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Circulating adrenaline released by sympathoadrenal activation elicits acute vasodilatation in the rat masseter muscle

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ARTICLE INFO

Article history:
Accepted 23 January 2009

Keywords:
Adrenal medulla
Splanchnic nerve
β-Adrenergic receptors
Anaesthetized rat
Jaw muscle

ABSTRACT

The present study was designed to examine the effects of circulating catecholamines released by sympathoadrenal system on the haemodynamics of the masseter muscle in deeply urethane-anaesthetized, artificially ventilated, cervically vagotomized and sympathectomized rats. Intravenous administration of adrenaline induced a biphasic change of blood flow in the masseter muscle (MBF). The change of blood flow showed an initial marked increase and successive slight decrease in a dose-dependent manner (0.01–1 μg/kg). The administration of noradrenaline had no significant effect on the MBF. The increase in the MBF evoked by exogenously applied adrenaline was markedly reduced by the intravenous administration of propranolol (100 μg/kg), whereas pretreatment with either hexamethonium (10 mg/kg), atropine (100 μg/kg), or phentolamine (1 mg/kg) failed to affect the MBF increase. Electrical stimulation of splanchnic nerve (SPLN) preganglionic neurones projecting to the adrenal medulla elicited frequency-dependent (1–20 Hz) increases in the MBF. The intravenous administration of the β_2-adrenergic receptor selective antagonist, ICI 118551 (0.5 mg/kg), almost abolished the MBF increase induced by SPLN stimulation, but pretreatment with the β_1-adrenergic receptor selective antagonist, atenolol (1 mg/kg), had no effect on this response. The results of the present study indicate that circulating adrenaline elicits acute vasodilatation through a β-adrenergic mechanism in the rat masseter muscle. Vascular β_2-adrenergic receptors in the masseter muscle may be activated preferentially by adrenaline released from the adrenal medulla, suggesting that the sympathoadrenal system is involved in the marked MBF increase during sympathoexcitation.

1. Introduction

Blood vessels in the rat masseter muscle are innervated by both parasympathetic vasodilator[1] and sympathetic vasoconstrictor fibres, similar to other orofacial tissues such as the lower lip[1–5] and submandibular gland.[4,6] The parasympathetic vasodilator response is a trigeminal mediated reflex,[1] whereas the sympathetic vasoconstrictor response is under tonic control from the superior cervical ganglion of the sympathetic trunk.[2] Therefore, vasomotor responses mediated by the autonomic nervous system regulates the basic physiological adjustments to haemodynamics in the masseter muscle.

Previously, we reported that electrical stimulation of sympathetic vasoconstrictor fibres consistently induces a frequency-dependent decrease of blood flow in the masseter muscle mediated by α-adrenergic receptors in the rat,[1,2] as

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0003–9969/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.archoralbio.2009.01.012

well as other animal species.[7,8] Further, we reported recently that parasympathetic reflex vasodilatation in the masseter muscle is markedly reduced by an increase in sympathetic activity.[2] These observations suggest that sympathoexcitation causes an inhibition of blood flow in the masseter muscle. However, sympathoexcitation with cold-pressor stimulation was reported to induce an increase in intramuscular blood volume in the human masseter muscle,[9] but the precise mechanism inducing this response is unclear. Cold-pressor stimulation has been reported to result in the release of adrenal medullary catecholamines through the sympathoadrenal system,[10–13] which is important in regulating the cardiovascular response by α- and β-adrenergic receptors under sympathoexcitation.[10,14] These studies suggest that the blood flow increase in the masseter muscle during sympathoexcitation is mediated by circulating catecholamines released by the sympathoadrenal system. However, it is unknown whether circulating catecholamines released by the sympathoadrenal system are involved in the vasodilator response in the masseter muscle under physiological conditions.

The present study was designed to examine the role of the sympathoadrenal system in the haemodynamics in the masseter muscle by investigating the effects of (1) exogenously applied catecholamines such as adrenaline and noradrenaline and (2) direct activation of the sympathoadrenal system using electrical stimulation of splanchnic nerve (SPLN) preganglionic neurones projecting to the adrenal medulla in deeply urethane-anaesthetized, artificially ventilated, cervically vagotomized and sympathectomized rats.

