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# Relationships between the parameters of uric acid exchange and electroencephalograms in humans

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## Summary

**Background**. During the implementation of the project "Physiological activity of uric acid", our group discovered four variants of the combination of levels of uricemia and uricosuria both in healthy rats and in people with chronic pyelonephritis and cholecystitis in the remission phase, which are accompanied by characteristic constellations of parameters of the autonomic nervous, endocrine, and immune systems, as well as the exchange of nitrogenous metabolites and electrolytes, the levels of which correlate with uricemia and/or uricosuria. The **aim** of this study is to clarify the relationship between parameters of uric acid metabolism and electroencephalogram (EEG) in humans. **Materials and methods.** Under an observations were 34 males and 10 females by age 24-76 years with chronic pyelonephritis and cholecystitis in the phase of remission. The object of the study was serum and urine levels of uric acid (uricase method) as well as EEG. **Results**. It was identified 12 parameters as characteristic of uric acid metabolism clusters. Another 42 EEG parameters were found to be out of the discriminant model, despite the clear recognition ability. A strong canonical correlation between EEG parameters and uricemia (R=0,729) and a moderate correlation with uricosuria (R=0,553) were revealed. Even stronger connections were found between changes in parameters of uric acid metabolism and EEG under the influence of balneotherapy: R=0,901 and 0,681 respectively. **Conclusion**. Uric acid has both activating and inhibitory effects on EEG parameters. The neurotropic effect of uric acid as a structural analogue of methylxanthines and adenosine is realized, apparently, through various adenosine receptors.

***Keywords***: uricemia, uricosuria, EEG, relationships, human.

## INTRODUCTION

During the implementation of the project "Physiological activity of uric acid" [13], our group discovered four variants of the combination of levels of uricemia and uricosuria both in healthy rats [3,4,14-17,32] and in people with chronic pyelonephritis and cholecystitis in the remission phase [5,6,18,19,33,42], which are accompanied by characteristic constellations of parameters of the autonomic nervous, endocrine, and immune systems, as well as the exchange of nitrogenous metabolites and electrolytes, the levels of which correlate with uricemia and/or uricosuria.

The **aim** of this study is to clarify the relationship between parameters of uric acid metabolism and electroencephalogram in humans.

## MATERIALS AND METHODS

Under an observations were 34 males and 10 females by age 24-76 years with chronic pyelonephritis and cholecystitis in the phase of remission. Testing was performed twice - on admission and after 7-10 days of standard balneotherapy on Truskavets Spa (drinking of Naftussya bioactive water, applications of ozokerite, mineral pools) [7,34].

The object of the study was serum and urine levels of uric acid (estimated by uricase method [11]) as well as electroencephalogram (EEG).

EEG recorded 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. Two minutes after the eyes had been closed, 25 sec of artifact free EEG data were collected by computer. Among the options considered the average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), absolute ($\mu V^2/Hz$) and relative (%) power spectral density (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 equations [29]:

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

We calculated also for each locus EEG the Entropy (h) of normalized PSD using Popovych’s IL [12,31,34,39] equation based on classic Shannon’s CE [41] equation:

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

Reference values are taken from the database of our laboratory [34].

Results processed using the software package "Statistica 6.4".

## RESULTS AND DISCUSSION

Following the pre-accepted algorithm [13], the recorded UA&EEG parameters were subjected to discriminant analysis [24]. The forward stepwise program identified 12 parameters as characteristic of uric acid metabolism clusters. In addition to uric acid parameters by default, 4 **delta-rhythm**, 2 **theta-rhythm**, 1 **alpha-rhythm** and 3 **entropy** parameters are included in the discriminant model (Tables 1 and 2).

Another 42 EEG parameters (19 **delta-rhythm**, 8 **theta-rhythm**, 3 **alpha-rhythm** and **entropy** as well as 9 **beta-rhythm**) were found to be out of the model, despite the clear recognition ability (Tables 3-6).

**Table 1. Summary of Stepwise Analysis for Uric acid and EEG Variables, ranked by criterion Λ**

| Variables currently in the model | F to enter | p-level | Λ | F-value | p-level |
|---|---|---|---|---|---|
| **Uricosuria** | 154 | $10^{-6}$ | 0,154 | 154 | $10^{-6}$ |
| **Uricemia normalized** | 13,46 | $10^{-6}$ | 0,104 | 58,3 | $10^{-6}$ |
| **PSD T4-δ, μV²/Hz** | 3,96 | 0,011 | 0,090 | 37,4 | $10^{-6}$ |
| **PSD O2-θ, %** | 3,51 | 0,019 | 0,080 | 28,6 | $10^{-6}$ |
| **Laterality δ, %** | 3,40 | 0,022 | 0,071 | 23,7 | $10^{-6}$ |
| **PSD C4 Entropy** | 1,94 | 0,129 | 0,066 | 20,1 | $10^{-6}$ |
| **PSD C3-δ, %** | 2,58 | 0,060 | 0,060 | 17,8 | $10^{-6}$ |
| **PSD F4 Entropy** | 2,02 | 0,118 | 0,056 | 15,9 | $10^{-6}$ |
| **PSD T6-α, %** | 1,72 | 0,171 | 0,052 | 14,4 | $10^{-6}$ |
| **PSD F7-θ, μV²/Hz** | 1,89 | 0,139 | 0,049 | 13,3 | $10^{-6}$ |
| **PSD T4 Entropy** | 1,45 | 0,235 | 0,046 | 12,2 | $10^{-6}$ |
| **PSD C3-δ, μV²/Hz** | 1,30 | 0,281 | 0,044 | 11,4 | $10^{-6}$ |

**Table 2. Discriminant Function Analysis Summary for Uric acid and EEG Variables, their actual levels for Clusters as well as Reference levels and Coefficients of Variability**

Step 12, N of vars in model: 12; Grouping: 4 grps; Wilks' Λ: 0,0435; appr. $F_{(36)}=11,4$; $p<10^{-6}$

| Variables currently in the model | **Clusters of Uric Acid Exchange (Males/Females)** | | | | **Parameters of Wilks' Statistics** | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **S-E2+ IV (18/4)** | **S± E+ I (16/5)** | **S2-E+ II (14/1)** | **S± E- III (20/10)** | Wilks' Λ | Partial Λ | F-remove | p-level | Tolerancy | Reference Cv/**σ** (112) |
| **Uricosuria, mM/24 h** | 5,94 | 3,94 | 3,88 | 2,27 | 0,274 | 0,159 | 129 | $10^{-6}$ | 0,893 | 3,00 0,250 |
| **Uricemia normalized, Z** | -0,70 | +0,09 | -1,89 | -0,53 | 0,070 | 0,619 | 15,0 | $10^{-6}$ | 0,835 | 0 |
| **Laterality δ, %** | -9,6 | -24,9 | -27,5 | +6,8 | 0,048 | 0,913 | 2,31 | 0,083 | 0,779 | +2,5 **39,8** |
| **PSD T4-δ, μV²/Hz** | 57 | 354 | 94 | 161 | 0,050 | 0,864 | 3,84 | 0,013 | 0,181 | 92 1,091 |
| **PSD C3-δ, %** | 25,7 | 42,1 | 32,4 | 30,5 | 0,046 | 0,939 | 1,59 | 0,199 | 0,282 | 28,0 0,602 |
| **PSD C3-δ, μV²/Hz** | 91 | 315 | 259 | 166 | 0,046 | 0,949 | 1,30 | 0,281 | 0,234 | 108 0,774 |
| **PSD O2-θ, %** | 6,3 | 5,1 | 5,3 | 9,1 | 0,054 | 0,803 | 5,96 | 0,001 | 0,642 | 7,1 0,554 |
| **PSD F7-θ, μV²/Hz** | 15,8 | 42,7 | 29,1 | 28,3 | 0,047 | 0,922 | 2,07 | 0,112 | 0,254 | 18,2 0,843 |
| **PSD T6-α, %** | 37,8 | 27,3 | 24,4 | 28,0 | 0,047 | 0,921 | 2,10 | 0,106 | 0,591 | 35,5 0,502 |
| **PSD C4 Entropy** | 0,83 | 0,87 | 0,80 | 0,85 | 0,049 | 0,881 | 3,30 | 0,025 | 0,317 | 0,867 0,109 |
| **PSD F4 Entropy** | 0,81 | 0,71 | 0,80 | 0,81 | 0,046 | 0,938 | 1,60 | 0,197 | 0,374 | 0,851 0,139 |
| **PSD T4 Entropy** | 0,84 | 0,76 | 0,82 | 0,82 | 0,047 | 0,930 | 1,84 | 0,147 | 0,342 | 0,844 0,137 |
| **Variable currently not in model** | | | | | Wilks' Λ | Partial Λ | F to enter | p-level | Tolerancy | Reference (112) |
| **Uricemia, mM/L** | 0,316 | 0,371 | 0,249 | 0,322 | 0,043 | 0,979 | 0,52 | 0,668 | 0,213 | 0,365 0,116 |

**Table 3. Parameters of EEG delta-rhythm not included in the model**

| Variables | Clusters of Uric Acid Exchange (Males/Females) | | | | Parameters of Wilks' Statistics | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | S- E2+ IV (18/4) | S± E+ I (16/5) | S2- E+ II (14/1) | S± E- III (20/10) | Wilks Λ | Partial Λ | F to enter | p-level | Tolerancy | Reference Cv (112) |
| **Amplitude δ, µV** | 13,2 | 29,5 | 18,9 | 20,4 | 0,043 | 0,994 | 0,15 | 0,927 | 0,482 | 14,9<br>0,431 |
| **PSD Fp1-δ, %** | 19,8 | 40,5 | 24,4 | 29,3 | 0,043 | 0,994 | 0,15 | 0,932 | 0,486 | 23,6<br>0,687 |
| **PSD Fp1-δ, µV²/Hz** | 39 | 560 | 63 | 102 | 0,043 | 0,986 | 0,35 | 0,790 | 0,734 | 58<br>1,132 |
| **PSD Fp2-δ, %** | 20,5 | 40,0 | 26,5 | 32,7 | 0,043 | 0,991 | 0,23 | 0,878 | 0,531 | 26,5<br>0,687 |
| **PSD Fp2-δ, µV²/Hz** | 39 | 636 | 71 | 119 | 0,043 | 0,983 | 0,42 | 0,737 | 0,717 | 74<br>1,260 |
| **PSD F4-δ, µV²/Hz** | 111 | 424 | 204 | 215 | 0,043 | 0,981 | 0,46 | 0,711 | 0,270 | 115<br>1,014 |
| **PSD F7-δ, %** | 22,5 | 53,2 | 32,3 | 35,1 | 0,043 | 0,982 | 0,44 | 0,724 | 0,625 | 31,4<br>0,706 |
| **PSD F7-δ, µV²/Hz** | 47 | 1309 | 128 | 151 | 0,043 | 0,989 | 0,26 | 0,857 | 0,722 | 80<br>1,759 |
| **PSD F8-δ, %** | 27,6 | 53,3 | 40,8 | 40,7 | 0,043 | 0,981 | 0,46 | 0,710 | 0,640 | 35,2<br>0,656 |
| **PSD F8-δ, µV²/Hz** | 59 | 579 | 129 | 194 | 0,043 | 0,998 | 0,05 | 0,983 | 0,584 | 92<br>1,642 |
| **PSD T3-δ, %** | 26,6 | 45,3 | 38,0 | 31,7 | 0,043 | 0,993 | 0,16 | 0,920 | 0,527 | 28,6 |
| **PSD T3-δ, µV²/Hz** | 73 | 368 | 215 | 146 | 0,043 | 0,992 | 0,19 | 0,905 | 0,413 | 86<br>1,055 |
| **PSD T4-δ, %** | 24,7 | 45,9 | 29,0 | 36,7 | 0,043 | 0,998 | 0,04 | 0,988 | 0,223 | 31,0<br>0,615 |
| **PSD C4-δ, µV²/Hz** | 94 | 250 | 193 | 197 | 0,043 | 0,990 | 0,25 | 0,864 | 0,124 | 114<br>0,813 |
| **PSD T5-δ, %** | 25,7 | 45,0 | 33,0 | 32,2 | 0,043 | 0,983 | 0,42 | 0,736 | 0,729 | 26,3<br>0,696 |
| **PSD T6-δ, %** | 21,3 | 38,3 | 35,1 | 33,9 | 0,043 | 0,989 | 0,26 | 0,857 | 0,470 | 26,1<br>0,626 |
| **PSD T6-δ, µV²/Hz** | 45 | 420 | 124 | 159 | 0,043 | 0,996 | 0,09 | 0,963 | 0,607 | 74<br>1,110 |
| **PSD P4-δ, µV²/Hz** | 81 | 203 | 193 | 180 | 0,043 | 0,982 | 0,44 | 0,726 | 0,564 | 107<br>0,886 |
| **PSD O2-δ, µV²/Hz** | 78 | 548 | 188 | 318 | 0,043 | 0,978 | 0,54 | 0,654 | 0,672 | 95<br>0,965 |

