of serum aAB to neuro-mediator receptors in the patients with symptomatic epilepsy can indicate the presence of various mechanisms of neuro-mediation and brain plasticity in case of idiopathic and symptomatic epilepsy.

On the basis of neuro-physiologic values of cognitive initiated potentials we detected characteristic disorders of the highest brain functions in case of epilepsy, reliable alterations of latent period and P300 amplitude dependently on the form of the disease. In cases of idiopathic and symptomatic forms there is absence of P300 wave amplitude asymmetry between hemispheres indicating function disorders. The values of P300 latent period are increased in cases of symptomatic epilepsy, different from idiopathic one and these values reflect inhibition of cognitive processes.

The inverse relation of latent period prolongation degree and amplitude to the presence and expression of neuro-immunologic values was detected in the analysis of interrelation of the latest ones and cognitive initiated potentials.

References:

- Vetrile L. A., Yevseyev V. A., Karpova M. N. Neuro-immune pathologic aspects of epilepsy//RAMS bulletin. 2004. – № 8. – p. 43–46.
- 2. Zinkovski K. A. Clinical-pathochemical, immunologic alterations and their correction in the patients with epilepsy: Abstract. Diss.. CMS. – M., 2004. – 30 p.
- Kropotov U. D. Quantitative EEG, cognitive BP of human brain and neurotherapy. Donetsk: Zaslavski,2010. – 512p.
- 4. Poletayev A. B., Alferova V. V., Abrosimova A. A., Komissarova I. A., Sokolov M. A., Gusev Y. I. Natural neurotropic auto antibodies and pathology of nerve system.//Neuroimmunology. – 2003. – Vol.1, №1. – P. 11–17.
- 5. Engel J.J. ILAE classification of epilepsy syndromes // Epilepsia. 2006. Vol. 70. P. 5–10.

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Exercise capacity in healthy perimenopausal women

Abstract: The work studies a relationship between the levels of endogenous sex hormones and exercise capacity in healthy women during their perimenopause. Seventy-one healthy perimenopausal women were included in the study. Mod BRUCE protocol has been used to assess exercise capacity. An effect of the follicle-stimulating hormone level on METs values has been detected. No similar effects have been found for estradiol, testosterone, aldosterone, and prolactin.

Keywords: women, perimenopause, climacteric period, exercise capacity, treadmill-test.

Despite the fact that menopause is a physiological stage in the life of every woman, very few patients go through this period smoothly and without symptoms. Great number of complaints presented by patients in perimenopause is related to the reduction in exercise capacity. E.g., according to the data of Ceylan B. and Ozerdoğan N., when assessing menopausal symptoms, 79.2% of women reported a feeling of tiredness [1, 1–18]. Vasconcelos-Raposo J., et al. found that vasomotor symptoms were more frequently reported by young women while older age group patients were in a greater degree concerned by feeling tired or lacking in energy, breathing difficulties [2, 257–260]. A reduction in exercise capacity in women in peri- and postmenopausal period

results in greater reduction in health-related fitness and contributes to an increase in various cardiovascular risk factors [3, 753–778]. This entire group of complaints can be combined into a reduction in exercise capacity associated with perimenopause. Exercise capacity is an estimate of the maximal oxygen uptake for a given workload and can be expressed in metabolic equivalents (METs). In addition, exercise capacity has been shown to be an independent predictor of the presence of CAD in women [4, 1018–1022]. It is known that it is difficult enough to interpret the workload test results in women for the diagnostics of ischemic heart disease. In this case, an exercise capacity assessment additional to the ST segment change allows increasing the specificity of this examination.

E.g., in the case of reaching a workload corresponding to 10 and more METs, the probability of ischemia is lower compared to those who reached less than 7 METs (0.4% versus 7.1%; p=0.001) [5, 538 – 545]. Another important property of the exercise capacity assessment in women is the prognostic value of this parameter [6, 1600 – 1607]. For symptomatic women for every 1-MET increase in exercise capacity, there was a 25% reduction in risk of all-cause mortality and a 23% reduction in risk of cardiac events [7, 2836 – 2841]. Prognostic value of exercise capacity was shown also for asymptomatic women. Gulti et al. detected that those asymptomatic women who were unable to achieve 5 METs on a Bruce protocol had a 3-fold increased risk of death compared with women who achieved more than 8 METs [8, 1554–1559].

The goal of this work was to assess the exercise capacity in patients in perimenopause depending on the level of sex hormones.

Materials and methods

Cross-sectional study with participation of 71 perimenopausal women was conducted. All women were examined by gynecologist for exclusion of gynecological diseases and confirmation of natural perimenopause.

