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Sexual dimorphism in the neuro-endocrine regulation of bicycle ergometric test parameters in untrained individuals with dysfunction of the neuro-endocrine-immune complex

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Abstract

Background. Ergometric physical working capacity (PWC) testing has a long tradition in occupational medicine. PWC can be tested, using performance indicators like VO_2max or the mechanical power. However, the calculated by bicycle ergometry PWC in reality reflects the reaction of the autonomic nervous system to muscle load, which, in turn, is strong, but still not absolutely complete, correlates with VO_2max as a real indicator of cardiorespiratory fitness. The purpose of this study is to clarify the relationship between PWC, calculated based on the result of two-stage bicycle ergometry, and the parameters of neuro-endocrine regulation as well as sexual differences in such relationships. **Materials and Methods**. The object of observation were 30 women 29-76 (49,4±11,0) years and 30 men 24-69 (47,4±12,0) years without a clinical diagnosis, but with the deviations from the norm in a number of parameters of the neuro-endocrine-immune complex as a manifestation of maladaptation. For estimation of PWC a two-stage bicycle ergometry used. Parameters of EEG, HRV and adaptation hormones levels registered twice with an interval of 4 or 7 days. **Results.** In men, PWC correlates negatively with plasma levels of cortisol (r=-0,52) and triiodothyronine (r=-0,47), but positively with levels of calcitonin (r=0,25) and testosterone (r=0,22). The coefficient of multiple correlation R=0,705. In women, the correlation of the twice lower PWC with cortisol and calcitonin is weaker (r=-0,31 and 0,18, respectively), and is absent with testosterone and triiodothyronine, instead it was found in relation to aldosterone (r=-0,24); R=0,394. The PWC regression model for men includes 6 HRV and 11 EEG parameters (R=0,846), while for women only the mode HRV (r=-0,56) and two EEG parameters (R=0,608). **Conclusion**. PWC levels in men are generally downregulated by cortisol, triiodothyronine, sympathetic tone, and θ-rhythm generating neurons, but upregulated by testosterone, calcitonin, vagal tone, and related α-rhythm generating neurons. In women, PWC levels are borderline downregulated by cortisol and aldosterone, but significantly upregulated by circulating catecholamines and β-rhythm generating neurons.
Keywords: bicycle ergometry, EEG, HRV, adaptation hormones, relationships, sexual dimorphism.

INTRODUCTION

Ergometric **physical working capacity** (PWC) testing has a long tradition in occupational medicine for assessing whether a sufficiently high level of physical performance for coping with the daily work requirements is given [33,36]. PWC can be tested maximally or submaximally, using performance indicators like VO_2max [6] or the mechanical power [11,46]. In the case of submaximal PWC testing measuring the mechanical power, the achieved power at a given heart rate serves as performance indicator. There are age- and sex-specific norm values [37] that can be used to judge whether differences or changes are within the normal range or can be considered significant. In addition, cardiorespiratory fitness is considered an attribute of health in general and non-specific resistance in particular [2,9,12,15], and is also an important target of adaptogenic agents [21,27,30,48-50].

However, it has been known for a long time that although the calculated submaximal PWC is considered as an indicator of cardiorespiratory fitness [13], in reality it reflects the reaction of the autonomic nervous system to muscle load, which, in turn, is strong, but still not absolutely complete, correlates with VO_2max as a real indicator of cardiorespiratory fitness. By the way, the correlation is significantly affected by the use of adrenergic and/or cholinergic blockers, as well as autonomic dysfunction as a manifestation of maladaptation [16,22,28].

The **purpose** of this study is to clarify the relationship between PWC, calculated based on the result of two-stage bicycle ergometry, and the parameters of neuro-endocrine regulation and sexual differences in such relationships.

MATERIAL AND RESEARCH METHODS

The object of observation were employees of the clinical sanatorium "Moldova" and PrJSC “Truskavets’ Spa”: 30 women 29-76 (49,4±11,0) years and 30 men 24-69 (47,4±12,0) years. The volunteers were considered practically healthy (without a clinical diagnosis), but the initial testing revealed deviations from the norm in a number of parameters of the neuro-endocrine-immune complex (details follow) as a manifestation of maladaptation, which actually prompted them to participate in the study with the hope of recovery.

