MODULATION OF VAGUS ESCAPE PHENOMENON BY AFFERENT VAGAL STIMULATION

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Summary: The present study was conducted on healthy adult mongrel dogs under chloralose urethane anaesthesia. After bilateral midcervical vagotomy, peripheral end of either vagus was stimulated continuously. This stimulation produced cardiac asystole followed by escape beats. Initially, the heart rate and arterial pressure were low, but both increased progressively and reached a steady-state level in 1-3 min while stimulation of peripheral vagus continued. During this plateau of vagus escape, stimulation of the central end of either vagus produced elevation of arterial pressure and cardio-acceleration. This modulation of vagus escape phenomenon by afferent vagal stimulation was reproducible.

Key words: vagus escape, arterial pressure, heart rate, afferent vagal stimulation, vagovagal reflex

INTRODUCTION

In an earlier work, (7), we have studied cardiac function during vagus escape and found that during continuous stimulation of peripheral vago-sympathetic trunk in dogs, a steady-state vagus escape is obtained in 1-3 min. During this plateau of the vagus escape, arterial pressure, heart rate and cardiac output are lower than the control, but the stroke volume is significantly increased.

In the present work, we have studied the effect of stimulation of the cut central end of the vago-sympathetic on the vagus escape phenomenon, as the relative role of various factors in the vagus escape mechanism is not well established. Also, the hemodynamic effects of central vago-sympathetic stimulation remain controversial. Some investigators have reported marked increase in arterial blood pressure (4) and an excitation of sympathetic efferent activity to the heart (14) on stimulation of central end of vagus. But the bulk of the evidence supports the view that afferent vagal stimulation leads to bradycardia and hypotension (1,2,3,5,8,9,12,13 and 15).
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MATERIALS AND METHODS

The present study was conducted on 11 dogs of either sex, weighing between 9.1 and 17.3 kg. The animals were anesthetized with chloralose (60 mg/kg) and urethane (300 mg/kg) given by slow intravenous injection. Tracheal cannulation was performed but the study was done on dogs breathing spontaneously. Both the common carotid arteries and vagosympathetic nerves were carefully dissected free in the middle of the neck. A polyethylene T-tube was positioned in one common carotid artery and its side limb connected to a mercury manometer to record carotid arterial pressure on Brodie-Starling (PALMER) kymograph. Heart rate was calculated from lead II electrocardiogram. Both the vagosympathetic nerves were bathed in mineral oil at 37°C.

Control heart rate and arterial pressure were recorded after bilateral midcervical vagotomy. The distal vagosympathetic on either side was placed on platinum bipolar electrodes and stimulated by Electronic Square Wave Stimulator (PALMER) at 50 Hz and 1 msec pulse duration. For each experiment the minimum strength of the stimulus producing cardiac stand-still followed by escape beats was determined and the stimulus actually delivered was 50% above that threshold. As a rule, it varied between 5 and 10 volts. Continuous stimulation of distal vagosympathetic produces "asytostole" followed by escape beats. When a steady-state of vagus escape was obtained, the central cut end of either vagosympathetic was stimulated at 50 Hz, 2 msec pulse duration and 5-15 volts to determine the effect of afferent vagal stimulation on the plateau of vagus escape.

RESULTS

The results are shown in Table I. The control recordings were taken about 1 hr after the induction of anaesthesia and after bilateral vagotomy. Mean heart rate was

![Carotid arterial pressure. From above downwards, arterial pressure: signal marker: time marker: B sec. A: Control after bilateral vagotomy. Downward deflection of the signal marker indicates the period during which cut distal vagus was stimulated. B: Plateau of vagus escape. Thick bars below the pressure tracing indicate stimulation of central vagus.](image-url)
160.8 ± 6.1/min. The mean arterial pressure was 102.4 ± 2.4 mm Hg. The effect of the efferent vagal stimulation on these parameters is shown in Figs. 1 and 2. In each dog, 3-5 observations were made and the results averaged. No significant difference was found between the effects of right and left vagosympathetic stimulation in this study. Stimulation of peripheral end of either vagosympathetic produced cardiac asystole within one or two seconds and the arterial pressure record registered a sudden and profound fall.

**TABLE I :** Heart rate and arterial pressure after bilateral vagotomy (V), during steady-state vagus escape (V.E.) and afferent vagal stimulation during the vagus escape (AFF. STI).

<table>
<thead>
<tr>
<th></th>
<th>V</th>
<th>V.E.</th>
<th>%change from V</th>
<th>AFF. STI</th>
<th>%change from V.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>160.8</td>
<td>54.1</td>
<td>-66.4</td>
<td>63.4</td>
<td>+17.1</td>
</tr>
<tr>
<td>Mean ± S.E.</td>
<td>±6.1</td>
<td>±3.7</td>
<td></td>
<td>±3.8</td>
<td></td>
</tr>
<tr>
<td>Art. Pr. (mmHg)</td>
<td>102.4</td>
<td>57.7</td>
<td>-43.7</td>
<td>97.0</td>
<td>+68.1</td>
</tr>
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<td>Mean ± S.E.</td>
<td>±2.4</td>
<td>±4.1</td>
<td></td>
<td>±5.6</td>
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</tr>
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However, the heart again started beating while the stimulation continued and this latency of vagus escape varied between 3-31 sec. During this vagus escape the heart rate and arterial pressure were much less initially but both increased progressively to reach a steady state level in 1-3 minutes. This plateau was maintained throughout the period of stimulation. During this plateau of vagus escape, the heart rate was 54.1 ± 3.7 as compared to the control value of 160.8 ± 6.1/min, mean deceleration being 66.4%. This is statistically significant, P value being < 0.001. Arterial pressure during the vagus escape was 100 ± 5.6 mm Hg, registering a profound fall of 43.7%.

