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Electrocardiogram, Vectocardiogram and Body Surface Maps in Patients with Panic Disorder

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Summary

An increased risk of myocardial ischemic changes was demonstrated in patients suffering from panic disorder (PD). Using classical ECG methods, this risk cannot be evaluated in most patients. We measured the vectocardiogram (VCG) using Frank orthogonal leads and body surface maps (BSM) including 12-lead ECG. In our study of 11 PD patients (2 men, 9 women), without any seizures and pharmacological treatment and without cardiovascular symptoms, we found marked sinus tachycardia (heart rate 90.1±12.2 min^{-1}) and a shorter R-R interval (678±93.6 ms) than in 27 controls (heart rate 73.6±7.7min^{-1}, R-R 822.7±86.4 ms) (5 men, 22 women) ($p<0.001$). The VCG measured spatial QRS-STT angle was more opened (70.3±24.5°) than in the control group (49.5±19.5°) ($p<0.05$). The maximum (extremum) in depolarization (DIAM max 30, 40) and repolarization (RIAM max 35) of body surface isoarea and isointegral (RIIM max) maps was less positive ($p<0.001$) and the minimum (DIAM min 40) was less negative than in the controls ($p<0.05$) even in the period free of a panic attack. Our results showed the changes in the heart electric field parameters occurred in PD patients when compared to the control group.

Key words
Panic disorder • ECG • VCG • Body surface maps

Introduction

Panic disorder (PD) is a common condition that includes symptoms which can resemble primary cardiovascular disease. PD includes recurrent episodes of sudden and unpredictable apprehension and is associated with such symptoms as dyspnea, palpitations, chest pain, choking and sweating. Because these symptoms mimic several medical conditions (e.g. cardiovascular disease), patients suffering from PD are frequent users of medical services.

On the other hand, many patients with cardiovascular disease also suffer from PD. No definitive pathophysiological mechanism for PD has yet been found (Jeejeebhoy *et al.* 2000). The prevalence of PD in both cardiology out-patients and patients with documented coronary artery disease (CAD) generally ranges from 0 % to 59 % (Kuijpers *et al.* 2000a). By a prospective questionnaire investigation in 83 % of the patients who visited First Heart Aid with cardiac complaints but not of cardiac origin, the PD or depression was diagnosed (Kuijpers *et al*. 2000b). According to another study of

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80 Emergency Department patients with primary complaints of chest pain, 48 % concerned noncardial chest pain and no CAD (Aikens *et al.* 1999). Out of the patients without known heart disease referred to out-patient clinics for investigation of chest pain in Norway, 38 % met the criteria for PD (Dammen *et al.* 1999). In an other study from Leiden it was shown that 39 % PD patients out of 2648 patients complained of unexplained chest pain (Van Peski-Oosterbaan *et al.* 1998).

The differences in cognition during chest pain of patients with PD and ischemic heart disease have been studied (Fraenkel *et al.* 1996-97), if the complaints of chest pain in PD patients are different from true angina pectoris symptoms. The authors concluded that the presence of frightening cognitions in the presence of chest pain, particularly at the onset of the clinical problem, makes psychiatric evaluation necessary with objective exclusion of PD (Fraenkel *et al.* 1996-97). However, patients with PD often complain of angina-like chest pain during panic attacks. In two out of three documented PD patients, cardiac ischemia progressed to myocardial infarction (Mansour *et al*. 1998).

It is also noteworthy that patients with PD have increased cardiovascular morbidity and mortality (Šimon 1999, Hofmann *et al.* 1999, Gorman and Sloan 2000, Fleet e*t al.* 2000, Potokar and Nutt 2000).

The risk of stroke in persons with lifetime diagnosis of PD was more than twofold of over that in persons with other or no psychiatric disorder (Weissman *et al*. 1990). Recent studies of men with an elevated level of anxiety (according to the Anxiety Symptom Scale) have proved that the risk of sudden cardiac death is distinctly higher in these men than in the control group (Kawachi *et al.* 1994, Fraenkel *et al.* 1996-97, Mansour *et al.* 1998).

An increased risk of cardiovascular disease in PD patients may be associated with an increased occurrence of cardiovascular risk factors (hypertension, smoking, high blood cholesterol level, low levels of exercise, psychological and/or other pathophysiological risk factors of PD).