**Table 4. Parameters of EEG theta-rhythm not included in the model**

| Variables | Clusters of Uric Acid Exchange (Males/Females) | | | | Parameters of Wilks' Statistics | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | S- E2+ IV (18/4) | S± E+ I (16/5) | S2- E+ II (14/1) | S± E- III (20/10) | Wilks Λ | Partial Λ | F to enter | p-level | Tolerancy | Reference Cv/σ (112) |
| Amplitude θ, µV | 7,4 | 10,0 | 8,9 | 9,1 | 0,042 | 0,972 | 0,69 | 0,564 | 0,341 | 7,75 0,376 |
| Laterality θ, % | -13,1 | -20,7 | -43,4 | -6,8 | 0,043 | 0,982 | 0,43 | 0,729 | 0,577 | -4,9 **38,9** |
| PSD Fp1-θ, % | 10,3 | 7,8 | 9,4 | 11,5 | 0,043 | 0,996 | 0,11 | 0,957 | 0,658 | 10,4 0,588 |
| PSD F7-θ, % | 9,5 | 7,4 | 10,2 | 9,2 | 0,043 | 0,990 | 0,24 | 0,871 | 0,528 | 10,0 0,458 |
| PSD T3-θ, $\mu V^2/Hz$ | 25 | 58 | 57 | 42 | 0,043 | 0,982 | 0,44 | 0,721 | 0,339 | 30 1,077 |
| PSD T4-θ, $\mu V^2/Hz$ | 21 | 44 | 28 | 40 | 0,043 | 0,991 | 0,22 | 0,885 | 0,294 | 28 1,114 |
| PSD T6-θ, % | 9,6 | 7,6 | 6,6 | 9,9 | 0,043 | 0,998 | 0,05 | 0,985 | 0,202 | 8,6 0,474 |
| PSD T5-θ, % | 11,4 | 8,9 | 7,7 | 9,9 | 0,043 | 0,998 | 0,06 | 0,981 | 0,201 | 9,7 0,471 |

**Table 5. Parameters of EEG alpha-rhythm and entropy not included in the model**

| Variables | Clusters of Uric Acid Exchange (Males/Females) | | | | Parameters of Wilks' Statistics | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | S- E2+ IV (18/4) | S± E+ I (16/5) | S2- E+ II (14/1) | S± E- III (20/10) | Wilks Λ | Partial Λ | F to enter | p-level | Tolerancy | Reference Cv/σ (112) |
| Laterality α, % | -1,2 | -14,6 | -29,1 | -9,6 | 0,043 | 0,997 | 0,07 | 0,977 | 0,580 | -1,1 **34,2** |
| PSD F7-α, % | 32,0 | 18,8 | 26,0 | 22,5 | 0,043 | 0,989 | 0,27 | 0,850 | 0,423 | 27,6 0,522 |
| PSD C4-α, % | 37,9 | 31,7 | 30,3 | 31,3 | 0,043 | 0,991 | 0,21 | 0,890 | 0,256 | 34,8 0,432 |
| PSD Fp1 Entropy | 0,83 | 0,74 | 0,80 | 0,82 | 0,043 | 0,979 | 0,52 | 0,669 | 0,567 | 0,848 0,116 |
| PSD F7 Entropy | 0,83 | 0,69 | 0,80 | 0,76 | 0,043 | 0,991 | 0,22 | 0,883 | 0,583 | 0,821 0,187 |
| PSD F8 Entropy | 0,80 | 0,66 | 0,70 | 0,77 | 0,042 | 0,961 | 0,98 | 0,407 | 0,584 | 0,815 0,202 |
| PSD O2 Entropy | 0,75 | 0,68 | 0,72 | 0,81 | 0,043 | 0,996 | 0,10 | 0,961 | 0,430 | 0,776 0,178 |

**Table 6. Parameters of EEG beta rhythms not included in the model**

| Variables | Clusters of Uric Acid Exchange (Males/Females) | | | | Parameters of Wilks' Statistics | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | S- E2+ IV (18/4) | S± E+ I (16/5) | S2- E+ II (14/1) | S± E- III (20/10) | Wilks Λ | Partial Λ | F to enter | p-level | Tolerancy | Reference Cv (112) |
| **Asymmetry β, %** | 22,1 | 17,7 | 17,9 | 25,6 | 0,042 | 0,968 | 0,79 | 0,504 | 0,677 | 23,4 0,679 |
| **PSD Fp2-β, %** | 33,6 | 22,2 | 34,4 | 27,6 | 0,043 | 0,987 | 0,31 | 0,815 | 0,682 | 30,7 0,504 |
| **PSD F3-β, %** | 22,8 | 17,4 | 26,4 | 23,8 | 0,043 | 0,979 | 0,53 | 0,665 | 0,601 | 26,7 0,463 |
| **PSD F7-β, %** | 36,1 | 20,6 | 31,5 | 33,1 | 0,043 | 0,981 | 0,46 | 0,712 | 0,710 | 31,0 0,558 |
| **PSD T3-β, %** | 31,6 | 18,9 | 24,1 | 32,2 | 0,043 | 0,999 | 0,02 | 0,995 | 0,670 | 30,7 0,462 |
| **PSD T4-β, %** | 31,4 | 21,4 | 36,8 | 28,3 | 0,043 | 0,990 | 0,25 | 0,860 | 0,567 | 30,4 0,483 |
| **PSD C3-β, %** | 25,6 | 17,6 | 24,8 | 25,4 | 0,043 | 1,000 | 0,01 | 0,999 | 0,432 | 25,5 0,420 |
| **PSD C4-β, %** | 25,1 | 21,4 | 28,1 | 22,9 | 0,043 | 0,985 | 0,37 | 0,775 | 0,407 | 25,9 0,405 |
| **PSD O1-β, %** | 27,8 | 17,0 | 24,5 | 25,3 | 0,043 | 0,983 | 0,42 | 0,737 | 0,734 | 26,3 0,542 |

Next, the 12-dimensional space of discriminant variables transforms into 3-dimensional space of a canonical roots. For Root 1 r*=0,929 (Wilks' Λ=0,044; $\chi^2_{(36)}$=248; p<$10^{-6}$), for Root 2 r*=0,706 (Wilks' Λ=0,317; $\chi^2_{(22)}$=91; p<$10^{-6}$), for Root 3 r*=0,607 (Wilks' Λ=0,631; $\chi^2_{(10)}$=36; p<$10^{-4}$). The major root contains 79,9% of discriminative opportunities, the second 12,6%, the minor 7,5%.

The calculation of the discriminant root values for each person as the sum of the products of raw coefficients to the individual values of discriminant variables together with the constant (Table 7) enables the visualization of each patient in the information space of the roots.

**Table 7. Standardized and Raw Coefficients and Constants for BP&EEG Variables**

| Coefficients | Standardized | | | Raw | | |
|---|---|---|---|---|---|---|
| **Variables** | Root 1 | Root 2 | Root 3 | Root 1 | Root 2 | Root 3 |
| **Uricosuria** | -1,044 | -0,022 | 0,082 | -1,733 | -0,037 | 0,136 |
| **Uricemia normalized** | -0,198 | 0,878 | 0,326 | -0,211 | 0,937 | 0,348 |
| **PSD T4-δ, μV²/Hz** | -0,215 | 1,099 | 0,552 | -0,001 | 0,005 | 0,002 |
| **PSD O2-θ, %** | 0,088 | -0,104 | 0,894 | 0,023 | -0,027 | 0,237 |
| **Laterality δ, %** | 0,082 | -0,126 | 0,514 | 0,002 | -0,004 | 0,015 |
| **PSD C4 Entropy** | -0,184 | 0,465 | -0,806 | -1,523 | 3,847 | -6,660 |
| **PSD C3-δ, %** | -0,267 | 0,386 | -0,472 | -0,014 | 0,021 | -0,025 |
| **PSD F4 Entropy** | -0,057 | -0,488 | 0,344 | -0,366 | -3,126 | 2,204 |
| **PSD T6-α, %** | -0,221 | 0,387 | 0,220 | -0,015 | 0,026 | 0,015 |
| **PSD F7-θ, μV²/Hz** | 0,247 | -0,290 | -0,761 | 0,007 | -0,008 | -0,022 |
| **PSD T4 Entropy** | -0,214 | 0,434 | 0,443 | -1,768 | 3,584 | 3,657 |
| **PSD C3-δ, μV²/Hz** | 0,046 | -0,606 | -0,296 | 0,0002 | -0,002 | -0,001 |
| | | | **Constants** | 10,20 | -4,279 | -0,091 |
| | | | **Eigenvalues** | 6,283 | 0,992 | 0,584 |
| | | | **Cumulative proportions** | 0,799 | 0,926 | 1 |

At the next stage of the analysis, the actual values of the parameters were normalized and grouped into three discriminant roots based on structural coefficients that reflect the strength and nature of the connection between the variable and the root. In addition, the table includes parameters that did not enter the discriminant model due to duplication/redundancy of information (Table 8).

