ORIGINAL ARTICLE

Sweat: a potential marker of clinical activity in panic disorder

Peter Kukumberg [1], Peter Valkovic [1,2], Pavel Blazicek [3], Anton Guth [4], Jana Martinkova [1], Vit Provaznik [5], Fedor Jagla [2*]

1. 2nd Department of Neurology, Comenius University, Bratislava;
2. Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava;
3. Department of Laboratory Medicine, TOP-MED a.s., Bratislava;
4. Department of Rehabilitation, Slovak Medical University, Bratislava;
5. Psychiatric Outpatient Department, Bratislava; Slovak Republic

Correspondence to: Fedor Jagla, M.D., Ph.D.
Institute of Normal and Pathological Physiology, Slovak Academy of Sciences
Sienkiewiczova 1, 81371 Bratislava, Slovak Republic
TEL.: +421/2/52926276; FAX: +421/2/52968516; EMAIL: fedor.jagla@savba.sk

Submitted: 2009-06-11 Accepted: 2009-07-01 Published online: 2009-09-01

Key words: **panic disorder; sweat; blood; clinical symptoms; sauna; neuropsychiatric disorders**

Neuroendocrinol Lett 2009; **30**(3): 400–402 **PMID:** 19855367 NEL300309A12

Abstract

OBJECTIVE: Panic disorder (PD) is a paroxysmal neuropsychiatric disorder with unclear etiology and obscure pathophysiology. Despite the frequency of its occurrence, PD still has no reliable laboratory markers. The sweat is a neglected human secrete reacting immediately to various neurovegetative challenges including psychic imupulses. We hypothesized a possible dysfunction of sweat homeosthasis in PD. **SUBJECTS AND METHODS:** 10 patients with active PD, 9 patients with PD in remission and 11 age-matched controls participated in this study. All subjects underwent a single 8-min session in the dry-heat sauna. Sweat and venous blood have been collected immediately after the end of this session. Concentrations of lactate, glucose, creatinine, natrium, potassium, chlorine, calcium and magnesium have been quantitatively estimated in both liquids and compared statistically among three groups. **RESULTS:** We did not find any significant difference in blood parameters of the three above groups. However, the patients with active PD had significantly higher sweat levels of lactate, glucose, creatinine and magnesium than both the other groups which did not differ. Moreover, sweat concentrations of natrium, potassium and chlorine were significantly higher in active PD comparing to the group of PD patients in remission. **CONCLUSIONS:** The sweat of patients with active PD in comparison to PD in its clinical remission exhibits surprisingly distinctive changes of selected parameters after dry-heat sauna exposure. Increased concentrations of lactate, glucose and magnesium in the sweat are not contradictory with presupposed neurotransmitter-metabolic firing mechanisms in PD. These findings appear to be perspective biochemical markers in PD and its course.

INTRUDUCTION

Panic disorder (PD) is a paroxysmal neuropsychiatric disorder with unclear etiology and obscure pathophysiology. Despite the frequency of its occurrence, PD still has no reliable laboratory markers. Sweating, however, is a typical feature of panic attacks (American Psychiatric Association, 1994). It is also an alternative mechanism to hyperventilation by which the body induces systemic alkalosis. Sweat might thus play a role in the pathophysiology of panic attacks (Janszky *et al.*

Table 1. Demographic data and the results of descriptive (mean ± SD) and comparative statistics (Tukey´s HSD post-hoc test).

	VALUES			STATISTICS		
	PD-act	PD-rem	Controls	PD-act vs.PD-rem	PD-act vs. Controls	PD-rem vs. Controls
Age (years)	33.0 ± 10.0	32.1 ± 9.6	33.2 ± 8.8			
Sex (M/F)	3 / 7	6 / 3	5 / 6			
Duration of PD	7.4 ± 11.2	8.5 ± 7.5	-			
B-Glucose	4.7 ± 0.4	4.6 ± 0.3	4.9 ± 0.2	NS	NS	NS
S-Glucose	0.15 ± 0.08	0.04 ± 0.02	0.07 ± 0.02	***	***	NS
B-Lactate	1.8 ± 0.6	1.8 ± 0.6	1.8 ± 0.7	NS	NS	NS
S-Lactate	35.0 ± 7.0	27.6 ± 3.8	28.0 ± 5.2	*	*	NS
B-Sodium	141.2 ± 2.3	140.3 ± 1.5	141.0 ±1.7	NS	NS	NS
S-Sodium	171.4 ± 69.5	79.2 ± 37.8	120.4 ± 63.3	**	NS	NS
B-Potassium	4.1 ± 0.4	4.2 ± 0.3	4.5 ± 0.3	NS	NS	NS
S-Potassium	19.1 ± 8.2	11.7 ± 3.0	14.2 ± 3.4	*	NS	NS
B-Chlorine	103.8 ± 2.4	104.7 ± 1.5	104.9 ± 1.7	NS	NS	NS
S-Chlorine	141.8 ± 62.4	64.1 ± 32.4	100.1 ± 60.5	*	NS	NS
B-Calcium	2.5 ± 0.1	2.5 ± 0.1	2.5 ± 0.1	NS	NS	NS
S-Calcium	4.1 ± 1.7	3.4 ± 1.8	2.5 ± 0.9	NS	NS	NS
B-Magnesium	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	NS	NS	NS
S-Magnesium	1.6 ± 0.6	1.1 ± 0.6	0.9 ± 0.3	*	*	NS
B-Phosphorus	1.2 ± 0.2	1.3 ± 0.2	1.2 ± 0.2	NS	NS	NS
S-Phosphorus	0.20 ± 0.08	0.30 ± 0.47	0.18 ± 0.05	NS	NS	NS

