Finally, the study of circadian rhythms of biochemical parameters in different seasons of the year can help to elucidate the mechanisms responsible for chronoresistance of the body to various toxic agents and during different periods of physiological activity [6, 7].

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CONTRIBUTION OF GENETIC CONSTITUTION TO FORMATION OF CIRCADIAN RHYTHMS OF SOME HEMODYNAMIC PARAMETERS

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Studies in twins are of great value to the elucidation of the relative role of environment and heredity in the formation of biorhythms. The main task of analysis of quantitative traits in twins is the ability to evaluate the relative role of heredity and environment in the realization of the phenomenon chosen for study. Circadian changes in a number of parameters are known to be more similar in monozygotic than dizygotic twins [1]. This suggests the existence of a sufficiently important genetic component in the formation of circadian rhythms of certain parameters, and in turn, this raises the question of mathematical methods for evaluating this importance.

The first studies using analysis of twins in biorhythmology [1-3] were based on separate analysis of observations at each time point. As a result of this method, the number of coefficients of genetic and environmental determination is proportional to the number of time cuts, and this makes evaluation of the degree of genetic determination of the rhythm of the test parameter difficult. This method also is more suitable for solving the problem of the rhythm of genetic (or environmental) determination than the problem of genetic determination of the rhythm, which is by no means the same thing. The main idea of our suggested generalization of unidimensional procedures in work with twins to the multidimensional case (which is what distinguishes analysis of chronobiological data from analysis of ordinary data) is that the initial time series is replaced by an acrophase-amplitude point on a plane, after which the resulting two-dimensional distribution is analyzed.

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TABLE 1. Parameters of Circadian Rhythm of Some Hemodynamic Parameters in Youths Aged 14-16 Years

Parameter	Acrophase, h, min	Confidence interval of acrophase, h. min	Amplitude	Confidence interval	Mesor	Confidence interval
HR	12,54	11,30—14,12	1,9	1—2,8	71	70—72
SP	15,36	15,6—16,00	5,9	5,2—6,5	114	113—115
DP	15,00	11,6—14,12	1,5	0,8—2	69,7	69—70

EXPERIMENTAL METHOD

The circadian rhythm of individual parameters of the circulation was studied in a group of twins (40 pairs), adolescent males (aged 14-16 years), residing permanently in Vinnitsa.

Zygosity was established on the basis of anthroposcopy, anthropometry, and dermatoglyphics: 17 pairs were accepted as monozygotic and 23 pairs as dizygotic. The heart rate (HR) was determined from the R–R interval of the ECG, and blood pressure was measured by Korotkov's method. Measurements were made seven times a day at 8 a.m. and 1, 4, 6, 9, and 11 p.m. The great uniformity of the groups tested, with respect to sex, age, and place of residence, must be emphasized. The results were subjected to cosinor analysis.

EXPERIMENTAL RESULTS

The presence of a circadian rhythm of all the parameters studied was established (the results of cosinor analysis are given in Table 1).

Even on visual analysis of the resulting distribution, the fact will be noted that individual cosinors of monozygotic twins are closer together than those of dizygotic twins (Fig. 1). Statistical analysis of the distances between the cosinors of monozygotic twins compared with distances between dizygotic twins (for comparison, the nonparametric Mann–Whitney test and Student's test were used) confirms this observation. The results of statistical analysis of the distances between cosinors of mono- and dizygotic pairs are given in Table 2.

It will be clear from Table 2 that individual rhythms of systolic (SP) and diastolic (DP) blood pressure of monozygotic pairs were closer than rhythms of dizygotic pairs, whereas the degree of similarity of individual rhythms of HR in monozygotic pairs did not differ from the degree of similarity of biorhythms of dizygotic pairs of twins. It can accordingly be concluded that hereditary factors have a greater influence on the character of rhythms of SP and DP, and that the environment has a significant effect on the character of rhythms of HR.

Generalized Coefficient of Genetic Determination. To assess the degree of the effect of genetic and environmental factors in the formation of biorhythms of the parameters examined above, it is natural to use methods analogous to those used in classical (unidimensional) analysis of twins.

Most frequently the mean square of deviations of features (phenotype) of individuals from the arithmetic mean (phenotypic variance) is used in calculations for analysis of twins.

The formula of phenotypic variance is as follows:

$$V_p = \sum_{i=1}^{n} (x_i - a)^2 / 2n,$$

where a denotes the mean, x_i the value of the feature studied in the i-th object, and n the number of objects.

