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## Peculiarities of Activation Processes the Cerebral Cortex in Oligomerrhea of Teenagers

**Olga Yu. Shilova<sup>a</sup> and Marina A. Bragina<sup>b\*</sup>**<sup>a</sup> *SII of Medical Problems of North, SB RAMS,  
3G P. Zhelezniak Str., Krasnoyarsk, 660022 Russia*<sup>b</sup> *Krasnoyarsk State Pedagogical University  
them. VP Astafeva  
89 Ada Lebedeva Str., Krasnoyarsk, 660049 Russia*

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*The article presents the data on the epidemiology of menstrual cycle disorders of Krasnoyarsk teenagers. The increase in the frequency of oligomenorrhea, indicating worsening of functional disorders of the reproductive system, has been revealed. Due to the possible relation between oligomenorrhea development and disruption of activation processes of cerebral cortex, the dynamic measurement of omega-potential of cerebral hemispheres was conducted. The study was carried out in a group of female patients before the hormone therapy and after its completion. It was revealed that the basic values of the omega-potential of the girls with oligomenorrhea are characterized with its increase, indicating a high level of mental stress. The results have revealed the dependence of normalization of the activation processes of the cerebral cortex and the option of hormonal correction of oligomenorrhea.*

*Keywords: omega-potential, oligomenorrhea, menstrual cycle, teenager.*

The quality of reproductive health is one of the main criteria of efficiency and social and economic policy and national security factor (Berezin, 1988; Gurkin, 2003; Zhukovets, 2012; Kuchma, 2011; Ocklenburg et al, 2012). The studies on reproductive health in the age category «female teenager», the so-called group of potential parents, are particularly relevant. Adolescent and teen-age periods are important steps in female postnatal development (Buralkina, 2009; Kozhevnikova et al, 2011; Trofymenko, 2012). Menstrual dysfunction in adolescence can lead to serious

disorders of the generative function in the future. The term «teenager» is widely used in domestic publications, despite the absence of this period in all known classifications of age periodization (Vasilchenko, 2008; Sizova, 2010; Chebrakova, 2012). Integration of adolescent (12-15 years) and teen-age (16-20 years) periods in a single age range is convenient from the perspective of a practical approach. This allows not only studying the characteristics of the reproductive function at its formation, but also undertaking the necessary preventive and curative measures in the case of

revealing disorders prior to the stage of formation of infertility (Zharov et al, 2006; Wada, 2009). Oligomenorrhea is a clinical manifestation of various forms of irregular menstrual cycle and is expressed by the lengthening of the menstrual cycle over 35-40 days (Shilova, 2011a; Berga et al, 2009).

Recently, researchers have stated the increase in the frequency of oligo- and amenorrhea in this age group, which may reflect worsening of functional disorders of the reproductive system (Vasilchenko, 2008; Shilova, 2011a; Ocklenburg et al, 2011). The data presented by the State health care institution of Administration of Krasnoyarsk city also shows the significant growth of menstrual cycle at the relative stability of the index of overall morbidity of girls from 0 to 14 (Table 1).

A more objective criterion of the morbidity rate in the population is morbidity indexes found during a routine inspection. However, this data shows a high menstrual disorder frequency rate in the group of 14-year-old females (Table 2). The share of menorrhagia in the group of the viewed was 39.1 %, of hypomenstrual syndrome – 60.9 %. The increase in the proportion of detected hypomenstrual syndrome with increasing age of adolescent girls is revealed (Fig. 1). There is evidence that the worsening of functional disorders of the reproductive system is expressed in the reliable increase in the average age of menarche, the greater frequency of puberty lagging pace, the increase in hypomenstrual syndrome frequency (Ilyuhina, 1982; Leutin et al, 1988; Parenkova, 2012; Uvarova, 2012). At the same time the trend of retardation of physical development in the generation of modern teenage girls is revealed (Uvarova, 2010; Shilova, 2011a; Shilova, 2007; Unestahl et al, 1996). Unfavorable dynamics and interdependence of processes of physical and sexual development suggests comprehensive approaches to the monitoring of female patients

with various forms of irregular menstrual cycle (Vasilchenko, 2008; Golubchikov, 1986; Uvarova, 2005; Chebrakova, 2012).

The most frequent clinical and laboratory version of oligomenorrhea is the hypothalamic-pituitary dysfunction relating to the second class of disorders of the WHO (Bulganina, 2012; Shilova, 2011a; Nepomnaschy et al, 2007). At the same symptom complex existing reproductive disorders are caused by dysfunction of the central structures, leading eventually to the breakdown of cyclic operation of the reproductive system.

