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DISTRIBUTION OF INDIVIDUAL CIRCULATORY BIORHYTHMS IN SCHOOLCHILDREN AGED 7-17 YEARS LIVING AT DIFFERENT ALTITUDES IN THE MOUNTAINS

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UDC 612.1-053.5"5"].08

KEY WORDS: biorhythms; hemodynamic processes; adaptation

The temporal organization of hemodynamic processes in permanent dwellers at high altitudes is of definite interest because biorhythmologic methods can broaden qualitatively our knowledge of a given functional system, changes in which play a key role in adaptation to a mountain climate. This explains the recent increase in the volume of research undertaken to study this problem [1-7]. However, the publications cited above represent the results of group comparisons of biorhythms of the circulation in inhabitants of different mountain zones. Yet, however, when problems of population adaptation are being considered, attention must be paid to interindividual differences in biorhythms [8, 9]. Besides an analysis of averaged data, the aim of the present investigation was also to assess the character of distribution of individual biorhythms depending on the height at which the population lives.

EXPERIMENTAL METHOD

To ensure maximal standardization of the subjects with respect to age, sex, and social organization, the investigation was based at boarding schools situated at altitudes of 760, 1700, and 2850 m above sea level. In each altitude zone 90 schoolchildren were investigated, divided into three groups depending on their age: 7-10, 11-14, and 15-17 years (30 in each group). The parameters of the systemic circulation were assessed by the electrical impedance method of Kubicek et al. [10] six times in the course of the 24-h period, i.e., every 4 h.

The primary data were analyzed by the special "Cosinor" chronobiological program.

The character of distribution of individual biorhythms in the populations was estimated as the circadian course of the cardiac index (CI), the ratio of the cardiac output to the body surface area. This was because this index eliminates natural anthropometric differences between the subjects studied.

Institute of Balneology, Bishkek, Kyrgyzstan. No. 60 Moscow General Hospital. (Presented by Academician of the Russian Academy of Medical Sciences Yu. A. Romanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 11, pp. 527-529, November, 1992. Original article submitted June 24, 1992.

 0007-4888/92/0010-1690$12.50

TABLE 1. Cosinor Estimation of Parameters of 24-Hourly Fluctuations of CI in Inhabitants of Different Altitude Zones

Age, years	Level, liters/m²/min	Amplitude, %	Acrophase, h
Low altitude			
7—10	3,36±0,12	14,88±0,89	13,9<15,4<16,6
11—14	2,84±0,07	25,70±0,70	15,4<16,0<16,6
15—17	2,76±0,08	19,57±0,72	15,2<16,0<16,9
Middle altitude			
7—10	3,46±0,12	18,79±0,87	14,6<15,5<16,5
11—14	3,19±0,13	15,67±0,63	14,5<15,5<16,7
15—17	2,74±0,12	20,80±0,82	15,5<16,3<17,2
High altitude			
7—10	3,30±0,12	12,73±0,91	13,5<15,1<16,6
11—14	2,43±0,07	16,05±1,11	14,5<15,5<16,5
15—17	2,51±0,11	19,52±0,80	15,6<16,5<17,5

TABLE 2. Biorhythmologic Kernel in Three Age Samples of Population Living at Different Altitudes, Per Cent

Age, years	Low altitude	Middle altitude	High altitude
7—10	80,0	60,0	60,0
11—14	80,0	83,3	60,0
15—17	86,7	76,7	66,7

EXPERIMENTAL RESULTS

Table 1 shows that significant circadian rhythms of CI were found in all the groups studied. Their acrophases occurred after mid-day. Similar age changes in the circadian rhythm of CI were observed in the inhabitants of all altitudes. During the 10-year period of life the mean daily level of CI decreased but the amplitude of its fluctuations increased and a phase shift of the rhythm by 1 h toward evening took place.

Incidentally, this averaged version of the biorhythm was characteristic, with a high degree of significance, only for a limited part of the population, for parameters of the biorhythms in some clinically healthy subjects differed significantly from the mean values for the group. Moreover, the probability of finding other forms of biorhythm depended on the altitude of residence. For instance, visual comparison of individual chronograms of CI in teenagers aged 15-17 years, living at low, middle, and high altitudes, revealed marked widening, under mountain conditions, of the biorhythmologic zone into which the biorhythms of most of the subjects fitted. A similar tendency also was noted when younger age groups were compared.