In the morning in basal condition we recorded simultaneosly electrocardiogram (ECG) and electroencephalogram (EEG). ECG recorded during 7 min in II lead to assess the parameters of heart rate variability (HRV) (hardware-software complex "CardioLab+HRV", "KhAI-Medica", Kharkiv, Ukraine). For further analysis the following parameters HRV were selected. Baevskiy’s parameters: heart rate (HR), the mode (Mo), amplitude of mode, the variation scope (MxDMn) [3]. Temporal parameters (Time Domain Methods): the standart deviation of all NN intervals (SDNN), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the percent of interval differences of successive NN intervals greater then 50 ms (pNN_{50}), triangular index (TNN). Spectral parameters (Frequency Domain Methods): absolute ($msec^2$) and relative (%) power spectral density (PSD) bands of HRV: high-frequency (HF, range 0,40÷0,15 Hz), low-frequency (LF, range 0,15÷0,04 Hz), very low-frequency (VLF, range 0,040÷0,015 Hz) and ultra low-frequency (ULF, range 0,015÷0,003 Hz) [5,18,34]. Calculated classical indexes: LF/HF, LFnu=100%•LF/(LF+HF), Centralization Index (CI)=(VLF+LF)/HF), Baevskiy’s Stress Index.

EEG recorded during 25 sec a hardware-software complex “NeuroCom Standard” (KhAI Medica, Kharkiv, Ukraine) monopolar in 16 loci (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, T5, T6, O1, O2) by 10-20 international system, with the reference electrodes A and Ref on the earlobes. Among the options considered the average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), absolute ($\mu V^2/Hz$) and relative (%) PSD of basic rhythms: β (35÷13 Hz), α (13÷8 Hz), θ (8÷4 Hz) and δ (4÷0,5 Hz) in all loci, according to the instructions of the device. In addition, calculated coefficient of Asymmetry (As) and Laterality Index (LI) for PSD each Rhythm using formulas [19]:

As, % = 100•(Max – Min)/Min; LI, % = Σ [200•(Right – Left)/(Right + Left)]/8.

We calculated for HRV and each locus EEG the Entropy (h) of normalized PSD using Popovych's IL [16,31] formulas based on classic Shannon's CE [35] formulas:

$hHRV = -[SPHF \cdot \log_2 SPHF + SPLF \cdot \log_2 SPLF + SPVLF \cdot \log_2 SPVLF + SPULF \cdot \log_2 SPULF]/\log_2 4$;

$hEEG = - [PSD\alpha \cdot \log_2 PSD\alpha + PSD\beta \cdot \log_2 PSD\beta + PSD\theta \cdot \log_2 PSD\theta + PSD\delta \cdot \log_2 PSD\delta]/\log_2 4$.

At last in portion of venous blood determined plasma levels of major hormones of adaptation [8,14,22-24,29]: Cortisol, Testosterone, Aldosterone, Triiodothyronine and Calcitonin (by the ELISA with the use of analyzer "RT-2100C" and corresponding sets of reagents from "Алкор Био", XEMA Co, Ltd and DRG International Inc).

For estimation of physical working capacity (PWC) a bicycle ergometer "Tunturi" (Finland) is used. The power of the first load was 0,5 W/kg (HR±SD: 100±11 beats/min) at a pedaling frequency of 60-75 rpm. The power of the second load (after 3 min) was 1,5 W/kg (131±15 beats/min). This corresponded to the recommendations for ergometer testing in occupational medicine, particular for patients with maladaptation [2,7,13,41]. Calculated submaximal PWC_{150} with the mechanical power in Watt per kilogram body weight (W/kg) as indicator of cardiorespiratory fitness [13].

Testing was performed twice with an interval of 4 or 7 days.

Reference values of hormones and HRV are taken from the instructions for the kits and the device, respectively. Instead, EEG reference values due to their absence in the instructions are taken from the database of the Truskavetsian Scientific School of Balneology (n=112).

Results processed using the software package "Statistica 6.4".

RESULTS AND DISCUSSION

Both cohorts were almost identical in terms of age and body mass index (Table 1). The latter slightly exceeded the norm (by 8% in men and by 11% in women). Aldosterone and triiodothyronine plasma levels were equally normal, and cortisol levels were equally reduced (by 19% in men and by 18% in women). The actual levels of calcitonin did not differ, however, taking into account the significant sexual dimorphism (males/females average ratio is 2,76), it was found to be reduced by 25% in men and increased by 76% in women. A similar excess of the average norm (by 62%) in the latter was also found for testosterone, while in men its level corresponded to the age norm.

