Modulation of neurocardiac function by oesophageal stimulation in humans

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(Received 10 May/12 August 1996; accepted 20 September 1996)

1. The heart and the oesophagus have similar sensory pathways, and sensations originating from the oesophagus are often difficult to differentiate from those of cardiac origin. We hypothesized that oesophageal sensory stimuli could alter neurocardiac function through autonomic reflexes elicited by these oesophageal stimuli. In the present study, we examined the neurocardiac response to oesophageal stimulation and the effects of electrical and mechanical oesophageal stimulation on the power spectrum of beat-to-beat heart rate variability in male volunteers.

2. In 14 healthy volunteers, beat-to-beat heart rate variability was compared at rest and during oesophageal stimulation, using either electrical (200 µs, 16 mA, 0.2 Hz) or mechanical (0.5 s, 14 ml, 0.2 Hz) stimuli. The power spectrum of beat-to-beat heart rate variability was obtained and its low- and high-frequency components were determined.

3. Distal oesophageal stimulation decreased heart rate slightly (both electrical and mechanical) (P < 0.005), and markedly altered heart rate variability (P < 0.001). Both electrical and mechanical oesophageal stimulation increased the absolute and normalized area of the high-frequency band within the power spectrum (P < 0.001), while simultaneously decreasing the low-frequency power (P < 0.005).

4. In humans, oesophageal stimulation, whether electrical or mechanical, appears to amplify respiratory-driven cardiac vagoafferent modulation while decreasing sympathetic modulation. The technique provides access to vagoafferent fibres and thus may yield useful information on the autonomic effects of visceral or oesophageal sensory stimulation.

INTRODUCTION

In humans, indirect evidence suggests that events occurring in the gastrointestinal tract influence cardiovascular function. Atypical chest pains, palpitations, syncope and other symptoms usually associated with cardiac pathology, often occur in the presence of gastrointestinal disorders including motility disorders, gastroesophageal reflux, dyspepsia and functional bowel disorders. In these conditions, it is often difficult to distinguish between symptoms originating from gastrointestinal and cardiovascular sources [1, 2]. Although the initial sensory stimulus may originate from the gastrointestinal tract, the integrated autonomic response to the gastrointestinal sensory input may produce clinically relevant changes in the efferent neural traffic to the heart and thereby produce symptoms.

In animals, it has previously been shown that sensory stimuli originating from the gut or other viscera can alter cardiac function. Colonic distension increases heart rate and arterial pressure in anaesthetized dogs [3], and in the rat, gastric distension also affects heart rate and blood pressure. Grundy and Davison [4] reported that gastric distension initially decreases, but subsequently increases heart rate, through vagal and sympathetic pathways respectively. In humans, the effects of gastrointestinal stimulation on cardiac autonomic function remain unknown. In particular, the effects of controlled oesophageal stimulation on neurocardiac function have not been examined. The vagal and sympathetic innervation of the oesophagus and the heart are closely related and there are numerous visceral afferent fibres originating in the distal oesophagus, thereby providing the afferent pathway through which oesophageal events may influence cardiac autonomic behaviour.

Sensitive methods now exist for the study of neurocardiac function in humans. While measurements of heart rate and arterial pressure may provide some index of autonomic outflow, more precise methods exist to assess the relationship or balance between sympathetic and vagal modulation of sino-atrial function. The power spectrum of the beat-to-beat variability in heart rate is a frequency

Key words: autonomic nervous system, heart rate variability, oesophageal stimulation, power spectrum analysis, visceral perception.

Abbreviations: AUC, area under curve; HF, high frequency; LF, low frequency.

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transformation from the standard ECG signal; it provides a non-invasive signature of efferent autonomic output. This method has been validated, and provides a clinically useful measurement of autonomic function [5, 6]. Power spectral analysis allows differentiation of two frequency bands representing the modulatory influence of sympathetic and vagal neural output on cardiac rhythm [7]. The high-frequency power (0.2-0.4 Hz) represents respiratory-driven vagal efferent output to the heart, while the low-frequency power band (0.05-0.15 Hz) is largely influenced by sympathetic modulation [8, 9].

We tested the hypothesis that oesophageal stimulation elicits a vagoaferent response which modifies the relative balance between the vagal and sympathetic components of neurocardiac modulation as expressed by the power spectrum of heart rate variability in healthy male volunteers. This was achieved by examining the effects of electrical stimulation and balloon distension of the oesophagus on heart rate and beat-to-beat variability.