**Table 8. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Uric acid and EEG Variables**

| Variables | Correlations Variables-Roots | | | S-E2+ IV (22) | S±E+ I (21) | S2-E+ II (15) | S±E- III (30) |
|---|---|---|---|---|---|---|---|
| *Root 1 (79,9%)* | R 1 | R 2 | R 3 | -3,61 | -0,44 | +0,31 | +2,80 |
| Uricosuria | -0,932 | -0,192 | -0,004 | +3,87 | +1,26 | +1,17 | -0,97 |
| *Root 2 (12,6%)* | R 1 | R 2 | R 3 | -0,21 | +1,36 | -1,70 | +0,05 |
| Uricemia normalized | 0,002 | 0,678 | 0,161 | -0,70 | +0,09 | -1,89 | -0,53 |
| PSD C4 Entropy | 0,025 | 0,149 | 0,017 | -0,44 | +0,07 | -0,67 | -0,14 |
| PSD T4-δ, μV²/Hz | 0,039 | 0,298 | -0,243 | -0,35 | +2,60 | +0,02 | +0,69 |
| PSD F7-δ, μV²/Hz | | | | -0,23 | +8,79 | +0,35 | +0,51 |
| PSD Fp1-δ, μV²/Hz | | | | -0,29 | +7,69 | +0,08 | +0,68 |
| PSD Fp2-δ, μV²/Hz | | | | -0,38 | +6,04 | -0,03 | +0,48 |
| PSD F8-δ, μV²/Hz | | | | -0,22 | +3,22 | +0,25 | +0,68 |
| PSD C3-δ, % | 0,020 | 0,139 | -0,245 | -0,14 | +0,83 | +0,26 | +0,26 |
| PSD F7-θ, μV²/Hz | 0,037 | 0,112 | -0,194 | -0,16 | +1,59 | +0,71 | +0,66 |
| Amplitude θ, μV | | | | -0,12 | +0,76 | +0,38 | +0,45 |
| PSD F8-δ, % | | | | -0,33 | +0,78 | +0,24 | +0,24 |
| PSD T5-δ, % | | | | -0,03 | +1,02 | +0,36 | +0,32 |
| Amplitude δ, μVz | | | | -0,26 | +2,29 | +0,62 | +0,87 |
| PSD F4-δ, μV²/Hz | | | | -0,03 | +2,66 | +0,76 | +0,86 |
| PSD T6-δ, μV²/Hz | | | | -0,35 | +4,23 | +0,62 | +1,05 |
| PSD O2-δ, μV²/Hz | | | | -0,19 | +4,92 | +1,00 | +2,41 |
| PSD Fp2-δ, % | | | | -0,33 | +0,74 | 0,00 | +0,34 |
| PSD T4-θ, μV²/Hz | | | | -0,22 | +0,50 | +0,01 | +0,39 |
| PSD T4-δ, % | | | | -0,33 | +0,78 | -0,11 | +0,30 |
| PSD F7-δ, % | | | | -0,40 | +0,98 | +0,04 | +0,17 |
| PSD Fp1-δ, % | | | | -0,23 | +1,05 | +0,05 | +0,35 |
| PSD F4 Entropy | 0,006 | -0,146 | 0,189 | -0,31 | -1,20 | -0,44 | -0,38 |
| PSD T4 Entropy | -0,010 | -0,118 | 0,163 | -0,05 | -0,70 | -0,24 | -0,21 |
| PSD F7 Entropy | | | | +0,07 | -0,83 | -0,12 | -0,41 |
| PSD Fp1 Entropy | | | | -0,14 | -1,14 | -0,52 | -0,24 |
| PSD Fp1-θ, % | | | | -0,02 | -0,43 | -0,17 | +0,17 |
| PSD F7-θ, % | | | | -0,12 | -0,58 | +0,04 | -0,17 |
| PSD T4-β, % | | | | +0,07 | -0,61 | +0,43 | -0,14 |
| PSD Fp2-β, % | | | | +0,19 | -0,55 | +0,24 | -0,20 |
| PSD C4-β, % | | | | -0,08 | -0,43 | +0,21 | -0,29 |
| PSD C3-β, % | | | | +0,01 | -0,74 | -0,06 | -0,01 |
| PSD F3-β, % | | | | -0,32 | -0,76 | -0,03 | -0,23 |
| PSD F7-β, % | | | | +0,30 | -0,60 | +0,03 | +0,13 |
| PSD O1-β, % | | | | +0,10 | -0,65 | -0,12 | -0,07 |
| PSD F7-α, % | | | | +0,31 | -0,61 | -0,11 | -0,35 |
| *Root 3 (7,5%)* | R 1 | R 2 | R 3 | +0,66 | -0,82 | -1,00 | +0,59 |
| Laterality δ, % | 0,077 | 0,026 | 0,406 | -0,30 | -0,69 | -0,75 | +0,11 |
| PSD O2-θ, % | 0,112 | 0,007 | 0,391 | -0,18 | -0,49 | -0,45 | +0,52 |
| PSD T6-α, % | -0,080 | 0,022 | 0,210 | +0,13 | -0,46 | -0,63 | -0,42 |
| Laterality α, % | | | | 0,00 | -0,39 | -0,82 | -0,25 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Laterality θ, %** | | | | -0,21 | **-0,41** | **-0,99** | -0,05 |
| **PSD T5-θ, %** | | | | +0,38 | **-0,17** | **-0,42** | +0,04 |
| **PSD T6-θ, %** | | | | +0,25 | **-0,24** | **-0,48** | +0,31 |
| **Asymmetry β, %** | | | | -0,08 | **-0,36** | **-0,35** | +0,14 |
| **PSD T3-β, %** | | | | +0,07 | **-0,83** | **-0,46** | +0,10 |
| **PSD F8 Entropy** | | | | -0,07 | **-0,95** | **-0,69** | -0,26 |
| **PSD O2 Entropy** | | | | -0,17 | **-0,71** | **-0,38** | +0,25 |
| **PSD C3-δ, μV²/Hz** | 0,026 | **0,069** | **-0,311** | -0,20 | **+2,47** | **+1,80** | +0,70 |
| **PSD T3-δ, μV²/Hz** | | | | -0,14 | **+3,12** | **+1,43** | +0,67 |
| **PSD C4-δ, μV²/Hz** | | | | -0,22 | **+1,46** | **+0,86** | +0,90 |
| **PSD T6-δ, %** | | | | -0,30 | **+0,75** | **+0,55** | +0,47 |
| **PSD P4-δ, μV²/Hz** | | | | -0,27 | **+1,01** | **+0,91** | +0,77 |
| **PSD T3-δ, %** | | | | -0,12 | **+0,98** | **+0,55** | +0,18 |
| **PSD T3-θ, μV²/Hz** | | | | -0,17 | **+0,86** | **+0,84** | +0,37 |

The result of the analysis is the visualization of each patient in the information space of discriminant roots (Fig. 1).

Patients with **hypouricosuria** are located in the extreme right zone of the axis of the first root. Instead, patients with pronounced **hyperuricosuria** are located at the opposite pole of the axis. An intermediate position is occupied by patients of I and II clusters with moderately increased excretion of uric acid, while both the average levels and their dispersion are practically the same.

The delimitation of these clusters occurs along the axis of the second root. The top position of the members of the I cluster reflects their **normal**, but maximum for the sample levels of **uricemia** and EEG entropy in the C4 locus, as well as to one degree or another increased levels of 16 parameters of the delta-rhythm and 3 parameters of the theta-rhythm, on the one hand, instead, the maximum for sample reduced entropy levels in loci F4, T4, F7 and Fp1, as well as 7 parameters of beta-, 2 theta- and one alpha-rhythms - on the other hand. In members of the II cluster, against the background of **hypouricemia**, the levels of the listed parameters are lower/higher, respectively.

In addition, both clusters, taken together, are separated from IV and III clusters along the axis of the third root. Their common lowest position reflects the maximum for the sample left-sided asymmetry of delta-, alpha- and theta-rhythms, maximally reduced entropy in loci F8 and O2, as well as levels of 3 parameters of theta-, 2 beta- and one alpha-rhythms, on the one hand, instead, the maximally increased levels of 6 parameters of delta-rhythm and one parameter of theta-rhythm - on the other hand.

The apparent clear demarcation of all four clusters in the information space of the three roots is documented by the calculation of Mahalanobis distances (Table 9).

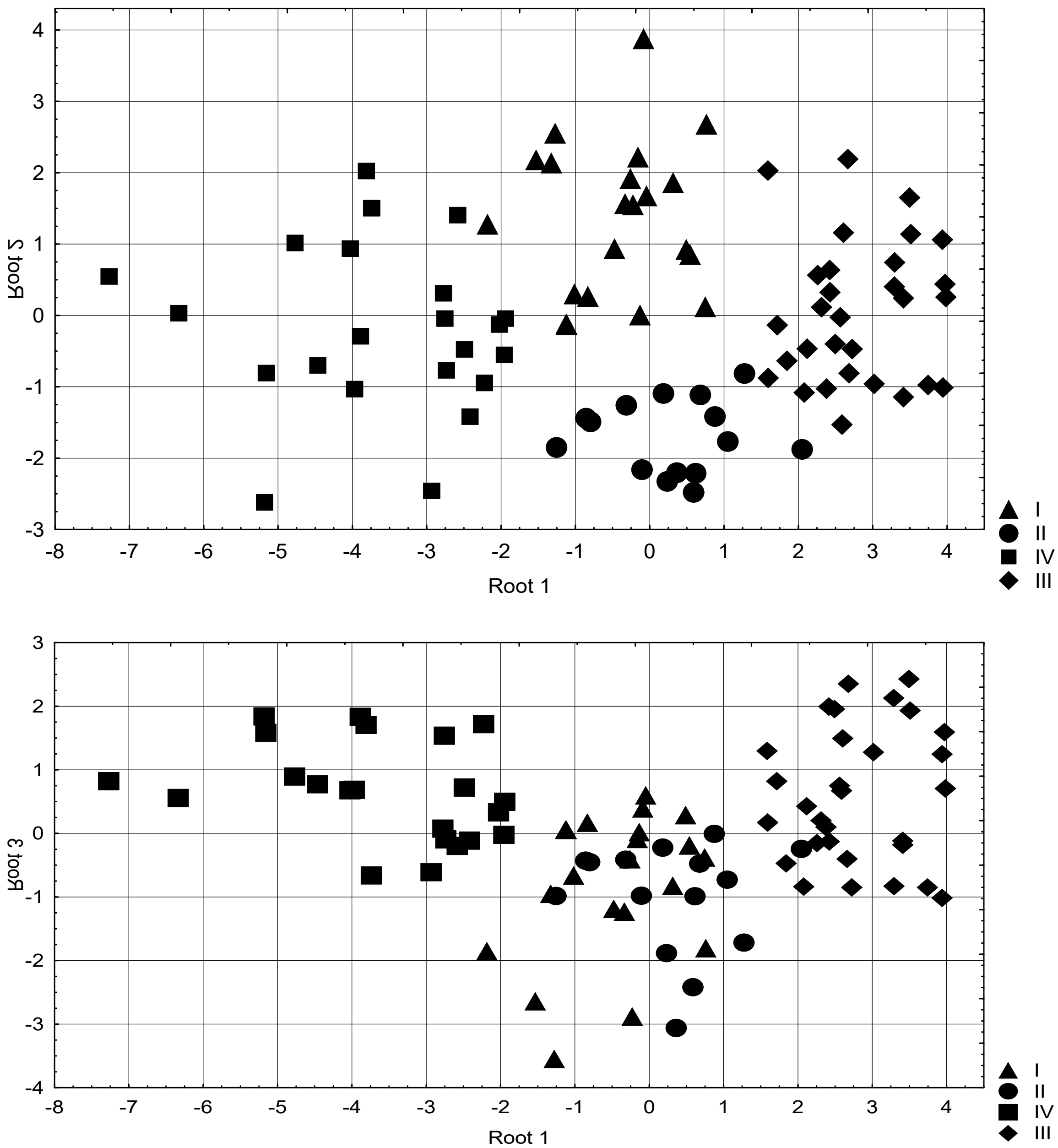



**Fig. 2. Scattering of individual values of the discriminant UA&EEG roots of patients of different uric acid clusters**

**Table 9. Squared Mahalanobis Distances between Clusters, F-values (df=12,7) and p levels**

| Clusters | **S±E+ I** | **S2-E+ II** | **S-E2+ IV** | **S±E- III** |
|---|---|---|---|---|
| **S±E+ I (21)** | 0 | 9,97 | 14,7 | 14,2 |
| **S2-E+ II (15)** | **6,3** $10^{-5}$ | 0 | 20,3 | 11,8 |
| **S-E2+ IV (22)** | **11,4** $10^{-6}$ | **13,1** $10^{-6}$ | 0 | 41,2 |
| **S±E- III (30)** | **12,7** $10^{-6}$ | **8,6** $10^{-6}$ | **24,1** $10^{-6}$ | 0 |

Another result of discriminant analysis is the possibility of retrospective identification of members of different clusters by calculating individual discriminant functions according to the coefficients and constants given in the Table 10.

**Table 10. Coefficients and Constants for Classification Functions for Uric acid Clusters**

| Clusters | S±E+ I | S2-E+ II | S-E2+ IV | S±E- III |
|---|---|---|---|---|
| **Variables** | p=,239 | p=,170 | p=,250 | p=,341 |
| **Uricosuria** | 17,83 | 16,62 | 23,58 | 12,45 |
| **Uricemia normalized** | 4,851 | 1,759 | 4,562 | 3,422 |
| **PSD T4-δ, μV²/Hz** | 0,058 | 0,043 | 0,057 | 0,052 |
| **PSD O2-θ, %** | 0,073 | 0,130 | 0,392 | 0,517 |
| **Laterality δ, %** | -0,165 | -0,155 | -0,145 | -0,132 |
| **PSD C4 Entropy** | 96,79 | 85,11 | 85,74 | 77,43 |
| **PSD C3-δ, %** | 0,478 | 0,409 | 0,454 | 0,370 |
| **PSD F4 Entropy** | -15,04 | -6,147 | -5,710 | -9,013 |
| **PSD T6-α, %** | 0,549 | 0,457 | 0,576 | 0,488 |
| **PSD F7-θ, μV²/Hz** | -0,286 | -0,251 | -0,328 | -0,283 |
| **PSD T4 Entropy** | 101,7 | 88,71 | 107,1 | 96,38 |
| **PSD C3-δ, μV²/Hz** | -0,011 | -0,003 | -0,009 | -0,008 |
| **Constants** | -133,3 | -113,5 | -164,4 | -97,11 |

Taking into account all features enables the retrospective recognition of members of all clusters almost without error: the classification accuracy is 98,9% (Table 11).

