Changes in Heart Rate Autonomic Regulation in Girls at The Age of 10–11 with Different Rates of Biological Maturation: A Two-year Study

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Abstract. The authors conducted a two-year study of 60 girls aged 10–11. The analysis of the features of heart rhythm autonomic regulation in girls with different biological maturation rates revealed the following. The girls with slower sexual and physical development rates at the age of 10 are marked with higher values of very-low-frequency (VLF) waves, lower values of the high-frequency component of HF than a group of children having the above-average level of physical and sexual development. The groups of 10-year-old girls with different physical and sexual development levels differ in basic anthropometric measurements, body composition parameters, and basal, specific, and norm-based metabolic rates. By the age of 11, girls with the due acquisition of secondary sexual characters demonstrate an increase in sympathetic influence and a decrease in parasympathetic effect on HR's variability. The obtained data indicate a relative lag in the functional development of the cardiovascular system autonomic regulation in girls with the delayed acquisition of secondary sexual characters at the age of 10 compared to the group of children with the above-average level of physical and sexual development.

Keywords: Heart rate variability · Sexual formula · Sexual development score · Physical development · Acceleration · Bioimpedansometry · Public health

1. Introduction

Negative trends continue to increase in women’s health indicators. They are associated with socioeconomic reasons and the influence of a set of environmental and geochemical factors [17, 23]. A drop in the birth rate was observed in many Russian regions since the beginning of the 1990s. The population decline in that period prevailed over its growth, which created an extremely alarming demographic situation [12]. Nowadays, the situation has changed for the better but not significantly. In these conditions, the protection of adolescent girls' health is essential because it will determine the nation’s reproductive potential. Environmental aggression, stress, and social and economic instability create unfavorable conditions for the development of the younger generation. The study of the physical development of adolescents and their functional state must be carried out, taking into account the parameters of sexual development, since the processes of sexual and physical development are closely interconnected. The heart rate (HR) variability analysis holds a significant place among modern methodological approaches to assessing the state of the cardiovascular system and the organism in general. The analysis of beat-to-beat fluctuations of heart rate (heart rate variability, HRV) is an established tool to quantify cardiac autonomic function [13] non-invasively. Apart from performing hydrodynamic functions, the cardiovascular system plays the role of a coordinating link in
the relationship of regulation and information mechanisms with the organism's morphological structures [20]. Recently, the bioimpedansometry method became widely used to assess body composition [10]. New parameters of the body composition, as measured by bioimpedance analysis (such as body fat mass (BFM), lean body mass (LBM), skeletal muscle mass (SMM), body fluid, extracellular fluid, active cell mass (ACM)) can be used as indicators for assessing energy metabolism [21]. The information on the specific features of the HR variability and the body composition of schoolchildren depending on the biological age, which does not always correspond to the stated age, is not available in the literature. Meanwhile, the biological age primarily reflects the individual's ontogenetic maturity, working capacity, and adaptive reactions [11].

The study aims to reveal the relationship between growth and biological maturation rates and heart rhythm autonomic regulation features in girls aged 10–11.

2. Materials and Methods

A two-year study of individuals in the second childhood period was carried out. At first, we examined 72 girls aged 10 (from 9 years 6 months to 10 years 5 months 29 days). The longitudinal studies are complicated by the fact that the composition of the examined group inevitably changes. In a year, we managed to re-examine 60 individuals. All girls are Caucasian and belong to the 1–2 health groups according to their medical records. The studies were conducted in the falls of 2017–2018.

Anthropometric studies included measuring body length (BL), body mass (BM), and chest circumference (ChC).

We used a comprehensive phenotypic assessment of sexual development, according to J. Tanner [5], to characterize the level of sexual development. We used the technique of L. G. Tumilovich et al. [22] to assess the degree of puberty. The basis of this technique is a digital (point-based) assessment of the degree of development of each gender and their biological significance.

The body composition was evaluated with the use of the apparatus for bioimpedansometry ABC-01 “Medass,” which allows determining fat mass, lean body mass, active cell mass, skeletal muscle mass, body fluid, extracellular fluid, basal metabolism (BM), and specific basal metabolism (SBM).