Table 1. Comparative characteristics of antropometric parameters and levels of adaptation hormones in men and women

Variable	Males (n=59)	Females (n=59)	Reference (n=30)		t/p for sexes	t/p for M reference	t/p for F reference
Age, years	47,4 1,6	49,4 1,7					
Hight, cm	178,2 0,7	163,8 1,1					
Weight, kg	83,0 0,7	71,5 1,3					
Body mass index, kg/m^2	26,2 0,3	26,8 0,6	24,2 0,6		0,94 ns	2,99 <0,01	3,07 <0,01
Aldosterone, pM/L	226 4	222 3	238 8		-0,68 ns	-1,39 ns	-1,82 >0,05
Triiodothyronine, nM/L	2,02 0,12	2,16 0,12	2,20 0,09		0,86 ns	-1,22 ns	-0,27 ns
Cortisol, nM/L	299 16	303 14	370 20		0,20 ns	-2,77 <0,01	-2,73 <0,01
			M	F			
Calcitonin, ng/L	10,51 0,89	8,87 0,90	13,95 1,26	5,05 0,45	-1,31 ns	-2,24 <0,05	3,80 <0,01
Testosterone, nM/L	13,1 0,8	3,83 0,42	14,4 0,5	2,37 0,14	-10,6 $<10^{-4}$	-1,46 ns	3,29 <0,01

In men, the level of PWC is significantly negatively correlated with plasma levels of cortisol (Fig. 1) and triiodothyronine (Fig. 2), on the other hand, at the limit of significance (for a sample of n=59, critical module r=0,26) positively with levels of calcitonin and testosterone (Table 2) in the complete absence of correlation with aldosterone (r=-0,03).

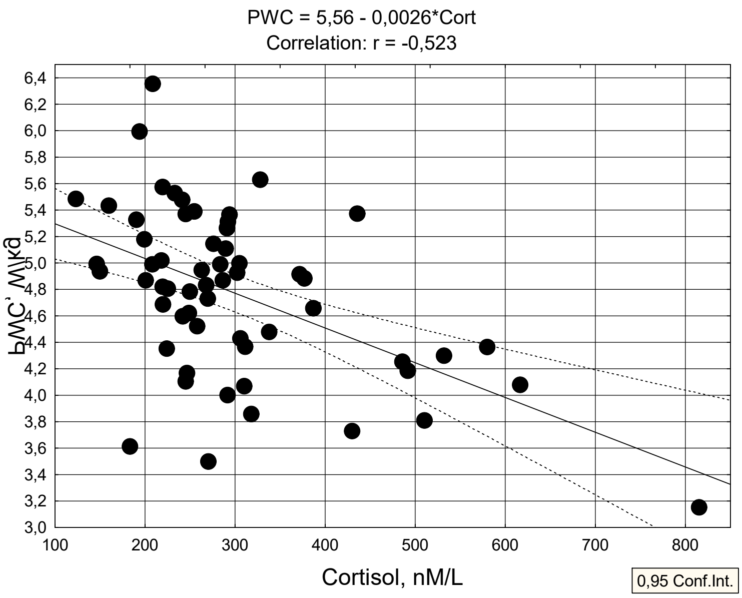


Fig. 1. Scatterplot of correlation between plasma cortisol level (line X) and PWC (line Y) in men

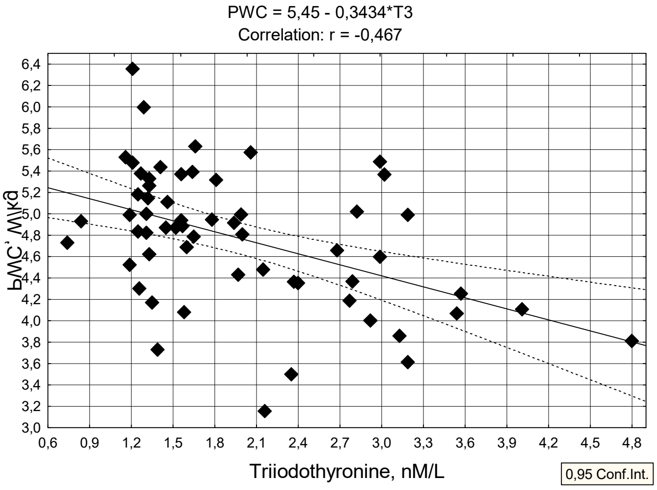


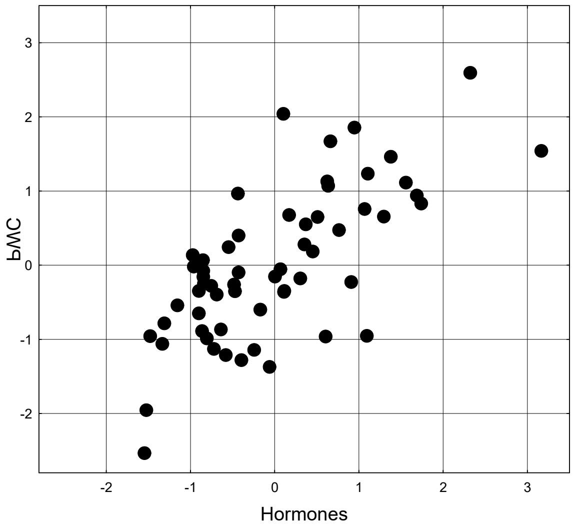
Fig. 2. Scatterplot of correlation between plasma triiodothyronine level (line X) and PWC (line Y) in men

Judging by the coefficient of multiple correlation, this hormonal constellation determines the level of PWC by 49,7% (Table 2 and Fig. 2).

