MECHANISM OF THE BAINBRIDGE EFFECT

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Vagotomy and extirpation of the stellate ganglia did not prevent the development of tachycardia in response to injection of Ringer's solution into the jugular vein. This effect was particularly demonstrable after application of chemical compounds to the region of the sino-atrial node. The experimental results did not confirm the concept of a reflex mechanism (or at least, an extracardial mechanism) of the Bainbridge phenomenon, but they indicated an important role of the sino-atrial node in its formation.

The conclusion that reflex tachycardia develops to stretching of the orifices of the venae cavae was drawn by Bainbridge from the fact that intravenous injection of defibrinated blood or saline solution in a volume of between 50 and 300 ml into an anesthetized dog rapidly leads to an increase in the heat rate [8]. Other workers obtained similar results [6, 17]. However, some investigators question the existence of the Bainbridge reflex [1, 4, 9, 12, 13, 16, 18] and suggest that the possible mechanism of the increase in heart rates is by a change in the activity of the sino-atrial node [11-13, 16] or excitation of the receptors of the pulmonary vessels [4, 14].

The object of the present investigation was to determine whether the hypothetical reflex from the orifices of the venae cavae on the heart exists. The basic assumption made was that intravenous injection of large volumes of fluid, in Bainbridge's experiments, could involve several different parts of the cardiovascular system in the response very quickly: the orifices of the venae cavae, the right atrium with the sino-atrial node, the right ventricle, and the pulmonary artery.

EXPERIMENTAL METHOD

Experiments were carried out on 32 animals (cats and dogs) anesthetized with urethane (1-1.5 g/kg). Artificial respiration was applied, the anterior part of ribs III-V was removed, the atrial segments of the venae cavae were dissected, and the pericardium was opened. The stimuli consisted of 3 M solutions of sodium chloride and lactic acid, and acetylcholine in a concentration of 10^{-3} g/ml. The substances used in the experiments satisfied two conditions: they pass readily through biological membranes [7, 19], and their concentration was sufficient to excite not only chemoreceptors and mechanoreceptors [3, 5], but also afferent fibers directly [5].

Pieces of filter paper or swabs soaked with one of the above-mentioned solutions (37°C) were applied to the orifices of the venae cavae, to the right ventricle, to the pulmonary artery (area of application 0.5 × 2 cm), and to the region of the sino-atrial node (area of application 0.5 × 0.5 cm). The site of stimulation was rinsed with warm Ringer's solution. The interval between individual stimuli applied to different segments was about 15 min, and between stimuli applied to the same segment, not less than 1 h. The pressure in the femoral artery was recorded and the heart rate estimated from the first-order waves. Only those experiments in which the blood pressure remained stable after the procedure, but the heart rate could vary, were regarded as technically successful.

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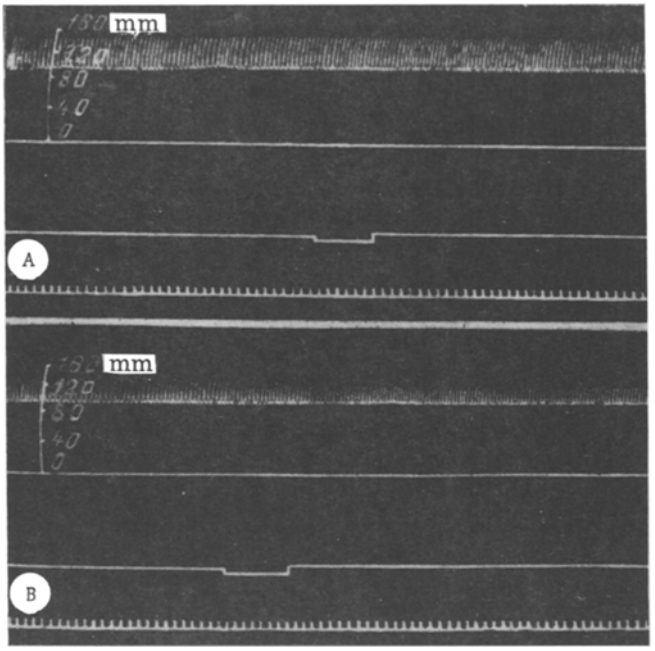

Fig. 1. Changes in the heart rate following injection of Ringer's solution into the jugular vein of a dog with intact innervation of its heart (A) and after vagotomy and extirpation of the stellate ganglia (B). From top to bottom: arterial pressure and zero line, marker of stimulation, time marker.

