

Received: 07.09.2010  
Accepted: 28.03.2011

A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Data Interpretation  
E – Manuscript Preparation  
F – Literature Search  
G – Funds Collection

# HYPERVENTILATION AND MONOPOLAR AFFECTIVE DISEASE-TYPE DEPRESSION

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## SUMMARY

### Background:

MAD-type depression is a mental disorder with many and various symptoms, which can be classified as emotional, cognitive, motivational, or somatic. These last two are strongly correlated with the cardiovascular system, which is linked with the respiratory system.

### Material/ Methods:

Material and methods: 98 women diagnosed with MAD (age 27 – 44 years) were examined with the STAI Inventory (X-1, X-2), and then twice more (before and after psychological conversation), using the FlexComp Infinity/BioGraph Infinity (Thought Technology Ltd.) to monitor the plethysmographic wave biosignal (PPG) behavior, along with computer evaluation related to the pulse wave and breathing depth.

### Results:

Results: A high level of fear and hyperventilation measured by PPG produces not only a synchronic component corresponding to cardiac contraction, but also a component related to breathing. Physiological hyperventilation caused by sinus node arrhythmia together with the intensified fear and anxiety characteristic of MAD can be attributed to this phenomenon. This regularity should be taken into consideration in both the diagnosis and therapy of the chronically recurrent and persistent depression characteristic of MAD.

### Conclusions:

Conclusion: More detailed conclusions require the continuation of research on larger subpopulations with excessive lung ventilation in relation to the organism's metabolic needs.

**Key words:** persistent affective (mood) disorders, recurrent depressive disorder, photoplethysmographic signal

## INTRODUCTION

The term depression has various meanings. In everyday language it means any temporary mood deterioration, whether or not it requires psychological or medical intervention. In medical terminology, however, depression is a pathological mood decrease lasting for a longer time (weeks, months, years), in most cases accompanied by complex disorganization of activity, a subjective experience of the futility of life, accompanied by a feeling of somatic disease [Catalan 2002, Piwoński et al. 2005]. According to ICD-10, depression constitutes a group of diseases with differentiated pathogenesis existing under the common name of affective disorders, numbered F31-F39; thus depression comprises as many as 36 nosological units, and the clinical picture may also be complicated by co-existing psychosomatic diseases. Due to nosological considerations, then, Pużyński (2005) has divided the entirety of affective disorders into three categories:

- depression occurring in the course of affective diseases (formerly known as endogenous depression and manic-depressive psychosis); the etiology is not well known, although it is often associated with a hypothetical endogenic factor;
- depressions occurring in various diseases with a somatic base, connected with drugs and other substances, also called somatogenic depression, symptomatic depression and organic depression;
- psychogenic depressions, whose occurrence is connected with various physical and emotional traumas.

The borders between these categories are not sharp, because it is possible to find in some patients the occurrence of two or even three groups of causal factors; in the current survey, then, depression does not constitute a disease unit, but rather a disorder complex of various etiology, as reflected in the newest classification of DSM-IV TR, where depression, regardless of the cause, may be diagnosed on the basis of the nature of the depressive episodes related solely to the first occurrence of depression:

- in the course of recurrent depressive disorders;
- in the course of bipolar affective disorders (if, in addition to depressive syndromes, there are manic episodes as well).

In this context it is important to remember that in the medical literature [Alagor 2005, Pużyński 2002, Pużyński 2005] two groups of disorders are under discussion, in which one of the significant symptoms is hyperventilation:

- mood changes (dysphoria), especially panic fear;
- brain stem function disorders, which may be developmental, vascular, post-traumatic, metabolic, degenerative or neoplastic.