Table 2. Regression Summary for PWC_{150} (W/kg) in men

$R=0,705$; $R^2=0,497$; Adjusted $R^2=0,460$; $F_{(4,5)}=13,3$; $p<10^{-6}$; SD=0,46 W/kg

N=59		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(54)}$	p-level
Variables	r		Intercpt	5,446	0,275	19,8	10^{-6}
Cortisol, nM/L	-0,52	-0,376	0,1037	-0,0019	0,0005	-3,63	0,001
Triiodothyronine, nM/L	-0,47	-0,432	0,0998	-0,3179	0,0735	-4,33	10^{-4}
Calcitonin, ng/L	0,25	0,160	0,1014	0,0147	0,0094	1,58	0,121
Testosterone, nM/L	0,22	0,262	0,0982	0,0282	0,0106	2,67	0,010



$R=0,705$; $R^2=0,497$; $\chi^2_{(4)}=38$; $p<10^{-6}$; Λ Prime=0,503

Fig. 2. Scatterplot of canonical correlation between hormonal variables (X-line) and PWC (Y-line) in men

As a result of the regression analysis with stepwise exclusion of variables until reaching the maximum value of Adjusted R^2, 6 HRV and 11 EEG parameters were included in the model (Table 3). The first 4 parameters of HRV are generally recognized markers of vagal tone, and Baevsky's stress index is a marker of sympathetic tone. The first 4 parameters of HRV are generally recognized markers of vagal tone, while Baevsky's stress index is a marker of sympathetic tone. The physiological interpretation of the VLF band remains a matter of debate.

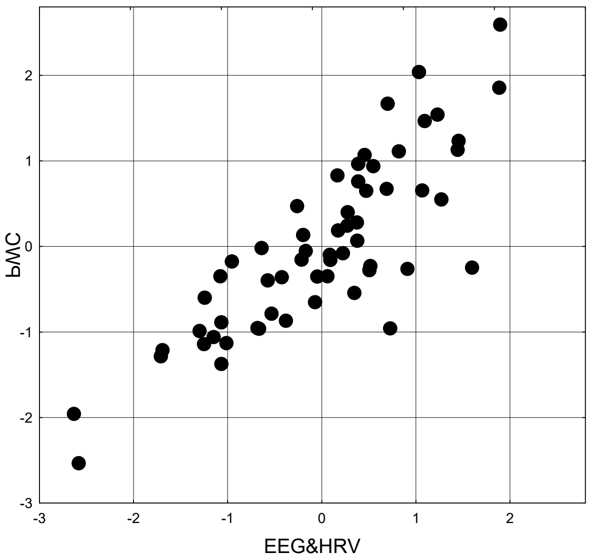
Table 3. Regression Summary for PWC_{150} (W/kg) in men
R=0,846; R^2=0,717; Adjusted R^2=0,599; $F_{(17)}$=6,1; p=10^{-6}; SD=0,40 W/kg

N=59		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(41)}$	p-level
Variables	r		Intercpt	-1,952	2,098	-0,93	0,358
Triangular index, units	**0,45**	0,976	0,304	0,1475	0,0459	3,21	0,003
MxDMn, msec	**0,41**	0,578	0,349	0,0043	0,0026	1,66	0,105
SDNN, msec	**0,38**	0,990	0,369	0,0287	0,0107	2,68	0,010
RMSSD, msec	**0,28**	-1,043	0,240	-0,0428	0,0098	-4,35	10^{-4}
P3-α PSD, %	**0,33**	-0,938	0,296	-0,0269	0,0085	-3,16	0,003
P3-α PSD, μV^2/Hz	**0,32**	1,749	0,497	0,0027	0,0008	3,52	0,001
P4-α PSD, μV^2/Hz	**0,32**	-1,375	0,610	-0,0022	0,0010	-2,25	0,030
T5-α PSD, %	**0,32**	-0,280	0,208	-0,0088	0,0066	-1,34	0,187
O2-α PSD, μV^2/Hz	**0,31**	0,898	0,407	0,0011	0,0005	2,20	0,033
Amplitude α, μV	**0,31**	-1,118	0,595	-0,0610	0,0325	-1,88	0,067
O1-α PSD, %	**0,30**	0,305	0,264	0,0082	0,0071	1,16	0,253
T6-α PSD, %	**0,29**	1,024	0,223	0,0321	0,0070	4,59	10^{-4}
Laterality β, %	**0,29**	0,279	0,107	0,0043	0,0017	2,60	0,013
VLF PSD, %	**-0,41**	-0,156	0,109	-0,0055	0,0039	-1,43	0,161
O2-θ PSD, %	**-0,36**	-0,377	0,108	-0,0524	0,0150	-3,49	0,001
Stress index, ln units	**-0,32**	1,316	0,357	1,0556	0,2866	3,68	0,001
T3-θ PSD, μV^2/Hz	**-0,31**	-0,179	0,117	-0,0058	0,0038	-1,53	0,135

