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Sexual dimorphism in relationships between of plasma urea and some psycho-neuro-endocrine parameters

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Summary

Background. Earlier we found a strong urato-neural relationships in both men and women. Moreover, in women, the factor structure of the neural root is almost completely different from that in men. In addition, significant differences were found between the profiles of urato-neural correlations of women of reproductive age and postmenopausal women. The **purpose** of this study is to analyze the relationships between the plasma urea level and some psycho-neuro-endocrine parameters in the same cohort. **Materials and Methods**. The object of observation were almost healthy volunteers: 31 males (24÷69 y) and 30 females, from among them 18 postmenopausal (48÷76 y) and 12 of reproductive age (30÷45 y). In basal conditions we determined plasma levels of urea and adaptation hormones, estimated the severity of the trait and reactive anxiety, recorded the ongoing HRV and EEG. After 4 or 7 days, repeated testing was performed. **Results**. By building regression models with stepwise exclusion, it was found that in men plasma urea positively determines (R^2=0,499) the level of circulating catecholamines and power spectrum density (PSD) of δ-, θ- and β-rhythms in different loci. In postmenopausal women, urea downregulates the amplitude and PSD of δ-rhythm in different loci, instead, it upregulates the PSD of α-rhythm in T5 locus, entropy of EEG in 2 loci and vagal tone. The degree of determination of neural parameters is 71,6%. In women of reproductive age the degree of determination of neural parameters is similar (69,9%), but the factor structure of the model is completely different. Urea upregulates the PSD of β-rhythm in F7 locus while downregulates the levels of reactive anxiety, vagal tone, entropy of EEG in 3 loci and P4-θ PSD as well as causes left lateralization of θ- and α-rhythms. **Conclusion.** Plasma urea has a modulating effect on EEG&HRV parameters, as

well as reactive anxiety, but this effect is significantly different in men and women of different ages.
Keywords: plasma urea, cortisol, testosterone, aldosterone, triiodothyronine, calcitonin, ongoing EEG, HRV, anxiety, men, women.

INTRODUCTION

Earlier we found a strong urato-neural relationships in both men (R=0,709) and women (R=0,812). Moreover, in women, the factor structure of the neural root is almost completely different from that in men, and also includes reactive anxiety and HRV parameters, which are absent in the factor structure of men. In addition, significant differences were found between the profiles of urato-neural correlations of women of reproductive age and postmenopausal women [14].

The **purpose** of this study, carried out as part of the "Neuro-endocrine activity of nitrogenous metabolites" project [3-5,14], is to analyze the relationships between the plasma **urea** level and some psycho-neuro-endocrine parameters in the same cohort.

The choice of tests is based on the concept of the existence of relationships between EEG& HRV parameters and adaptation hormones [7,8,12,16,17].

MATERIAL AND METHODS

The object of observation were employees of the clinical sanatorium "Moldova" and PrJSC "Truskavets' Spa": 31 males (24÷69 y) and 30 females, from among them 18 postmenopausal (48÷76 y) and 12 of reproductive age (30÷45 y). 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 as a manifestation of maladaptation [4,5].

Testing was performed twice with an interval of 4 (in 11 men and 10 women; "Moldova") or 7 (in 10 men and 10 women; "Truskavets' Spa") days.

We determined the plasma levels of the Urea (by urease method by reaction with phenol hypochlorite) [6] as well as main adaptation hormones Cortisol, Aldosterone, Testosterone, Triiodothyronine and Calcitonin (by the ELISA with the use of corresponding sets of reagents from "Алкор Био", XEMA Co. Ltd, and DRG International Inc).

The analyzers "Pointe-180" ("Scientific", USA), "Reflotron" (Boehringer Mannheim, BRD) and "RT-2100C" (PRCh) were used.

The levels of the trait and reactive anxiety estimated by STAI of Spielberger ChD [20] in modification of Khanin YL [13].

The state of the autonomic and central nervous systems was evaluated according to the parameters of heart rate variability [1,2,10,19] (software-hardware complex "CardioLab+HRV", KhAI-MEDICA, Kharkiv) and QEEG (hardware-software complex "NeuroCom Standard", KhAI MEDICA, Kharkiv). Kerdö's Vegetative Index [11] was also calculated.

In addition to routine parameters, Shannon's CE [18] Entropy of HRV and EEG were calculated [9,15]. See the previous articles for details [3-5].

Results processed by using the software package "Statistica 6.4".