The study of the HR variability was carried out with the use of the “Poly-Spectr-8 \ EX” electrocardiograph, the software being provided by the “Neyrosoft” company (Ivanovo, Russia). A cardiac rhythmogram was recorded at rest at short 5-minute intervals, with the patient lying on his back, breathing being calm, and the external stimuli being absent. The analysis of heart rate variability was carried out following the guidelines developed by a group of Russian authors [3] and the standard of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [13]. To study HR's autonomic neural regulation, the method of temporal and spectral analysis of HR variability was used. The heartbeat rate (bpm) was recorded. The time indices were determined: RRNN, ms – average duration of the RR intervals; SDNN, ms – standard deviation of the RR intervals; RMSSD – standard deviation of the inter-interval differences; pNN50 – a fraction of adjacent intervals differing by more than 50 ms; CV – variation range. The spectral analysis evaluated VLF (ms², %) – wave power in the very-low-frequency range (0–0.04 Hz), LF (ms², %) – wave power in the low-frequency range (0.04–0.15 Hz), HF (ms², %) – wave power in the high-frequency range (0.15–0.4 Hz), TP (ms²) – total spectrum power.

Statistical processing of the material was carried out using the SPSS 21.0 software. In the tables, the quantitative characters having a normal distribution are presented as the arithmetic mean (M), the standard deviation (SD); the values with a distribution different than normal are presented as the median value (Me) and the percentile ranking (Q25–75 = 25 and 75 percentiles). The data samples were checked for normality of distribution with the use of the Shapiro-Wilk criterion at the significance level of p<0.05. The Kruskal-Wallis multiple comparison criterion was used to compare groups. When comparing age-related changes, we used the t-test for dependent samples in the case of a character normal distribution and the non-parametric Wilcoxon paired test if the indicator does not fit into the normal distribution. The differences in the values of the studied parameters were considered statistically significant at a 95% probability threshold (p <0.05). The analysis of the
characters correlation relationship was carried out using the non-parametric Spearman correlation method with the calculation of the correlation coefficient and the p level.

3. Results

The level of puberty or sexual development is determined by the time of the succession of secondary sexual characters appearance and the degree of their development. It is effectively used in the “adolescence” period, i.e., from 7–8 to 16–17 years of age. It is most often applied as a criterion of physiological age in mass screening [8]. There exists a direct correlation between sexual and physical development. Therefore, peculiarities of the sexual development and the estimation of the secondary sexual characters (SSC) manifestation rate are necessary for a comprehensive assessment of the girl's physical development. Secondary sexual characters are known to appear in strict succession. First, the mammary glands start developing (thelarche). Then, a growth spurt is observed, and pubic hair growth appears (pubarche). Only after that, menarche follows [24], which is worth paying attention to. A part of the girls did not yet start acquiring SSC (82%, N = 49), while particular representatives of the sample group (18%, N = 11) demonstrated the appearance of SSC. By the age of 11, some girls still did not start developing SSC (13%, N = 8). In the remaining part of the group, SSC either began to appear, or the process of sexual development continued. We divided the girls into three groups: 1 – a group of girls who did not start developing SSC (with a delayed appearance of SSC), 2 – girls who started to acquire SSC at the age of 11 (with the due appearance of SSC), 3 – girls that started acquiring SSC at the age of 10 (with the advanced appearance of SSC).

| Groups (Z) | Degree of secondary sexual characters development (sexual formula) | Menstrual function | Sexual development score (Me, Q_{25-75}) |
|------------|------------------------------------------------------------------|-------------------|----------------------------------------|
|            | Age (years old)                                                   | Age (years old)   | Age (years old)                        |
| 10 11      |                                                                  |                   |                                        |
| 1          | M_{10,AX_0}P_0                                                    | M_{10,AX_0}P_0    | Me_0                                   |
| 2          |                                                                  |                   | 0                                      |
| 3          |                                                                  |                   | 1.5                                    |
| 11         |                                                                  |                   | 2.4                                    |
|            |                                                                  |                   | 4.4                                    |

Note: Group 1 – girls that did not start developing SSC, 2 – girls that started developing SSC, 3 – girls that developed SSC at the age of 10.

Source: Compiled by the authors.