Considering the above, accurate diagnosis and correct treatment of the depression brings usually quick improvement of patient status and relief in suffering, as the patient suffers due to lowered mood, energy loss, activity decrease, and sleep and appetite disorders. The following types are described most often in the medical practice: major depression, dysthymia (also called minor depression), seasonal affective disorder (SAD), and affective disease [Święcicki 2006]. In this

last case, there are only recurrent depressive episodes, so it exists in medical nomenclature under the name MAD (monopolar affective disease), while disturbances characterized by the occurrence of alternating depressive and manic episodes are called BAD (bipolar affective disease).

MAD-type depression is considered in the psychophysiological aspect [Hammen 2004, Kalueff et al. 2004, Nowak 2005] to include mental disorders characterized by numerous and diverse symptoms, which may be grouped as follows:

- *emotional*: lowered mood (sadness, often accompanied by fear, weeping, loss of the joy of life characteristic for dysphoria, impatience and irritability);
- *cognitive*: negative self image (lowered self-evaluation, self-accusation, pessimism and resignation), and in extreme cases delusions may also occur;
- *motivational*: problems with mobilization to any kind of action, which may also cause a form of psychomotor slowness, as well as problems with making decisions;
- *somatic*: circadian rhythm disorders, loss of appetite (in mild depression it is sometimes possible to observe an increase and not a loss of body mass), weakness and tiredness, repeated complaints about migrating pains and physical discomfort.

Affect and its neurovegetative representations are partly linked with the hypothalamus, which is the source of various kinds impulses in the autonomous nervous system. Certain cognitive impulses connected with memory and attention are linked with the dorsolateral cortex and precortical abnormalities, when the changes in the frontal limbic network affect emotional, motivational and cognitive modulation. Between episodes, the patient person with MAD [Dudek 2004, Fajkowska-Stanik et al., 2003], as compared with the healthy persons, demonstrates greater sensitivity, unstable self-evaluation, and more frequent attitude disorders (expecting acceptance and striving after perfection). According to the opinion of these investigators, the main features of the depressive world are darkness and heaviness; the past, the present and the future are dark, and this changes the quality of life of each person with this mood disorder, as even breathing is usually excessively accelerated (tachypnea) due to intensive and increasing panic anxiety and fear. This breathing, accompanied by hyperventilation often impairing the oxygen inflow to the brain, manifests itself very often by chest pain, chills or hot flashes, vertigo, and whole-body trembling characteristic for intense pain.

Extreme respiratory movements during hyperventilation bring the respiratory system to excessive lung ventilation in relation to the metabolic need for lung ventilation, which causes various measurable changes, such as acidosis, hypoxia, fever, thyroid gland hyperfunction, pneumothorax, gaseous alkalosis, decreased ionized calcium in serum, dysesthesia with tingling sensation, tetany, and even epileptic seizure, the detailed description of which exceeds the bounds of the present survey. Pressure reduction and a significant increase of carbon dioxide in arteries, veins and capillary vessels (up to 35 mm Hg) are the most frequent, where the amplitude and frequency respiration successive is slowed. Hence the effect of hyperventilation results from its influence on the carbon dioxide level, as rapid

and deep breaths reduce the carbon dioxide amount, which is the main element stimulating the respiratory center [Piwoński et al. 2005, Rosenthal 2002].

Breathing disorders, measured by breath depth and frequency, can be measured by the plethysmographic wave (PPG) biosignal, also called the blood volume pulse (BVP), as conditioned by cardiac rhythm and respiratory rhythm. It may be measured by the reflex method or, at the same time, by the transmission method (as the signal is subject to considerable fluctuations with each heart beat and each breath) in the peripheral vessels, using a photoplethysmographic sensor placed, for example, on the examined person's finger, imaged by means of a band filter.