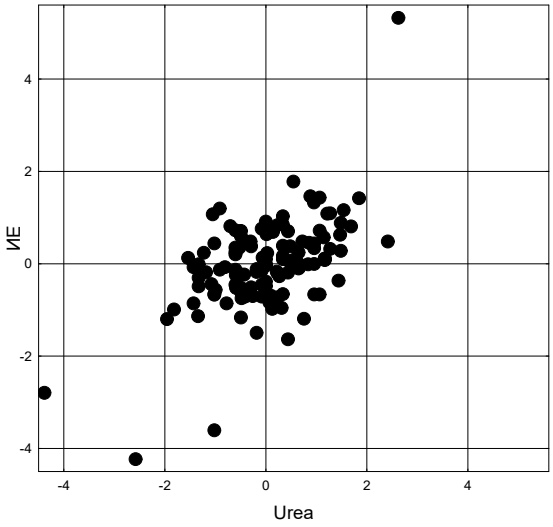
RESULTS AND DISCUSSION

At the first stage, following the algorithm of Truskavetsian Scientific School of Balneology [9,15], regression models were built by step-by-step exclusion of the variable until the maximum value of Adjusted R^2 was reached.

For the cohort as a whole, the regression model includes only three HRV and 4 EEG parameters in the absence of anxiety and hormone parameters. The degree of determination of neural parameters by plasma urea level was very moderate (Table 1 and Fig. 1).

Table 1. Regression Summary for Urea plasma in total cohort
R=0,558; R^2=0,311; Adjusted R^2=0,269; $F_{(7,1)}$=7,4; $p<10^{-5}$

N=122		Beta	St. Err. of Beta	B	SE of B	$t_{(114)}$	p-level
Variables	r		Intercpt	6,302	0,528	11,9	10^{-6}
C4-δ PSD, μV²/Hz	**-0,26**	-0,292	0,081	-0,00038	0,00010	-3,61	0,0005
Deviation-β, Hz	**-0,23**	-0,203	0,079	-0,2499	0,0980	-2,55	0,012
Entropy HRV	**-0,22**	-0,164	0,080	-1,357	0,661	-2,05	0,042
Total Power HRV, msec²	**0,24**	0,182	0,083	0,00004	0,00002	2,20	0,030
Baevskiy's ARSI, units	**0,24**	0,160	0,085	0,060	0,032	1,89	0,061
F7-δ PSD, μV²/Hz	**0,18**	0,241	0,080	0,00014	0,00004	3,01	0,003
Deviation-α, Hz	**0,16**	0,181	0,079	0,3485	0,1516	2,30	0,023



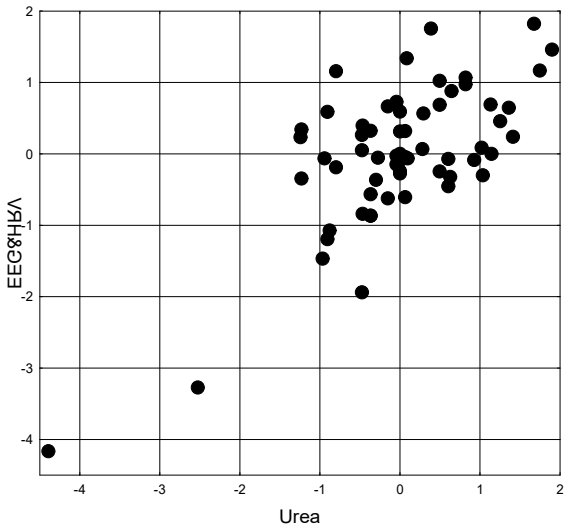
R=0,558; R^2=0,311; $\chi^2_{(7)}$=43; $p<10^{-6}$; Λ Prime=0,689

Fig. 1. Scatterplot of canonical correlation between Urea plasma (X-line) and HRV&EEG parameters (Y-line) in total cohort

However, a separate analysis revealed a quantitatively and qualitatively different picture. In particular, in men, the level of plasma urea upregulates the level of circulating catecholamines and power spectrum density (PSD) of δ-, θ- and β-rhythms in different loci. The degree of determination of neural parameters is 49,9% (Table 2 and Fig. 2).

