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Acute pain increases heart rate: Differential mechanisms during rest and mental stress

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Abstract

The main aim was to investigate if acutely stressed subjects have abnormal heart rate variability responses to acute pain. Efferent cardiac autonomic activity was assessed by analyzing RR interval variation in 26 male volunteers. Heart rate variability was measured as mean and standard deviation of normal RR intervals (mean RR, SDNN) and by power spectral analysis where high frequency (HF) and low frequency (LF) power were used as indexes of vagal function and of sympatho-vagal interaction, respectively. Coefficient of component variance in the LF and HF bands (CCV-LF, CCV-HF) was estimated to adjust for possible influences of different mean RR levels on power amplitude. Subjects received painful and non-painful sural nerve stimulations during rest, during attention to pain, and during mental stress. Our results show that pain significantly decreased mean RR and increased LF power and CCV-LF during rest and during attention to pain. SDNN, HF power, and total power were not affected by pain. During mental stress, pain significantly decreased mean RR but failed to affect other heart rate variability parameters. We conclude that acute pain induced efferent cardiac sympathetic activation during rest and during attention to pain as LF power and CCV-LF increased without alterations of pure vagal heart rate variability measures. During mental stress, pain inhibited mean RR without changing heart rate variability measures suggesting that pain does not increase efferent cardiac sympathetic activity during mental stress. Pain induced decrease of mean RR during mental stress may be caused by the release of catecholamines into the systemic circulation.

Keywords: Attention; Autonomic nervous system; Heart rate variability; Humans; Mental pressor test; Neurohumoral activity; Pain

1. Introduction

Noxious stimuli and the resulting pain affect the activity of the sympathetic nervous system. The sympathetic activation pattern is characterized by an instantaneous defense behavior with piloerection, sweat secretion, increases in heart rate, blood pressure, cardiac output, and blood flow in skeletal muscles and corresponding blood flow reductions in skin, kidneys, and splanchnic region (Janig, 1985, 1995). As a biochemical correlate to such stress, catecholamines are released from the adrenal medulla into the circulation together with other metabolic changes (Pacak et al., 1998). In experimental studies, painful sural nerve stimulations have been used to induce a spinal polysynaptic defense response characterized by heart rate increases and withdrawal of the extremity away from the noxious stimulus, the so-called nociceptive withdrawal reflex (Terkelsen et al., 2004).

Other threatening stimuli than noxious stimuli can elicit defense behavior. Mental arithmetic (Freyschuss et al., 1988; Lindvall et al., 1991) such as the Paced Auditory Serial Addition Task (PASAT) (Gronwall and Wrightson, 1974) induces circulatory reactions resembling the classical defense reaction and has been utilized as a laboratory psychological stressor (McCann et al., 1993).

Thus, both pain and acute mental stress can induce major cardiovascular changes. Prior chronic stress is known to

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alter cardiovascular responses to acute stress (Konarska et al., 1989). However, it is unknown if prior acute stress alters the heart rate variability responses to a second acute stressor like pain. This question is clinically relevant because subjects in acute pain are often simultaneously in a highly stressful situation. For example, when soldiers wounded in battle or patients exposed to major injuries like traumatic amputations or lacerations fail to experience pain at the time of the injury (Melzack et al., 1982). The mechanisms behind this analgesic effect are not known in detail, but both humoral and neural mechanisms may be involved (Lewis et al., 1981; Randich and Maixner, 1984).

In the present study, heart rate variability was used to describe mechanisms involved during pain and psychological modulation. Oscillatory changes in efferent autonomic cardiac activities cause heart rate variability, measured as a variation in time (RR intervals) between consecutive heartbeats (Akselrod et al., 1981; Pomeranz et al., 1985; Task Force, 1996). By using power spectral analysis of RR intervals, pure vagal respiratory-dependent activity is assessed by the HF power (0.15–0.4 Hz) (Akselrod et al., 1981; Pomeranz et al., 1985; Hayano et al., 1991) while baroreflex-dependent sympatho-vagal modulation is estimated by LF power (0.04–0.15 Hz) (Pomeranz et al., 1985; DeBoer et al., 1987). Heart rate variability is proposed to characterize, quantitatively, autonomic nervous system regulation of cardiovascular activity (Pomeranz et al., 1985) and has made it possible to separate cardiac parasympathetic activity from sympathetic activity.