**MATERIALS AND METHODS**

**Subjects**

Fourteen healthy male volunteers (aged 18–39 years) comprised the study group. All fasted overnight before the study, which took place between 09.00 and 11.00 hours. A complete medical history and physical examination excluded anyone with gastrointestinal, cardiac or neurological disease. Subjects refrained from smoking, alcohol, caffeine or any medication for 14 days before the study.

Written informed consent was obtained from each subject. The protocol was approved by the Ethics and Research Advisory Committees of McMaster University Medical Centre.

**Oesophageal stimulation**

To provide electrical and mechanical stimulation, we used a 12 French modified manometry catheter (Wilson-Cook Medical, Winston-Salem, NC, U.S.A.). A silastic rubber balloon (2 cm in length), placed 5 cm proximal to the distal end of the assembly, provided intermittent oesophageal balloon distension. Electrical stimulation of the oesophagus was performed using a stimulating electrode made of stainless steel wire wrapped around the manometric tube immediately proximal to the balloon (diameter, 7 mm; width, 7 mm).

Electrical stimulation was carried out using a 16 mA, 200 μs square wave stimulus delivered at a rate of 0.2 Hz, for 128 s, through an electrostimulator normally used for somatosensory-evoked potential studies (Somatosensory Probe, Bio Logic Systems, Mundelein, IL, U.S.A.). Intermittent oesophageal balloon distension was achieved using a customized pump (Air Pump 2; Wilson-Cook Medical). This pump can provide rapid (170 ml/s) inflations. A 14 ml volume was administered for a distension time of 0.5 s, at a rate of 0.16 Hz for 128 s. With this distension volume, the outer diameter of the balloon was 2.5 cm. These parameters are identical to parameters we have previously found to produce a definite perception of the stimulus, and reproducible cortical-evoked responses, but below those associated with pain [10–12].

After positioning the balloon and stimulating electrode in the distal oesophagus (5 cm proximal to the lower oesophageal sphincter), the patient was allowed to settle comfortably for 10 min. Electrical stimulation was performed for a period of 128 s, followed by a rest period of 10 min. Electrical stimulation was performed twice more; each followed by a rest period. After the third rest period, three series of intermittent balloon distensions were performed, each followed by a 10 min rest period. The assembly was then withdrawn 15 cm and the entire protocol repeated in the proximal oesophagus. Each individual sequence (rest, electrical or balloon stimulation, proximal or distal oesophagus) was recorded separately for subsequent analysis.

The duration of the stimulation period has previously been determined to be optimal between 120 and 240 s, as the response and the signal are stable during recordings of such duration [7].

**ECG recording, monitoring and data acquisition**

To examine the effects of oesophageal stimulation on heart rate and beat-to-beat variability, ECG recordings were obtained during each period, using three limb leads placed in the lead II configuration. The signal was amplified using a Hewlett-Packard 7807E amplifier, and fed to a continuous data acquisition system on a personal computer where the amplified analog ECG signal was displayed continuously (frequency response of ECG recording = 0.5–100 Hz). A 12-bit analog-to-digital converter digitized the ECG recording at a rate of 0.5 kHz, for further processing on an 80486-based personal computer (DataQ Instruments, Akron, OH, U.S.A.). The QRS complex was detected using a special detection algorithm described previously [13, 14]. Each sequence was also examined by direct visual inspection for the presence of ectopic beats, but in our healthy volunteers, none was observed. Mean heart rate was measured for every recording period at rest, and during electrical and balloon stimulation. Power spectral analysis was then performed on each series, using a ninth-order autoregressive model. The number of coefficients was constant for all studies [7]. The following indices obtained from the power spectral data were then analysed separately: the peak power spectral density, the central frequency of low-frequency (LF) and high-frequency (HF) peaks, the normalized area under the LF and
HF bands (area under curve, AUC) at rest and during electrical or mechanical stimulation. For analysis of the absolute LF and HF power, the normalized area under the LF and HF bands was used.

**Statistical analysis**

One-, two- and three-way analysis of variance, as appropriate, were applied to the heart rate and power spectral data for each parameter of interest (central frequency, AUC and power spectral density) to separate the variability within subjects from the variability between subjects and between stimuli. A paired t-test compared the power spectral response at rest with those during electrical or balloon stimulation. A P-value <0.05 was considered to be statistically significant.

Mean heart rate values were determined using the RR interval between each QRS complex for each subject individually. All data are given as means ± SD.