In the second and the third groups, the growth spurt is observed at the age of 10–11, while in the first group, the growth rates correspond to those in the prepubertal period.

As our study showed, at the age of 10, there were statistically significant differences between the groups in terms of BMI (table 2), BFM, LBM, SMM, and ACM in absolute and relative values (table 3). The basal metabolic rate is higher in the second and the third groups (table 3) at a statistically significant level. However, the specific basal metabolic rate (BM's ratio to body surface area) was lower in girls of the second and the third groups (table 3). According to the parameters of body composition, the division allows us to compare the energy expenditure of different people, even within the same sex and age group. The value of the norm-based basal metabolism (per LBM, kg) was also lower in girls of the second and the third groups (table 3). At the age of 11, the tendency to distribute the bioimpedansometry parameters in groups remained the same. The second group displays the maximum increase in BFM by the age of 11 (table 3). Due to the pubertal acceleration of growth rate, the difference in BFM (%) value was negative (table 3), reaching the maximum in the third group. The BM index increased in all groups by the age of 11. However, the indices of SBM and norm-based BM decreased by the age of 11.
Table 2. Anthropometric parameters of 10–11-year-old girls with different rates of biological maturation.

| Groups | Age (years old) | Δ Differences between the ages of 10 and 11 | Differences between groups |
|--------|-----------------|-------------------------------------------|---------------------------|
|        | M | SD | M | SD | p | M | SD | M | SD | p |
| Body length, cm | 1 133.0 | 3.66 | 138.1 | 3.87 | 5.1 | 0.003 |
| Body mass, kg | 1 24.6 | 1.41 | 26.9 | 1.46 | 2.3 | 0.011 |
| Chest circumference, cm | 1 61.1 | 2.95 | 64.3 | 2.12 | 3.1 | 0.003 |
| BMI, kg/m² | 1 14.0 | 1.35 | 14.2 | 1.41 | 0.2 | 0.000 |

Notes: The groups are similar to the groups in table 1.
Source: Compiled by the authors.

Table 3. The specification of bioimpedansometry parameters in 10–11-year-old girls with different rates of biological maturation.

| Parameters | Groups | Age (years old) | Δ %11 years of age | Differences between groups |
|-----------|--------|-----------------|-------------------|---------------------------|
|          | N | M | SD | M | SD | p | M | SD | M | SD | p |
| Body fat mass, kg | 1 8 | 4.0 | 1.64 | 4.3 | 1.97 | 8 | 15 | <0.001 |
| Body fat mass, % | 1 8 | 16.1 | 6.03 | 15.6 | 6.78 | 8 | 15 | <0.001 |
| Lean body mass, kg | 1 8 | 20.7 | 1.43 | 22.6 | 1.42 | 9 | 15 | <0.001 |
| Active cell mass, kg | 1 8 | 11.6 | 2.51 | 12.2 | 1.71 | 5 | 8 | <0.001 |
| Skeletal muscle mass, kg | 1 8 | 10.4 | 1.22 | 11.8 | 1.22 | 13 | 15 | <0.001 |
| Basal metabolism, kcal/day | 1 8 | 982.8 | 79.66 | 1000.6 | 53.73 | 2 | 15 | <0.001 |

Note: Differences between groups, p ≤ 0.001.
In our study, mean CVs at the age of 10 were lower in girls of the second group. CV
pNN50 showed that the activity of the autonomic regulation loop at the age of 10 was the most
prominent in the girls of the second group. CV (coefficient of variation, %) is analogous to the SDNN
index in a physiological sense. In our study, mean CVs at the age of 10 were lower in girls of the
second group of girls at the age of 10. The RMSSD index reflects the contribution of the parasympathetic division to the cardiac function control. The second group of girls at the age of 10 was marked with an evident vagal activity in the heart rhythm. The analysis of pNN50 showed that the activity of the autonomic regulation loop at the age of 10 was the most prominent in the girls of the second group. CV (coefficient of variation, %) is analogous to the SDNN index in a physiological sense. In our study, mean CVs at the age of 10 were lower in girls of the second group.

Notes: The groups are similar to the groups in table 1.

Source: Compiled by the authors.

