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Effect of Considering the Initial Parameters on Accuracy of Experimental Studies Conclusions

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Abstract. The presented paper contains the evidences of the necessity to take into account the initial level of physiological parameters while conducting the biomedical research; it is exemplified by certain indicators of cardiorespiratory system. The analysis is based on the employment of data obtained via the multiple surveys of medical and pharmaceutical college students. There has been revealed a negative correlation of changes of the studied parameters of cardiorespiratory system in the repeated measurements compared to their initial level. It is assumed that the dependence of the changes of physiological parameters from the baseline can be caused by the biorhythmic changes inherent for all body systems.

Modern biorhythmology notes the existence of a number of simultaneous rhythms of different frequencies for each life indicator (1, 2). Despite this, the majority of biomedical researches do not take into account the rhythmic organization of living systems (3). To a large extent this is due to such factors as methodological difficulties and the necessity of long-term dynamic studies in both experimental and control groups. Nevertheless, the lack of attention to the recurring changes can significantly reduce the accuracy of the findings of the experimental data analysis. This is especially true for the researches related to the prediction of the behavior of functional systems, determining the success of corrective actions or the effects of various factors.

MATERIALS AND METHODS

The paper analyzes the data of multiple surveys of 173 students during 2 months, including the periods before and after exam sessions: there were carried out 8 measurements with an interval of 7 days and the 9th measurement was conducted after the final exam completion. In order to eliminate the influence of circadian rhythms, the survey was conducted in the same time of day. Such variables as heart rate (HR), the recovery heart rate after the load (RHR), systolic blood pressure (sBP), diastolic blood pressure (dBP), pulse pressure (PP), vital capacity of lungs (VC), and functional vital capacity of lungs (FVC) were measured. Measurements of the cardiovascular system parameters, excluding RHR, were implemented in a sitting position after 10 minutes of rest.

The critical level of significance in the process of testing statistical hypothesis was assumed to be 0.05. Statistical analysis of the results and graphs plotting was produced by means of the software package "Stastistica for Windows, 8.0" and MS Excel 2010.

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RESULTS AND DISCUSSION

Biological rhythms are oscillatory processes that can be described by a generalized hypothetical curve characterizing the rhythmic change of the indicator (Fig. 1). Basing on this type of a hypothetical curve (Fig. 1), it can be assumed that double measurements of any index demonstrate the way of changes of this index in time, its decrease or increase, and this direction depends on the stage of the cycle where the first and the second measurements were produced. If the first measurement of the indicator takes place at the stage which is below the average level by 25%, then the possibility of obtaining higher value of the same indicator at the second measurement is significantly higher. It can be explained by the fact that the curve segment, where the indicator value is low, is substantially shorter than the segment with higher values. Thus, the closer to the minimum value the 1st measurement of the indicator occurs, the relatively larger is the area on which the indicator value is higher at the second measurement compared to the 1st one.

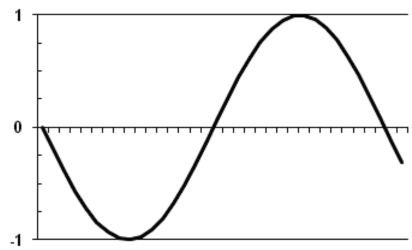

FIGURE 1. Hypothetical aggregate biorhythmic curve

Similarly, there can be considered the case when the first measurement of the index reaches the segment of the curve of 25% higher than the average level. In this instance, the interval at which the index demonstrates higher value at the repeated measurement is significantly smaller than the interval at which, respectively, there is a decline of index value in time.

From the above it follows that, irrespective of the number of simultaneous beats, the values which are lower than the average level can probably manifest the increase in values, while the indicators which are higher compared to the average level can show the reduction over time. The validity of this provision would mean that the direction of changes by the initial index over time could be predicted in group measurements.

In that case, if, to consider the repeated group observations, index dynamics in time actually depends on the segment of the biorhythm curve at which the first measurement takes place, then the analysis of data obtained at investigating the big groups, there should be observed negative correlation between the initial group values of the tested parameters and the value of their changes over time. Therefore, to test this hypothesis, there were calculated correlation coefficients r between the original values of the tested parameters and the magnitude of changes over time – r (X; ΔX).

Multiple measurements of physiological parameters showed the rhythmic changes of their values. This dynamics curves were individual in nature (Fig. 2). At the same time, the calculations showed that for all parameters, regardless of the time interval between two measurements, there were observed significant negative ($r \geq -0{,}5$) correlation coefficients r (X; ΔX). It is exemplified by the correlation coefficients r (X; ΔX) for change with respect to the first measurement (Tab. 1).