Patients with coronary heart disease, cardiac failure, severe arterial hypertension (arterial pressure 180/110 mm Hg), thyroidal hormone producing function disorders, gastric and duodenal ulcerative disease, diseases limiting the life span to 1 year, menopause duration exceeding 5 years, and surgical menopause were excluded from the study. Patients received no therapy prior to exclusion to the study.

Follicle-stimulating hormone (FSH) serum content was tested by enzyme-linked immunoassay using a set of reagents Gonadotropin IFA-FSH from Alkor Bio Company LLC. PROGESTERONE-IFA from KHEMA LLC was used for progesterone test, PROLACTIN-IFA from KHEMA LLC was used for prolactin test, and TESTOS-TERONE-IFA from KHEMA LLC was used for testosterone test. Estradiol was tested using Estradiol ELISA kit from DRG Instruments GmbHSemi-automatic immunoenzyme analyzer Immunochem-2100 was used for the test. The menopause was diagnosed if FSH level was higher than 25 IU/l.

For assessing the exercise capacity, all patients were subjected to a workload treadmill-test. For the treadmilltest, we used the digital electrocardiographic complex with a treadmill "Cardio-Perfect MD" (Cardio-Control, Netherlands). Prior to the workload test, all patients discontinued beta-adrenergic blocking agents and calcium channel antagonists in advance. For blood pressure control during the workload test, ACE inhibitors or angiotensin II receptor blockers have been used. The test was conducted in a well-ventilated room at a temperature of 20–22 C before noon, 1–2 hours after a light breakfast. Mod BRUCE protocol has been used, initial rate was 2.7 km/h, treadmill angle — 0.0%, duration of each stage 3 minutes. The patients with positive treadmill-test results were excluded from the further analysis and examined in accordance with the ischemic heart disease protocol. For assessing the exercise capacity, we assessed the metabolic equivalent (MET), which was calculated automatically by "Cardio-Perfect MD" software according to the formula: 1 ME = 3.5 ml O2/min/kg body weight.

The study protocol was approved by local ethics commission of L. T. Malaya National Institute of Therapy of Ukraine. The aim of the study was explained to all patients and informed consent was signed before any study related procedures.

SPSS 21 for Windows PC software was used for statistical data processing. Data were represented as median and 25% and 75% quartiles (Me [25%-75%]). To test null hypothesis Mann-Whitney test and chi-squared test were used.

Results

Table 1 represents comparison results for patient groups depending on the FSH level in the blood. The group 2 showed significantly lower values of progesterone, prolactin, and estradiol levels.

	FSH < 25, IU/l	FSH > 25, IU/l	
	(group 1) n=34	(group 2) n=37	
Age, years, Median [25%-75%]	52 [45-53]	53 [49-59]	p=0,21
BMI, kg/m ² , Median [25%-75%]	27 [24–33]	28 [26–31]	p=0,65
Age of menopause, years, Median [25%-75%]	49 [45-51]	50 [49-53]	p=0,25
EF,%, Median [25%-75%]	62 [56-66]	63 [59–66]	p=0,57
Women with hypertension/women without	26/8	28/9	p=0,12
hypertension, n/n			_
Smoking/non smoking women, n/n	3/31	3/37	p=0,34
Progesterone, nmol/l, Median [25%-75%]	2,87 [2,3–5,4]	2,72 [2,1–3,4]	p=0,02

 Table 1. – Characteristic of study patients depending on hormonal status

Testosterone, mmol/l, Median [25%-75%]	0,56 [0,33-0,77]	0,6 [0,4–0,7]	p=0,10
Prolactin, mmol/l, Median [25%-75%]	247,4 [196,3–415,9]	182,7 [142,6–235,3]	p=0,05
Estradiol, pg/ml, Median [25%-75%]	110 [55,5–217]	39,14 [27,9–61,2]	p=0,001
FSH, IU/l, Median [25%-75%]	8,3 [5,7–16,0]	62,4 [46,2–79,7]	p=0,0001

The group 2 showed significantly lower METS value, while heart rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP), Duke Index were not different significantly between the groups (table 2).

