CHANGES IN THE TONE OF THE VAGAL CENTER FOR THE HEART IN THE COURSE OF MORPHINE-ETHER ANESTHESIA IN ADULT DOGS

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Investigations carried out in this laboratory have shown that the reaction to stress-producing stimuli of various kinds in both puppies, after the age of 2.5-3 months at which time tonic excitation becomes established in the vagus center for the heart, and fully grown dogs is one of initial bradycardia followed by tachycardia [2-7, 11, 14]. Diphasic effects have also been demonstrated in the action of certain pharmacological agents, notably some narcotic substances [8-10, 12, 13]. A natural assumption is that the first phase of the reaction is connected with increased and the second phase with reduced vagal tone.

An attempt was now made to assess changes in the state of tonic excitation prevailing in the vagus center by recording outgoing impulse activity in fibers of the vagus nerve.

METHODS

The experiments were carried out on puppies of 3-6 months and fully grown dogs (43 animals in all). Morphine (10-20 mg/ kg) was injected and, after an interval, one vagus nerve was dissected out, divided at the level of the first rib and cleared of its membranes. In some experiments the vagus was separated from the sympathetic trunk. Freed from their membranes, fibers of the central part of the nerve were placed on the electrodes. Action potentials were recorded on a multichannel electromyograph. An ECG in standard lead II was recorded in the second channel of the instrument and action potentials from the diaphragm or external intercostal muscles in the third. As the results obtained with dogs between the ages of three and six months were similar to those for the fully grown animals, they are given in combined form.

RESULTS

Morphine was used as it produces a considerable degree of stable vagal tone. Parallel recording of electrocardiograms and impulse activity in the central part of the vagus could be expected to provide clear evidence of any relationship between changes in the rate of cardiac contractions and the nature of impulse activity in the vagus nerve. Initially, efforts were made to bring a small number of fibers (4-6) on to the electrodes with a view of recording synchronous impulse activity (Fig. 2, a), but this type of experiment was subsequently rejected as the elimination of fibers in which impulse activity was constant took a great deal of time. It was found better to record the irregularly spreading impulse activity of a large number of fibers (half or more) in the vagus nerve, and the results proved to be even more striking.

If the dissection had been carried out successfully, the slow "morphine" rhythm of the cardiac contraction, generally accompanied by respiratory arrhythmia, was usually associated with vigorous impulse activity in the vagus nerve. When the heart rate was reduced and respiratory arrhythmia increased by, say, continued absorption of morphine or a further injection of the preparation, intensified impulse activity could be observed in the nerve. Fig. 1a, and b, shows that slowing of the heart from 96 to 60 was associated with pronounced increase of impulse activity. Both impulse rate and amplitude were increased. The increased amplitude indicated that, when vagal tone was intensified, number of fibers carrying impulses was increased as well as the impulse frequency. Because of the pronounced respiratory arrhythmia, the rate of cardiac contractions was determined from counts made over periods of five minutes.

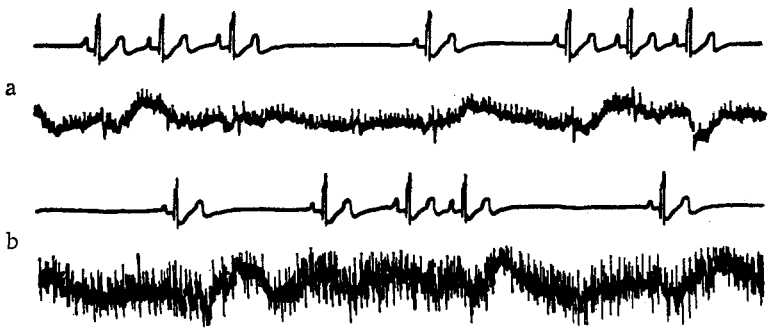

Fig. 1. Change in vagus impulse activity during bradycardia produced by injection of small (a) and large (b) quantities of morphine. Above—ECG; below—impulse activity in central part of vagus.

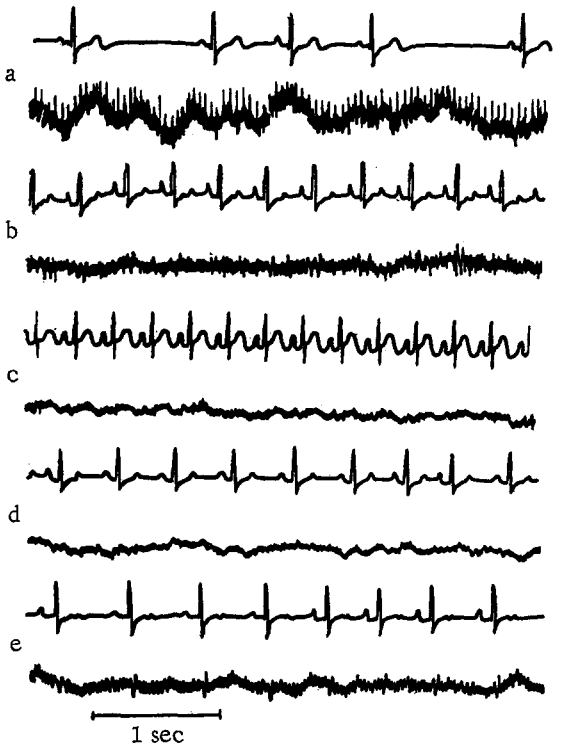

Fig. 2. Change in impulse activity in vagus nerve and in heart rate in various kinds of anesthesia; a) morphine; b) ether (light); c) ether (deep); d) urethane; e) chloral hydrate. Notation as in Fig. 1.