In series I (6 experiments) 5-50 ml Ringer's solution was injected into the jugular vein in the course of 8-10 sec. To determine the causes of the tachycardia, the heart was denervated, but in contrast with Bainbridge's experiments, in addition to bilateral vagotomy, the stellate ganglia with adjacent segments of the sympathetic chain were also removed in the neck.

In series II (9 experiments) the action of chemical and mechanical stimuli was studied. In the latter case (3 experiments), a rigid catheter was used. Although not interfering with the blood flow, this enabled the blood vessels and chambers of the heart to be stretched.

In series III (17 experiments) the animals received a preliminary intravenous injection of atropine (1 mg/kg) which prevented the development of bradycardia.

EXPERIMENTAL RESULTS AND DISCUSSION

After injection of Ringer's solution into the jugular vein tachycardia occurred in 4 of the 6 experiments and it persisted not merely after division of the vagus nerves in the neck, but also after bilateral extirpation of the stellate ganglia (Fig. 1). These results cast doubts upon the reflex origin of the Bainbridge effect.

In the experiments of series II, application of solutions of lactic acid, sodium chloride, or acetylcholine to the orifices of the venae cavae led to the development of bradycardia in 7 of 9 cases (Fig. 2A); in the other 2 experiments bradycardia did not develop. Application of these substances to the right atrium, the right ventricle, and the trunk of the pulmonary artery as a rule caused arrhythmia and bradycardia. Similar effects appeared on stretching the orifices of the venae cavae or the chambers of the right heart by means of a rigid catheter (Fig. 2B). The heart rate was reduced after application of sodium ions to the wall of the vein by 6±0.8 beats/min, and during slight stretching with the catheter it was reduced by 10±2.3 beats/min. However, during stretching of the orifices of the venae cavae by the rigid catheter there is no guarantee that the wall of the right atrium is not also stretched to some extent.

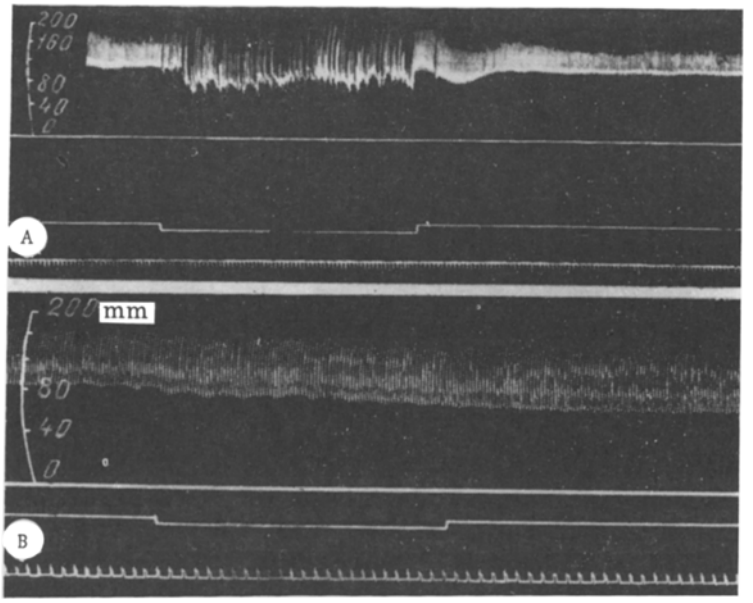

Fig. 2. Bradycardia evoked by stretching orifices of venae cavae by lactic acid solution (A) or by a rigid catheter (B). Legend as in Fig. 1.