It has also been found that related oscillations in further sequence have more effect on the neurons' autonomic activity than mechanical factors themselves involving the breathing process [Hammen 2004, Kukwa et al. 2003, Pecyna 2005, Pecyna 2006, Pecyna et al. 2009]. This phenomenon may be unquestionably confirmed by the analog and digital record, i.e. in the visual record of long term change in these parameters. It is difficult, however, to fully explain whether such prevailing factors may become synchronic fluctuations related to the cardiac contraction, as this would be only the mechanical effect related to step increase of the ejected blood volume. Hence it seems likely that the PPG biosignal should be considered in the diagnosis of the development of depression symptoms in young men, which should be overarching aim of any therapy. Their analysis may become a significant element characterizing this process, hence it may be a turning point in the diagnostics and treatment of depression symptoms. Thus the hypothesis expressed in this manner constitutes an attempt to answer the question that is the focus of the present article.

## **MATERIAL AND METHODS**

### ***Research group characteristics and study methods***

The research group consisted of 98 women diagnosed with MAD (recurrent depressive episodes complicated by strong fear and anxiety), ranging in age from 27 to 44 years (mean age  $35.3 \pm 6.72$ ). For statistical purposes two age groups were separated: A (younger – 27-35 years) and B (older – 36-44 years). All these patients were examined in two-stages. In the first state, the State-Trait Anxiety Inventory (STAI, X1 – X2) [Spielberger et al. 1970] was used, in the Polish adaptation [Wrześniewski et al., 2002]. This method was used to define the fear level in each woman, both as a trait, i.e. the acquired behavioral disposition to react fearfully, and as an affective state, understood as the subjective and conscious perception of tension and anxiety. The Inventory consists of the two independent parts, comprising 20 statements each. The fear level treated as the current emotional state was defined using the STAI X-1, while the STAI X-2 was used to measure the personality dynamics of fearfulness. The subject was asked to describe her attitude towards each statement, selecting one of four possibilities. The fear level was expressed by the number of points gained by adding up the values

from the particular responses. The scores for each part of the Inventory can vary from 20 up to 80 points, where a high score means a higher level of fear.

In the second stage, a non-invasive examination [Struckman & Mathiesen, 1985] using the FlexComp Infinity /BioGraph Infinity (Thought Technology Ltd.) to obtain a plethysmographic (PPG) wave biosignal, and the component related to the cardiac contraction in the breathing rhythm mode was measured twice (before and after two hours of psychological conversation), using digital processing based on amplitude demodulation in the RT mode, simultaneously recorded in three forms: raw results (raw), range (amplitude) and frequency (rate).

For statistical purposes, the additive components related to rhythmic breathing and heart oscillation were separated by the use of the bottom-pass filter built into the system, and then corrected by appropriate mathematical models, considering individual variability. For differentiation purposes, the component filtered from the PPG signal was called the DRS (Derived Respiratory Signal), which is drawn as a new biosignal in the form of a linear curve (see Fig. 1).

It has also been noticed that, as a result of changes in the blood vessels, the PPG biosignal is visualized and synchronized with breathing fluctuations in the form of a free component PPG-DRS (photoplethysmography-derived respiratory signal), illustrating breathing frequency and depth [Nicolaidis et al. 1987, Nicolaidis et al. 1991, Nicolaidis 2000], which reflects the mutual interaction of these systems. Hence it is possible to read from a recorded photoplethysmographic curve the vein capacity expressed in the proportional biosignal change (PPG%).

Then in turn, the plethysmographic summary analog records set analyzed in the three forms of biosignals is shown in Fig. 2.

Detailed statistical evaluation of these signals, expressed both in numbers and in the form of polyplethysmographic spindles, was performed using the t-Student test.

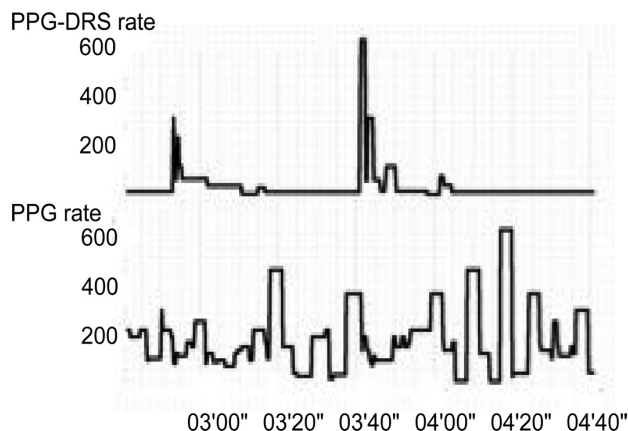


Fig. 1. Digital record of the analog signals PPG (blood flow wave related to myocardial contractions) and its component PPG-DRS (representing the breathing process) in a 24-year-old female patient diagnosed with MAD