TABLE 1. Spearman's rank correlation coefficient (r) between the baseline of the 1st control point and the amount of change in the next 8 cardiorespiratory system measurements ($p < 0{,}001$)

	r (x1;x2-x1)	**r (x1;x3-x1)**	**r (x1;x4-x1)**	**r (x1;x5-x1)**	**r (x1;x6-x1)**	**r (x1;x7-x1)**	**r (x1;x8-x1)**	**r (x1;x9-x1)**
VC	-0,49	-0,51	-0,55	-0,56	-0,76	-0,56	-0,50	-0,50
FVC	-0,71	-0,58	-0,56	-0,54	-0,7	-0,70	-0,64	-0,66
HR	-0,50	-0,49	-0,50	-0,67	-0,54	-0,56	-0,49	-0,56
sBP	-0,51	-0,54	-0,54	-0,56	-0,73	-0,6	-0,56	-0,62
dBP	-0,51	-0,49	-0,53	-0,51	-0,77	-0,60	-0,51	-0,58
PP	-0,50	-0,52	-0,54	-0,54	-0,75	-0,60	-0,54	-0,60
RHR	-0,59	-0,56	-0,56	-0,81	-0,72	-0,73	-0,63	-0,65

The presence of such correlations indicates that the magnitude and direction of the changes in the parameters over time depends on their initial level. To test this hypothesis, there were analysed the frequency and magnitude of the increase and decrease of indicators in different ranges of the original values. Furthermore, at the first stage of the analysis, those control points which mean values did not differ were included.