However, this rule requires mathematical verification. A program was therefore devised to assess quantitatively the degree of biorhythmologic dispersion in the suggested samples. Two stages of Cosnor analysis are represented in the top part of the block diagram. The factual data are first approximated by 24-hourly harmonics (individual Cosinor analysis), which are subsequently averaged (group Cosinor analysis). The original material for creating the program consisted of data of individual Cosinor analysis. Statistical nonhomogeneity of the biorhythmologic sample with a level of significance accepted in physiology (95%) was taken as the working hypothesis. For this purpose all individual harmonics were verified against a mutual increase of deviation, equal to 2 sigmas, relative to the mean value of the rhythm, and with respect to amplitude, acrophase, and mesor. The presence of one or more off-scale elements of the set to be analyzed, with respect to any parameter of the biorhythm, led to their rejection. Selections of curves not satisfying the narrowed range (±2 sigmas), newly created for the "purified" group have in turn been subjected to a "purified" group. This operation, which can be continued for an infinitely long time in the form of a cyclic algorithm (in Fig. 2 only three cycles are shown conventionally), was stopped in two cases: either the biorhythm of one person was left, indicating 95% nonhomogeneity of the set analyzed, or the program preserved a statistically homogeneous group. In other words, in this case the program formed the "biorhythmologic kernel" of the given population. Its fraction in per cent is the equivalent of the degree of homogeneity of the biorhythmologic sample (Table 2).

Two tendencies can be discerned: first, independently of the altitude of residence, the percentage of individuals having homogeneous parameters of the circadian rhythm of their systemic circulation increases in the population as it moves into adulthood. This is evidence that in the period of ontogenetic human growth and development, i.e., when the human circadian system is formed, a wider polymorphism of biorhythms is observed within the population. It is quite possible that the cause lies in the multivariance of forms of maturation of the circadian system. Second, the size of the biorhythmologic kernel in mountain dwellers, compared with lowlanders of the same age, was reduced in proportion to the altitude of the locality. At low altitudes its mean value for the groups was 82%, at middle altitudes 73%, and at high altitudes 62%. It will be clear that the lowland population was closest to the normal gaussian distribution. A more extremal type of mean was accompanied by the accumulation of individuals in the population with versions of biorhythms that differ from the mean for the group. Whereas at low altitudes they amounted to under 20% of the sample, at an altitude of 2850 m above sea level, they applied to 40% of the subjects. If this rule is extrapolated to higher altitudes, an altitude limit, above which the statistical mean biorhythmologic norms will really describe under 50% of the population, is perfectly probable.

This individualization of biorhythms is not a sign of "loosening" of the circadian system. As our own observations show, stable relations between individual components of the circadian structure are preserved in the mountain dwellers. However, in a high proportion of subjects they may differ appreciably from the statistical mean values. From the methodologic standpoint this points to a decrease in the informative value of statistical mean methods of evaluation of biorhythms and raises the problem of the elaboration of finer criteria of the "biorhythmologic norm" in inhabitants of high altitudes.

This broadening of the spectrum of forms of circadian activity of the cardiovascular system which are found can be explained by the multivariance of methods of adaptation to chronic hypoxia [11, 12]. However, this last suggestion will need to be verified in the future, for we do not yet know whether this phenomenon extends to biorhythms of other functional systems, which do not play so active a part in the adaptation process. Nevertheless, there is every reason to suppose that the degree of polymorphism of circulatory biorhythms is a reliable marker of the harshness of the climate in the mountain locality where the subjects-tested live.

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RADIO-ISOTOPIC PLATELET LABELING WITH MONOCLONAL ANTIBODY AGAINST MEMBRANE GLYCOPROTEIN IIb-IIIa. MEASUREMENT OF PLATELET ADHESION/AGGREGATION TO THE SUBSTRATE

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UDC 616.155.25-073:916

KEY WORDS: platelets; adhesion; aggregation

Adhesion and aggregation of platelets on the surface of an injured vascular wall are key reactions initiating thrombus formation. Methods of investigation of adhesion and aggregation are widely used to assess the functional state of platelets in patients with cardiovascular and hematologic diseases and to investigate the action of various drugs on platelets. To study aggregation in suspension, Born [4] suggested a method of recording aggregates based on the change in scattering of light in mixed platelet suspension. However, the method does not allow adhesion processes and aggregate formation to be studied on the substrate surface. To study these processes, microscopic and radio-isotopic methods are used. To study interaction of platelets with the surface active substrates stimulating adhesion, spreading, and aggregation of platelets are used. They include various types of collagens, fibronectin, and adhesive proteins. Mazurov and co-workers [1, 9] suggested that the platelets should first be activated by plasma inducers, and only after that should they be incubated with the substrate. In that case adhesion and aggregation were stimulated even on an inactive substrate. By the use of microscopic methods, the number of adherent platelets can be directly counted and the morphology of processes such as pseudopodium formation, changes in shape, and spreading of platelets can be studied in detail [1, 3, 9]. However, microscopic methods are difficult to carry out when quantitative measurements are needed. For quantitative assessment of the total number of platelets adherent to the substrate, radio-isotopic methods are the most convenient. Isotopes ^{51}Cr [5] and ^{111}In [6] are most frequently used to label platelets [6] ^{51}Cr is incorporated in the adenylate pool of the platelets [14], but the mechanism of binding of ^{111}In with platelets has not yet been elucidated.

In this paper we suggest a new method of labeling platelets, using ^{125}I-labeled monoclonal antibody (McAb) against the membrane glycoprotein IIb-IIIa complex. Labeled platelets were used to measure platelet adhesion/aggregation on the surface of the substrate. The method was tested in a study of antiplatelet activity of the antianginal drug trapidil and the antiatherogenic agent probucol.

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