	FSH < 25, IU/1	FSH > 25, IU/l	
	(group 1) n=34,	(group 2) n=37,	
	Median [25%-75%]	Median [25%-75%]	
Heart rate, baseline, beats per min.	82,0 [69,0-87,6]	81,0 [71,0-88,0]	p=0,68
Heart rate maximal. Beats per min	153,0 [144,0–156,0]	146 [140,0–160,0]	p=0,76
SBP, baseline, mm Hg,	120,0 [110,0-135,0]	127,5 [120, —135,0]	p=0,34
SBP maximal, mm Hg,	170,0 [150,0-180,0]	175,0 [160,0–200,0]	p=0,56
DBP, baseline, mm Hg,	80,0 [80,0-90,0]	80,0 [80,0–100,0]	p=0,08
DBP, maximal, mm Hg,	90,0 [80,0-100,0]	90,0 [80,0–105,0]	p=0,6
METs	14,1 [9,0–15,0]	7,0 [4,6–7,0]	p=0,048
Duke index	6,2 [4,5-8,5]	5,0 [1,0–7,0]	p=0,11

Table 2. – Treadmill-test results of women with different hormonal status

For detecting the effect of sex hormones on METs, we carried out a stepwise regression analysis, which showed that only FSH had a significant effect on this parameter (table 3).

Table 3. – Influence of sex hormones on METs in health perimenopausal women

	beta	Standard error of beta	В	Standard error of B	p-level
FSH	-0,11259	0,04821	-0,0326	0,01398	0,01995
Estradiol	-0,05784	0,04821	-0,0057	0,00477	0,23083

Graph 1 shows the change of METs values with an increase in FSH. E. g., a significant reduction in this value is observed with an increase in FSH for more than 14.5 IU/L with a subsequent more marked

reduction after FSH reached a level of 30 IU/L. With further FSH increase, METs values do not change significantly and remains stably low (Fig. 1).

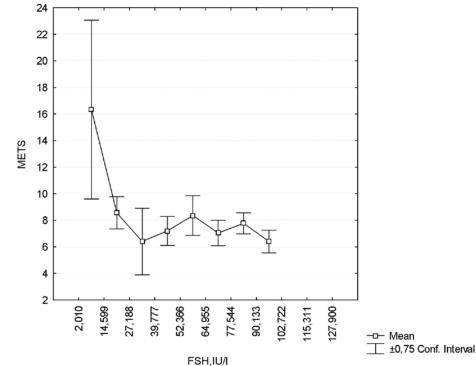
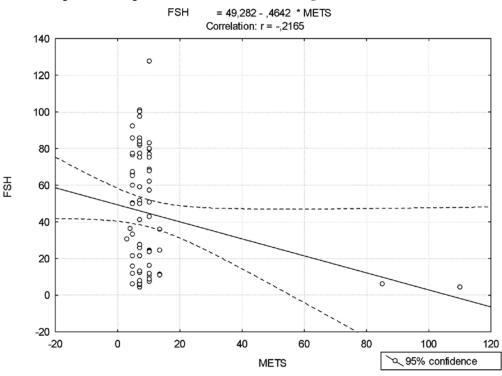
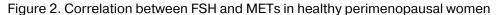


Figure 1. The ration between FSH and METs in healthy perimenopausal women.







Thus, we detected a relationship between the folliclestimulating hormone level and exercise capacity in women in perimenopause. Higher follicle-stimulating hormone levels are associated with lower exercise capacity.

It is known that reproductive ageing in women is accompanied by a reduction in exercise capacity; however, there is a deficiency of works related to studies of relationships between endogenic steroid levels and exercise capacity. E.g., Mieczkowska J. et al. in their work studied a relationship between the levels of estradiol, total testosterone, dehydroepiandrosterone sulphate, sex hormone binding globulin and the degree of exercise capacity. Testosterone level correlated positively with exercise duration, level of free testosterone was associated with systolic blood pressure increase during exercise and exercise duration and bioavailable testosterone positively correlated with heart rate increase during exercise and with exercise duration. Authors concluded that exercise capacity of postmenopausal women may be influenced by sex hormones, which levels in blood could be useful in the qualification for physical recreation plan [9, 295–303].

Enough contradictory data are provided in the literature regarding the effect of exogenous estrogens on exercise capacity in women. It is shown that estrogen replacement therapy is associated with exercise capacity as measured by maximal oxygen uptake and anaerobic threshold in postmenopausal women without coronary artery disease [10, 739–744]. At the same time, during the hormonal replacement therapy in a study conducted by Snabes M. C., although an increase in estradiol concentration in the blood and reduction of heart rate in rest were observed, exercise capacity did not show any increase [11, 110–114]. Similar data were also obtained in a study conducted by Aldrighi J.M., where no positive effect of exogenous estradiol on exercise capacity in women in postmenopause was also detected [12, 324–329]. A positive effect of testosterone on exercise capacity was detected in women with cardiac insufficiency [13, 1310–1316].