In 1845 Weber demonstrated that vagovagal reflex that vagovagal reflex increased the heart rate and arterial pressure. In Chen et al. (3) indicated the excitatory effect and results have been obtained.

But on the other hand, Schwartz et al. (14) have observed that excitation of efferent vagal afferents produced vagovagal reactions. Chauvin (2) has demonstrated that vagovagal reactions caused marked increase in arterial pressure. It is interesting to note that the afferent vagal stimulation produces vagovagal reactions. Such observations and results have been obtained.

**Fig. 2 :** Heart rate and arterial pressure during steady-state vagus escape and afferent vagal stimulation during vagus escape. Control is taken after bilateral vagotomy and expressed as 100%.
mm Hg. The effect of Figs. 1 and 2. In each no significant difference in this study.

During steady-state vagus escape (AFF. STI).

<table>
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<tr>
<th>V</th>
<th>AFF. STI</th>
<th>%change from V.E.</th>
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<tr>
<td>4</td>
<td>63.4</td>
<td>+17.1</td>
</tr>
<tr>
<td>1)</td>
<td>±3.8</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>7</td>
<td>97.0</td>
<td>+68.1</td>
</tr>
<tr>
<td>11)</td>
<td>±5.6</td>
<td>(P&lt;0.001)</td>
</tr>
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</table>

During continued and this latency period the heart rate progressively to reach a steady state compared to 54.1±3.7 as compared being 66.4%. This is statistically significant (P<0.05).

DISCUSSION

In 1845 Weber brothers demonstrated the dramatic cardioinhibitory effect of vagal stimulation. But even today, the relative role of various factors in the vagus escape mechanism is not well established. The hemodynamic effects of central vagal stimulation also remain controversial. According to the textbooks of physiology the activity in afferent vagal fibers causes bradycardia and hypotension (1). This is supported by bulk of the literature (2,3,5,8,9,12,13,15).

In 1900-1901, Brodie and Russell (2) demonstrated that the excitation of central ends of different branches of vagus produces reflex cardiac inhibition. According to Rushmer (13) stimulation of internal organs can involve vagal afferents producing bradycardia and even drastic cardiac inhibition as a result of vagovagal reactions. After studying 1200 cardiac arrest cases, Stephenson (15) observes that vagovagal reflex is responsible for as many as 25% of such cases. The results of Chen et al. (3) indicate that the collective influence of vagal afferents can produce a vasodilatory effect and have a restraining influence on systemic arterial pressure. Similar results have been obtained by Öberg and White (9).

But on the other hand, Cotten and Moran (4) found that central vagal stimulation caused marked increase in arterial pressure due to reflex increase in sympathetic activity. Schwartz et al. (14) have demonstrated that the stimulation of cardiac afferents leads to excitation of efferent sympathetic outflow to heart. The afferent limb of this cardio-vagal reflex passes through sympathetic and vagal nerves. Our experimental observations reported in this paper are in agreement with the findings of Cotten and Moran (4) and show that the afferent vagal stimulation can produce cardio-acceleration and a rise in arterial pressure. It is interesting to note that in all the observations in the present series of experiments, we obtained only one type of response i.e. cardio-acceleration and a rise in arterial blood pressure on afferent vagal stimulation during the steady-state vagus escape. Ledsome and Linden (6) have demonstrated that an increase in the perfusion pressure of atrial pouch causes tachycardia and that the afferent pathway for this reflex is in the vagus. Such observation and the present study differs from the observations of other workers (2,3,13,15) and that of Öberg and White (9) who believe that the vagal afferents exert a tonic restraint on the medullary vasomotor center and that the stimulation of cardiac nerves...
generally induces a profound bradycardia. Mancia et al. (8) have concluded that the receptors in the cardio-pulmonary region with their afferents in the vagus exert a continuous restraint on the sympathetic adrenergic outflow to the capacitance and resistance vessels. Daly et al. (5) have found that inflation of the lungs causes vasodilatation and hypotension. Pillsbury et al. (12) are of a similar opinion.

We invariably got tachycardia and a rise in arterial pressure by afferent vagal stimulation when the literature reports that the central vagal stimulation can produce either tachycardia and hypertension or bradycardia and hypotension and that the latter type of response has been reported by the bulk of the literature. Paintal (10,11) has classified the vagal afferents according to their conduction velocity and reflex effects. Some of the afferents produce bradycardia and/or hypotension while others produce tachycardia and/or hypertension. It is quite possible that by using the same stimulation parameters (5-15 volts, 2 msec pulse and 50 Hz) in all the experiments, we might have stimulated only those vagal afferents whose reflex effects are tachycardia and hypertension.

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REFERENCES