Akselrod S et al [1] in pioneering experiment illustrated that after parasympathetic blockade the amplitude of the VLF peak is reduced; β-sympathetic blockade tends to reduce the VLF peak's amplitude, but this effect is not consistent because of the low tonic level of sympathetic activity in the resting dog. Increasing the activity of either the sympathetic or parasympathetic nervous system augments the area under the VLF peak. Therefore, both SNS and PSNS may mediate the VLF fluctuations. Selective blockade of renin-angiotensin system (by converting enzyme inhibitor) lead to 2-4,5-fold increase in the area under the VLF peak. Taylor JA et al [38] in young healthy subjects observed that β-adrenergic blockade had no significant effect on VLF power. ACE blockade modestly (approximately 21%) increased VLF power in the supine (but not upright tilt) position; atropine, given alone or with atenolol, decreased VLF band by 92%. Authors concluded that although VLF band are influenced by the renin-angiotensin-aldosterone system, they depend primarily on the presence of parasympathetic outflow. However very recently Del Valle-Mandragon L et al. [10] showing that during hemodialysis angiotensin II had a **positive** correlation with VLF band (r=0,390) and with LF/HF (r=0,359) while a negative correlation with LF (r=-0,262) and HF (r=-0,383) bands. Therefore, the contradictions regarding the nature of VLF connections with vagal and sympathetic tone as well as the renin-angiotensin-aldosterone system remain unresolved. Besides it was shown that low VLF power has been correlated with low levels of testosterone, while cortisol have not [17,39]. In the cohort of men observed by us, the **relative** PSD of VLF band correlates negatively with markers of vagal tone (r=-0,44÷-0,54), but positively with the stress index (r=0,27) and AMo (r=0,31), as well as cortisol (r=0,44) in the complete absence of a connection with both aldosterone (r=-0,05) and testosterone (r=-0,03). So, in this specific situation, the **relative** PSD of VLF band acts as a marker of sympathetic tone and cortisol.

Among the EEG parameters included in the regression model, the activity of the α-rhythm generating neural structures, which project to the temporal, parietal and occipital both right and left loci of the scalp, are positively correlated with PWC.

Judging by the scheme of Winkelmann T et al [45], on the P3/P4 loci is projected supramarginal gyrus, on the T5/T6 loci transverse temporal cortex, and on the O1/O2 loci lingual gyrus of left/right hemisphere, the **thickness** of which are positively correlated (r=0,43 for P3; 0,51 for T6 and 0,47 for O2 resrectively) with vagally mediated HRV (HF band and RMSSD). This is in excellent agreement with our data on vagal upregulation of PWC. At the same time, the activity of θ-rhythm-generating neurons of right lingual gyrus (O2) and leftt superior temporal gyrus (T3) makes down regulation of PWC. Taken together, neurogenic influences determine the level of PWC in men by 71,7% (Table 3 and Fig. 3).



R=0,846; R^2=0,717; $\chi^2_{(16)}$=58; p=10^{-6}; Λ Prime=0,307

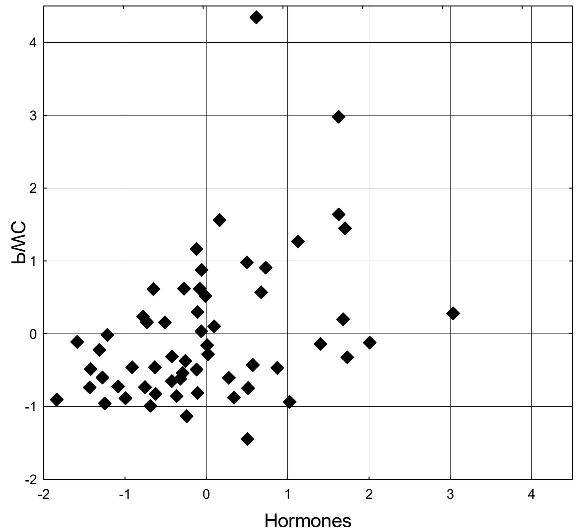
Fig. 3. Scatterplot of canonical correlation between EEG&HRV variables (X-line) and PWC (Y-line) in men

In women, the neuro-endocrine regulation of PWC differs from that in men both quantitatively and qualitatively. In particular, downregulation on the part of cortisol and upregulation on the part of calcitonin are weaker, and on the part of triiodothyronine and testosterone they come to nothing (r=-0,13 and -0,04 respectively), instead there is a weak downregulation on the part of aldosterone, absent in men. Accordingly, the measure of hormonal determination is very weak (15,5%), but statistically significant (Table 4 and Fig. 4).