In the present study, we have determined how pain and psychological modulation like attention and mental stress interact on cardiac function using power spectrum analysis of heart rate variability as marker of sympathetic and parasympathetic activity. The main aim is to investigate the heart rate variability responses in acutely stressed subjects exposed to a second painful stressor.

2. Materials and methods

2.1. Subjects

The experiment was carried out on 26 healthy male volunteers (mean age 24 years, range 21–31 years) with a normal 12-lead electrocardiogram (ECG). Subjects had mean systolic blood pressure of 116 mmHg (range 100–130), mean diastolic blood pressure of 64 mmHg (range 50–75), and mean BMI of 22 kg m^{-2} (range 17–28). None were taking any medication or suffered from neurological, cardiovascular, or psychiatric disorders. They refrained from smoking, alcohol, and coffee the last 12 h, excessive physical activity the last 24 h, and did not participate in medical experiments the previous month. The investigation conforms to the principles outlined in the Declaration of Helsinki (WMA Inc., 1997), and the Local Ethical Committee approved the study (No. 97/4036). Subjects received a thorough written and oral explanation describing the experiment but not the purpose of the study, and they signed an informed consent document. Four subjects were excluded (abnormal ECG in two, anxiety in one, rheumatic disease in one). The remaining 26 subjects completed the study. All subjects were participants of a study eliciting the nociceptive withdrawal reflex by painful sural nerve stimulation (Terkelsen et al., 2004).

2.2. Sural nerve stimulation

The methods for sural nerve stimulation and estimation of the nociceptive withdrawal reflex threshold have been described in detail previously (Andersen et al., 1996; Terkelsen et al., 2001). Briefly, solid gel surface electrodes (Neuroline disposable 700 01-SC, Medicotest, Oelstykke, Denmark) were placed on the right foot at the distal cutaneous area of the sural nerve. In the experimental sessions, painful and non-painful sural nerve stimulations were randomly delivered in a time span between 13 and 17 s as trains of five 1-ms constant current rectangular pulses, repeated at 200 Hz.

Electrical detection, pain, and unpleasantness thresholds were defined as the point where the subject first feels the electrical stimulus, the point where the stimulation changes to a sharp pinprick-like pain, and the point where the stimulation changes to unpleasantness, respectively. Perception thresholds were estimated by a staircase-limit method, consisting of three series of increasing and decreasing stimuli. Mean electrical detection threshold was 1.3 mA (range 1.0–2.1). Mean electrical unpleasantness and pain thresholds were 6.3 mA (range 1.6–13.9) and 6.8 mA (range 2.6–14.3), respectively.

At experimental sessions of non-painful sural nerve stimuli, subjects were stimulated with intensities below their individual electrical pain and unpleasantness threshold and above mean electrical detection threshold. At intermittent painful sural nerve stimulation, subjects were stimulated with intensities of mean 31.9 mA (range 15 to 69) corresponding to 1.5 times the intensity eliciting the nociceptive withdrawal reflex. This high stimulus intensity ensured that subjects received a clear painful stimulus eliciting a defense response.

2.3. Numeric pain rating scale

Subjects received a numeric rating scale (NRS) consisting of 10 levels for rating pain. Zero was defined as “no pain”, whereas 10 was defined as “maximal imaginable pain”.

2.4. Continuous recording of heart rate

By electrocardiography (lead II), 3-min segments of beat-to-beat QRS complexes were sampled at 1000 Hz with surface electrodes (L-00-S blue sensor, Medicotest) connected to an ECG-amplifier.