**RESULTS**

**Effects of oesophageal stimulation on cardiac rhythm**

When the effects of proximal and distal stimulation were analysed separately, there was a small but significant effect of distal oesophageal electrical and balloon stimulation on heart rate (P<0.005), while proximal oesophageal stimulation had no effect (Fig. 1), but overall, there was no difference between the mean heart rate at rest and during electrical or balloon stimulation. There was a small but significant rebound in heart rate on cessation of distal oesophageal electrical stimulation (P<0.001) and balloon distension (P<0.001) in the period immediately after stimulation.

Neither mode of stimulation produced any dysrhythmia. The QRS complex and PR interval were identical before, during and after either electrical or mechanical stimulation.

**Effects of oesophageal stimulation on the instantaneous heart rate record**

An example of the effect of oesophageal stimulation on instantaneous heart rate is shown in Fig. 2. There was a small but significant decrease in average heart rate (P<0.005), but the effects of oesophageal stimulation were much more pronounced on the beat-to-beat variance of heart rate. Overall, the mean variance in instantaneous heart rate significantly decreased during electrical stimulation (from 4.821 ± 0.245 beats/min to 3.756 ± 0.181 beats/min, P<0.001) and during balloon distension (from 4.821 ± 0.245 beats/min to 3.988 ± 0.242 beats/min, P<0.02). The beat-to-beat variance also significantly increased immediately upon stopping the stimulus when compared with the variance observed before or during electrical stimulation (5.762 ± 0.147 beats/min, P<0.001) or balloon distension (6.478 ± 0.226 beats/min, P<0.001). Both proximal and distal oesophageal stimulation had similar effects on RR variance.

**Effects of oesophageal stimulation on power spectral analysis of heart rate variability**

The typical power spectra observed at rest and during electrical and balloon stimulation are illustrated in Fig. 3. The specific cardiac responses to oesophageal stimulation in terms of peak amplitude (power spectral density), frequency and area (AUC) are detailed in Table 1 for the LF peak and Table 2 for the HF peak.
**Effects of oesophageal stimulation on LF (sympathetic) peak.** The central frequency of the LF peak significantly increased during electrical ($P<0.05$) and balloon ($P<0.05$) stimulation (Table 1 and Fig. 4). There was a significant rebound decrease in the LF central frequency in the rest period after either electrical ($P<0.05$) or balloon stimulation ($P<0.001$). The effect was similar with proximal and distal oesophageal stimulation.

The area of the LF band decreased by 12% during electrical stimulation ($P<0.05$) and by 18% during balloon stimulation ($P<0.05$) (Table 1 and Fig. 4).

Table 1. Effect of oesophageal stimulation on the LF power of heart rate variability. Statistical significance: *$P<0.05$ compared with response during resting period, \( ^{b}P<0.05 \) compared with response during electrical stimulation, \( ^{c}P<0.001 \) compared with response during balloon distension, \( ^{d}P<0.005 \) compared with response during electrical stimulation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oesophageal location</th>
<th>Rest</th>
<th>Electrical stimulation</th>
<th>Recovery period</th>
<th>Balloon distension</th>
<th>Recovery period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak amplitude</td>
<td>Distal</td>
<td>N/A</td>
<td>64.83 ± 3.50</td>
<td>70.66 ± 2.97</td>
<td>51.86 ± 4.64 ( ^{d} )</td>
<td>76.19 ± 3.86</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>62.32 ± 4.51</td>
<td>72.46 ± 3.73</td>
<td>56.66 ± 6.71 ( ^{b} )</td>
<td>69.51 ± 8.41</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>75.61 ± 4.04</td>
<td>63.58 ± 2.70 ( ^{a} )</td>
<td>71.56 ± 2.40 ( ^{b} )</td>
<td>54.26 ± 3.63 ( ^{d} )</td>
<td>72.85 ± 3.50 ( ^{a} )</td>
</tr>
<tr>
<td>Central frequency</td>
<td>Distal</td>
<td>N/A</td>
<td>9.869 ± 0.234</td>
<td>9.247 ± 0.199</td>
<td>10.307 ± 0.311 ( ^{d} )</td>
<td>8.813 ± 0.259</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>9.869 ± 0.302</td>
<td>9.077 ± 0.250</td>
<td>9.707 ± 0.450 ( ^{b} )</td>
<td>8.669 ± 0.564</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>9.143 ± 0.265</td>
<td>9.869 ± 0.196 ( ^{a} )</td>
<td>9.181 ± 0.159 ( ^{a} )</td>
<td>10.114 ± 0.261 ( ^{c} )</td>
<td>8.791 ± 0.245 ( ^{c} )</td>
</tr>
<tr>
<td>Normalized area</td>
<td>Distal</td>
<td>N/A</td>
<td>50.61 ± 1.43</td>
<td>57.96 ± 1.21</td>
<td>44.95 ± 1.89 ( ^{d} )</td>
<td>60.36 ± 1.57</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>50.49 ± 1.84</td>
<td>57.62 ± 1.52</td>
<td>49.50 ± 2.74 ( ^{c} )</td>
<td>59.10 ± 3.43</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>56.48 ± 1.61</td>
<td>50.56 ± 1.19 ( ^{b} )</td>
<td>57.83 ± 0.96 ( ^{b} )</td>
<td>46.61 ± 1.58 ( ^{d} )</td>
<td>60.17 ± 1.48 ( ^{a} )</td>
</tr>
</tbody>
</table>