Table 4. Regression Summary for PWC_{150} (W/kg) in women

R=0,394; R^2=0,155; Adjusted R^2=0,109; $F_{(3,6)}$=3,4; p=0,025; SD=0,17 W/kg

N=59		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(55)}$	p-level
Variables	r		Intercpt	2,645	0,213	12,4	10^{-6}
Cortisol, nM/L	**-0,31**	-0,263	0,128	-0,000	0,000	-2,06	0,045
Aldosterone, pM/L	**-0,24**	-0,219	0,125	-0,002	0,001	-1,76	0,085
Calcitonin, ng/L	**0,18**	0,118	0,128	0,003	0,003	0,92	0,361



R=0,394; R^2=0,155; $\chi^2_{(3)}$=9,3; p=0,025; Λ Prime=0,845

Fig. 4. Scatterplot of canonical correlation between hormonal variables (X-line) and PWC (Y-line) in women

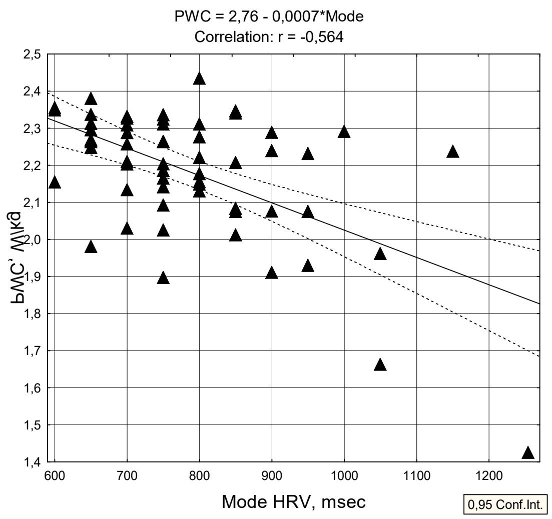


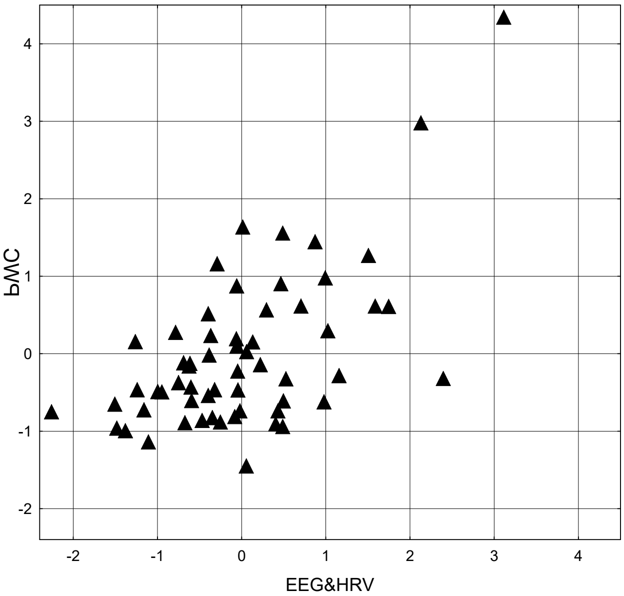
Fig. 5. Scatterplot of correlation between Mode HRV (line X) and PWC (line Y) in women

Among the HRV parameters, the connection with the mode (Fig. 5), which is an inverse marker of the level of circulating catecholamines [3], turned out to be the most significant. A significant positive correlation was also found with the sympathetic tone marker LFnu (r=0,30) and P3-β PSD (0,27), but these parameters were formally outside the model. Instead, PSD entropy at the P3 locus and T5-β PSD were included in the model. As a result, the measure of neurogenic determination of PWC turned out to be very strong (37,0%), but significantly weaker than that in men.