Fig. 2. Full analog plethysmographic signal digital record (counting from the bottom, in formats PPG raw, PPG rate and PPG amplitude as well as PPG-DRS raw, PPG-DRS rate and PPG-DRS amplitude) registered from the same patient (cf. Fig. 1)

## RESULTS

The results obtained from the two-part Inventory, STAI (X-1 – X-2) showed a significantly increased fear level in both groups, both as a state and as a trait, where a slightly higher level was registered in the younger group (72 points in group A and 66 in group B). These differences were not statistically significant, however ( $t=1,85$ ), hence age did not serve as a differentiation criterion. However, the very high result obtained in the Inventory for both parts, with point scores on the level of 7 and 8, evidences the fact that the women from both groups experienced successive episodes of major depression, characteristic for MAD. The entire PPG biosignal illustrating the pulse course, together with its main component, the PPG-DRS, was measured and subjected to detailed statistical analysis twice (before and after two hours of psychological conversation). The following indices were used: PPG raw, PPG rate, and PPG amplitude, and then PPG-DRS raw, PPG-DRS rate and PPG-DRS amplitude. The values given here were based on the calculation of changes in the peripheral blood flow measured by the finger photoplethysmograph, which were then used to develop an algorithm of the digital processing of biosignals developed by MAD-type depression, in order to show the probability of slow and shallow breathing. For this purpose there was a 7-

minute plethysmographic wave biosignal recorded for each distinguished woman, thus obtaining globally 134,228 numerical data for each group, which are presented in Tables 1 and 2.

Table 1. Selected indices in the research groups of younger women (A) and older women (B) diagnosed with MAD, obtained before the psychological conversation

Index	Group A ( $\bar{x} \pm SD$ )	Group B ( $\bar{x} \pm SD$ )	T	p
PPG <i>raw</i>	29.88±12.29	22.39±13.41	2.08	0.05
PPG <i>rate</i>	89.46±23.42	75.23±32.69	3.09	0.01
PPG <i>amplitude</i>	23.68±11.35	17.46±10.12	1.97	0.05
PPG-DRS <i>raw</i>	17.42±8.87	11.34±4.28	2.08	0.05
PPG-DRS <i>rate</i>	11.46±6.82	6.17±5.39	1.99	0.05
PPG-DRS <i>amplitude</i>	1.59±0.69	0.94±0.48	1.28	na.
Min PPG-DRS <i>raw</i>	26.35±0.81	25.49±0.43	0.98	na
Min PPG-DRS <i>rate</i>	17.34±7.28	11.99±10.57	1.67	na
Min PPG-DRS <i>amplitude</i>	3.11±1.06	1.99±0.97	0.82	na
Max PPG-DRS <i>raw</i>	31.57±0.43	29.88±9.62	1.29	na
Max PPG-DRS <i>rate</i>	33.53±22.52	27.65±13.84	2.21	0.05
Max PPG-DRS <i>amplitude</i>	0.39±0.62	0.22±0.33	0.59	na

Table 2. Selected indices in the research groups of younger women (A) and older women (B) diagnosed with MAD, obtained after the psychological conversation