Table 2. Regression Summary for Urea plasma in Men
R=0,706; R^2=0,499; Adjusted R^2=0,423; $F_{(8,5)}$=6,6; $p=10^{-5}$

N=62		Beta	St. Err. of Beta	B	SE of B	$t_{(53)}$	p-level
Variables	r		Intercpt	6,823	0,641	10,6	10^{-6}
1/Mode HRV, msec⁻¹	**0,42**	-0,424	0,104	-0,0029	0,0007	-4,09	10^{-4}
T5-δ PSD, μV²/Hz	**0,30**	0,364	0,296	0,0004	0,0004	1,23	0,224
F8-θ PSD, μV²/Hz	**0,29**	0,242	0,181	0,0040	0,0030	1,34	0,186
F7-δ PSD, μV²/Hz	**0,28**	0,504	0,279	0,0002	0,0001	1,80	0,077
F7-θ PSD, μV²/Hz	**0,27**	-0,628	0,284	-0,0140	0,0064	-2,21	0,031
C3-β PSD, %	**0,28**	0,180	0,128	0,0159	0,0113	1,40	0,166
Fp1-β PSD, %	**0,23**	0,285	0,132	0,0187	0,0087	2,16	0,036
T3-β PSD, μV²/Hz	**0,22**	0,228	0,113	0,0054	0,0027	2,02	0,049



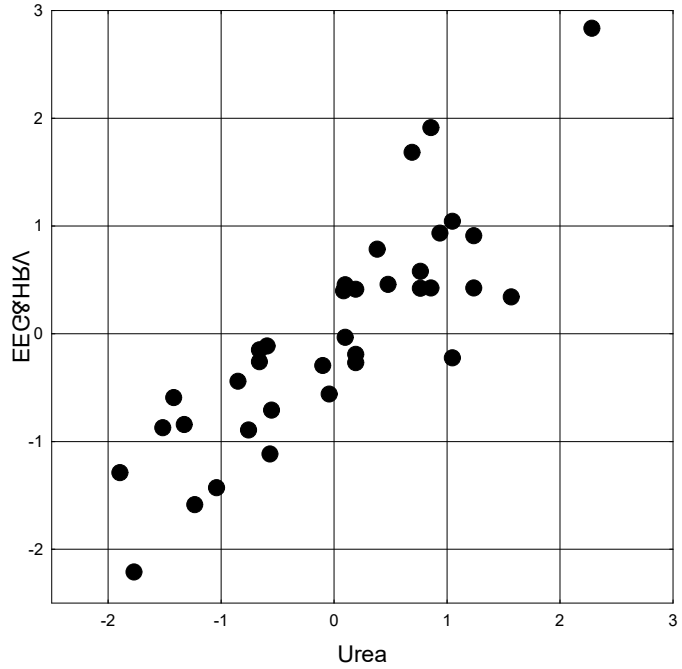
R=0,706; R^2=0,499; $\chi^2_{(8)}$=39; $p<10^{-5}$; Λ Prime=0,501

Fig. 2. Scatterplot of canonical correlation between Urea plasma (X-line) and EEG&HRV parameters at Men (Y-line)

In postmenopausal women, urea downregulates the amplitude and PSD of δ-rhythm in different loci, instead, it upregulates the PSD of α-rhythm in T5 locus, entropy of EEG in two loci and markers of vagal tone. The degree of determination of neural parameters is 71,6% (Table 3 and Fig. 3).

Table 3. Regression Summary for Urea plasma in postmenopausal (48÷76 y) Women
R=0,846; R^2=0,716; Adjusted R^2=0,548; $F_{(13,2)}$=4,3; p=0,014

N=36		Beta	St. Err. of Beta	B	SE of B	$t_{(22)}$	p-level
Variables	r		Intercpt	2,695	2,000	1,35	0,192
Fp1-δ PSD, μV²/Hz	**-0,41**	2,869	0,976	0,0040	0,0014	2,94	0,008
F4-δ PSD, μV²/Hz	**-0,38**	-1,583	0,539	-0,0019	0,0007	-2,94	0,008
T5-δ PSD, μV²/Hz	**-0,37**	-0,779	0,384	-0,0009	0,0004	-2,03	0,055
F8-δ PSD, μV²/Hz	**-0,36**	-1,848	0,576	-0,0016	0,0005	-3,21	0,004
Index θ, %	**-0,33**	-0,696	0,189	-0,0263	0,0071	-3,69	0,001
Deviation β, Hz	**-0,31**	-0,327	0,129	-0,3339	0,1317	-2,54	0,019
T5-δ PSD, %	**-0,27**	0,628	0,327	0,0322	0,0168	1,92	0,068
Amplitude δ, μV	**-0,27**	0,822	0,324	0,0389	0,0153	2,54	0,019
Entropy C4	**0,32**	0,425	0,203	2,725	1,305	2,09	0,049
Entropy F4	**0,29**	-0,405	0,278	-2,248	1,539	-1,46	0,158
T5-α PSD, %	**0,28**	0,500	0,210	0,0281	0,0118	2,38	0,027
MxDMn HRV, msec	**0,28**	0,368	0,132	0,0060	0,0021	2,80	0,011
Kerdö Vegetative Ind, un.	**0,28**	0,452	0,126	0,0180	0,0050	3,59	0,002