Table 5. Regression Summary for PWC_{150} (W/kg) in men

R=0,608; R^2=0,370; Adjusted R^2=0,336; $F_{(3,6)}$=10,8; $p=10^{-5}$; SD=0,14 W/kg

N=59		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(55)}$	p-level
Variables	r		Intercpt	2,524	0,162	15,5	10^{-6}
Mode HRV, msec	**-0,56**	-0,523	0,109	-0,0007	0,0001	-4,80	10^{-5}
P3 PSD Entropy	**0,24**	0,1825	0,108	0,2169	0,1286	1,69	0,097
T5-β PSD, µV2/Hz	**0,23**	0,136	0,109	0,0002	0,0002	1,26	0,214

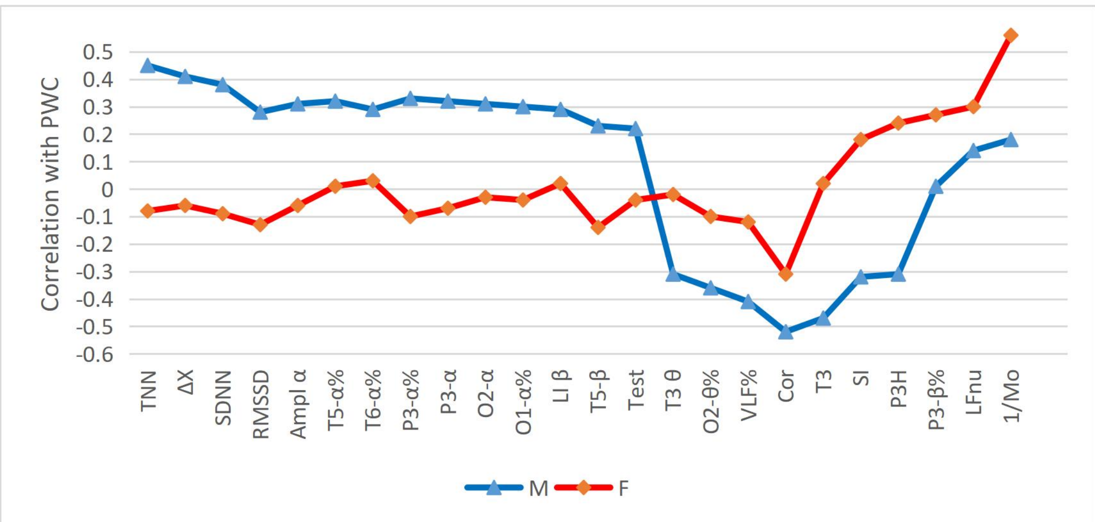


R=0,608; R^2=0,370; $\chi^2_{(3)}$=26; p=10^{-5}; Λ Prime=0,629

Fig. 6. Scatterplot of canonical correlation between EEG&HRV variables (X-line) and PWC (Y-line) in women

It is very interesting that in the already cited study of Winkelmann T et al [45] a negative correlation (r=-0,45) was found between the thickness of the isthmus cingulate cortex LH, which also projects to the P3 locus, and vagally mediated HRV. This suggests that the β-rhythm generating neurons of this area of the cortex, as well as of transverse temporal cortex RH (T6) are responsible for increasing the sympathetic tone and/or the level of circulating catecholamines through medullary sympathoexcitatory neurons [43,44] and other structures of the central autonomic network [4,20,25,26,32,40,42].

The described sexual dimorphism in the neuro-endocrine regulation of PWC is visualized in the form of profiles of correlation coefficients (Fig. 7).



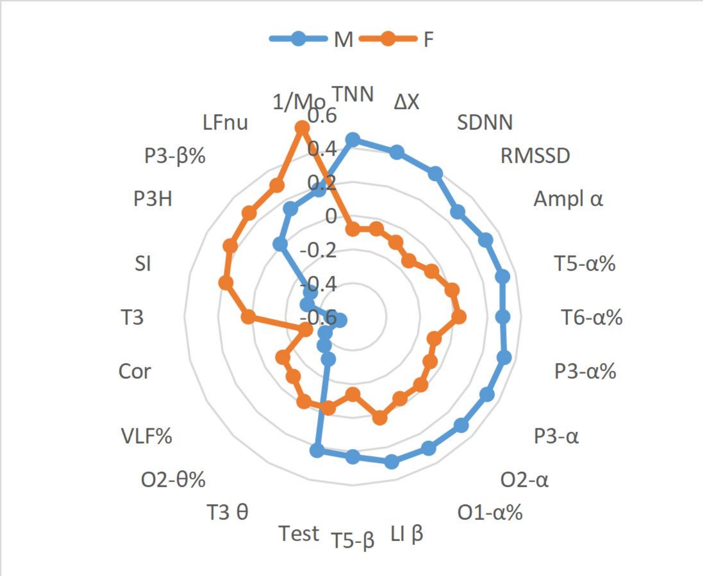


Fig. 7. Profiles of correlation coefficients between EEG&HRV parameters and PWC in men and women

The sexual dimorphism in the neuro-endocrine regulation of PWC is manifested against the background of the absence of significant differences in the HRV parameters involved, with the exception of a 9% higher sympathetic tone in men, which, in turn, exceeded the norm in both sexes in combination with a decrease in vagal tone and an increase the level of circulating catecholamines (Table 6).