This work studied a relationship between endogenous sexual steroids and exercise capacity in women in perimenopause. No effect of prolactin, testosterone, or estradiol on exercise capacity was detected in healthy women, while an increase in follicle-stimulating hormone level was related to lower exercise capacity. An increase in the follicle-stimulating hormone level for more than 25 IU/L is a marker of the reproductive ageing and can be observed long before the onset of menopause. The effect of the hormonal background on workload test results and first on METs value should be taken into account when interpreting the workload test results in women.

Conclusion: an increase in follicle-stimulating hormone level during menopause in women is associated with a reduction in exercise capacity.

References:

- 1. Ceylan B., Ozerdoğan N. Menopausal symptoms and quality of life in Turkish women in the climacteric period. Climacteric. 2014 Jun 2: 1–18.
- Vasconcelos-Raposo J., Coelho E., Fernandes H. M., Rodrigues C., Moreira H., Teixeira C. Factor structure and normative data of the Greene Climacteric Scale among postmenopausal Portuguese women. Maturitas. 2012 Jul; 72 (3): 256–262.
- 3. Asikainen T. M., Kukkonen-Harjula K., Miilunpalo S. Exercise for health for early postmenopausal women: a systematic review of randomised controlled trials. Sports Med. 2004;34 (11): 753–778.
- 4. Al-Mallah M., Alqaisi F., Arafeh A., Lakhdar R., Al-Tamsheh R., Ananthasubramaniam K. Long term favorable prognostic value of negative treadmill echocardiogram in the setting of abnormal treadmill electrocardiogram: a 95 month median duration follow-up study. J Am Soc Echocardiogr. 2008 Sep;21 (9): 1018–1022.
- Bourque J. M., Holland B. H., Watson D. D., Beller G. A. Achieving an exercise workload of 0 or 10 metabolic equivalents predicts a very low risk of inducible ischemia: does myocardial perfusion imaging have a role? J Am Coll Cardiol. 2009;54: 538 – 545.
- Mora S., Redberg R. F., Cui Y., Whiteman M. K., Flaws J. A., Sharrett A. R., Blumenthal R. S. Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the Lipid Research Clinics Prevalence Study. JAMA. 2003;290: 1600 –1607.
- 7. Roger V. L., Jacobsen S. J., Pellikka P. A., Miller T. D., Bailey K. R., Gersh B. J. Prognostic value of treadmill exercise testing: a population-based study in Olmsted county, Minnesota. Circulation. 1998;98: 2836–2841.
- Gulati M., Pandey D.K., Arnsdorf M.F., Lauderdale D.S., Thisted R.A., Wicklund R.H., Al-Hani A.J., Dlfck H.R. Exercise capacity and the risk of death in women; the St James Women Take Heart Prpject. Circulation. 2003; 108: 1554–1559
- Mieczkowska J., Mosiewicz J., Rutkowska E., Jedrych M., Prystupa A., Lachowska-Kotowska P. Selected problems of medical qualification for physical fitness in postmenopausal women. J Sports Med Phys Fitness. 2013 Jun;53 (3): 295–303.
- Redberg R. F., Nishino M., McElhinney D. B., Dae M. W., Botvinick E. H. Long-term estrogen replacement therapy is associated with improved exercise capacity in postmenopausal women without known coronary artery disease. Am Heart J. 2000 Apr;139 (4): 739–744.
- 11. Snabes M. C., Herd J. A., Schuyler N., Dunn K., Spence D. W., Young R. L. In normal postmenopausal women physiologic estrogen replacement therapy fails to improve exercise tolerance: a randomized, double-blind, placebo-controlled, crossover trial. Am J Obstet Gynecol. 1996 Jul;.175 (1): 110–114.
- Aldrighi J. M., Calvoso-Júnior R., Alecrin I. N., Trombetta I. C., Negrão C. E. Estrogen replacement and exercise capacity in postmenopausal women: a randomized placebo-controlled study. Gynecol Endocrinol. 2005 Dec;21 (6): 324–329.
- Iellamo F., Volterrani M., Caminiti G., Karam R., Massaro R., Fini M., Collins P., Rosano G. M. Testosterone therapy in women with chronic heart failure: a pilot double-blind, randomized, placebo-controlled study. J Am Coll Cardiol. 2010 Oct 12;56 (16): 1310–1316.

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Changes of indicators of viscosity of the blood in the remote postoperative period after operations on the damaged lien

Abstract: Studying of changes of rheologic properties of a blood is spent at 85 patients operated on the injured lien, in time not less than one year after operation. From them to 35 patients the splenectomy, 20 — organ saving operations has been executed, 30 patients have transferred autolientranspolantation. Terms after carrying out of op-