**Table 11. Classification matrix for clusters**

Rows: observed classifications; columns: predicted classifications

| | Percent | S±E+ I | S2-E+ II | S-E2+ IV | S±E- III |
|---|---|---|---|---|---|
| **Clusters** | correct | p=,239 | p=,170 | p=,250 | p=,341 |
| **S±E+ I** | 100 | **20** | 0 | 0 | 0 |
| **S2-E+ II** | 93,3 | 0 | **14** | 0 | **1** |
| **S-E2+ IV** | 100 | 0 | 0 | **22** | 0 |
| **S±E- III** | 100 | 0 | 0 | 0 | **30** |
| Total | 98,9 | 20 | 16 | 22 | 30 |

Two approaches were used to clarify the relationship between uric acid and EEG parameters. In the first approach, the object of analysis was the average values of clusters grouped into patterns. The linear nature of the relationship was revealed only in relation to the entropy of the PSD in the C4 locus (Fig. 12). Constellations of other EEG parameters are related to uric acid in a non-linear manner. In 4 constellations, which contain 31 EEG parameters, the coefficients of their determination by uricemia significantly outweigh those by uricosuria: 0,987÷0,758 vs 0,543÷0,332 (Figs. 13-18 and 21-22). In 2 constellations, which contain 18 EEG parameters, the coefficients of their determination by uricemia and uricosuria are equally high (Figs. 19-20 and 23-24). It is interesting that in all cases the curves of uricemia and uricosuria are quasi-mirror, and there is no correlation between them (Fig. 25).

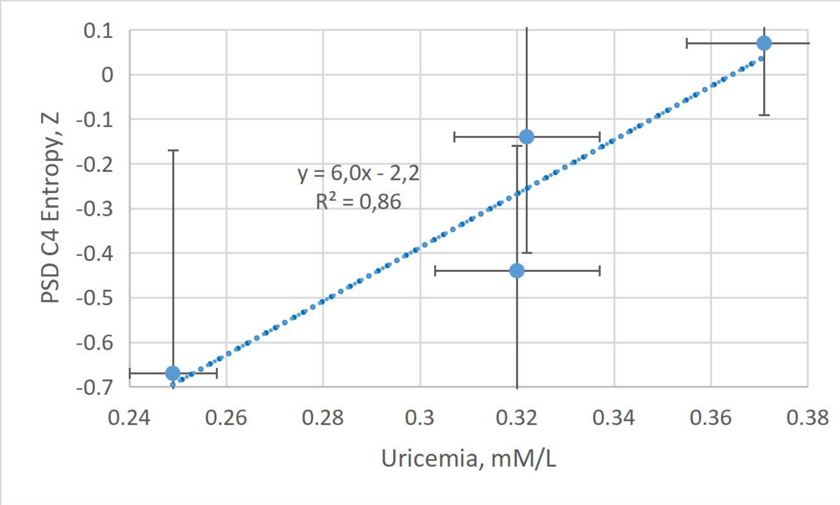



**Fig. 12. Linear relationship between uricemia and entropy of PSD at the C4 locus**

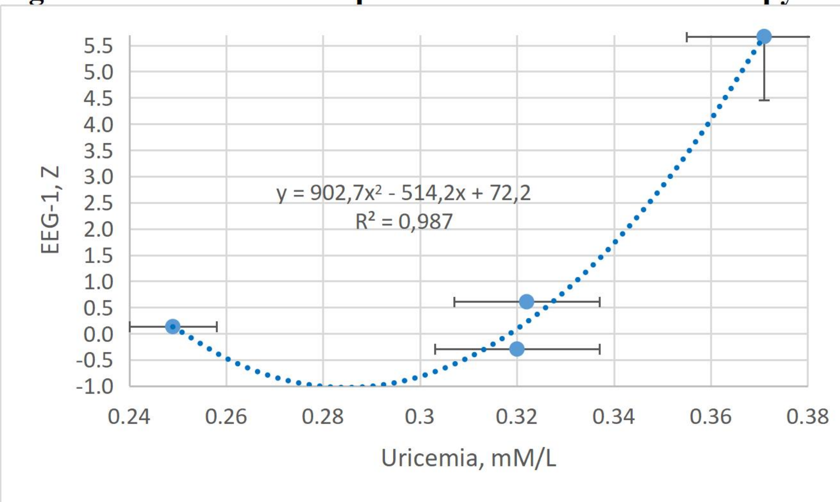



**Fig. 13. Nonlinear relationship between uricemia and PSD delta-rhythm in loci Fp1, Fp2, F7, F8 and T4**

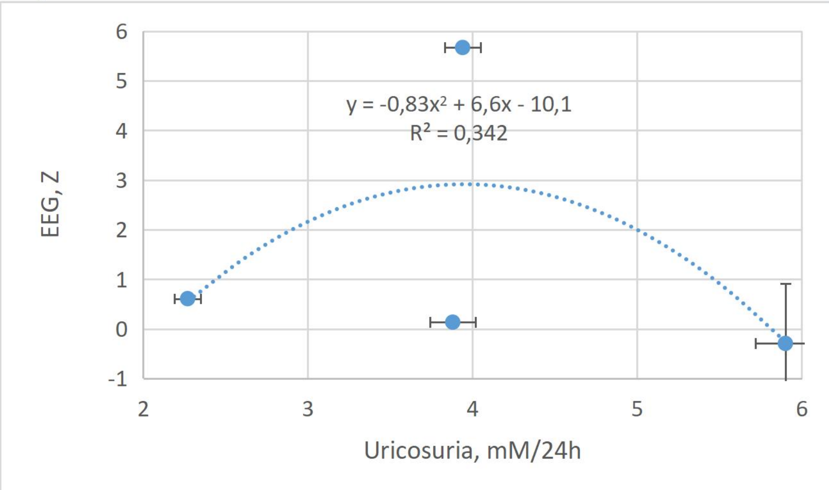



**Fig. 14. Non-linear relationship between uricosuria and PSD delta rhythm in loci Fp1, Fp2, F7, F8 and T4**

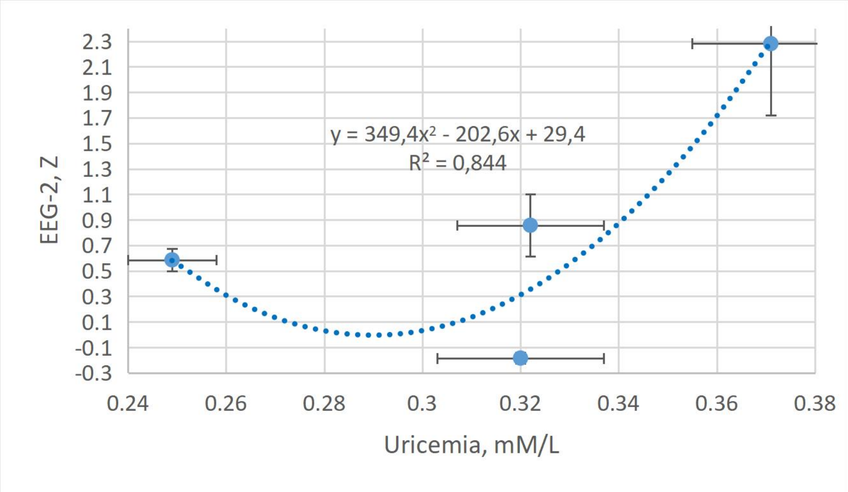



**Fig. 15. Non-linear relationship between uricemia and PSD delta-rhythm in loci F4, F8%, T5%, T6, O2 and its amplitude; PSD of the theta-rhythm at the F7 locus and its amplitude**

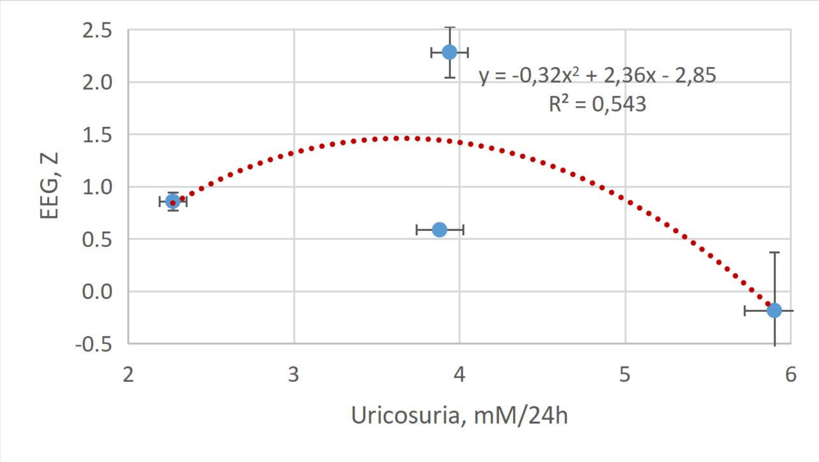



**Fig. 16. Non-linear relationship between uricosuria and delta-rhythm PSD in loci F4, F8%, T5%, T6, O2 and its amplitude; PSD of the theta-rhythm in the F7 locus and its amplitude**

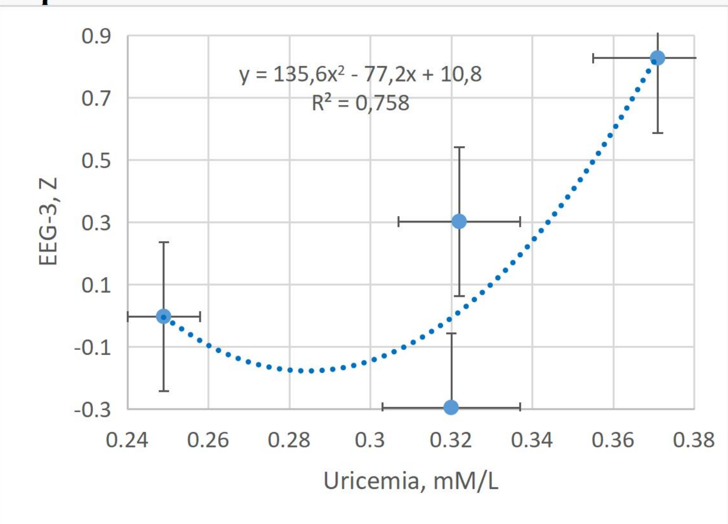



**Fig. 17. Nonlinear relationship between uricemia and PSD of the delta-rhythm in the Fp1%, F7%, T4% loci and theta-rhythm in the T4 locus**

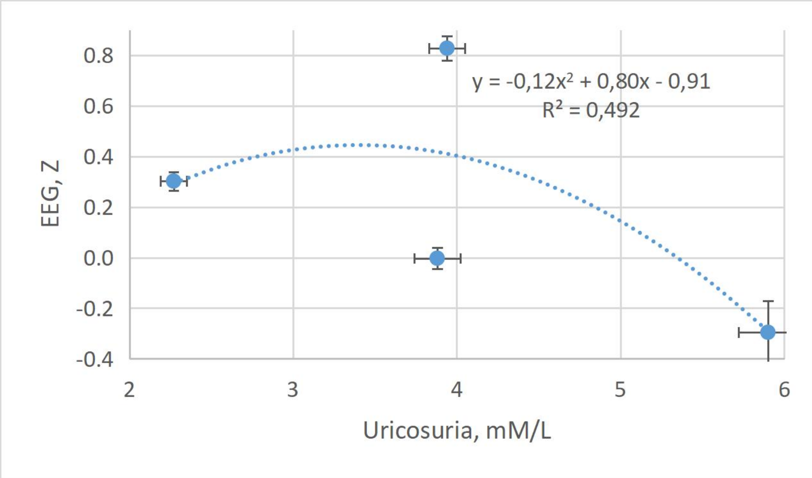



**Fig. 18. Nonlinear relationship between uricosuria and PSD of the delta-rhythm in the Fp1%, F7%, T4% loci and theta-rhythm in the T4 locus**