There has recently been a growing interest to studying the interaction between superslow physiological processes (SSPP) of the brain and the processes of neurosecretion and humoral regulation of autonomic and visceral functions (Dolzenko, 2004; Ilyuhina, 1981; Kulakov, 2005; Medvedeva, 1981; Minicheva, 1984; Parenkova, 2012). Sustainable millivolt range potential, including the class SSPP, is an omega-potential (OP). OP plays an important role in the control of various functional systems and in the regulation of normal and pathological conditions and reactions of the organism (Bolova, 2008; Bulganina, 2012; Malyshev et al, 1999; Sineeveva, 2012; Shilova, 2009). According to the classification by V.A. Ilyuhina, OP is characterized (Ilyuhina, 1981; Ilyuhina et al, 1979; Irgasheva, 2008) by the stability over time (from 1-2 minutes to hours), its changes are manifested in the form of smooth or abrupt shifts of varying intensity (the very few or tens of Mb). Omega-potential plays an important role in the formation of functional states and adaptive responses. In this regard, the relationship between disorders of activation processes of cortex and regulation of the menstrual cycle is assumed, which dictates the need in the research in this area.

*The purpose of the study.* Study of features of activation processes of the cerebral cortex of

Table 1. Dynamics of some indexes of girls' morbidity (0-14 years) in Krasnoyarsk

|                           | 2007   | 2008   | 2009   | 2010   | 2011   | Increase by 2007 |
|---------------------------|--------|--------|--------|--------|--------|------------------|
| Menstrual disorder        | 14.2   | 16.6   | 16.1   | 28.2   | 23.4   | +64.8            |
| Morbidity (of both sexes) | 2699.2 | 2679.1 | 3067.7 | 2997.0 | 2682.6 | -0.6             |

\* The index is calculated as at the female population of 10-14 years old

Table 2. Some indexes of 14-year-old females of Krasnoyarsk according to the routine inspection of 2011

| Diseases                                      | Code in ICD-10 | Total found absolute number | Morbidity (per 1000 of respective age) |
|-----------------------------------------------|----------------|-----------------------------|----------------------------------------|
| Malnutrition                                  | E40-E46        | 250                         | 56.1                                   |
| Obesity                                       | E66            | 436                         | 97.9                                   |
| Disorder of rhythm and nature of menstruation | N91-N94.5      | 144                         | 32.3                                   |
| Total viewed girls -4454                      | A00-T98        | 6200                        | 1392.0                                 |

adolescents with oligomenorrhea to improve therapeutic approaches to its management.

*Material and methods.* In the first phase 208 girls aged 16-19 ( $16,8 \pm 1,2$  years) who applied with the complaints of missed menses in 2002-2012 were surveyed. The following standard set of examinations was conducted, including: clinical and instrumental examination (ultrasound investigation of pelvic organs and thyroid), laboratory determination of hormones on the third day of the induced or spontaneous cycle (LH, FSH, TSH, prolactin, total testosterone, hormone binding globulin, 17-OH progesterone, DEA-S). After the in-depth examination a group of girls with hypothalamic-pituitary dysfunction (134 pers.) was identified. The criteria for inclusion in the group are: 1) the duration of cycle disorders for more than a year, and 2) the absence of menstrual periods from 2 months to 2.5 years ( $5.8 \pm 4.4$  months on the average) after a period of regular or irregular menstrual periods, and 3) normal basal level of gonadotropin Pituitary hormones and prolactin in serum (average value of FSH was  $6,2 \pm 2,3$  IU/l), and 4) no evidence

of hypoenestrogenism. The group did not include the patients with symptoms of PCOS, as the current diagnostic and therapeutic approaches to the management of female patients with PCOS require the allocation of this disease in a separate group (Rotterdam consensus, 2003).

The activation processes of the cerebral cortex using the method of dynamic measurement of omega-potential of the cerebral hemispheres of all the female patients in this group were examined. The level of excitability of the cerebral cortex, the quantitative and qualitative hemispheric asymmetry of brain activity (Savchenkov, 2013; Savchuk, 2012; Adolescent Health., 2002) was assessed on the basis of the values of omega-potential. The background values of omega-potential of right and left hemispheres are defined. The examination was carried out with the help of omega-tester (OT-2) performing dynamic registration of omega-capacity with discretisation of 1 sec., which allows measuring, recording and storing in memory and displaying fixed values on the tester's display on two channels. The values

are visualized in the form of graphs, which are subsequently interpreted on a computer using a specially developed program. The readings were taken with the help of self-adhesive chloride silver electrodes from the projections of the frontal lobes relative to the opposite hands: left hand – relative to the right hemisphere, and vice versa (Ilyuhina, 1981; Ilyuhina et al., 1979; Irgasheva, 2008). The registration of omega potentials lasted for 10 minutes in a sitting position with open eyes in a room an isolated from outside influences.