The difference between the degree of expression of a feature in individuals in a population may be determined by both genetic and environmental factors. Accordingly, two important parameters are used in genetics: H, the coefficient of genetic determination, and E, the coefficient of environmental determination of the feature. Now:

$$H + E = 1.$$

The so-called Holzinger's coefficient [9] is one of the coefficients of genetic determination that is used most often:

$$H = \frac{V_{DZ} - V_{MZ}}{V_{DZ}}.$$

TABLE 2. Mean Values of Distances between Individual Cosinors of Pairs of Twins

Parameter	Monozygotic	Dizygotic	Significance
HR	5,5±0,6	5,8±0,4	—
SP	2,8±0,4	4,7±0,4	$p<0{,}01$
DP	3,4±0,2	4,8±0,4	$p<0{,}01$

TABLE 3. Relative Values of Hereditary (H) and External Environmental (E) Factors in Formation of Rhythm of Some Hemodynamic Paramters in Youths Aged 14-16 Years

Parameter	H	E
SP	0,61	0,39
DP	0,56	0,44
HR	0,01	0,99

In this case the parameter of environmental determination of the feature is calculated by the equation:

$$E = 1 - H.$$

Unfortunately the value of H, as has repeatedly been stated in the genetic literature (E. T. Lil'in, 1980), is not a well-grounded assessment (in the statistical sense) of genetic determination, and for that reason results obtained in that way can be only a very approximate characteristic of the relative role of heredity. Despite this fact, Holzinger's formula is widely used in studies of twins. This is partly due to the fact that it was historically the first attempt at assessing the relative roles of heredity and environment. The parameter H also, as will be shown below, is easily generalized to the chronobiological case. Incidentally, H varies within natural limits from 1 in the case of entirely hereditary determination of the feature to 0 in the case of complete environmental determination.

Attention is drawn to the fact that the parameter H can be expressed in a form which depends only on differences of the studied value in partners of pairs of twins. It is this fact which enables this parameter naturally to be generalized to the multidimensional case. In doing so, we shall set out from the proposition that we use a certain amplitude-acrophase reflection of chronobiological observations on a plane, for which we may use individual cosinor analysis.

In this case each time series is represented by a point on the plane, characterized either by polar coordinates (A, φ) or cartesian coordinates (x, y). It will be evident that the square of the difference in the above-mentioned formulas means the square of the distance between the points on the numerical axis. The square of the distances on the numerical axis is easily generalized as the square of distances on the plane between the points (x_1, y_1) and (x_2, y_2). Generalization of Holzinger's coefficient H is thus represented in the following form

$$\frac{\dfrac{\sum_{i=1}^{n_{DZ}} R_{iDZ}^2}{2n_{DZ}} - \dfrac{\sum_{i=1}^{n_{MZ}} R_{iMZ}^2}{2n_{MZ}}}{\dfrac{\sum_{i=1}^{n_{DZ}} R_{iDZ}^2}{2n_{DZ}}},$$

where R_1 denotes the distance between two amplitude–phase points, corresponding to the representatives of the pairs of twins, and n_{MZ} and n_{DZ} denote the number of monozygotic and dizygotic pairs respectively. In this case the parameter is calculated just as in the unidimensional case:

$$E = 1 - H.$$

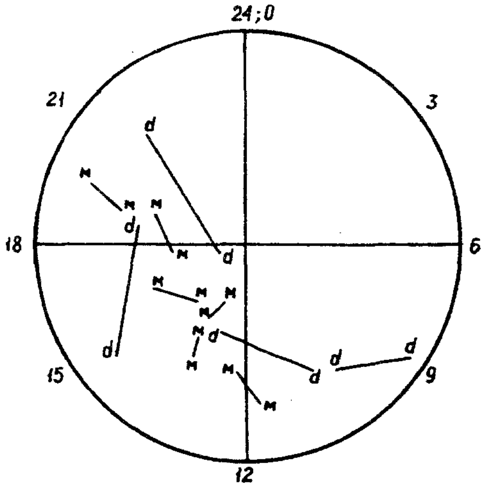

Fig. 1. Individual cosinors of systolic blood pressure of monozygotic (m) and dizygotic (d) twins.

The results of calculations of generalized Holzinger's coefficients are given in Table 3.

As Table 3 shows, the generalized Holzinger's parameter gives results in full agreement with the conclusions reached from Table 2. The rhythm of HR has a very small coefficient of genetic determination, unlike the blood pressure rhythms.

The simplicity of generalization of the Holzinger formula for analysis of time series was based on the fact that its analytical expression in the unidimensional case was based not so much on the use of the actual value studied, as on the use of a certain measure of difference between this value in one representative of a pair of twins and its value in the other representative of the same pair.

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