Concentrations of all laboratory parameters are given in mmol/l. Abbreviations: Prefix "**B**" in the first article means concentration of a parameter in blood, and "**S**" indicates concentration in sweat. **PD-act** = patients with active panic disorder, **PD-rem** = patients with panic disorder in remission, **NS** = not significant, * ($p \leq 0.05$), ** ($p \leq 0.01$), *** ($p \leq 0.001$).

1997). From a practical viewpoint, sweat is also a ready source of biological material for laboratory analysis.

Of the eccrine and apocrine sweat glands, only the eccrine ones are responsible for the sweat response. These glands are richly supplied by both the blood vessels and sympathetic nerve fibers, but they are unusual in that they receive sympathetic innervation, which is cholinergic (Sato & Dobson, 1970). Recent studies on subjects with anhidrosis due to deficits in cholinergic transmission indicate that adrenergic stimulation is also present on the palms and soles (Nakazato *et al.* 2004).

In our preliminary study with a non-selected groups of PD patients and age-matched controls, we found significantly increased sweat concentrations of lactate, glucose, and other minerals in PD subjects (Kukumberg *et al.* 2005). These results, however, can be correctly interpreted only when based on a better selection of patients and the correlation of sweat and blood parameters will be done.

To the best of our knowledge, this is the first consistent investigation of sweat in PD. The aim of our study was to verify possible differences in levels of various ubiquitous biochemical parameters between PD and healthy subjects. We were also interested in whether these changes appear in relation to the clinical activity of PD or if they are "permanent" features of this disorder.

MATERIAL & METHODS

Nineteen patients with PD and 11 age-matched control subjects participated in the study. Prior to examination, written informed consent was obtained in accordance with the Declaration of Helsinki. The diagnosis of PD was established using the DSM IV criteria (American Psychiatric Association, 1994). For the purpose of this study we arbitrarily divided PD patients into two groups based on the clinical activity of the disease at the time of assessment. Patients with "active PD" (*PD-act*; n=10) had to have at least two clinical panic attacks in the preceding 4 weeks. Patients in the group of "PD in remission" (*PD-rem*; N=9) must been attack-free for at least 4 weeks. All other subjects were otherwise mentally and physically healthy. The participants´ demographic and clinical data are given in *Table 1*. Any treatment received was not taken into consideration in this study.

All subjects underwent a single 8-min session in the dry-heat sauna. Sweat and venous blood were collected immediately after the end of this session (the sweat was sampled as the first). Immediately before sauna exposure, subjects took a cleansing shower followed by careful drying of the skin. Sweat was collected by means of absorbent swabs over the chest bone, between the scapulas, and over the arms. Saturated swabs were scrolled, inserted into sterile plastic tubes, and stored on ice. Quantitative laboratory analysis was done within 90 min by means of the Hitachi 917 automated analyzer (Roche Diagnostics).

STATISTICAL ANALYSIS

Statistical analysis was done using the SPSS 13.0 statistical package. Concentrations of lactate, glucose, sodium, potassium, chlorine, calcium, and magnesium in both fluids were statistically compared among the three groups using ANOVA and Tukey's HSD post hoc test. Correlation analysis between values in the blood and sweat was done by Pearson´s method.

RESULTS

None of the subjects had clinical signs of panic attack during or immediately after sauna exposure. Mean values ± standard deviations of all assessed parameters in sweat and blood are given in Table 1. All three groups were comparable in age and both patient groups were not statistically different as regards the duration of PD since diagnosis. We did not find any significant difference between the three groups in any of the blood parameters. However, statistical analysis revealed that patients in the group PD-act had significantly higher values of lactate, glucose, and magnesium in sweat in comparison with the other two groups. Moreover, PD-act patients had significantly higher sweat concentrations of sodium, potassium, and chlorine than PD-rem patients. We did not detect any significant difference between the PD-rem patients and the control group, neither in blood nor in sweat. There was also no significant correlation between blood and sweat levels of any of the measured parameters (data not shown).