3 levels of omega potential were empirically isolated (Dolzenko, 2004; Ilyuhina, 1981; Kulakov, 2005; Lomarev, 1995; Medvedeva, 1981; Minicheva, 1984; New possibilities..., 2009; Zdziebło, 2009). Understanding the differences of adaptive-functional reserves of the organism for each level was a prerequisite to the successful interpretation of the results of the study.

Level I with the values of omega-potential from 0 to 20 Mb reflected the decrease in active wakefulness: adaptive functional reserves of the body were limited. Normal adaptive responses remained subject to the load distribution over time.

Two groups of individuals were identified with low values of omega-potential. Group I was characterized with high exhaustibility after great physical stress, high lability of the primary processes, high trainability under strict dosing of load distribution over time, low thresholds of reactions to stimuli, unstable adaptive responses, need in psycho-social protection, vulnerability to neurotic reactions. Group 2 is characterized by severe exhaustibility after minor physical and mental stress, decreased lability, poor learning ability (premorbid condition, illness).

Level II with the values of omega-potential from 20 to 40 Mb reflected the optimal level of wakefulness: adequate behavioral reactions. Well tolerated long-term mental and physical

stress while maintaining high working efficiency, optimal mobility of nervous processes. Thresholds of reactions to load are optimal.

Level III with the value of omega-potential from 40 to 60 Mb reflected stressful state of a person, inappropriate behavioral reactions in response to any exogenous and endogenous effects on the mental component as well as on the motor one.

Two groups with high levels of omega-potential were identified:

Group 1 is practically healthy people. The group is characterized by high thresholds of adaptive responses, hyperstability, viscosity of reactions, reduced lability of primary processes, difficulty of adaptive rearrangements in behavior. These symptoms can probably be found in nearly healthy people who experience mental and physical overloads and modifiable pathological disorders in the body. Group 2 is characterized by a distinct hyperstability of reactions to any impact; duration of their reactions is months and years. Thresholds of reactions are high, lability of primary processes is low with impaired adaptive rearrangements in behavior. Education and recall of professional and behavioral skills is impossible. It is typical of chronic and long-term ongoing diseases.

In order to evaluate the effectiveness of different variants of hormonal regulation of existing menstrual disorders, the sample of the patients with hypothalamic-pituitary dysfunction was randomized into two groups. In group I (68 women) monophasic combined hormonal contraceptives were used. In group II (66 women) progestogens were prescribed in a cyclic mode, i.e. from the 16<sup>th</sup> to the 25<sup>th</sup> days of the menstrual cycle. Prior to the hormonal therapy the periods were induced with a daily dose of progestogens during 10 days: 20 mg of dydrogesterone daily or 5 mg of norethisterone daily. In both groups, treatment was prescribed for six menstrual

cycles. After the cessation of hormone therapy the rhythm of the periods was assessed for six months, ultrasound and hormonal markers of ovulation were examined under the regular cycle. At this stage, the control measurements of omega potential were conducted. The therapy was regarded as effective when the ovulatory menstrual cycle was reactivated and the activation processes of the cerebral cortex were normalized.

Calculation of relative values and determination of their validity were carried out under statistical processing in most cases. The differences between the relative values of the compared groups were evaluated using the criterion  $\phi^*$  (angular transformation of Fisher). The criterion assesses the accuracy of differences between the percentages of the two samples in which the effect we are interested in is registered. As for absolute values, the average values and their errors were determined for them.

*Results and discussion.* By the end of the six-month period of examination after cessation of hormonal therapy, 38.4 % of the girls of group I and 44.6 % of the girls of group II had regular menstrual cycles. In this case, only 12.3 % of patients of group I and 18.9 % of patients of group II had ovulatory menstrual cycles recovered. The girls with preserved oligomenorrhea of group I had a menstrual cycle lasted for  $72 \pm 8.0$  days and the girls of group II had a menstrual cycle lasted for  $53 \pm 4.9$  days ( $p < 0.05$ ). There were also more follicles of classes 7 and 8 in group II found by means of ultrasound examination of the pelvic organs, held during the expected second phase of the cycle.