The study of ECG body surface maps (BSM) in ontogeny of healthy persons (Green *et al.* 1985, Kozmann *et al.* 1989, 1999, Slavíček *et al.* 2001) and in coronary artery disease (Kittnar *et al.* 1993), in hypertension (Tichý *et al.* 2001), or in patients treated with antidepressants (prominent adrenergic action) was used (Slavíček *et al.* 1995, 1998, Paclt *et al.* 1995) for the detection of changes in the heart electric field. But the heart electric field parameters in PD patients have not yet been extensively studied (Paclt *et al.* 2000).

In the present work, we registered the 12-lead ECG, VCG and the BSM in patients suffering from PD without any attacks during the examination, without cardiovascular symptomatology and without pharmaco-logical PD treatment. These were compared with a control group of healthy persons with the aim to find differences in their heart electric field parameters.

Methods

Two groups of patients were evaluated:

1. Out-patients with diagnosis of PD without cardiovascular symptoms and pharmacological treatment. The Hamilton Anxiety Scale was ≥25 in each patient during the assessment (n=11, 2 men and 9 women, age 38.6±10.8 years). The patients were examined by a cardiologist with negative results.

2. The control group consisted of volunteers without any cardiovascular or psychiatric disease in their medical history (n=27, 5 men and 22 women, age 36.9±9.8 years) also examined by a cardiologist. There were differences in the number of men and women in the controls and the PD patients. For this reason a) men and women were compared in the controls, b) 22 control women were compared with 9 PD women only, c) the PD group (2 men, 9 women) was compared with 5 men and 22 women of the control group (Table 1), because similar results were obtained in b) as in c).

In both groups of persons, normal lipemia, blood pressure and blood glucose were found. The control group consisted of non-smokers and in 10 % of PD patients 10 cigarettes per day were smoked. Electro-cardiogram (ECG), vectocardiogram (VCG) in frontal, transversal and left sagittal plane were recorded and isopotential, isointegral and isoarea maps were registered using the diagnostic system CARDIAG 112.2. (Kittnar *et al.* 1993, Kittnar and Šťovíček 1993, Slavíček *et al.* 1995, 1998, Paclt *et al.* 1995). Forty-nine parameters were evaluated. The following characteristics were obtained:

ECG: Heart rate (min^{-1}), PQ, QRS, QT, QTc, RR intervals duration (ms).

VCG: the Frank orthogonal leads were used: QRS axis and QRS-STT angle in the frontal, transversal and left sagittal plane were measured. Spatial angle of QRS-STT was computed by diagnostic system Cardiag.

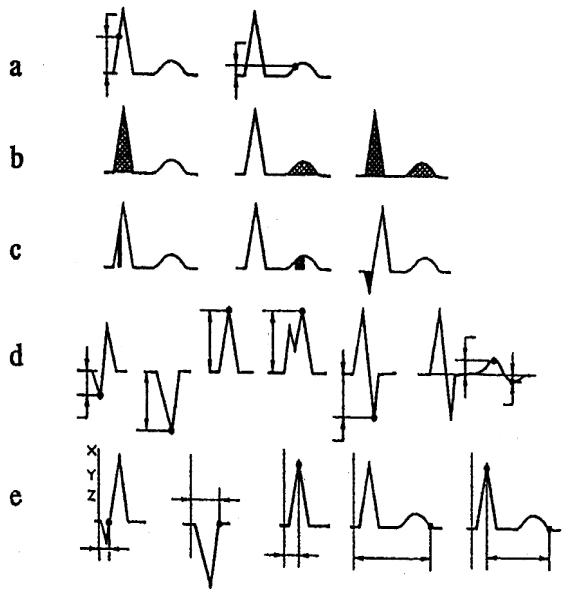

Fig. 1. *Types of body surface maps of electric heart activity according to the values shown in the maps. a – isopotential (depolarization, repolarization), b – isointegral (depolarization, repolarization, of the whole ventricular Q and QS waves), c – isoarea (depolarization, repolarization), Q wave d – of asynchronous potential maxima and minima (of Q and QS waves, of R1 wave, R2 wave, S wave, T1 or T2 wave), e – isochronal (duration of Q and QS wave, ventricular activation time, duration of ventricular electric activity QT/QTc, duration of ventricular repolarization RT/RTc)*