Fig. 3. Typical power spectral representation of beat-to-beat variability for 128 s epochs in a single healthy volunteer before (interrupted line), during and after oesophageal stimulation (solid line). Note the presence of two distinct peaks (LF and HF) with respective central frequencies of 0.1 Hz and 0.25 Hz on a normal power spectral representation (interrupted line). During electrical stimulation or balloon distension, the relative power (amplitude) of the LF band is markedly decreased while the relative power of the HF band is nearly doubled.
Table 2. Effect of oesophageal stimulation on the HF power of heart rate variability. Statistical significance: \( \ast P<0.05 \) compared with response during resting period, \( \ast \ast P<0.001 \) compared with response during electrical stimulation, \( \ast \ast \ast P<0.001 \) compared with response during balloon distension, \( \ast P<0.05 \) compared with response during electrical stimulation, \( \ast \ast P<0.05 \) between distal and proximal sites.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oesophageal position</th>
<th>Rest</th>
<th>Electrical stimulation</th>
<th>Recovery period</th>
<th>Balloon distension</th>
<th>Recovery period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak amplitude (beats/min²/Hz)</td>
<td>Distal</td>
<td>N/A</td>
<td>48.27 ± 2.89</td>
<td>38.36 ± 2.45</td>
<td>62.39 ± 3.71 ( \ast \ast \ast )</td>
<td>31.21 ± 3.18</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>50.60 ± 3.72</td>
<td>39.10 ± 3.07</td>
<td>49.32 ± 5.14 ( \ast \ast \ast )</td>
<td>40.27 ± 6.94</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>40.44 ± 3.38</td>
<td>49.44 ± 2.30 ( \ast \ast \ast )</td>
<td>38.73 ± 2.03 ( \ast \ast \ast )</td>
<td>55.85 ± 4.45 ( \ast \ast \ast \ast )</td>
<td>36.74 ± 3.64 ( \ast \ast \ast \ast )</td>
</tr>
<tr>
<td>Central frequency (10⁻² Hz)</td>
<td>Distal</td>
<td>N/A</td>
<td>22.51 ± 0.60</td>
<td>22.96 ± 0.51</td>
<td>21.39 ± 0.80</td>
<td>20.77 ± 0.66</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>22.04 ± 0.77</td>
<td>22.54 ± 0.64</td>
<td>19.97 ± 1.15</td>
<td>23.29 ± 1.44</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>21.97 ± 0.69</td>
<td>22.28 ± 0.51</td>
<td>22.75 ± 0.41</td>
<td>20.68 ± 0.68</td>
<td>21.61 ± 0.64</td>
</tr>
<tr>
<td>Normalized area (%)</td>
<td>Distal</td>
<td>N/A</td>
<td>49.39 ± 1.43</td>
<td>42.04 ± 1.21</td>
<td>55.05 ± 1.89 ( \ast \ast \ast \ast )</td>
<td>39.64 ± 1.57</td>
</tr>
<tr>
<td></td>
<td>Proximal</td>
<td>N/A</td>
<td>49.51 ± 1.84</td>
<td>42.38 ± 1.52</td>
<td>50.50 ± 2.74</td>
<td>40.90 ± 3.43</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>43.52 ± 1.61</td>
<td>49.44 ± 1.19 ( \ast \ast \ast \ast )</td>
<td>42.17 ± 0.96 ( \ast \ast \ast \ast )</td>
<td>53.59 ± 1.58 ( \ast \ast \ast \ast )</td>
<td>39.83 ± 1.48 ( \ast \ast \ast \ast )</td>
</tr>
</tbody>
</table>

Fig. 5(top). The effect was greater with balloon distension than with electrical stimulation in the distal oesophagus \( (P<0.05) \) but the effects of either modality were similar at the proximal site. There was a significant rebound increase in the LF area after cessation of either electrical or balloon stimulation (13% and 23% respectively, \( P<0.001 \) for both).