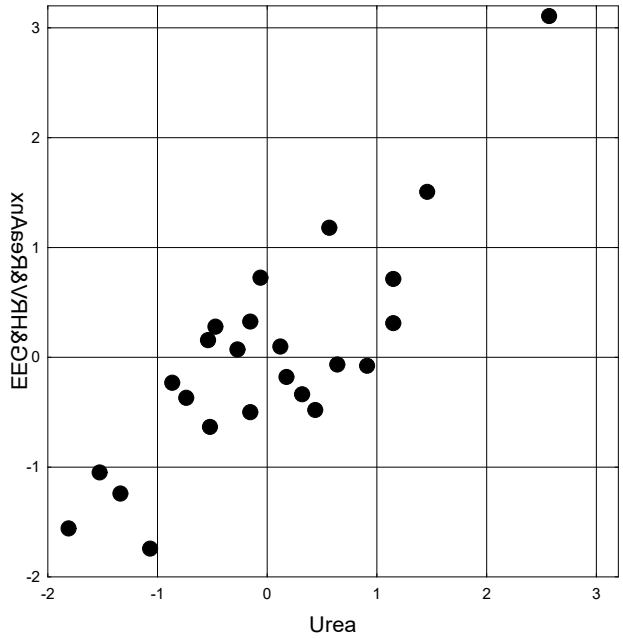
R=0,846; R^2=0,716; $\chi^2_{(13)}$=35; $p<10^{-3}$; Λ Prime=0,284

Fig. 3. Scatterplot of canonical correlation between Urea plasma (X-line) and EEG&HRV parameters at postmenopausal Women (Y-line)

In women of reproductive age (Table 4 and Fig. 4) the degree of determination of neural parameters is similar (69,9%), but the factor structure of the model is completely different. Urea upregulates the PSD of β-rhythm in F7 locus while downregulates the levels of reactive anxiety, vagal tone, entropy of EEG in 3 loci and P4-θ PSD as well as causes left lateralization of θ- and α-rhythms.

Table 4. Regression Summary for Urea plasma in premenopausal (30÷45 y) Women
R=0,836; R^2=0,699; Adjusted R^2=0,467; $F_{(10,1)}$=3,0; p=0,033

N=24		Beta	St. Err. of Beta	B	SE of B	$t_{(13)}$	p-level
Variables	r		Intercpt	9,023	1,517	5,95	10^{-4}
Entropy P4	**-0,39**	-1,245	0,376	-8,753	2,643	-3,31	0,006
Laterality Index θ, %	**-0,37**	0,991	0,361	0,0329	0,0120	2,75	0,017
Laterality Index-α, %	**-0,34**	-0,837	0,247	-0,0254	0,0075	-3,38	0,005
Entropy Fp1	**-0,32**	0,424	0,311	2,436	1,789	1,36	0,197
HF HRV PSD, %	**-0,32**	-0,721	0,247	-0,0614	0,0210	-2,92	0,012
T4-θ PSD, %	**-0,31**	-0,415	0,178	-0,1028	0,0440	-2,34	0,036
Reactive anxiety, points	**-0,29**	-0,425	0,204	-0,0491	0,0236	-2,08	0,058
Entropy T5	**-0,28**	0,450	0,227	2,734	1,378	1,98	0,069
P4-θ PSD, %	**-0,28**	0,719	0,280	0,1659	0,0645	2,57	0,023
F7-β PSD, $\mu V^2/Hz$	**0,29**	0,954	0,274	0,0275	0,0079	3,48	0,004



R=0,836; R^2=0,699; $\chi^2_{(10)}$=20; p=0,026; Λ Prime=0,301

Fig. 4. Scatterplot of canonical correlation between Urea plasma (X-line) and Psycho-Neural parameters at premenopausal Women (Y-line)

In order to visualize the strength and directionality of the relationships between plasma urea levels and psycho-neuro-endocrine parameters at premenopausal and postmenopausal women as well as men, three profiles were created (Fig. 5).

Next, the parameters were grouped into clusters (Fig. 6).

It seems that the differences between the neurotropic effects of urea in the three groups of people are related to the levels of sex hormones, but cannot be completely reduced to them. This will be the subject of a separate study.

