A sympathetic hypertensive reflex from the heart of conscious dogs

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Summary

1. The aim of the present experiments was to study in conscious animals the effect of chemical stimulation of cardiac sensory innervation by bradykinin, a physiological substance known to activate both vagal and sympathetic cardiac sensory nerve endings, at doses devoid of systemic haemodynamic effects.

2. In conscious dogs with implanted catheters bradykinin (100 ng/kg) injected into a cannulated branch of the left coronary artery induced significant (P < 0.01, n = 5) reflex increases in mean arterial pressure and heart rate as well as increases in left ventricular pressure, left ventricular dP/dt max. and coronary blood flow.

3. These changes were obtained in the absence of pain reactions.

4. The concept, derived from experiments on anaesthetized animals, that chemical stimulation of the intact sensory supply of the heart always elicits a cardiovascular depressor reflex mediated by cardiac vagal afferents has to be modified, as pressor sympathetic reflexes may occur after an appropriate stimulus to the fully innervated heart of conscious dogs.

Key words: bradykinin, heart, pressor sympathetic reflex.

Introduction

In 1975 we advanced the hypothesis that excitatory cardiovascular reflexes mediated by sympathetic afferent nerves could be involved in the pathogenesis of arterial hypertension, as a disease of regulation [1]. However, a major limitation of the hypothesis was that it was based on experiments in anaesthetized and vagotomized cats [2]. Since then we have shown that physiological distension (~9%) of the descending thoracic aorta mediates a powerful pressor sympathetic reflex in the fully innervated conscious dog in the absence of pain reactions [3, 4]. These findings seem to support the hypothesis that positive feedback sympathetic reflexes initiated by the stimulation of aortic sympathetic mechanoreceptors might be instrumental in the maintenance of hypertension [5].

The role of stimulation of cardiac sympathetic afferent nerves [6] is more difficult to evaluate, as any stimulus applied to the heart could activate both vagal and sympathetic sensory endings. It is claimed that in such a case the vagally mediated depressor influences invariably predominate [7, 8]. However, the opposite can also be true, depending on the experimental conditions and the nature of the stimuli [9].

In the present experiments we studied in conscious animals the effects of chemical stimulation of the cardiac sensory innervation by bradykinin, a physiological substance known to activate both vagal [8] and sympathetic [10] sensory endings, at doses devoid of direct systemic haemodynamic effects.

Methods

Dogs were anaesthetized with pentobarbitone sodium (30 mg/kg intravenously) and, under aseptic conditions and with positive-pressure ventilation, a thoracotomy was performed in the fifth left intercostal space. A Tygon catheter was implanted in the thoracic aorta through a puncture, and secured with a suture. After the pericardium had been opened and with minimal dissection so as to avoid any damage to the pericoronary nerves, a small silicone (Dow
Corning) catheter was implanted by the technique described by Herd & Barger [11] in either the left anterior descending or circumflex coronary artery. In the latter case a Doppler flow probe was placed around the same coronary artery. Additionally a solid-state pressure gauge (Konigsberg) was implanted in the left ventricle, through the apical dimple. After closure of the thoracotomy all wires and catheters were exteriorized at the base of the neck.

Experiments were performed 1–3 weeks after surgery, when the animals were again vigorous and healthy. While the conscious, unrestrained dogs were lying on a recording table, systemic arterial, coronary artery and left ventricular pressure, left ventricular dP/dt, heart rate and left coronary blood flow were recorded continuously on magnetic tape and with a strip chart recorder, before, during and after the intracoronary injection of graded doses of bradykinin. This substance was freshly prepared for every experiment, the dose used being 30–100 ng/kg in a volume of 0.5–1.0 ml.

At the end of the experiments the intracoronary position of the catheter, the patency of the artery and lack of infarction of the myocardium perfused by it, were verified at autopsy.

Results are expressed as means ± se. Every animal underwent several (three to five) trials on different days. Significance of the changes from control was evaluated with the t-test for paired observations.

Results

In the conscious dog the intracoronary injection of bradykinin (100 ng/kg) produced a consistent pressor response in the absence of pseudoaffective reactions.

After a latency of approximately 15 s, significant (P < 0.01) reflex increases in mean arterial pressure (31 ± 3% from 85 ± 2 mmHg), and in heart rate (34 ± 3% from 84 ± 9 beats/min) were observed, together with increases in left ventricular pressure and dP/dt max. (33%) and coronary blood flow. It is important to mention that a pressor response was obtained when the injection of bradykinin was performed in either the left circumflex or left anterior descending coronary artery.

The reflex nature of the pressor response was shown by its disappearance after a-adrenoceptor blockade with phentolamine (1 mg/kg, intravenously).

In several trials larger doses of bradykinin (300–600 ng/kg) were injected into the can-
Sympathetic pressor reflex in conscious dogs

References