Effects of oesophageal stimulation on HF (vagal) peak. There was no difference in the central frequency of the vagal (HF) peak during either electrical or balloon stimulation (Table 2). There was no difference in the rate or pattern of breathing between rest and stimulation.

Electrical and balloon stimulation both increased the mean area and peak amplitude of the HF band \( (P<0.005 \) and \( P<0.001 \) respectively) [Table 2 and Fig. 5(bottom)]. The area of the HF band rapidly returned to baseline (resting) values in the period after stimulation. The effect of balloon stimulation on the HF area was greater than the effect of electrical stimulation at the distal site, but in the proximal site the effects of either forms of stimulation were comparable \( (P<0.02) \) (Table 2).

Effects of oesophageal stimulation on LF/HF area ratio. Overall, the ratio of the normalized LF/HF area markedly decreased during both electrical and
vagal modulation as shown by a significant decrease in the absolute power in the HF band of the heart rate autospectrum. There was also a significant decrease in the absolute power within the LF band, indicating a possible sympathetic-inhibitory effect. We also observed a significant rightward shift in the central frequency of the LF peak, a finding consistent with a vagal effect [15]. However, oesophageal stimulation did not produce a measurable shift in the central frequency of the HF peak as would have been expected if the effect on cardiac vagal tone was due to a direct entrainment of the breathing frequency by oesophageal stimulation. This suggests that the effect is due to afferent pathways originating from the oesophagus, rather than by synchronization of the breathing frequency via oesophageal ‘pacing’.

We have previously shown in humans that direct electrostimulation of the left cervical vagoafferent nerves increases cardiac vagal modulation [13, 16], and obtained reproducible cortical-evoked responses during left vagal electrostimulation, due to activation of vagal afferent pathways [17]. We have subsequently shown that intermittent oesophageal mucosal electrostimulation produced a similar cortical-evoked response [12, 18]. These findings suggest the involvement of similar vagoafferent pathways in both instances (vagal and oesophageal stimulation). The findings of DeVault et al. [19], who reported that the cortical-evoked responses obtained after oesophageal mechanical stimulation in healthy volunteers and in quadriplegic patients with complete cervical transection were comparable, further support the involvement of vagoafferent pathways during oesophageal stimulation. The magnitude of the neurocardiac responses to electrical and balloon oesophageal stimulation observed in the present study is comparable to the neurocardiac effect of left vagal stimulation [13] and probably involves the same afferent and efferent vagal pathways. The changes in cardiac autonomic function are greater with distal than with proximal oesophageal stimulation, particularly with balloon distension. This observation could suggest a denser sensory innervation of the distal oesophagus, a higher threshold to mechanical stimulation in the proximal oesophagus, or a different balance in the integrated response of the sympathetic and vagal pathways to stimulation of different oesophageal regions.

Oesophageal stimulation does not result in any dysrhythmia and the overall effect on heart rate is small. Furthermore, the effect of mechanical or electrical stimulation is similar, implying that the response to oesophageal stimulation more than likely occurs through a reflex arc rather than through a direct cardiac effect across the oesophageal wall.

The potential limitations of our experimental approach should be examined. Heart rate was stable before and during each stimulation period, and movement minimized, but it is possible that random noise or movement artefact could have interfered with our signal processing. We have separately confirmed that our automated detection algorithm corresponded to the actual number of beats in each sample. The signal processing, transform methods and autoregressive coefficients used in the present study have been validated previously [20]. In the present study, the stimulation frequency was close to the respiratory frequency, and entrainment of the HF peak could have resulted. We have preliminary evidence showing that, over a wide range of stimulation frequencies (0.1–1 Hz), oesophageal stimulation had a consistent effect on the HF peak over the whole range, showing that the effect is not merely due to entrainment [21].