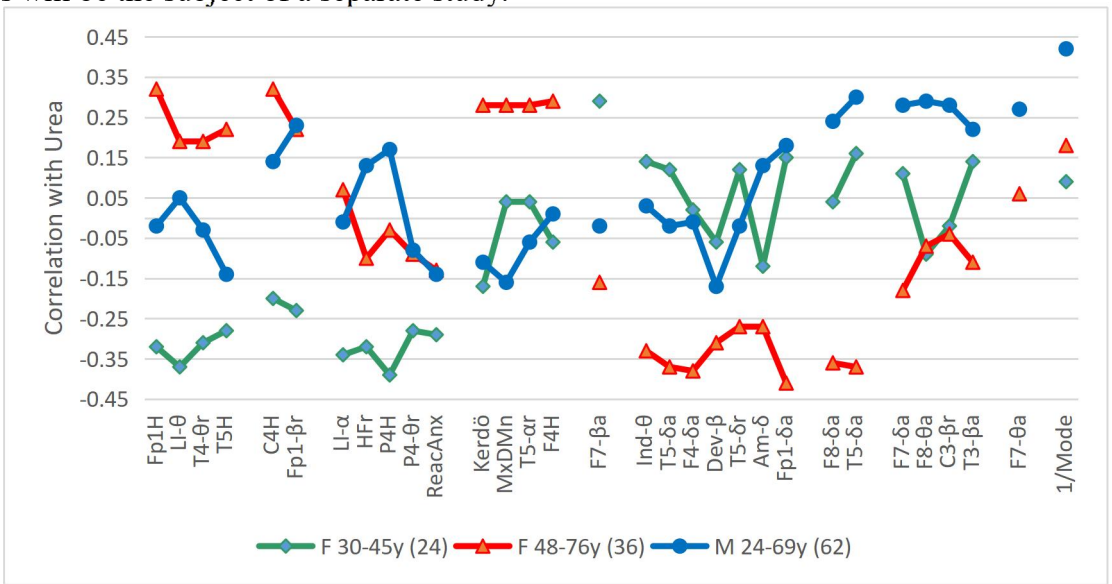


Fig. 5. Profiles of relationships between plasma Urea and Psycho-Neuro-Endocrine parameters at premenopausal and postmenopausal Females as well as Males

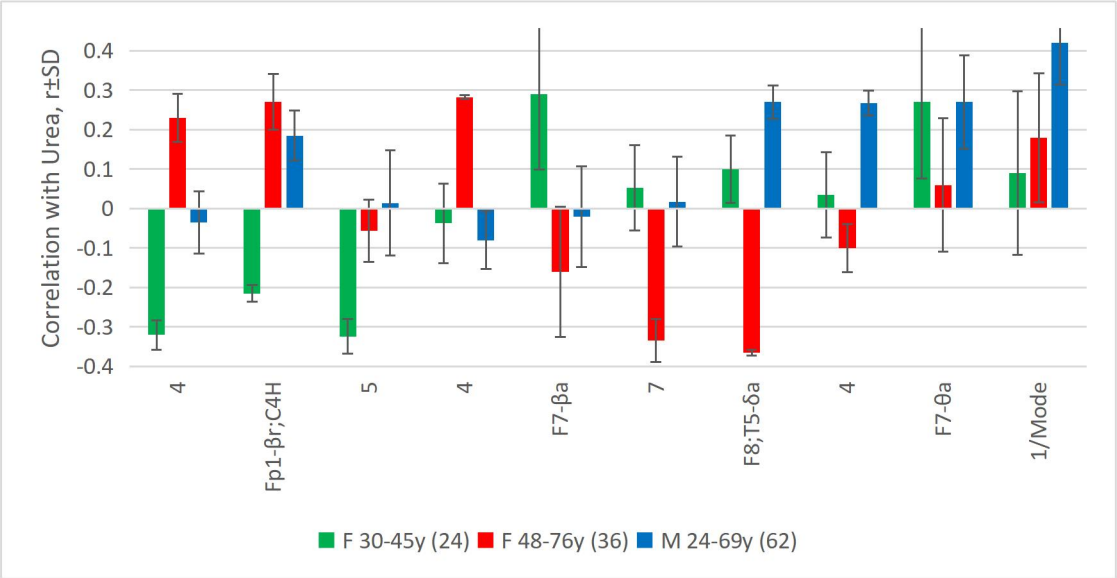


Fig. 6. Clusteres of relationships between plasma Urea and Psycho-Neuro-Endocrine parameters at premenopausal and postmenopausal Females as well as Males. The number of variables in the cluster is given

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are carried out in accordance with positions of Helsinki Declaration 1975 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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