Table 4. Time indices of HR variability in 10–11-year-old girls with different rates of biological maturation.

| Indices | Groups | Age (years old) | Δ % | Differences between the ages of 10 and 11 |
|---------|--------|-----------------|-----|----------------------------------------|
|         |        | 10              | 11  |                                         |
|         |        | M/Me            | SD/ Q25.75 | M/Me | SD/ Q25.75 |
| HBR     | 1 8    | 95.5            | 10.10 | 94.7 | 6.40 | -1 |
|         | 2 41   | 88.7            | 11.82 | 90.0 | 9.61 | 0.006 |
|         | 3 11   | 88.1            | 12.04 | 88.5 | 11.90 | 0.002 |
|         | Σ 60   | 89.4            | 11.70 | 90.3 | 9.78 | 0.006 |
| RRNN, ms| 1 8    | 628.8           | 63.78 | 636.5 | 42.64 | 1 |
|         | 2 41   | 686.7           | 95.97 | 677.5 | 76.46 | -1 |
|         | 3 11   | 691.4           | 93.64 | 689.5 | 92.76 | 0 |
|         | Σ 60   | 679.9           | 92.87 | 674.2 | 76.69 | -1 |
| SDNN, ms| 1 8    | 66.6            | 21.96 | 59.6 | 13.87 | -11 |
|         | 2 41   | 62.5            | 19.58 | 63.7 | 23.72 | 2 |
|         | 3 11   | 62.3            | 17.91 | 64.9 | 22.42 | 4 |
|         | Σ 60   | 62.9            | 19.26 | 63.4 | 22.24 | 1 |
| RMSSD, ms| 1 8    | 57.0            | 30.69 | 49.7 | 18.90 | -13 |
|         | 2 41   | 62.8            | 32.73 | 55.0 | 31.37 | -12 |
|         | 3 11   | 57.8            | 21.94 | 57.2 | 33.83 | -1 |
|         | Σ 60   | 61.1            | 30.33 | 46.5 | 37.0 – 62.0 | -10 |
| pNN50, %| 1 8    | 12.3            | 16.21 | 11.2 | 8.80 | -9 |
|         | 2 41   | 27.3            | 22.59 | 19.2 | 18.81 | -30 |
|         | 3 11   | 25.5            | 19.94 | 22.6 | 21.18 | -11 |
|         | Σ 60   | 25.5            | 19.26 | 22.6 | 21.18 | -11 |
| CV      | 1 8    | 10.4            | 2.72  | 9.5  | 2.50 | -9 |
|         | 2 41   | 9.1             | 2.51  | 9.4  | 3.08 | 3 |
|         | 3 11   | 9.0             | 2.23  | 9.4  | 2.64 | 4 |
|         | Σ 60   | 9.2             | 2.48  | 9.4  | 2.89 | 2 |

Notes: The groups are similar to the groups in table 1.

Source: Compiled by the authors.

The average values of heart rate variability parameters (tables 4, 5) were obtained. SDNN is one of the main parameters of HRV, an integral index depending on the combined effect on the sinoatrial node of the sympathetic and parasympathetic divisions of the ANS. Our study showed a decrease in mean SDNN values from the first group to the third one at the age of 10. The RMSSD index reflects the contribution of the parasympathetic division to the cardiac function control. The second group of girls at the age of 10 was marked with an evident vagal activity in the heart rhythm. The analysis of pNN50 showed that the activity of the autonomic regulation loop at the age of 10 was the most prominent in the girls of the second group. CV (coefficient of variation, %) is analogous to the SDNN index in a physiological sense. In our study, mean CVs at the age of 10 were lower in girls of the second group.
second and the third groups. The heart rate variability index did not display a statistically significant difference between 10-year-old and 11-year-old girls.