In anaesthetized rats, gastric distension transiently decreases heart rate and arterial blood pressure, but sustained stimulation eventually increases arterial pressure [4], Abdominal (subdiaphragmatic) vagotomy abolishes the cardiovascular effects of gastric distension, showing that vagal afferent pathways are involved, but others have questioned the importance of vagal afferent pathways in the cardiovascular response to gastric stimulation [22]. In cats, splanchnic sympathetic pathways mediate the cardiovascular effects of gastric distension, a
response that was not affected by prior vagotomy [23]. In pigs, gastric distension increases heart rate and arterial blood pressure [24]. Atropine had no effect on these responses, which were prevented by prior abdominal vagotomy, showing that the afferent input travels via vagal afferent pathways but that cholinergic, vagal efferent pathways are not necessary. Since bretylium tosylate, a sympathetic ganglionic blocker, blocked the response to gastric distension, sympathetic efferent pathways are probably involved [25]. It is likely that, in pigs, the response is mediated differently than in rats, involving a reflex arc that includes vagal afferent and sympathetic efferent pathways. In our study, heart rate and blood pressure are not markedly influenced by oesophageal stimulation. Marked alterations in autonomic balance will eventually affect heart rate and blood pressure [26, 27], but the power spectral analysis of heart rate variability is a more sensitive method of assessing modulatory adjustments in sympatho-vagal balance [7, 9, 28].

Since previous studies have established the involvement of vagal afferent pathways in the mediation of the cortical-evoked responses to oesophageal stimulation using identical stimulation parameters to those used in the present study, and since the overall cardiac response to the same stimuli primarily involves vagal efferent pathways, we suggest that the response in humans involves a vago-vagal reflex, similar to the pathways previously reported with gastric distension in rats [4, 29].

In humans, direct vagoafferent electrostimulation increases cardiac vagal modulation and decreases heart rate slightly [13, 16]. This effect occurs with chronic as well as acute, short-term stimulation [17]. It is quite possible that more intense oesophageal stimulation, in particular mechanical stimulation, could elicit significant changes in heart rate. Events such as bradycardia are a common occurrence during procedures such as endoscopy and colonoscopy which may be associated with intense mechanical distension.

The reflex changes in sympato-vagal balance observed in the present study are not merely of statistical significance but are qualitatively and quantitatively similar to those observed under physiological conditions such as simulated flight [30] or exercise [9]. High sympathetic cardiac tone, or, alternatively, depressed HR variance secondary to reduced vagal tone, is strongly associated with an increased incidence of sudden cardiac death after myocardial infarction [31]. This increased mortality correlates with a decrease in heart rate variability and an increase in cardiac sympathetic tone, believed to be a predisposing factor to ventricular fibrillation in patients with myocardial infarction [32]. Conversely, high vagal tone appears to be protective under experimental conditions and in high-risk patients predisposed to sudden cardiac death [33].

While our study examined the effect of oesophageal stimulation on cardiac autonomic function, it is likely that similar effects occur with stimulation of other parts of the gut, or from other vagally innervated viscera. The vagally mediated effects of oral and pharyngeal stimulation on gastric acid secretion are probably mediated along the same pathways as well [34].

The potential role of oesophageal events in the generation of recurring chest pain has been studied [35]. Primary oesophageal motor events such as high-amplitude contractions (nutcracker oesophagus) or diffuse oesophageal spasm have been implicated in many patients [36]. Oesophageal mucosal irritation can also produce angina-like chest pain in some patients [37]. More recently, evidence has accumulated to associate angina with abnormalities of the coronary microcirculation but without direct evidence of large vessel coronary disease; an entity termed microvascular angina [38]. In a subgroup of patients with microvascular angina, a high association also exists between abnormal oesophageal motor events, changes in microvascular circulation and chest pain. The findings in the oesophagus and in the heart may be epiphenomena, or perhaps related to a generalized abnormality of visceral nociception as suggested previously [39]. In some patients, another possible explanation is that oesophageal stimulation may produce reflex changes in the cardiovascular neural balance, possibly resulting in the production of symptoms such as those found in microvascular angina.

Afferent neural pathways closely associated with cardiac and visceral innervation constitute the sensory link between these organs and the central nervous system. The autonomic and sensory innervation of the oesophagus and of the heart are closely related. It is known that many gut reflexes, such as stimulated acid output due to sham feeding and gastric receptive relaxation, occur through reflex arcs involving sensory afferent as well as efferent vagal pathways. Our study indicates that it is possible to alter the cardiac autonomic balance through oesophageal stimulation in healthy volunteers. Whether these responses can be altered in patients with angina-like or atypical chest pain remains to be examined.

ACKNOWLEDGMENT

We thank the Medical Research Council of Canada, and the De Groote Foundation.

REFERENCES