Index	Group A ( $\bar{x} \pm SD$ )	Group B ( $\bar{x} \pm SD$ )	t	p
PPG <i>raw</i>	18.24±8.53	19.48±11.72	0.68	na
PPG <i>rate</i>	64.46±23.42	69.63±24.26	2.02	0.05
PPG <i>amplitude</i>	9.81±9.27	7.93±2.48	0.97	na
PPG-DRS <i>raw</i>	11.42±6.39	7.14±6.13	1.99	0.05
PPG-DRS <i>rate</i>	11.46±6.82	6.17±5.39	1.99	0.05
PPG-DRS <i>amplitude</i>	1.33±0.54	0.99±0.48	0.78	na
Min PPG-DRS <i>raw</i>	12.54±4.21	10.23±6.89	1.37	na
Min PPG-DRS <i>rate</i>	1.09±0.83	0.98±0.43	0.21	na
Min PPG-DRS <i>amplitude</i>	11.60±0.58	18.29±11.29	2.29	0.05
Max PPG-DRS <i>raw</i>	23.08±11.02	22.06±12.84	0.29	na
Max PPG-DRS <i>rate</i>	24.76±16.32	25.39±13.68	0.26	na
Max PPG-DRS <i>amplitude</i>	7.01±6.58	6.85±3.48	0.43	na

Comparing the plethysmographic biosignal indices values enumerated in Table 1, statistical significance was noted in the following variants:

- $p < 0.01$  only in PPG rate;
- $p < 0.05$  in PPG Raw and PPG amplitude, and in the indices filtered from this biosignal the smallest value of the component Pk-Pk (peak-to-peak) PPG-DRS raw and PPG-DRS rate, as well as their maximum Max PPG-DRS rate describing blood vessel cyclical stretching and shrinking caused by blood flow in the heart rhythm and breathing frequency, and depth calculated in three types: raw and amplitude forms given in the percentage results, and rate in the frequency bpm (beats per minute).

Soon after two-hours of psychological conversation (see Table 2.), there was a general decrease of all examined parameters, with statistical significance at  $p < 0.05$  only in the indices of PPG rate, PPG-DRS raw and rate, as well as Min PPG-DRS amplitude.

The results presented in the tables confirm the findings described in the literature, that the PPG signal contain not only the synchronic component related to cardiac contraction, but also a component related to breathing rhythm, measured as the result of so called II raw blood pressure oscillation. Thus the physiological respiratory arrhythmia of the sinus node is attributed only to this phenomenon. An increased number of heart beats (up to 97/min.) as well as breaths (up to 32/min., characteristic for hyperventilation) was registered in all subjects during detailed analysis in the first examination.

## **DISCUSSION**

Plethysmographic (PPG) biosignal digital analysis is a very sensitive and non-invasive diagnostic method enabling the evaluation of the behavior of two systems, the cardiovascular system and respiratory system, in women diagnosed with depression of the MAD type. Furthermore, it made it possible to clear up, to a certain extent, an age-long diagnostic problem concerning the co-operation of these two systems in the course of hyperventilation caused by increasing fear, as the breathing process by itself is not limited only to the bronchi and lungs, since it also involves the most proximally and/or distally located regions of normally functioning blood vessels.

The data given above indicate that hyperventilation is also subject to differentiation by age, since there is a very strong connection between the plethysmographic biosignal quantitative analysis, including the PPG-DRS component filtered from it, and the breathing disturbances range defined by hyperventilation. These observations, confirmed by various monitoring methods and results, show that the described forms existed in reality, and were modified both by fear as trait (learned fear related to early childhood) and state fear (subjectively and consciously perceived) in Spielberg's conception. The characteristic feature of fear as state is significant variability under the influence of the response to various endogenous and exogenous endangering factors, hence their mutual relations may



be defined as *reactive fear* as opposed to *chronic fear*, which in the groups of examined women did constitute differentiating variables. Regardless of the type of situation, together with higher fear as trait, the higher the level of fear as state, as in interpersonal and physical situations in which the conscious endangering of the ego is expressly present.

## CONCLUSION

More detailed conclusions would require continuation of this research with larger populations with excessive lung ventilation problems in relation to the organism's metabolic needs.

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