Table 5. Spectral indices of HR variability in 10–11-year-old girls with different rates of biological maturation.

| Indices | Groups | N | 10 | 11 | Δ %10-11 years of age | Differences between groups | Differences between the ages of 10 and 11 |
|---------|--------|---|----|----|----------------------|---------------------------|--------------------------------------|
|         |        |   |    |    |                      | 1st measure               |                                      |
|         |        |   |    |    |                      | p                         |                                      |
| VLF, %  | 1     | 8 | 38.8 | 12.99 | 31.7 | 13.70 | -18 | P_{1,2} = 0.001 | <0.001 |
|         | 2     | 41| 24.1 | 9.58  | 35.8 | 14.67 | 49 | P_{1,3} = 0.002 | 0.001 |
|         | 3     | 11| 32.2 | 11.75 | 31.1 | 8.70  | -3 | P_{2,3} = 0.27  |
| Σ       | 60    | 932.0 | 625.5 | 1,564.0 | 954.0 | 680.3 | 2,405.3 | 2 |
| VLF     |        | Me | Q_{25;75} | Me | Q_{25;75} |                    |                                      |
|         | 1     | 1,110 | 499.0 | 4,075.0 | 2,217.0 | 1,698.77 | 11 |
|         | 2     | 1,251.0 | 727.0 | 2,130.0 | 1,495.6 | 1,143.69 | 5 |
|         | 3     | 1,540.0 | 1,142.36 | 2,085.5 | 1,629.56 | 35 |
| Σ       | 60    | 1,512.5 | 1,095.47 | 1,698.1 | 1,327.66 | 12 |
| LF, %   | 1     | 8 | 38.2 | 6.66  | 37.1 | 14.68 | -3 |
|         | 2     | 41| 33.5 | 14.11 | 32.6 | 10.15 | -3 |
|         | 3     | 11| 32.2 | 14.15 | 38.0 | 11.81 | 18 |
| Σ       | 60    | 33.8 | 13.37 | 34.2 | 11.11 | 1 |
| HF      |        | Me | Q_{25;75} | Me | Q_{25;75} |                    |                                      |
|         | 1     | 8 | 1,854.0 | 678.0 | 1,534.0 | 943.4 | 312.38 | -25 |
|         | 2     | 41| 1,270.5 | 931.5 | 3,172.0 | 1,151.0 | 605.0 | 1,645.3 | -9 |
|         | 3     | 11| 1,721.9 | 1,466.49 | 1,632.3 | 1,722.04 | -5 |
| Σ       | 60    | 1,186.0 | 701.3 | 2,950.3 | 1,092.0 | 671.3 | 1,606.3 | -8 |
| HF, %   |        | Me | Q_{25;75} | Me | Q_{25;75} |                    |                                      |
|         | 1     | 8 | 23.0 | 14.95 | 31.3 | 25.06 | 36 | P_{1,2} = 0.016 |
|         | 2     | 41| 28.5 | 17.29 | 31.6 | 15.76 | -25 | P_{1,3} = 0.034 |
|         | 3     | 11| 37.9 | 14.86 | 30.9 | 14.71 | -13 |
| Σ       | 60    | 38.7 | 17.57 | 31.4 | 16.57 | -19 |
| TP      |        | Me | Q_{25;75} |                    |                                      |
|         | 2     | 41| 4,453.5 | 2,583.27 | 3,528.0 | 2,222.0 | 5,730.0 | 11 |
|         | 3     | 11| 4,544.0 | 2,571.02 | 5,459.1 | 3,974.59 | 20 |
| Σ       | 60    | 4,704.8 | 2,891.76 | 5,082.2 | 3,847.56 | 8 | <0.001 |

Notes: The groups are similar to the groups in Table 1.
Source: Compiled by the authors.

The High-frequency component (HF, 0.15–0.4 Hz) is related to the respiratory activity and parasympathetic control [13]. Variations exist in the interpretation of the LF range. Some authors attribute this indicator to the activity of the sympathetic link of autonomous regulation of HR [14]. Other authors suggest participation in the formation of this range and vagal influences [4]. The parasympathetic system’s activity contributes to the formation of the power of the LF range 50%, 25% – sympathetic activity, 25% – other factors according to the calculations of G. Billman. The power of the HF range is 90% due to the vagus’ activity, and 10% due to the activity of the sympathetic nerve [4].

The results of the spectral analysis of HR variability exposed the changes in the frequency components of heart rate fluctuations. When comparing the spectral indicators of HR variability in the
third group, we noticed a tendency (table 5) to the rise in the high-frequency component HF (%) of the cardiac rhythm as compared to the first and the second groups, which indicates an increase in the parasympathetic component of the heart rate variability [7]. In the second and the third groups, there is a tendency for a decrease in heartbeat rate (table 4). The indices of the HR variability spectral analysis did not demonstrate statistically significant differences between the groups at the age of 11.