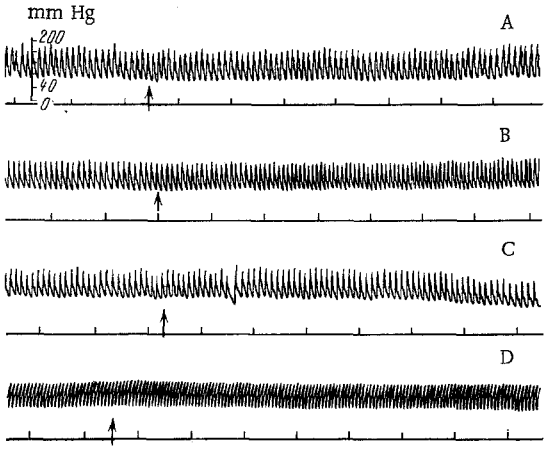

Fig. 3. Heart rate during stimulation of orifices of venae cavae (A), region of the sinoatrial node (B), the wall of the right ventricle (C), and the pulmonary artery (D) with lactic acid. From top to bottom: blood pressure, time marker (5 sec); arrow marks application of stimulus.

It was clear from Fig. 3A that application of lactic acid to the wall of the venae cavae after injection of atropine caused no increase in heart rate: before and after application the heart rate was 144/min. Tachycardia likewise did not develop, with one exception, in the other experiments, regardless of which substance was used for stimulation. In one experiment application of lactic acid to the orifices of the venae cavae increased the heart rate by 14 beats/min.

If the stimulus was applied to the region of the sinoatrial node, the heart rate was always increased. For instance, in the experiment recorded in Fig. 3B, application of lactic acid increased the heart rate by 30 beats/min. The increase in the heart rate during application of sodium ions averaged 27±7.6, during application of lactic acid, it averaged 25±2.9, and in response to acetylcholine the increase was 16±4.5 beats/min. Application of any one of these substances to the surface of the right ventricle was accompanied by tachycardia in 6 experiments (increases in heart rate 5-10 beats/min), while in 32 cases it caused no appreciable change in the heart rate. In the experiments of this group, the blood pressure rose, primarily through an increase in systolic pressure (Fig. 3C), indicating strengthening of inotropic influences [12].

Tachycardia developed in response to stimulation of the pulmonary artery after atropinization (Fig. 3D). The mean heart rate in 5 experiments with acetylcholine was increased by 10±3.1 beats/min. These results agree with those obtained by other workers [4].

One of Bainbridge's main conclusions is that the increase in heart rate in response to stretching of the orifices of the venae cavae is a reflex because it disappears after division of the vagus nerves. Judging from some of the records described by Bainbridge, the attempt to reproduce tachycardia after vagotomy took place in dogs in which the initial heart rate was about 200 beats/min [8]. However, to elicit Bainbridge's

phenomenon, the initial heart rate must be at a certain optimum level [10, 12]. In some of the present writers' experiments it was also noted that no increase in heart rate took place against the background of well-marked tachycardia.

Hence, after extracardial denervation of the heart, intravenous injection of Ringer's solution induces tachycardia. In the atropinized animal this effect appears systematically after application of the stimulus to the region of the sino-atrial node and pulmonary artery. Stimulation of two other areas, namely, the orifices of the venae cavae and the right ventricle, was rarely followed by tachycardia. On the whole, the increase in heart rate was most marked in response to stimulation of the sino-atrial node. This can be explained by direct stimulation of the tissue of the pacemaker and by an increase in its excitability [11-13, 16].

Depending on the frequency of the positive effect, zones whose stimulation induced tachycardia in Bainbridge's experiments were distributed as follows: the sino-atrial node, pulmonary artery, right ventricle, orifices of the venae cavae. After removal of the stellate ganglia and vagotomy, a positive chronotropic effect developed only in response to stimulation of the sino-atrial node.

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