DISCUSSION

The results of our study confirm our preliminary hypothesis about the significance of sweat in PD. We demonstrated unequivocal differences in the composition of sweat which depended on the concomitant presence of PD „per se" and presence of the relapsing period in its course. Patients with "active" PD had substantially higher sweat concentrations of lactate, glucose, and other ions than patients with PD in the period of remission or healthy subjects. Interestingly, no significant differences were found in the blood; this clearly excludes the possibility that the differences found in sweat in PD simply reflect those in blood.

Due to the unique nature of our study design and only limited possibility of referring to previous research with healthy subjects, we can at present offer only a partial interpretation of our results. It may be argued that our sweat concentrations are markedly higher relative to literature. However, values referred by others were found in studies where sweat was collected after longer (30 min) sauna exposure (Hoshi *et al.* 2001), during physical exercise (Shirreffs & Maughan, 1997), or both (Bar-Or, 1998). Significantly increased levels of lactate in the sweat of patients with active PD support its crucial role in the pathophysiological matrix of PD. It is known that changes in blood lactate are independent of sweat lactate concentration (Green *et al.* 2000). Our results confirm this notion also in the opposite direction, since blood lactate was similar in all subjects. The sweat glucose elevation in normoglycemic subjects with active PD is the most suprising finding. We can only surmise that it reflects specific and direct neurovegetative activation of the stress axis in the possibly panicogenic environment of a sauna in connection with active PD. Magnesium is an important cation involved in the generally enhanced neuromuscular excitability of PD patients (Kukumberg & Strečko, 1993); however, its selective increase in the active period of PD remains elusive. Higher sweat levels of sodium, potassium, and chlorine in active PD patients in comparison with PD patients in remission but not healthy controls could be caused by specific ion channel changes at the site of the eccrine sweat gland or of their control in the central nervous system. These could be unbalanced in one direction in the active phase of PD and in the opposite direction during the period of remission. Another explanation is that these shifts simply reflect a higher rate of sweating in active PD, and the sodium and chloride concentrations increase with increasing sweat rate (Cage & Dobson, 1965).

In conclusion, sweat appears to be a promising medium for the detection of valuable biochemical markers to diagnose the paroxysmal neuropsychiatric entity – PD and its clinical course. Future extensive research is needed to confirm and further elucidate our findings.

Acknowledgement. We wish to thank Judy Benson for copyediting the manuscript.

REFERENCES

1 American Psychiatric Association (1994). Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Washington, DC.
2 Bar-Or O (1998). Effects of age and gender on sweating pattern during exercise. Int J Sports Med. **19** (Suppl 2): S106–S107.
3 Cage GW, Dobson RL (1965). Sodium secretion and reabsorption in the human eccrine sweat gland. J Clin Invest. **44**: 1270–1276.
4 Green JM, Bishop PA, Muir IH, McLester JR, Jr., Heath HE (2000). Effects of high and low blood lactate concentrations on sweat lactate response. Int J Sports Med. **21**: 556–560.
5 Hoshi A, Watanabe H, Kobayashi M, Chiba M, Inaba Y, Kimura N, Ito T (2001). Concentrations of trace elements in sweat during sauna bathing. Tohoku J Exp Med. **195**: 163–169.
6 Janszky I, Szedmak S, Istok R, Kopp M (1997). Possible role of sweating in the pathophysiology of panic attacks. Int J Psychophysiol, **27**: 249–252.
7 Kukumberg P, Blažíček P, Valkovič P, Račková Z, Barčíková A, Gúth A (2005). Vyšetrenie potu u panickej poruchy. Pilotná štúdia. [(Assessment of sweat in panic disorder. Pilot study.) (In Slovak.)] Neurol pro praxi. **6**: B28.
8 Kukumberg P, Strečko A (1993). Increased neuronal excitability in panic disorder. Br J Psychiatry. **163**: 839–840.
9 Nakazato Y, Tamura N, Ohkuma A, Yoshimaru K, Shimazu K (2004) Idiopathic pure sudomotor failure: anhidrosis due to deficits in cholinergic transmission. Neurology. **63**: 1476–1480.
10 Sato K, Dobson RL (1970). Regional and individual variations in the function of the human eccrine sweat gland. J Invest Dermatol. **54**: 443–449.
11 Shirreffs SM, Maughan RJ (1997). Whole body sweat collection in humans: an improved method with preliminary data on electrolyte content. J Appl Physiol. **82**: 336–341.