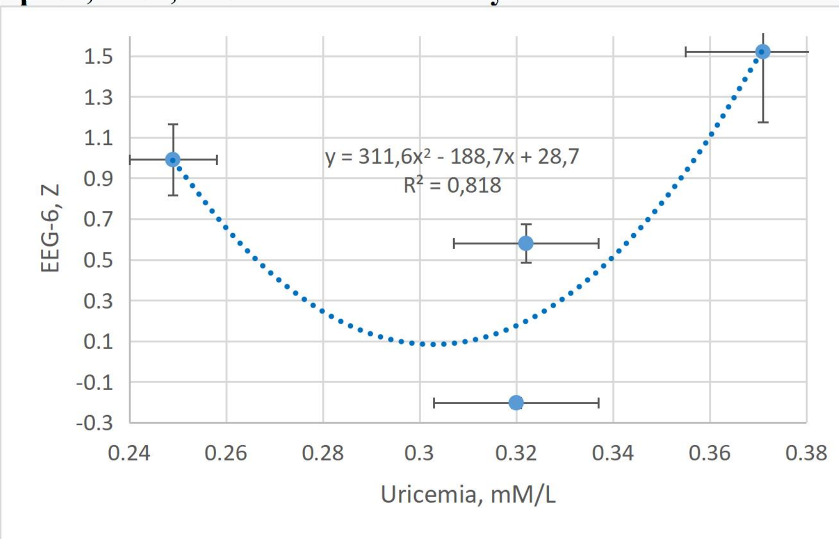



**Fig. 19. Nonlinear relationship between uricemia and PSD of the delta-rhythm in the T3%, T3, C3, C4, T6%, P4 loci and theta-rhythm in the T3 locus**

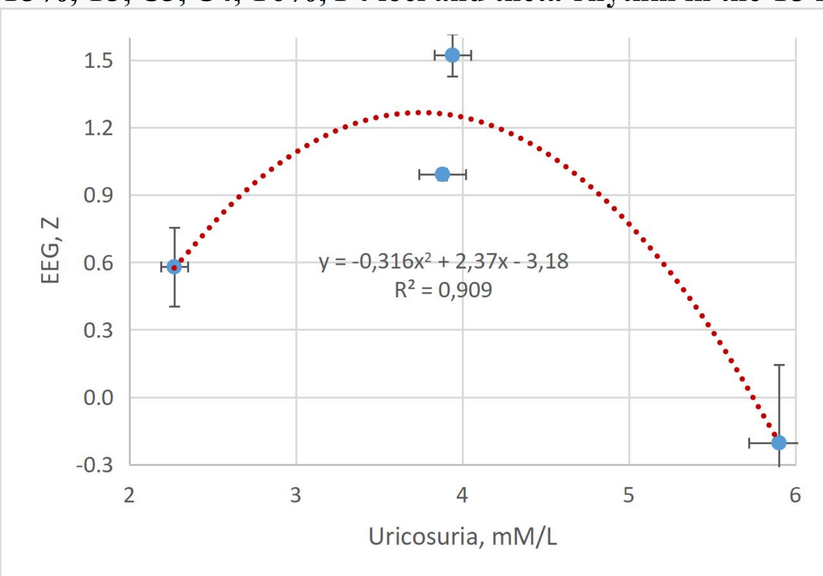



**Fig. 20. Nonlinear relationship between uricosuria and PSD of the delta-rhythm in the T3%, T3, C3, C4, T6%, P4 loci and theta-rhythm in the T3 locus**

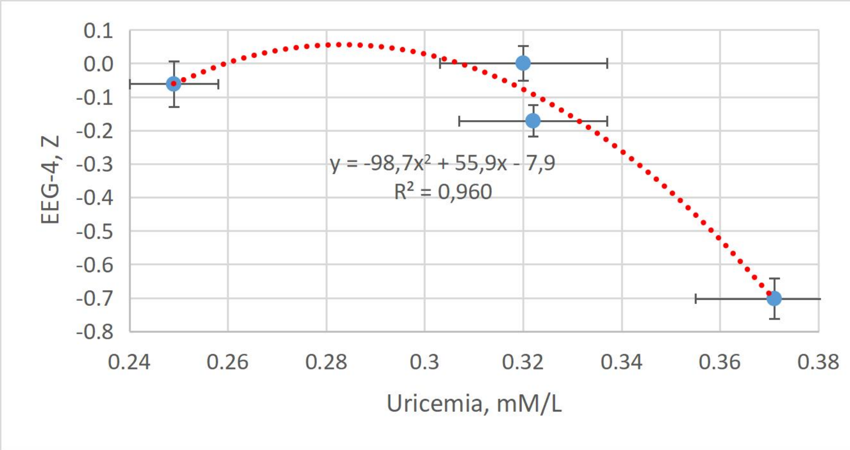



**Fig. 21. Nonlinear relationship between uricemia and PSD beta-rhythm in loci Fp2%, F3%, F7%, T4%, C3%, C4%, O1%; theta-rhythm in the Fp1% and F7% loci; alpha-rhythm in the F7% locus and PSD entropy in the Fp1, F4, F7 and T4 loci**

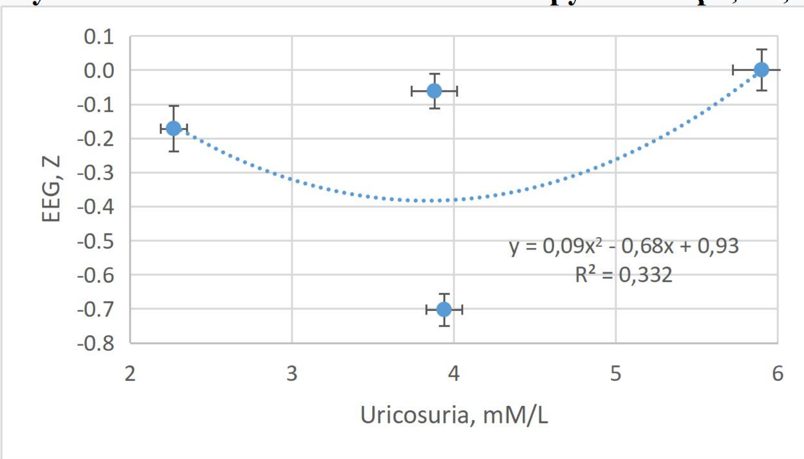



**Fig. 22. Non-linear relationship between uricosuria and beta-rhythm PSD in loci Fp2%, F3%, F7%, T4%, C3%, C4%, O1%; theta-rhythm in the Fp1% and F7% loci; of the alpha-rhythm in the F7% locus and the entropy of the PSD in the Fp1, F4, F7 and T4 loci**

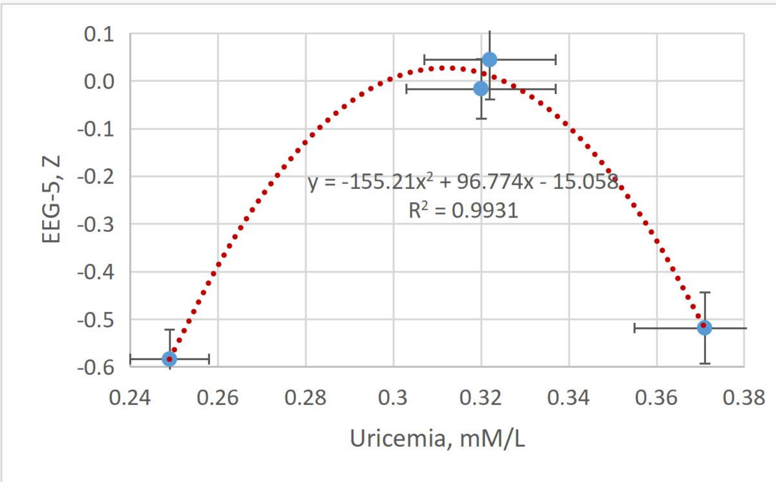



**Fig. 23. Non-linear relationship between uricemia and PSD theta-rhythm in loci T5, T6, O2% and its lateralization; alpha-rhythm in the T6% locus and its lateralization; beta-rhythm in the T3% locus and its asymmetry; lateralization of the delta-rhythm, as well as PSD entropy in the F8 and O2 loci**

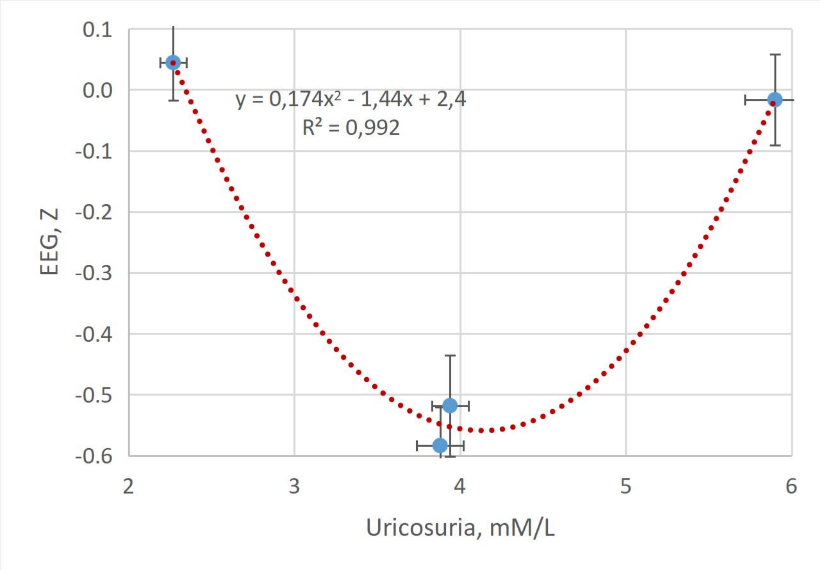



**Fig. 24. Non-linear relationship between uricosuria and PSD theta-rhythm in loci T5, T6, O2% and its lateralization; alpha-rhythm in the T6% locus and its lateralization; beta-rhythm in the T3% locus and its asymmetry; lateralization of the delta-rhythm, as well as PSD entropy in the F8 and O2 loci**

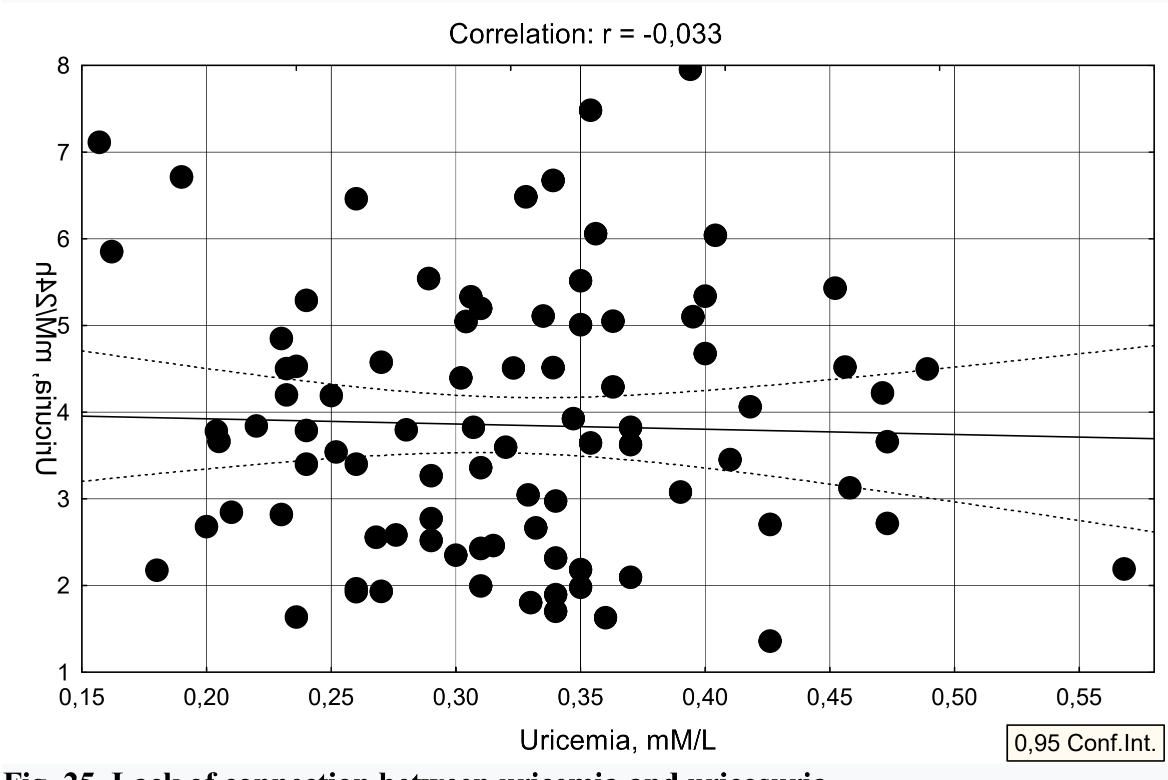



**Fig. 25. Lack of connection between uricemia and uricosuria**

In the second approach, the object of analysis was individual parameters of uric acid metabolism and EEG. As a result of the screening, a correlation matrix was created (Table 12). Since it turned out that the relationships with EEG parameters of sex- and age-normalized levels of uricemia are weaker than those of actual uricemia or even insignificant, the canonical correlation was calculated only in relation to the latter.