ECG body surface potential maps (BSPM, Fig. 1): Depolarization, repolarization isopotential maps (DIPM, RIPM), their maximum and minimum in μVs. Depolarization, repolarization and total isointegral maps, their maximum and minimum values in μVs (DIIM max, DIIM min, RIIM max, RIIM min, DRIIM max, DRIIM min). Depolarization isoarea maps, their maximum and minimum in μVs (isointegral maps from the beginning of QRS to the 30th and 40th ms of depolarization – DIAM max 30, DIAM min 30, DIAM max 40, DIAM min 40), repolarization isoarea maps, their maximum and minimum in μVs (isointegral maps from the point J to the 35th and 80th ms of repolarization - RIAM max 35, RIAM min 35, RIAM max 80, RIAM min 80). Maximum amplitude of R wave in μV (IPMAM-R). Activation time in ms between the beginning of depolarization in the orthogonal lead and maximum of R wave in individual chest leads (ICHVAT). Map of Q duration in ms (Q-ICHM, Stojan 1991a,b, Stojan *et al.* 1993). The localization of maximum and minimum (extreme values) on the surface of the thorax was evaluated. Statistical comparisons were made using Student´s two-sample T-test.

Results

The results showed significant changes of several parameters in PD patients when compared to the control group (Table 1).

The differences of other parameters were not significant (not shown in the Table). In PD patients, a marked sinus tachycardia and shortened R-R interval was observed. The opening of transversal QRS-STT angle and spatial QRS-STT angle in PD patients was significant, but its absolute value was below 90 degrees, the value for development of global ischemia. Less positive maximum (extreme) depolarization (DIAM) and repolarization (RIAM) isoarea maps, even in the period free of a panic attack was observed. The minimum (extreme) was less negative in depolarization isoarea map of PD patients (DIAM min 40), while the minimum in repolarization isoarea map (RIAM min 35) was less negative in the controls. Thus, in patients with PD, both depolarization and repolarization phases of the heart cycle were affected.

The localization of extreme values on the surface of thorax (RIIM max, RIAM max 35, RIAM min 80) was different in PD patients as compared to the controls ($p<0.05$): the mean maximum (extreme in repolarization isointegral map (RIIM max) of controls was situated in the position of Wilson electrode V5, while the same value of PD patients was in the V3 electrode position. The maximum (extremum) in repolarization isoarea map (RIAM max 35) of control persons was located in the position of Wilson V3 electrode, while in PD patients to the V2 electrode. Two minimums (extremum) in repolarization isoarea map (RIAM min 80) were placed in the controls on the surface of thorax: on the right anterior thorax (2nd intercostal space, in right medioclavicular line) and on the back thorax (second intercostal space in the right scapular line). In PD patients one extreme (minimum) was on the posterior thorax (second intercostal space in the left scapular line).

Table 1. The comparison of heart electric field parameters in patients with PD and in controls

	Controls n=27	**Panic disorders n=11**	**p Significance level**
Heart rate (min^{-1})	73.6 ± 7.7	90.1 ± 12.2	0.0001
R-R (ms)	822.7 ± 86.4	678.0 ± 93.6	0.001
Transversal QRS-STT angle (degrees)	–46.1 ± 30.0	–82.4 ± 36.4	0.01
Spatial angle QRS-STT (degrees)	49.5 ± 19.5	70.3 ± 24.5	0.01
RIIM (μV)	63.9 ± 22.6	42.5 ± 15.8	0.01
DIAM MAX 30 (μVs)	5.42 ± 2.0	3.01 ± 1.3	0.001
DIAM MAX 40 (μVs)	12.0 ± 4.4	7.34 ± 3.4	0.01
DIAM MIN 40 (μVs)	–4.8 ± 1.7	–3.54 ± 1.3	0.05
RIAM MAX 35 (μVs)	3.67 ± 0.9	2.96 ± 0.9	0.05
RIAM MIN 35 (μVs)	–1.43 ± 0.5	–2.07 ± 0.7	0.05