The physiological meaning of the VLF range remains not fully deciphered. The VLF power is related to control of energy metabolism and thermoregulation, changes in peripheral chemoreceptor activity, and fluctuations in the renin-angiotensin system [13, 18].

In the first group, the prevalence of the spectral power and the contribution (%) of the slow-wave VLF ranges in the HR spectrum is observed (table 5).

Correlation analysis helps to understand the relationship between VLF and LF waves in the HR spectrum and metabolic parameters. At the age of 11, positive correlations appear between the amount of SMM (%) and the relative power of very low frequencies VLF (r = 0.470, p <0.001), VLF% share (r = 0.301, p = 0.018), the relative power of low frequencies LF (r = 0.260, p = 0.043). Negative correlation is observed between SMM% and the fraction of high frequencies HF% (r = −0.294, p = 0.021). We did not find a significant correlation between indicators of very low and low frequencies in the variability of HR and metabolic parameters. However, the basal metabolic rate is associated with a positive strong relationship with the SMM at the age of ten (r = 0.829, p <0.001) and eleven years (r = 0.787, p <0.001). The value of normalized metabolism (per kg LBMI) is associated with a negative strong relationship with the SMM indicator at the age of ten (r = 0.719, p <0.001) and eleven years (r = 0.809, p <0.001).

The wave structure of the spectrum of girls of the first (VLF> HF>LF – at 10 years old, LF> VLF>HF – 11 years old) and the second (HF>LF> VLF – at 10 years old, LF>HF> VLF – 11 years old) groups changed towards the dominance of the low-frequency component of the spectrum (LF). The wave structure of the spectrum in girls of the third group by the age of 11 displayed a redistribution of the VLF, and HF ranges relative power (HF>LF> VLF – at 10, LF> VLF>HF – at 11), an increase in the low frequencies contribution (table 5), which is most likely associated with a growth spurt (table 2) and intense neuroendocrine restructuring of the organism. This was accompanied by the most notable decrease in BFM (table 3) by 11.

4. Discussion

HR variability features depending on the rate of biological maturation are well explained by age-related changes in the influence of the autonomic nervous system departments on HRV. The studies show an increase in the impact of the parasympathetic department of the autonomic nervous system with age within the period of 7–17 years of age [1, 6, 9]. At 15–16, the stabilization of heart rate regulation was revealed, which allowed the authors to conclude that adaptive alterations were completed, and the optimal regulation was formed by this stage of ontogenesis [9]. The younger the child is, the stronger the effect of the SNS on the heart rate is [6, 9]. Girls with an advanced appearance of secondary sexual characters at the age of 10 show a tendency towards a moderate activation of the parasympathetic regulation link, which is confirmed by an increase in the HF index (table 5).

We found out that the girls with higher rates of physical development and puberty level demonstrate higher indices of lean body mass and body fat mass, while their norm-based metabolic rate decreases. The data obtained on the increase in the BMI in the second and the third groups are consistent with the results of P. L. Okorokov, O. V. Vasyukova, and T. Yu. Shiryaeva. Their study showed that the absolute values of the basal metabolic rate at rest naturally increased with the progression of sexual development. As well as other authors [15, 16], we revealed a decline in the intensity of basal metabolism at rest with the progression of puberty (table 3), which may be explained by a growing need for additional energy to ensure growth and development.
5. Conclusion
The data obtained in our work indicate a relative lag in the functional development of the autonomic regulation of the cardiovascular system in girls with a delayed appearance of secondary sexual characters at the age of 10 as compared to the group of children having the above-average level of physical and sexual development.

All the studies were conducted following the principles of biomedical ethics formulated in the Helsinki Declaration of 1964 and its subsequent updates and were approved by the local bioethical committee of the Altai State University. Parents of all the children participating in the survey provided a voluntary informed consent statement in a written form, signed by them after being explained the potential risks, benefits, and the nature of the study. The authors declare no apparent or potential conflicts of interest related to the publication of this paper.

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