CHANGES IN AMPLITUDES OF CIRCADIAN RHYTHMS IN POSTNATAL ONTOGENY

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Our investigations on laboratory animals and on human subjects of different ages have shown regular changes in amplitude of the circadian rhythm of many homeostatic systems during postnatal ontogeny [1].

The amplitude of these rhythms rises initially and reaches a maximum in organisms of reproductive age. During aging the amplitude diminishes, and at times disappears completely. On this basis we have formulated a "spinning top" hypothesis. We judged changes in amplitude both visually and on the basis of the results of Cosinor analysis [2].

To obtain further proof and confirmation of our hypothesis we undertook dispersion analysis, which does not require a model describing the shape of the oscillations. The "Cosinor" procedure assumes a sinusoid, and on that basis it postulates that the decrease in amplitude calculated by the "Cosinor" procedure is connected only or partially with a change in shape of the oscillatory process, as it differs increasingly from a sinusoid. The second factor which can determine an apparent reduction of amplitude is connected with desynchronization between animals, for circadian curves represent the sum of the data for many individuals. In grouped "Cosinor" analysis better coincidence can be expected between circadian rhythms and synchronization, whereas in early ontogeny the mechanisms of protraction are only just maturing, and in the late stages they are gradually lost.

Because of differences of age, definite dispersion can be expected between individuals. This factor must have a greater effect during aging than in the period of growth. The aim of the present investigation was to assess the possible role of these factors in age changes in the amplitude of the circadian rhythm established previously.

EXPERIMENTAL METHOD

The conditions under which the animals were kept and the experiments conducted, and also the methods of determination of the parameters chosen were described in detail in the previous publication [1].

Dispersion analysis was carried out on the C64 computer. The program was devised to take account of G. F. Lakin's suggestions [3].

EXPERIMENTAL RESULTS

The results of dispersion analysis are given in Table 1 (parameters 2-4). For comparison, we also give amplitudes calculated by the "Cosinor" method (parameter 1). It will be seen (parameter 2) that the sum of the squares of deviations between the time points increases up to the adult age, then decreases, i.e., the differences between the time points increases and decreases. Dependence of the values on clock time is greater in the adult period. This reflects coincidence in principle with the "Cosinor" results. In the latter case changes in the amplitudes are actually less marked, which is due to some mismatching in the shape of the circadian curve (sinusoid). Thus, the results of dispersion analysis not only confirm the results obtained previously [1], but they also show that ontogenetic changes of amplitude may be even more marked than it appeared to us on the basis of the "Cosinor" data.

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TABLE 1. Characteristics of Amplitudes of Circadian Rhythm of Some Biological Parameters during Ontogeny of Rats Based on Results of "Cosinor" and Dispersion Analysis

Parameter	Age of rats					
	infantile	juvenile	young	adult	presenile	senile
Liver glycogen						
1	67,1	62,2	69,7	100	59,3	31,9
2	41,1	34,5	71,6	100	15,2	9,2
3	313,6	444,7	384,1	1060,2	30,2	58,0
4	3,7	2,6	3,0	1,1	28,5	17,1
5	42,2	35,0	73,0	100	21,0	11,0
Blood glycogen						
1	55,4	55,4	82,6	100	62,0	21,5
2	58,1	30,8	69,7	100	39,7	4,8
3	76,8	56,6	255,0	203,8	133,2	29,2
4	13,5	17,5	4,5	5,6	8,3	29,1
5	64,1	35,2	69,0	100	40,9	6,4
Blood glucose						
1	54,2	64,2	93,2	100	50	31,6
2	52,6	106,0	102,7	100	70,5	36,7
3	93,7	183,9	306,0	232,3	285,7	61,7
4	11,4	6,1	3,8	4,9	4,0	16,3
5	56,5	107,3	101,4	100	69,8	41,7
ICE:						
1	82,9	87,7	92,9	100	67,9	61,7
2	47,5	44,3	72,1	100	35,0	25,9
3	529,0	799,7	953,8	723,4	833,0	677,2
4	2,2	1,5	1,2	1,6	1,4	1,7
5	47,8	44,2	71,8	100	34,9	25,9
Blood lactate						
1	53,0	78,8	93,9	100	62,1	48,5
2	40,6	57,0	79,8	100	41,4	26,3
3	84,0	50,9	91,0	201,2	49,2	23,9
4	12,5	19,1	11,6	5,6	19,6	33,3
5	43,8	66,5	85,2	100	48,6	37,2
Blood pyruvate						
1	22,1	55,2	73,6	100	39,2	16,4
2	4,1	34,4	59,2	100	32,7	2,3
3	131,5	980,5	1954,5	4211,3	2074,7	186,2
4	8,4	1,2	0,6	0,3	0,6	6,1
5	4,4	34,7	59,4	100	32,8	2,4
Body temperature						
1	66,7	90,9	72,7	100	103,0	57,6
2	40,1	55,0	63,6	100	79,7	24,7
3	21,5	25,7	58,2	73,1	57,3	13,3
4	35,8	31,8	17,1	14,1	17,3	47,4
5	53,5	69,5	65,9	100	83,0	40,3
pH blood						
1	30,9	82,4	97,1	100	88,2	69,1
2	66,7	88,9	111,1	100	88,9	66,7
3	7,6	17,7	15,8	34,3	41,6	73,3
4	61,4	40,4	43,2	25,9	22,4	14,1
5	115,4	100	138,5	100	76,9	46,2

