reproducibility of the manual stimuli was tested and confirmed by similar application of pressure to a small balloon connected to a pressure gauge. The stimulation was applied every 10 min. In the drug-administration experiments, three control stimulations were applied before the drug was administered, and the effect of the drug was studied during 9 consecutive stimulations (90 min).

2.4. Statistical analysis

Data are expressed as mean ± SEM. Comparison was made with one-way ANOVA and the Fisher's post hoc test.

### Table 1

<table>
<thead>
<tr>
<th>Site of stimulation</th>
<th>Time after the onset of stroking (s)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Ventral + lateral</td>
<td>388 ± 24</td>
</tr>
<tr>
<td>Ventral</td>
<td>390 ± 25</td>
</tr>
<tr>
<td>Lateral</td>
<td>388 ± 27</td>
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</table>

Values are mean ± SEM (n = 5). * P < 0.05; * * P < 0.01, significantly different from prestimulus control values using one-way ANOVA and the Fisher's post hoc test.
Fig. 2. (A–E) Sample recordings showing the effects of various frequencies of abdominal stroking on arterial blood pressure. (A) Only one stroking. (B–E) Stroking was applied every 12 s (B), 6 s (C), 3 s (D) and 1.5 s (E) for 1 min. (F) A sample recording showing effect of prolonged stimulation by stroking (for 5 min) on arterial blood pressure. Stroking was applied every 1.5 s for 5 min. See Fig. 1 for other details.

3. Results

3.1. Effect of massage-like stroking on blood pressure and heart rate

3.1.1. Stimulus area dependence

The massage-like stroking of the ventral and/or the lateral sides of the abdomen caused a decrease in blood pressure, as shown in Fig. 1A–C. The blood pressure decreased immediately after the onset of the 1-min-long stimulation and returned to the pre-stimulus control level within 1 min after its cessation. As summarized in Fig. 1D, the stroking of either the ventral or both ventral and lateral sides decreased blood pressure by approx. 50 mmHg. The stroking of the lateral sides decreased blood pressure by approx. 30 mmHg.

These strokings also slowed the heart rate (Table 1), although there were no significant differences in the magnitude of the heart rate responses to stimulation of the ventral and/or lateral sides of the abdomen.

3.1.2. Stimulus frequency dependence

The frequency of the stroking was varied between 0.017 and 0.67 Hz in experiments where the ventral plus the lateral sides of the abdomen were stimulated. As shown in Fig. 2A, one stroke induced a decrease in blood pressure of about 40 mmHg. Stroking at frequencies between 0.083 and 0.67 Hz caused a decrease of about 50 mmHg during the stimulation period, although the response to the lower frequency fluctuated more and was more short-lasting (Fig. 2B–E). When the stimulus duration was prolonged to 5 min (0.67 Hz), the decrease of blood pressure persisted over the entire stimulation period (Fig. 2F).

3.2. Effect of administration of an oxytocin antagonist and/or oxytocin on blood pressure

Stimulation was applied for 1 min to the ventral plus lateral sides of the abdomen, at a frequency of 0.67 Hz. And the effect of the oxytocin antagonist and/or oxytocin on the response of blood pressure to stroking was evaluated by comparing the values of the decrement of the blood pressure at 20 s after the onset of the stimulation.

3.2.1. Effect of an oxytocin antagonist

Administration of 1 mg/kg of the oxytocin antagonist had no effect by itself on the basal blood pressure during a 90-min-long observation period (Table 2). The antagonist did not influence the decrease in blood pressure caused by stroking (hatched columns in Fig. 3).

3.2.2. Effect of oxytocin

Basal blood pressure was significantly increased in response to 1 mg/kg of oxytocin but not by 0.01 and 0.1 mg/kg of oxytocin (Table 2). We chose the dosages of 0.01 and 0.1 mg/kg of oxytocin to investigate the effect of oxytocin on the response of blood pressure to stroking, since these dosages did not affect the basal blood pressure. The stroking effects on blood pressure were reduced after administration of 0.1 mg/kg of oxytocin as shown in Fig. 4A and B. As summarized in Fig. 4E (dotted columns), the effect of oxytocin on the response to stroking was observed in 4 animals between 15 min and 75 min after the injection. The maximum effect was seen 35 min after the injection. 0.01 mg/kg of oxytocin showed no effect on the response of blood pressure to stroking (data not shown). The inhibitory effect of oxytocin on stroking-induced