2. Materials and methods

2.1. Preparation of animals

Experiments were performed on adult male Wistar rats between 10 and 20 weeks of age and weighing 310–450 g. After induction with inhalation anaesthesia (ether), urethane (1 g/kg) in a volume of 1 ml/(100 g body weight) was injected subcutaneously into the back of the animals. One femoral vein was cannulated to allow drug injection, and one femoral artery was cannulated and connected to a Statham pressure transducer to monitor the systemic arterial blood pressure (SABP) and heart rate. The anaesthetized animals were intubated, paralysed by intravenous (i.v.) injection of pancuronium bromide (Mioblock; Organon, Teknika, The Netherlands; 0.6 mg/kg initially, supplemented with 0.4 mg/kg every hour or so after testing the level of anaesthesia; see below), and artificially ventilated by a tracheal cannula with a mixture of 50% air–50% O_2. The ventilator (model SN-480-7; Shinano, Tokyo, Japan) was set to deliver a tidal volume of 8.5–10 cm^3/kg at a rate of 20–23 breaths/min, and the end-tidal concentration of CO_2 was determined by means of an infrared analyser (Capnomac Ultima; Datex, Helsinki, Finland), as reported previously.[1–3] Rectal temperature was maintained at 37–38 °C with the use of a heating pad. Before the injection of additional pancuronium bromide, we checked that the depth of anaesthesia was adequate by the absence of a flexion response to a noxious stimulus, such as pinching the digit for approximately 2 s. When the depth of anaesthesia was considered inadequate, additional urethane (i.e., intermittent doses of 100 mg/kg, i.v.) was administered.

At the end of the experiment, all the rats were killed by an overdose (approximately 100 mg) of pentobarbital sodium. The experimental protocols were conducted in accordance with the Guidelines for the Care and Use of Laboratory Animals in the Health Sciences University of Hokkaido. All the animals were cared for in accordance with the recommendations in the current National Research Council guide.

2.2. Electrical stimulation of the lingual nerve and splanchnic nerve

The central cut end of the lingual nerve (LN) (Fig. 1a) and the peripheral cut end of the SPLN (Fig. 1b), which regulates catecholamine secretion from the adrenal medulla,[11,12,15] were electrically stimulated using a bipolar silver electrode attached to an electrical stimulator (model SEN-7103; Nihon Kohden, Tokyo, Japan). These nerves were isolated from surrounding tissues and sectioned unilaterally under a binocular microscope. The LN was stimulated for 20 s with supramaximal intensity (20 V) at 20 Hz using 2 ms pulse durations.[1] Electrical stimulation of the SPLN was delivered for periods of 1 min with supramaximal intensity (10 V) at various frequencies (1–20 Hz) using 2 ms pulse durations.[11,12] This period of SPLN stimulation was chosen because the levels of catecholamines released from the adrenal medulla have been reported to reach maximum values at around 20–30 s after onset.[11] The cervical vagi and sympathetic trunk were cut bilaterally in the neck before the experiments. This effectively ruled out the involvements of both vagal and sympathetic fibres as the effector in the present study.

2.3. Measurement of the blood flow and SABP

Changes in the blood flow in the masseter muscle (MBF) (Fig. 1c), lower lip (LBF) (Fig. 1d) and gracilis muscle (GBF) were monitored on either side using a laser-Doppler flowmeter (LDF; FLO-C1, Omegawave, Tokyo, Japan), as described elsewhere.[1–3] Parasympathetic reflex vasodilatations in both the masseter muscle and lower lip have been shown to be evoked by LN stimulation in the cat[3,5] and rat.[1,2] Therefore, these blood flows were recorded as controls for the evoked vasodilator responses in the present study. After incising the skin and identifying the muscle, the probes were placed against the muscle without exerting pressure on the tissue. The LDF values obtained by this method represent the blood flow in the superficial vessels in each tissue.[16,17] Electrical calibration for zero blood flow was performed for all recordings. Several gain levels could be selected and the maximum output of a particular gain level (defined electrically) was set as 100%. The analogue output of the equipment did not give absolute values, but indicated relative changes in blood flow (for technical details and an evaluation of the LDF method, see Stern et al.[18] The output from the devices was continuously displayed on an eight-channel chart recorder (model W5000; Graphtec, Tokyo, Japan) at a speed of 10 mm/min. The blood flow changes were assessed by measuring the height of the response. The SABP was recorded from the femoral catheter