Legend. 1) Amplitude in % of amplitude at adult age; 2) sum of squares of deviations, intergroup (i.e., between time points in % of adult age); 3) dispersion relations, degree of freedom 3 and 36; 4) sum of squares of deviations, intragroup (i.e., within time points, in % of total sum of squares); 5) total sum of squares of deviations (in % of adult age).

Interindividual dispersion can be judged from the values of parameters 3 and 4 in Table 1. The dispersion relations indicate high statistical significance of the circadian rhythm and the increased contribution of interindividual differences in the early and late stages. The latter is clearly visible in data in line 4 of each column. The lowest interindividual dispersion is observed at young and adult ages. With increasing distance from this stage of development, interindividual dispersion increases; the highest values are recorded, moreover, at presenile and senile ages. This is in agreement with our hypothesis that it is at those ages that biological age differs to the greatest degree from the calendar age. The exceptions are insulin-containing erythrocytes (ICE) and blood pH. In the first case the contribution of interindividual sum of squares of deviations from the total sum throughout ontogeny is very low, and is almost unchanging, whereas in the second case it gradually falls.

It can accordingly be concluded that interindividual dispersion changes in the course of ontogeny, and in most cases it does so parallel with changes in amplitudes. However, the first is not the only cause of the second. If it were so, the total sum of squares of the deviations (parameter 5) ought to remain more or less constant. However, it changes to the same degree as scatter

between the time points. Moreover, the amplitude of the circadian rhythm of ICE and blood pH rises and falls, just as in the case of the other parameters, but the interindividual dispersion does not change in the first case and falls continuously in the second. Amplitudes of circadian rhythms of blood glucose and pyruvate, however, start to fall before interindividual dispersion increases.

The statements made above do not rule out the possibility that changes in amplitudes are to a definite degree connected with desynchronization between animals. However, its contribution to this process is exceedingly small.

If we speak of increasing desynchronization between animals with increasing distance from the adult age, besides the phase shift, changes in mesors and amplitudes, which also determine the increase in interindividual dispersion, must also be taken into account. Only an individual approach can determine the contribution of individual changes to the general picture. However, the following conclusion can already be formed from the data given above together with analysis of the calculated acrophages: some improvement in internal and external synchronization can be observed in early ontogeny, with their worsening in late ontogeny, but changes take place primarily and most strongly in the amplitude of circadian rhythms, and this may provide important material in respect of biological age, especially in the final stages of ontogeny.

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EFFECT OF IMMOBILIZATION ON MYOCARDIAL MITOCHONDRIAL ENERGY METABOLISM AND ULTRASTRUCTURE IN RATS OF DIFFERENT ZOOSOCIAL RANKS

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The writers' previous investigations showed that a single exposure to immobilization stress causes changes in the ultrastructural organization of heart muscle cells of rats, the intensity of which depends on the animal's zoosocial rank in the group. The most marked disturbances of myocardial ultrastructure are observed in rats belonging to the zoosocial rank of dominants [1].

There is reason to suppose that the cause of the lower resistance of the heart of dominant rats to immobilization stress is the greater energy dependence of their myocardium. To test this hypothesis we studied mitochondrial metabolism in the myocardium of rats belonging to different zoosocial ranks under normal conditions and after immobilization.

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