When the dog, exhibiting "morphine bradycardia," was switched to the inhalation of ether, there was, after the initial increase of vagal tone, cardiac acceleration, the degree of which depended on the depth of ether anesthesia. The development of tachycardia was associated with reduced impulse activity in the vagus nerve; when high rates were attained, impulse activity disappeared completely (Fig. 2b, c). Tachycardia also developed when other anesthetic substances were administered. Reduced impulse activity in the vagus nerve and tachycardia were observed when urethane and chloral hydrate were administered intravenously (Fig. 2d, e). It may be noted that the same heart rate was not necessarily associated with the same level of impulse activity in the vagus nerve (see Fig. 1).

These observations are of some importance in their bearing on changes in the nature of impulse activity in the vagus in respiratory arrhythmia. The latter is particularly marked when the heart is under the influence of morphine. The natural assumption is that cardiac acceleration in the phase of inspiration should be associated with reduced impulse activity in the vagus and slowing of the heart during expiration, with intensified activity. The actual picture is, however, somewhat more complex.

First of all, the usual form of sinus respiratory arrhythmia was recorded from the left vagus when the nerve on the right side was intact. When, however, impulse activity was recorded from the right vagus, the left being intact, it was found that there was typical atrioventricular block in the phase of expiration (Fig. 3a). The authors have already reported that this phenomenon can usually be recorded when the peripheral end of the divided left vagus is stimulated [1].

Three types of impulse activity in the vagus nerve associated with sinus respiratory arrhythmia were observed in our experiments. In some, impulse activity in the vagus remained unchanged in both inspiratory and expiratory phases (see Fig. 1a, b and Fig. 2a). In other experiments impulse activity increased immediately when inspiration ended. It was of short duration, however, and typical slowing during expiration developed after one (Fig. 3b) or after two cardiac contractions (Fig. 3c). In this case the inhibitory effect on the heart developed rather as an after-effect, and not synchronously. Figure 3c likewise shows that cardiac acceleration only developed towards the end of inspiration, and not at the beginning of the phase. In a third group of experiments impulse activity in the vagus

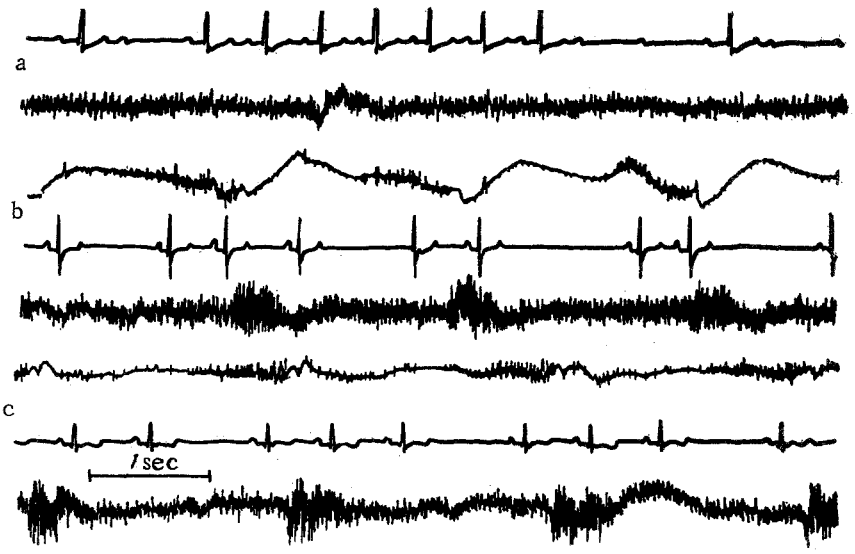

Fig. 3. ECG and impulse activity in central part of right vagus (left vagus intact) and change in impulse activity in different forms of respiratory arrhythmia. a) ECG and impulse activity in vagus; b) and c) respiration, ECG and impulse activity in vagus.

was already beginning to increase during inspiration and this activity ended in the early part of expiration, during which phase the heart rate again became slower.

Despite the obvious complexity of this somewhat variable relationship between the level of impulse activity in the vagus and the heart rate in respiratory arrhythmia these experiments did, however, establish that vagal tone was present in dogs from the age of three months and that there was a relationship between changes in the rate of cardiac contractions and the level of impulse activity in the vagus nerve. This relationship was a perfectly exact one in respect to the heart rate generally. It was, however, less evident when changes in the heart rate during inspiration and expiration (in respiratory arrhythmia) were compared with changes in the intensity of impulse activity in the vagus. At the same time, some authors suggest that the tachycardia associated with muscular work is the result of the direct action of adrenaline, brought by the blood, on the heart as well as of reduction of tone in the vagus nerve.

The present authors do not personally have any direct evidence of this.

They have observed, however, in many experiments that the heart in the phase of tachycardia produced by stress stimuli might exceed the rate seen after division of both vagus nerves or after atropinization. The following phenomenon was observed in this investigation. The administration of ether was followed by the development of persistent tachycardia, with associated arrest of impulse activity in the vagus nerve, and this was followed by a phase in which, during inspiration, the vagus center generated quite considerable impulse activity. Despite this, the heart rate remained unchanged during both inspiration and expiration.

These findings suggest that the phase of tachycardia which developed in these experiments was determined partly by inhibition in the vagus center, but also by the concurrent effect of catecholamines or other adrenaline-like substances discharged into the blood. The direct effect of these substances on the heart is probably so considerable that it cannot be overcome by the transient impulse activity developing periodically in the vagus center.

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