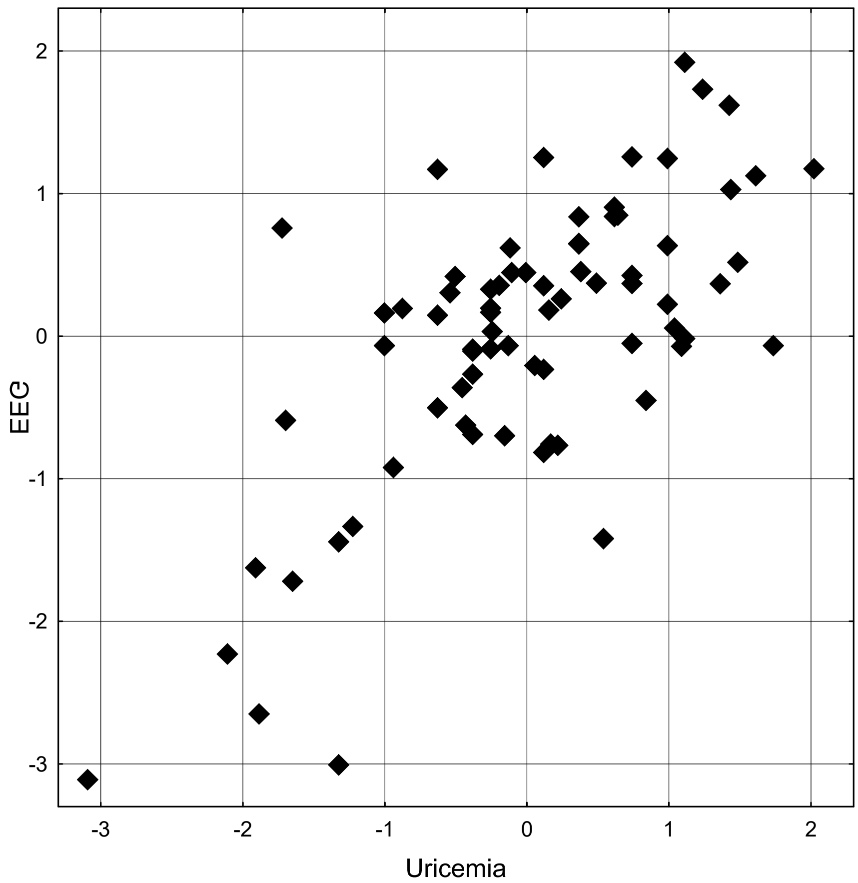
**Table 12. Correlation matrix for parameters of uric acid metabolism and EEG**

| Variable | Correlations N=74 | | |
|---|---|---|---|
| | UaS | UaSz | UaEx |
| UaS | 1,00 | 0,85 | -0,05 |
| UaSz | 0,85 | 1,00 | -0,08 |
| UaEx | -0,05 | -0,08 | 1,00 |
| DT | 0,01 | 0,02 | 0,30 |
| IRB | -0,27 | -0,23 | -0,02 |
| LID | -0,03 | -0,04 | -0,23 |
| FP2H | -0,24 | -0,15 | -0,04 |
| FP2T% | -0,22 | -0,09 | -0,09 |
| FP2D% | -0,02 | 0,10 | -0,24 |
| F3T | -0,21 | -0,09 | -0,14 |
| F4B% | 0,20 | 0,01 | 0,11 |
| F7H | -0,34 | -0,24 | 0,09 |
| F7T% | -0,24 | -0,08 | 0,02 |
| F7B | 0,07 | 0,04 | -0,20 |
| F8H | -0,27 | -0,14 | 0,05 |
| F8B% | 0,21 | 0,07 | 0,11 |
| F8A% | -0,06 | -0,05 | 0,27 |
| F8D% | -0,08 | -0,02 | -0,23 |
| T3B% | 0,20 | 0,06 | -0,05 |
| T3T% | -0,23 | -0,12 | -0,00 |
| T4B% | 0,23 | 0,05 | 0,09 |
| T4A% | 0,08 | 0,04 | 0,25 |
| T4D% | -0,19 | -0,05 | -0,21 |
| C3T | -0,20 | -0,06 | -0,05 |
| T5H | -0,20 | -0,15 | 0,01 |
| T5T% | -0,23 | -0,05 | 0,06 |
| T5D | 0,22 | 0,22 | 0,03 |
| T6H | -0,35 | -0,24 | -0,02 |
| T6A% | -0,04 | -0,03 | 0,21 |
| T6T% | -0,23 | -0,03 | -0,10 |
| T6D% | -0,05 | 0,02 | -0,23 |
| T6B | 0,29 | 0,29 | -0,10 |
| P3H | -0,21 | -0,18 | -0,11 |
| P3B% | -0,01 | -0,20 | 0,03 |
| P3A% | 0,30 | 0,24 | 0,04 |
| P3T% | -0,31 | -0,18 | -0,07 |
| P3D% | -0,23 | -0,09 | -0,04 |
| P4A% | 0,27 | 0,20 | 0,07 |
| P4T% | -0,26 | -0,10 | -0,13 |
| P4D% | -0,25 | -0,10 | -0,16 |
| O2T% | -0,15 | 0,05 | -0,29 |

It was found that uricemia is significantly (|r|≥0,23) or borderline negatively correlated with 18 EEG parameters and positively with 8. After stepwise exclusion, 14 parameters remained in the regression model, the constellation of which is determined by uricemia by 53% (Table 13 and Fig. 26).

**Table 13. Regressive model for uricemia and EEG parameters**

| N=74 | R=,729; R^2=,531; Adjusted R^2=,420; F(14)=4,8; p<,00001; Std.Error of estimate:,062 | | | | | |
|---|---|---|---|---|---|---|
| | Beta | St. Err. of Beta | B | St. Err. of B | t(59) | p-value |
| Intercpt | | | 0,1780 | 0,2058 | 0,87 | 0,390 |
| IRB | -0,330 | 0,115 | -0,0020 | 0,0007 | -2,86 | 0,006 |
| F4B% | -0,467 | 0,195 | -0,0025 | 0,0011 | -2,40 | 0,020 |
| F7H | -0,143 | 0,128 | -0,0585 | 0,0522 | -1,12 | 0,267 |
| F8H | -0,214 | 0,133 | -0,0797 | 0,0497 | -1,61 | 0,114 |
| T3B% | 0,196 | 0,132 | 0,0010 | 0,0007 | 1,49 | 0,143 |
| T4B% | 0,571 | 0,183 | 0,0028 | 0,0009 | 3,12 | 0,003 |
| C3T | -0,180 | 0,113 | -0,0002 | 0,0002 | -1,59 | 0,117 |
| T6H | -0,355 | 0,178 | -0,1746 | 0,0878 | -1,99 | 0,051 |
| T6T% | 0,417 | 0,152 | 0,0067 | 0,0024 | 2,74 | 0,008 |
| T6B | 0,172 | 0,111 | 0,0002 | 0,0001 | 1,55 | 0,126 |
| P3H | 0,381 | 0,168 | 0,2367 | 0,1046 | 2,26 | 0,027 |
| P3A% | 1,180 | 0,323 | 0,0048 | 0,0013 | 3,65 | 0,001 |
| P3D% | 0,850 | 0,291 | 0,0036 | 0,0012 | 2,92 | 0,005 |
| P4D% | -0,243 | 0,166 | -0,0011 | 0,0007 | -1,46 | 0,149 |



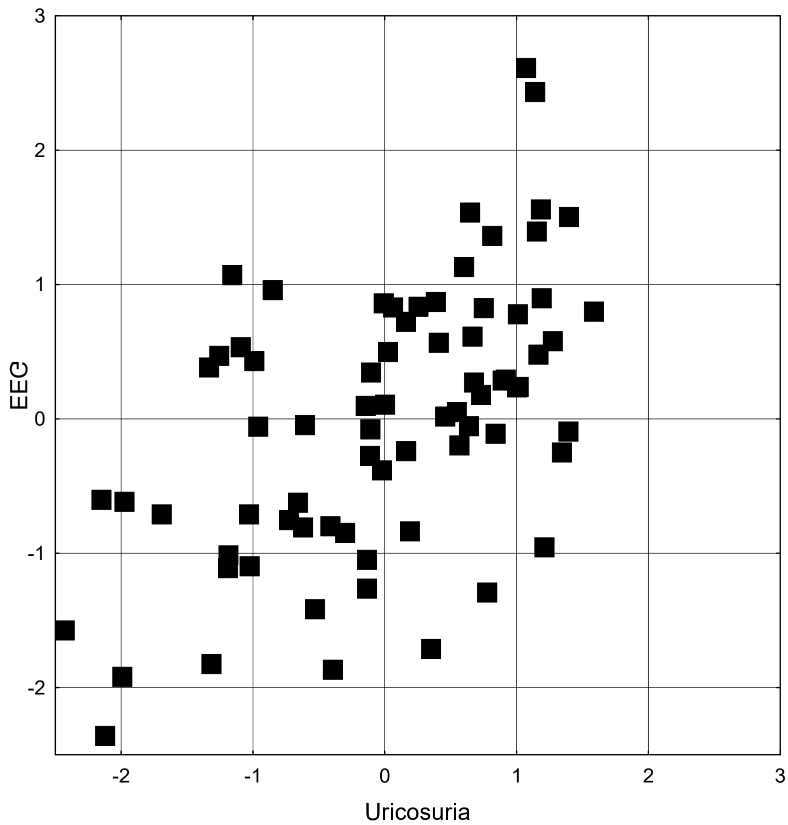

R=0,729; $R^2$=0,531; $\chi^2_{(14)}$=42; p=$10^{-4}$; Λ Prime=0,521

**Fig. 26. Scatterplot of canonical correlation between Uricemia (X-line) and EEG parameters (Y-line) in Human**

Instead, the connections of uricosuria with EEG parameters are less numerous and generally weaker (Table 12). After a step-by-step exclusion of 11 parameters in the regression model, 6 remained, the constellation of which is determined by uricosuria by 31% (Table 14 and Fig. 27).

**Table 14. Regressive model for uricosuria and EEG parameters**

| N=74 | R=,553; R^2=,306; Adjusted R^2=,244; F(6,7)=4,9; p<,0003; Std.Error of estimate:1,25 | | | | | |
|---|---|---|---|---|---|---|
| | Beta | St. Err. of Beta | B | St. Err. of B | t(67) | p-value |
| Intercpt | | | 3,2034 | 0,6825 | 4,69 | 0,00001 |
| DT | 0,346 | 0,105 | 1,0857 | 0,3290 | 3,30 | 0,00155 |
| LID | -0,239 | 0,105 | -0,0087 | 0,0038 | -2,28 | 0,02609 |
| F7B | -0,133 | 0,107 | -0,0032 | 0,0026 | -1,24 | 0,21753 |
| F8A% | 0,146 | 0,123 | 0,0133 | 0,0112 | 1,19 | 0,23963 |
| T6D% | -0,127 | 0,118 | -0,0085 | 0,0079 | -1,08 | 0,28581 |
| O2T% | -0,174 | 0,107 | -0,0575 | 0,0354 | -1,62 | 0,10941 |