Prior to the start of hormonal therapy the average values of omega-building of the right hemisphere exceeded the parameters of omega-potential of the left hemisphere. In this case, the moderate hemispheric asymmetry was found. It amounted to  $9,53 \pm 5,44$  Mb. In both groups, the

average values of omega-potential of the right hemisphere were 35 Mb, of the left hemisphere – 31 Mb. In 61.2 % of the cases the value of omega-potential of the right and left hemisphere was more than 40 Mb, which was ranked as high values and characterized by a high level of mental stress (Aladzhanova, 1979; Arshavsky et al, 1984; Bekhtereva, 1980; Bekhtereva, 1974; Rusinov, 1969; Shilova, 2011b), which inevitably depletes the body's resources (Yashchuk, 2012; Unestahl et al, 1996).

In 23.1 % of the cases the value of omega-potential of the left and right hemisphere was less than 20 Mb, which was assessed as low and characterized by high values of exhaustibility, fast psychodivisibility of mental and physical functions and limitation of functional reserves of the body. In 15.7 % of the cases there was an optimal value of omega-potential (20-40 Mb). In most cases, the dynamics of the values of omega-potential of the right and left hemispheres was characterized by the appearance of spontaneous, rhythmic and superslow fluctuations of potentials on the background of omega-waves with a period from 2 to 4 seconds which are called zeta-waves (Ilyuhina et al, 1979). The appearance of these waves is characterized by psycho-emotional stress, emotional activation (Table 3).

The revealed features of activation processes of the cerebral cortex of adolescents with oligomenorrhea on the background of the hypothalamic-pituitary dysfunction are expressed in increasing proportion of young people with high levels of omega-potential, which leads to disadaptation and metabolic disorders in the central nervous system. Estimation of parameters of the menstrual cycle of the female patients with hypothalamic-pituitary dysfunction on the stage of cessation of hormone therapy led to the conclusion of the greater efficiency of the cyclic regime of progestogens' prescription. Using the cyclic regime of hormonotherapy in

Table 3. Structural features of activation processes of cortex on the value of omega-potential before and after hormonal therapy

| Level of omega-potential | Structure of omega-potential index prior to hormonal therapy (%±m) N=134 | Structure of omega-potential index after taking COCs (%±m) N=68 | Structure of omega-potential index after prescription of progestogens (%±m) N=66 |
|--------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------|----------------------------------------------------------------------------------|
| Less than 20 Mb          | N = 31 mV (23,1 %±3,5)                                                   | N = 18 (26,5 %±5,3)                                             | N = 10 (15,1 %±4,4)                                                              |
| 20 Mb – 40 Mb            | N = 21 (15,7 %±3,1)                                                      | N = 11 (16,2 %±4,5)                                             | N = 33 (50 %±6,1) *                                                              |
| Over 40 Mb               | N = 82 (61,2 %±4,2)                                                      | N = 39 (57,3 %±6,0)                                             | N = 23 (34,4 %±5,9)                                                              |

\* Value  $\phi^*$  (angular criterion by Fisher) is in the area of significance (2.334)

this group of female patients has a regulating effect on the reproductive system, presumably through the recovery of a special rhythm of GnRH, which can lead to further recovery of

regular spontaneous menses. This hypothesis is supported by the increase in the proportion of young people in the group with normal values of omega-potential.

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## **Особенности активационных процессов коры головного мозга при олигоменорее у подростков**

**О.Ю. Шилова<sup>а</sup>, М.А. Брагина<sup>б</sup>**

*<sup>а</sup>Красноярский государственный педагогический университет  
им. В.П. Астафьева*

*Россия 660049, Красноярск, ул. Ады Лебедевой, 89*

*<sup>б</sup>НИИ медицинских проблем Севера СО РАМН,  
Россия 660022, Красноярск, ул. П. Железнякa, 3г*

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*В статье приводятся данные по эпидемиологии нарушения менструального цикла подростков г. Красноярска. Выявлено увеличение частоты олигоменореи, что свидетельствует об усугублении функциональных расстройств репродуктивной системы. В связи с возможной зависимостью развития олигоменореи и нарушением активационных процессов коры головного мозга проведено динамическое измерение омега-потенциала полушарий мозга. Исследование проведено в группе пациенток до начала гормональной терапии и после ее окончания. Выявлено, что базовые значения омега-потенциала у девушек с олигоменореей характеризуются его повышением, что свидетельствует о высоком уровне психического напряжения. Выявлена зависимость нормализации активационных процессов коры головного мозга и варианта гормональной коррекции олигоменореи.*

*Ключевые слова: омега-потенциал, олигоменорея, менструальный цикл, подросток.*

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