Mean ± S.D., n - number of persons. Heart rate (min^{-1}). R-R interval (ms). Transversal QRS-STT angle – QRS-STT angle in the transversal (horizontal) plane of VCG. Spatial angle QRS-STT – space QRS-STT angle computed from VCG (degrees). RIIM max – the absolute value of maximum (extreme) in repolarization isointegral map (T wave – μVs). DIAM max 30 – the absolute value of maximum (extreme) in depolarization isoarea map (isointegral map from the beginning of QRS to 30th ms of depolarization – μVs). DIAM max 40 – the absolute value of maximum (extremum) in depolarization isoarea map (isointegral map from the beginning of QRS to 40th ms of depolarization – μVs). DIAM min 40 – the absolute value of minimum (extremum) in depolarization isoarea map (isointegral map from the beginning of QRS to 40th ms of depolarization – μVs). RIAM min 35 – the absolute value of minimum (extremum) in repolarization isoarea map (isointegral map from the point J to 35th ms of repolarization – μVs).

Discussion

Our results have shown changes of some heart electric field parameters in PD patients without cardiovascular diseases symptomatology (Table 1). The increased heart rate and shortening of the R-R interval in PD patients is probably due to activation of the adrenergic system, blocking of cholinergic innervation and loss of autonomic nervous system control. There is a link between psychopathology, anxiety disorders and heart disease (Gorman and Sloan 2000). Patients with PD have a higher rate of sudden cardiac death than those from the average population.

It would be expected that noradrenergic modulation would have large effects on anxiety and anxiety disorders including PD. In panic disorder, α_2 probes, that increase noradrenergic function (e.g. yohimbine - an antagonist that blocks noradrenergic autoreceptors). have the effect of precipitating panic attacks in about 60 % of PD patients and about 5 % of the controls (Charney *et al*. 1984).

The specific serotonine reuptake inhibitors (SSRI) are convenient for treating PD similarly to depressions, which are emerging as a first line choice for the treatment of PD (Kuijpers *et al.* 2000a, Potokar and Nutt 2000, Gorman and Sloan 2000).

Until now, we have not found reports studying in detail the heart electric field parameters in PD patients. The effect of PD on heart electric field parameters in the present work was comparable to the effect of tricyclic antidepressants in therapeutic doses (amitriptyline, dosulepin), which increased the heart rate (antimuscarinic effect) by blocking the cholinergic and stimulating the adrenergic system (Slaviček *et al.* 1995, 1998, Paclt *et al.* 1995, Kitzlerová *et al.* 2003). The spatial angle between integral vectors QRS and STT is an indicator of adrenergic tonization of the working myocardium (Andrásyová *et al.* 1998).

The opening of spatial angle QRS-STT in our PD patients depends on the different depolarization and repolarization pattern. Although the difference in the spatial angle was significant, its absolute level (70.3°) in PD patients is less than the value of 90°. Global ischemia, left ventricular overload and hypertrophy is diagnosed when the QRS-STT angle is greater than 90° (Ruttkay-

Nedecky 1983, MacFarlane and Lawrie 1989, Stojan 1991a, Horinaka *et al.* 1993).

The absolute maximum and minimum values in ECG body surface depolarization and repolarization isoarea maps are convenient for measuring local depolarization and repolarization changes, disclosing the regularity of local activation and recovery. Significant differences of the parameters (Table 1) were found by the more sensitive method of BSM than the classical 12-lead ECG for detecting changes in local activation and repolarization. The decrease in repolarization isointegral map extreme and the change of their localization on the surface of the thorax were recently found in CAD positive patients (Kittnar *et al.* 1993). Our results confirmed the opening of VCG space QRS-STT angle by the different localization of extreme values of isointegral and isoarea maps in PD patients when compared with the controls.

In summary, in our PD patients (38.6±10.8 years old) the measurement of heart electric field parameters showed differences in local depolarization and repolarization patterns during the period free of panic attack in comparison with the controls. A further investigation of PD patients during the panic attack, when the adrenergic effect is more prominent, and measurements of BSM parameters during the treatment of PD (the adrenergic effect is decreased) could be suitable for explaining the pathophysiological mechanism of PD as a possible risk factor for cardiovascular diseases.

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Reprint requests

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