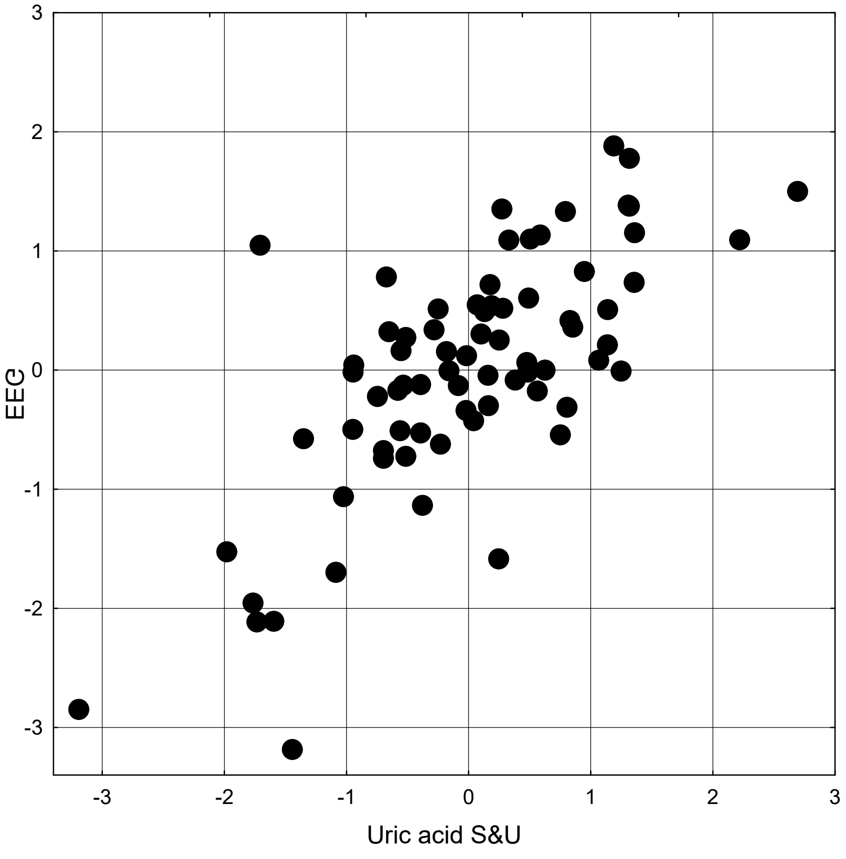

R=0,553; $R^2$=0,306; $\chi^2_{(6)}$=25; p=0,0003; Λ Prime=0,694

**Fig. 26. Scatterplot of canonical correlation between Uricosuria (X-line) and EEG parameters (Y-line) in Human**

The combined effect of uricemia and uricosuria on EEG parameters does not differ from that of uricemia alone (Table 15 and Fig. 27).

**Table 15. Factor structure of canonical roots of parameters of uric acid metabolism and EEG**

| *Left set* | R |
|---|---|
| Uricemia | -0,939 |
| Uricosuria | 0,394 |
| *Right set* | R |
| PSD F7 Entropy | 0,482 |
| PSD F8 Entropy | 0,369 |
| PSD T5 Entropy | 0,259 |
| PSD P3 Entropy | 0,208 |
| PSD T5-θ, % | 0,323 |
| PSD C3-θ, $\mu V^2/Hz$ | 0,234 |
| PSD P3-δ, % | 0,280 |
| PSD P4-δ, % | 0,240 |
| Index β, % | 0,342 |
| PSD T6-β, $\mu V^2/Hz$ | -0,425 |
| PSD T3-β, % | -0,279 |
| PSD T4-β, % | -0,251 |
| PSD F4-β, % | -0,199 |
| PSD P3-α, % | -0,366 |
| PSD F8-α, % | 0,210 |
| Deviation θ, Hz | 0,133 |
| PSD F7-β, $\mu V^2/Hz$ | -0,183 |
| PSD O2-θ, % | 0,052 |
| PSD T6-δ, % | -0,048 |
| Laterality δ, % | -0,075 |




R=0,721; $R^2$=0,520; $\chi^2_{(40)}$=74; p=0,0008; Λ Prime=0,300

**Fig. 27. Scatterplot of canonical correlation between Uricemia&Uricosuria (X-line) and EEG parameters (Y-line) in Human**

Next, the relationships between changes in uric acid parameters and EEG under the influence of balneotherapy were analyzed. Following the previous algorithm, a correlation matrix was first created from significant (|r|≥0,33) and marginal coefficients (Table 16).

**Table 16. Matrix of correlations between changes in parameters of uric acid metabolism and EEG**

| Variable | Correlations N=35 UaS | UaEx |
|---|---|---|
| AF | 0,05 | -0,35 |
| BF | 0,02 | -0,28 |
| IRA | 0,23 | -0,30 |
| AT | -0,33 | 0,18 |
| AA | -0,28 | -0,01 |
| LIT | 0,13 | -0,37 |
| FP2B% | -0,29 | 0,16 |
| FP2B | -0,28 | -0,06 |
| F7H | -0,33 | 0,22 |
| F7B% | -0,01 | 0,28 |
| F7A% | -0,29 | 0,06 |
| F8H | -0,31 | -0,09 |
| F8D | 0,36 | -0,05 |
| T3B% | -0,43 | 0,05 |
| T3T% | 0,11 | 0,38 |
| T3B | -0,44 | 0,08 |
| T4B% | -0,53 | 0,20 |
| T4B | -0,54 | 0,08 |
| C3H | 0,14 | 0,36 |
| C3B% | -0,31 | 0,24 |
| C4B% | -0,32 | 0,31 |
| T5A% | -0,30 | 0,05 |
| T5D% | 0,29 | -0,15 |
| T6B% | -0,42 | 0,29 |
| T6D% | 0,29 | -0,16 |
| P3B% | -0,58 | 0,17 |
| P3A | 0,29 | -0,03 |
| P4B% | -0,51 | 0,37 |
| P4A | 0,31 | -0,12 |
| O1T% | -0,36 | 0,30 |
| O2B% | -0,00 | 0,41 |
| O2T% | -0,28 | -0,11 |
| O2D | 0,36 | 0,02 |

Inverse relationships between changes in uricemia and beta-rhythm PSD in the P3 (Fig. 28) and T4 (Fig. 29) loci turned out to be the closest, and among the direct relationships, the correlation with the dynamics of alpha-rhythm PSD in the P3 locus is noteworthy (Fig. 30).

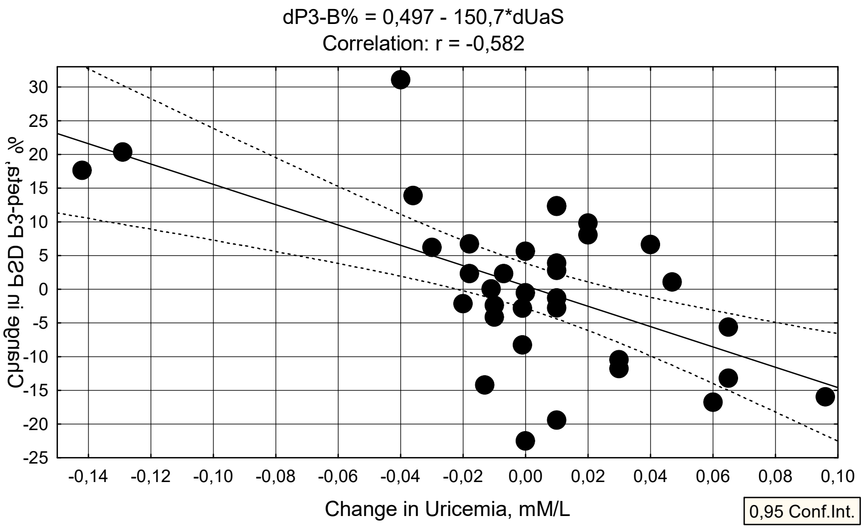



**Fig. 28. Scatterplot of correlation between changes in Uricemia (X-line) and PSD P3-beta (Y-line) in Human**

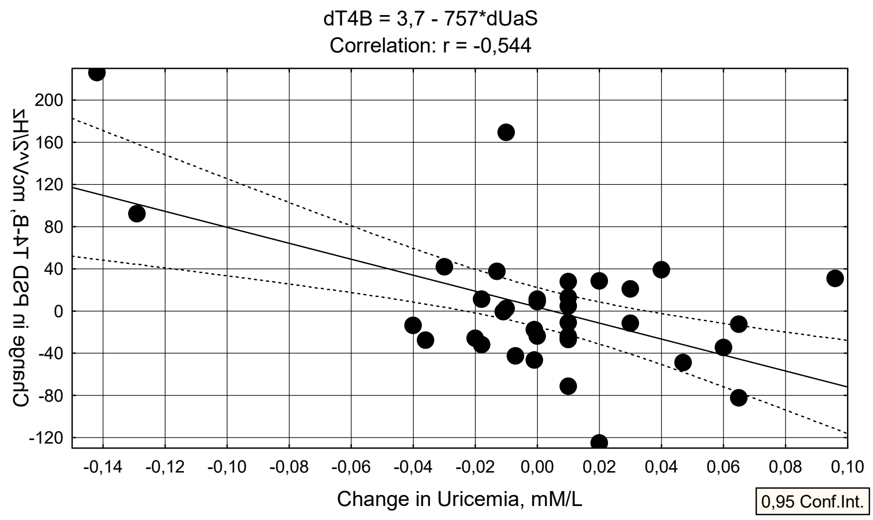



**Fig. 29. Scatterplot of correlation between changes in Uricemia (X-line) and PSD T4-beta (Y-line) in Human**

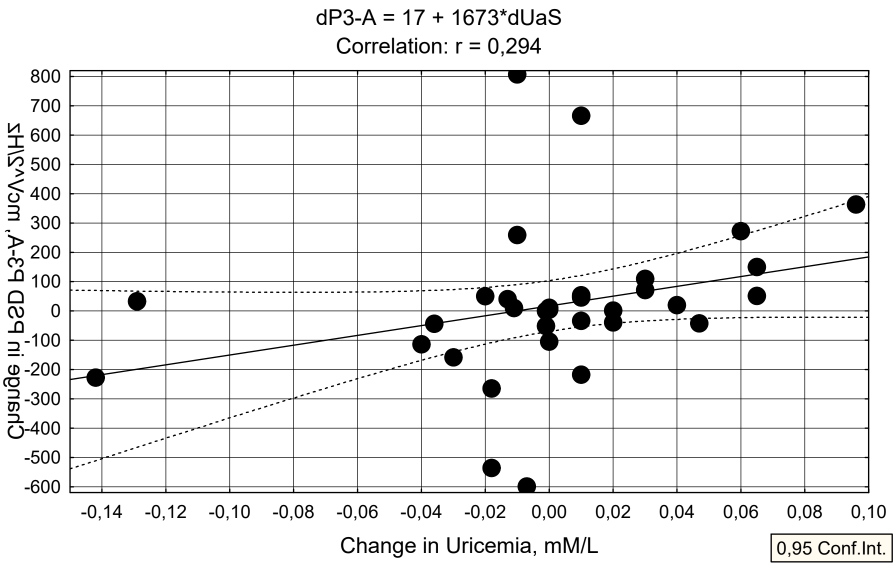
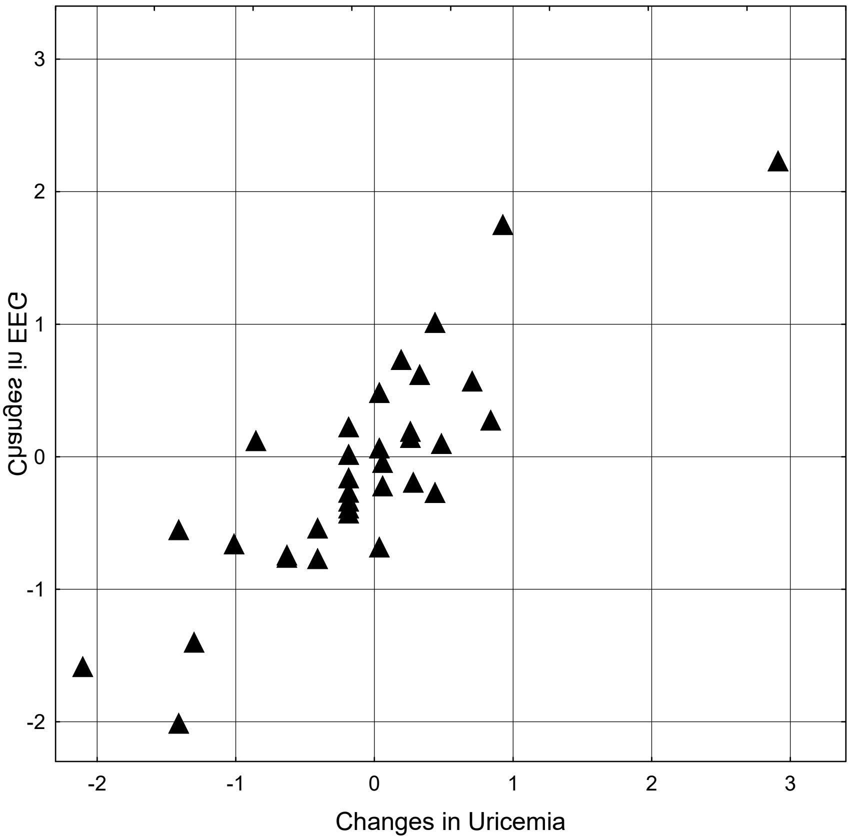



**Fig. 30. Scatterplot of correlation between changes in Uricemia (X-line) and PSD P3-alpha (Y-line) in Human**

It was found that changes in the level of uricemia determine changes in 9 EEG parameters by 81% (Table 17 and Fig. 31).