Among the EEG parameters (Table 7), the PSD of the θ-rhythm in the T3 locus was found to be more than two times lower in men than in women, as well as a 32% lower PSD of the β-rhythm in the T5 locus, which, however, did not differ from the average norm, and in women exceeded it by 84% and 35%, respectively.

In addition, males had 16-20% lower than normal PSDs of the α-rhythm at all 4 loci, while females only at the P3 locus.

Table 6. Comparative characteristics of HRV parameters correlated with PWC

Variable	Males (n=59)	Females (n=59)	Reference (n=118)	t/p for sexes	t/p for M reference	t/p for F reference
Mode, msec	775 18	787 18	870 9	0,44 ns	-4,24 <0,001	-4,24 <0,001
MxDMn, msec	209 11	232 10	245 6	1,58 >0,05	-2,88 <0,01	-1,15 ns
Stress index, units	203 24	171 24	134 5	-0,97 ns	2,86 <0,01	1,53 >0,05
Stress index, ln units	5,01 0,10	4,83 0,10	4,89 0,09	-1,28 ns	0,85 ns	-0,49 ns
Triangular index, units	10,8 0,5	11,7 0,5	11,2 0,2	1,09 ns	-0,65 ns	0,80 ns
SDNN, msec	44,2 2,8	48,7 2,5	56,2 2,5	1,19 ns	-3,21 <0,01	-2,12 <0,05
RMSSD, msec	22,9 2,1	27,5 2,3	30,1 1,3	1,48 ns	-2,94 <0,01	-1,01 ns
LFnu PSD, %	81,7 1,4	74,8 1,7	64,4 1,5	-3,10 <0,01	8,44 $<10^{-4}$	-4,24 <0,001
VLF PSD, %	47,2 2,4	43,4 2,2	53,6 1,8	-1,18 ns	-2,19 <0,05	-4,24 <0,001

Table7. Comparative characteristics of EEG parameters correlated with PWC

Variable	Males (n=59)	Females (n=59)	Reference (n=112)	t/p for sexes	t/p for M reference	t/p for F reference
T3-θ PSD, μV²/Hz	26,4 2,5	55,4 7,9	30 3	3,51 <0,01	-0,92 ns	3,01 <0,01
T5-β PSD, μV²/Hz	65 5	96 13	71 5	2,20 <0,05	-0,81 ns	1,80 >0,05
P3-α PSD, %	35,7 2,8	35,3 2,7	42,7 2,0	-0,09 ns	-2,03 <0,05	-2,18 <0,05
O1-α PSD, %	33,5 3,0	36,7 2,8	42,0 2,0	0,78 ns	-2,35 <0,05	-1,55 >0,05
T6-α PSD, %	28,6 2,6	31,8 2,4	35,5 1,7	0,92 ns	-2,25 <0,05	-1,24 ns
T5-α PSD, %	28,6 2,6	32,7 2,4	35,1 1,7	1,16 ns	-2,10 <0,05	-0,82 ns
P3-β PSD, %	20,4 1,5	20,1 1,4	22,7 1,1	-0,18 ns	-1,21 ns	-1,51 >0,05
Laterality β, %	-4 5	-6 4	-1 3	-0,35 ns	-0,53 ns	-1,11 ns
P3 PSD Entropy	0,79 0,02	0,80 0,02	0,80 0,01	0,10 ns	-0,29 ns	-0,17 ns
Amplitude α, μV	16,3 1,5	18,3 1,6	17,4 1,0	0,93 ns	-0,67 ns	0,47 ns
P3-α PSD, μV²/Hz	279 53	326 67	287 36	0,56 ns	-0,13 ns	0,51 ns
O2-α PSD, μV²/Hz	292 65	332 67	301 43	0,42 ns	-0,12 ns	0,38 ns
O2-θ PSD, %	7,4 0,6	8,0 0,6	7,1 0,4	0,71 ns	0,41 ns	1,26 ns

Identified deviations from the norm are, apparently, a manifestation of dysfunction of the neuro-endocrine-immune complex and maladaptation [16,23,28].

CONCLUSION

PWC levels in men are generally downregulated by cortisol, triiodothyronine, sympathetic tone, and θ-rhythm generating neurons, but upregulated by testosterone, calcitonin, vagal tone, and related α-rhythm generating neurons. In women, PWC levels are borderline downregulated by cortisol and aldosterone, but significantly upregulated by circulating catecholamines and β-rhythm generating neurons.

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are carried out in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all participants the informed consent is got and used all measures for providing of anonymity of participants.

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