<table>
<thead>
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<th>Treatment</th>
<th>Time after drug administration (min)</th>
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<tr>
<td></td>
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<tr>
<td>OXY 0.01 mg/kg</td>
<td>116 ± 11</td>
</tr>
<tr>
<td>OXY 0.1 mg/kg</td>
<td>128 ± 3</td>
</tr>
<tr>
<td>OXY 1.0 mg/kg</td>
<td>123 ± 8</td>
</tr>
<tr>
<td>OA 0.1 mg/kg</td>
<td>129 ± 8</td>
</tr>
<tr>
<td>OA 1.0 mg/kg</td>
<td>119 ± 4</td>
</tr>
</tbody>
</table>

Values are mean ± SEM (n = 4). * P < 0.01, significantly different from preadministration control values using one-way ANOVA and the Fisher's post hoc test.
4. Discussion

The present study demonstrates that both arterial blood pressure and heart rate decreased following massage-like stroking of the abdomen in anesthetized rats.

The blood pressure and heart rate decreased immediately after the onset of the stroking of the abdomen in the present study, suggesting a neurally mediated response. We have previously reported that cutaneous brushing of the abdomen decreases efferent sympathetic nerve activity in anesthetized rats [2,12]. It is also possible that the blood pressure and heart rate decreased in response to stroking due to the direct mechanical compression of the vena cava. However, this possibility can be excluded because the decrease diminished after the administration of oxytocin. Taken together, these data strongly suggest that the decreases in blood pressure and heart rate caused by stroking were elicited, at least partly, via a reduction of the efferent sympathetic nerve activity.

The constancy of the manual stroking to the ventral and/or lateral parts of the abdomen was intermittently confirmed during experiment by similar application of pressure to a small balloon connected to a pressure gauge. Under this condition, stroking the ventral part of the abdomen elicited a bigger decrease in blood pressure than did the stroking of the lateral parts of the abdomen. This difference in response magnitude could be due either to a different density of somatosensory afferent innervation or to different patterns of connection between peripheral nerves and the central nervous system in these two areas. Furthermore, it is also possible that the stroking activates visceral afferents, and that the stimulation of the ventral part of the abdomen may excite these more than does stimulation of the lateral parts.
In a recent study we demonstrated that the massage-like stroking used in the present investigation increases withdrawal latency to heat and to mechanical stimulation [1]. The effect on withdrawal latency to heat stimuli was blocked by the previous administration of an oxytocin antagonist directed against the uterine receptor (1 mg/kg), as was the increase in withdrawal latency brought about by oxytocin injection [13]. However, the decreased blood pressure in response to stroking was not reversed by 1 mg/kg of the oxytocin antagonist in this study. These results indicate that, in contrast to the stroking-induced anti-nociception, the decrease in blood pressure caused by this stimulation does not involve intrinsic oxytocinergic transmission, or that a non-uterine type of oxytocinergic receptor is involved in this response. Furthermore, since the stroking induced anti-nociception was shown in conscious animals, and since the blood pressure response in the present experiments was investigated under anesthesia, it is also possible that anesthesia had inhibited the activity of oxytocinergic neurons.

In contrast to the lack of effect of the oxytocin antagonist, the lowering of blood pressure in response to stroking was lessened after oxytocin administration. This effect was itself antagonized by the oxytocin antagonist, indicating a possible inhibitory influence of oxytocin via the oxytocin receptor in this stroking-induced effect.

Plasma, as well as central oxytocin levels increase in response to various kinds of stress such as hemorrhage, ether inhalation, hypothermia and electric shock, etc. [3–6,14]. The present results indicate that the lowering of blood pressure in response to stroking may be reduced under stressful conditions in part by the elevated secretion of oxytocin.

In summary, massage-like stroking decreases blood pressure and heart rate by means of a reflex action. The same kind of non-noxious stimulation is able to reduce tail temperature [1], as well as catecholamine secretion from the adrenal gland [2], and to increase withdrawal latency [1] as well as oxytocin level in the peripheral plasma [18]. All these responses may reflect to the sedative effect of stroking demonstrated by Kanetake [8]. Further investigation of the autonomic, endocrine and behavioral responses to stroking are required.

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References