**Table 17. Regressive model for uricemia and EEG parameters**

| N=35 | R=,901; R^2=,812; Adjusted R^2=,745; F(9,3)=12,0; p<,00000; Std.Error of estimate:,023 | | | | | |
|---|---|---|---|---|---|---|
| | Beta | St. Err. of Beta | B | St. Err. of B | t(25) | p-value |
| Intercpt | | | 0,00728 | 0,00421 | 1,73 | 0,09579 |
| AA | -0,382 | 0,098 | -0,00096 | 0,00025 | -3,92 | 0,00062 |
| T4B | -0,560 | 0,098 | -0,00040 | 0,00007 | -5,74 | 0,00001 |
| C3B% | 0,352 | 0,169 | 0,00104 | 0,00050 | 2,08 | 0,04823 |
| C4B% | -0,330 | 0,151 | -0,00098 | 0,00045 | -2,20 | 0,03764 |
| T5A% | -0,642 | 0,271 | -0,00191 | 0,00080 | -2,37 | 0,02599 |
| T5D% | -0,665 | 0,295 | -0,00090 | 0,00040 | -2,26 | 0,03303 |
| P3B% | -0,612 | 0,144 | -0,00236 | 0,00056 | -4,25 | 0,00026 |
| P3A | 0,584 | 0,212 | 0,00010 | 0,00004 | 2,76 | 0,01074 |
| P4A | -0,391 | 0,203 | -0,00009 | 0,00005 | -1,93 | 0,06526 |



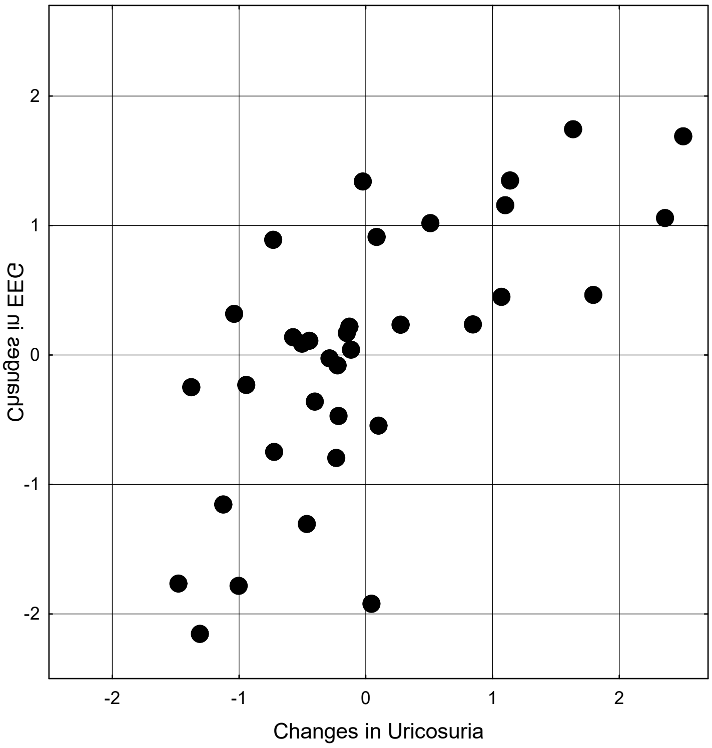

R=0,901; $R^2$=0,812; $\chi^2_{(9)}$=48; p=$10^{-6}$; Λ Prime=0,187

**Fig. 31. Scatterplot of canonical correlation between changes in Uricemia (X-line) and EEG parameters (Y-line) in Human**

Neurotropic determination from the side of uricosuria is much weaker and amounts to 46.5% (Table 18 and Fig. 32).

**Table 18. Regressive model for uricosuria and EEG parameters**

| N=35 | R=,682; R^2=,465; Adjusted R^2=,326; F(7,3)=3,4; p<,0106; Std.Error of estimate:1,30 | | | | | |
|---|---|---|---|---|---|---|
| | Beta | St. Err. of Beta | B | St. Err. of B | t(27) | p-value |
| Intercpt | | | -0,109 | 0,246 | -0,44 | 0,661 |
| IRA | -0,236 | 0,197 | -0,014 | 0,012 | -1,20 | 0,242 |
| LIT | -0,358 | 0,156 | -0,011 | 0,005 | -2,29 | 0,030 |
| T3T% | 0,176 | 0,165 | 0,058 | 0,054 | 1,07 | 0,296 |
| C3H | 0,222 | 0,159 | 2,012 | 1,443 | 1,39 | 0,174 |
| T6B% | -0,420 | 0,328 | -0,033 | 0,025 | -1,28 | 0,210 |
| P4B% | 0,381 | 0,276 | 0,047 | 0,034 | 1,38 | 0,180 |
| O2B% | 0,232 | 0,211 | 0,024 | 0,022 | 1,10 | 0,282 |




R=0,681; $R^2$=0,465; $\chi^2_{(7)}$=18; p=0,010; Λ Prime=0,535

**Fig. 32. Scatterplot of canonical correlation between changes in Uricosuria (X-line) and EEG parameters (Y-line) in Human**

Finally, the canonical correlation between changes in both parameters of uric acid metabolism, on the one hand, and EEG parameters, on the other, was analyzed.

The lion's share of the factor load on the causal canonical root belongs to uricemia (Table 19). The factor structure of the neural root is represented, first of all, by the PSD beta-rhythm in the P3, T4, C4 and C3 loci, as well as the alpha-rhythm in the T5 locus and its asymmetry, which are subject to downregulation by uricemia.

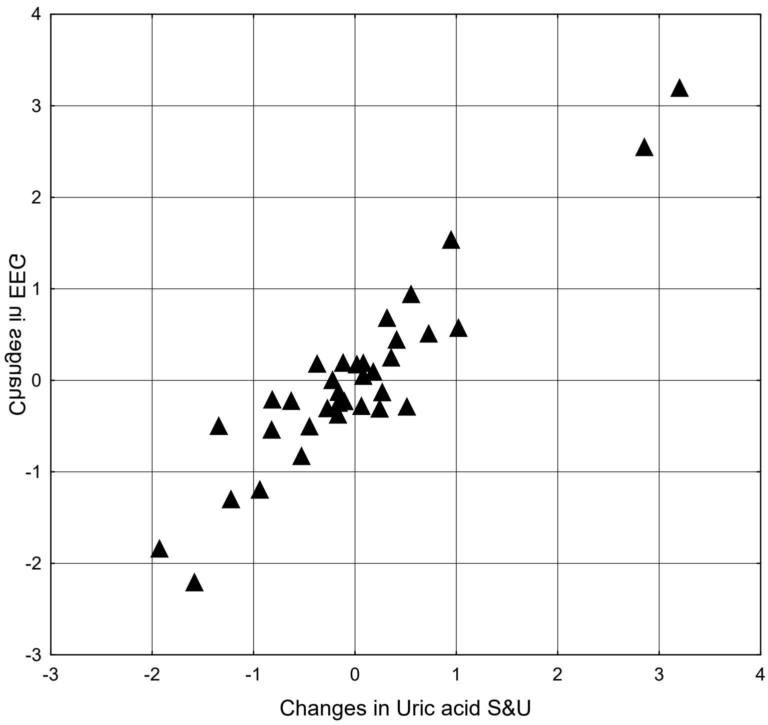
PSD of the beta-rhythm in the P4 and T6 loci are subject to both downregulation by uricemia and upregulation by uricosuria. On the other hand, PSDs of the delta-rhythm in the T5 locus, as well as the alpha-rhythm in the P4 and P3 loci are upregulated by uricemia. Alpha-rhythm index and theta-rhythm lateralization are subject to significant downregulation by uricosuria and weak upregulation by uricemia.

Finally, PSD of theta-rhythm in the T3 locus and beta-rhythm in the O2 locus, as well as entropy in the C3 locus are subject to significant upregulation by uricosuria and weak upregulation by uricemia.

**Table 19. Factor structure of the canonical roots of changes in parameters of uric acid metabolism and EEG**

| ***Left set*** | **R** |
|---|---|
| **Uricemia** | **-0,984** |
| **Uricosuria** | **0,209** |
| ***Right set*** | **R** |
| **PSD P3-β, %** | **0,643** |
| **PSD T4-β, μV²/Hz** | **0,585** |
| **PSD C4-β, %** | **0,395** |
| **PSD C3-β, %** | **0,371** |
| **PSD T5-α, %** | **0,323** |
| **Asymmetry α, %** | **0,292** |
| **PSD P4-β, %** | **0,608** |
| **PSD T6-β, %** | **0,494** |
| **PSD T5-δ, %** | **-0,336** |
| **PSD P4-α, μV²/Hz** | **-0,344** |
| **PSD P3-α, μV²/Hz** | **-0,313** |
| **Index α, %** | **-0,301** |
| **Laterality θ, %** | **-0,209** |
| **PSD T3-θ, %** | **-0,044** |
| **PSD C3 Entropy** | **-0,079** |
| **PSD O2-β, %** | **0,079** |

Taken together, changes in the parameters of uric acid exchange determine changes in the listed EEG parameters by 87% (Fig. 33).




R=0,934; $R^2$=0,872; $\chi^2_{(32)}$=70; p=0,0001; Λ Prime=0,058

**Fig. 33. Scatterplot of canonical correlation between changes in Uricemia&Uricosuria (X-line) and EEG parameters (Y-line) in Human**

## CONCLUSION

Unfortunately (or fortunately?), we managed to find only one study on the correlation between serum uric acid level and EEG on the PubMed resource [45]. We will be grateful to colleagues who point to other works.

The significant negative and positive correlations between uric acid and EEG parameters as a whole, and even more so between their changes, revealed in this study, provide grounds for stating the ability of uric acid to exert both inhibitory and activating effects on nerve structures, which generate all registered rhythm types. In a previous study on the same cohort of patients, we found positive relationships of uric acid with HRV-markers of sympathetic tone and negative connections with markers of vagal tone [5], which indicates the ability of uric acid to influence the brainstem and subcortical autonomous nuclei [2,40]. So, we have shown that uric acid has neurotropic activity, in addition to its immunotropic activity detected in the same cohort of patients [13]. The combination of such effects is possible due to bilateral functional connections between the central and autonomic nervous and immune systems within the framework of the neuroendocrine-immune complex [31,34-37].

According to the concept of our laboratory [13,22], this is due to the similarity molecule of the uric acid (**2,6,8**-tri**oxipurine**) with the molecules of theophylline (**2,6**-di**oxi**-1,3-dimethyl**purine** or 1,3-dimethyl**xantine**), caffeine (**2,6**-di**oxi**-1,3,7-trimethyl**purine** or 1,3,7-trimethyl**xantine**) and other methylxanthines, which, in turn, are structural homologues of adenosine [(2R,3R,4R,5R)-2-(6-amino**purine**-il)-5-(hydroximethyl) oxolan-3,4-diol)].

It is known that the effects of adenosine as well as methylxanthines are realized through its receptors ($A_1$, $A_{2A}$, $A_{2B}$, $A_3$), which express virtually all populations of immunocytes such as T, NK, B lymphocytes, macrophages, neutrophils, dendritic and endothelial cells [1,10,20,21,28,44] as well as neurons of central and autonomous neural systems [8,9,23,26,30,38].

Our data confirms and develops both old [43] and modern [10,27] hypotheses about the physiological activity of uric acid.


## ACKNOWLEDGMENT

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## ACCORDANCE TO ETHICS STANDARDS

Tests in patients are conducted 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 parent of participants the informed consent is got and used all measures for providing of anonymity of participants.

For all authors any conflict of interests is absent.

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