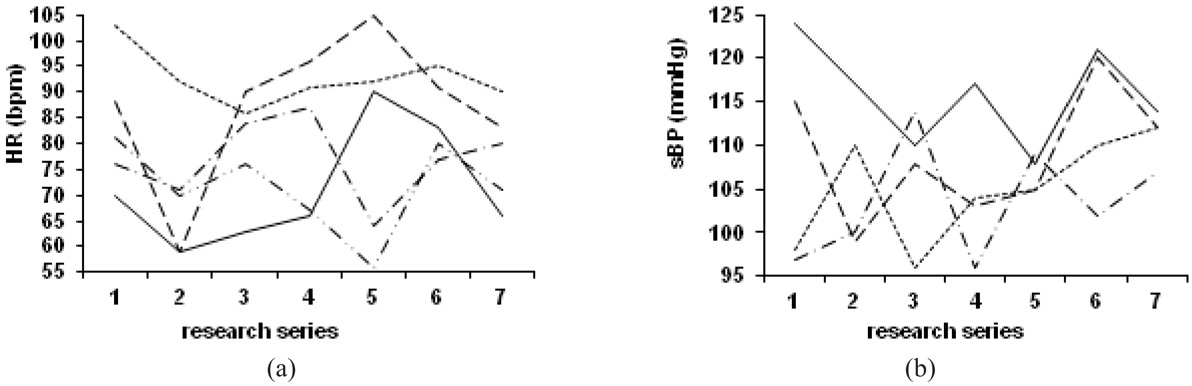

FIGURE 2. Individual sample values and dynamics, a – HR, b – sBP

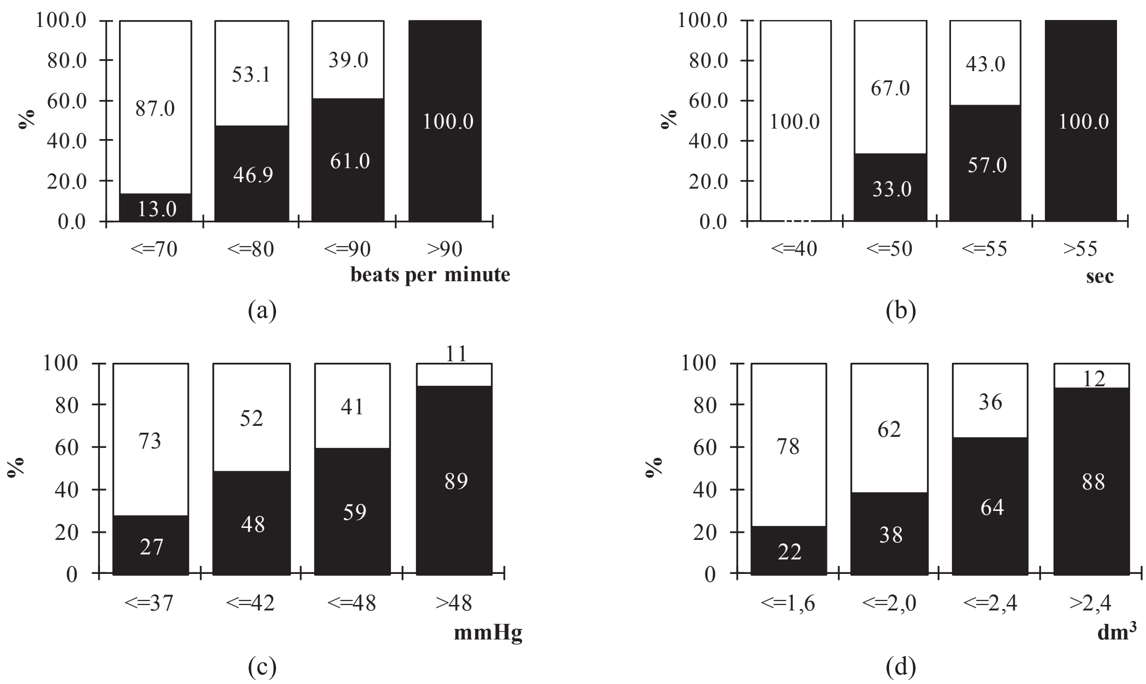

FIGURE 3. The percentage of positive (white bars) and negative (black bars) changes of physiological parameters according to their initial values. Note: a – HR (measurement interval is 7 days); b – RHR (measurement interval is 28 days); c – Pulse Pressure (measurement interval is 42 days.) d – FVC (measurement interval is 49 days.) (the y-axis – ranges of initial values, the x-axis is the proportion of occurrence of the events in%)

To analyze the received data of the tested parameters by initial values, they were divided into four groups, so that differences between the groups were revealed most clearly. The initial assessment of changes direction depending on the initial value indicators confirmed the assumption: lower initial values in a high percentage of cases increased, while higher values decreased (Fig.3). Herewith, the area of the original values, where positive and negative shifts are equiprobable, is located approximately in the middle of the range of the initial values. Subsequent analysis of the indicators changes showed their direct dependence on the initial values. At the extreme values of determined parameters, their deviation in positive or negative to both positive and negative directions were more emphasized and reached 20-60% of their initial value (Fig. 4).

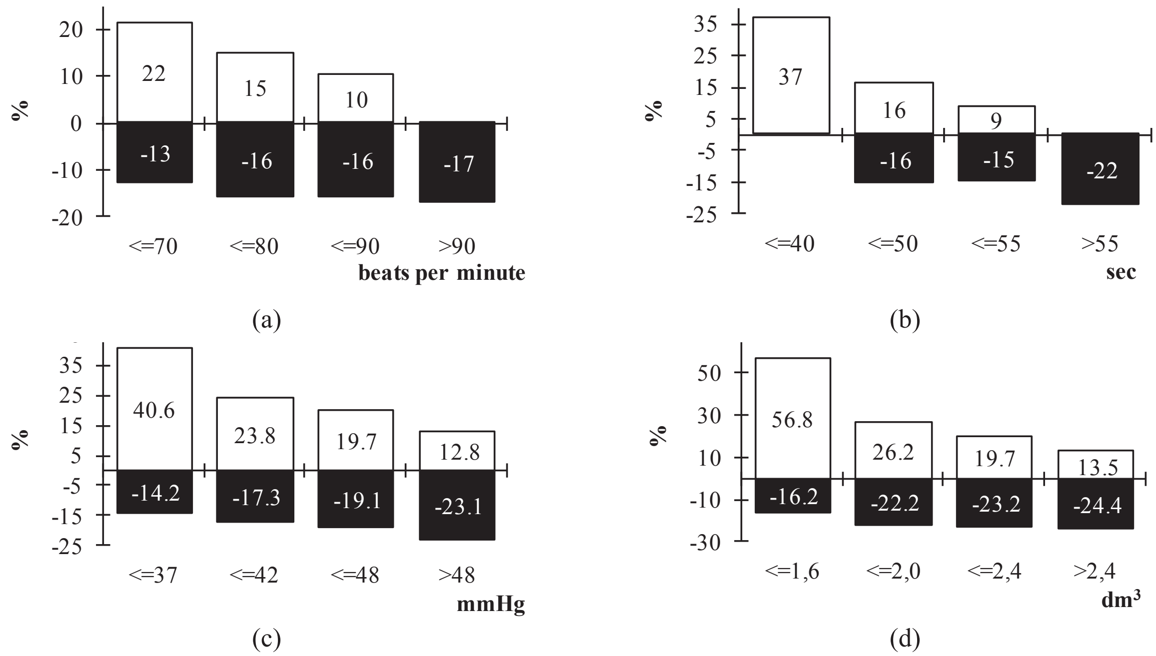

FIGURE 4. The relative magnitudes of the positive (white bars) and negative (black bars) changes in physiological parameters depending on the initial values of the parameters; Note: a – HR (measurement interval is 7 days); b – RHR (measurement interval is 28 days); c – Pulse Pressure (measurement interval is 42 days.) d – FVC (measurement interval is 49 days.) (y-axis - ranges of initial values, x-axis - the relative change in %)

As a result, the probability of the direction and magnitude of change over time can be predicted for each range of the initial values of the investigated physiological parameters. The special interest is presented by the interpretation of the values range in which the direction of the indicators changes is equiprobable. It can be assumed that this segment can be seen as a «dynamic optimum» of the measured physiological parameters which is the most corresponding to the body's needs at a particular time.

A further object of this study was a comparative analysis of the findings obtained by analyzing data with and without initial level considering.

The results of the experimental data interpretations, presenting different results depending on the fact of considering or not the initial level of measured indicators are shown below.

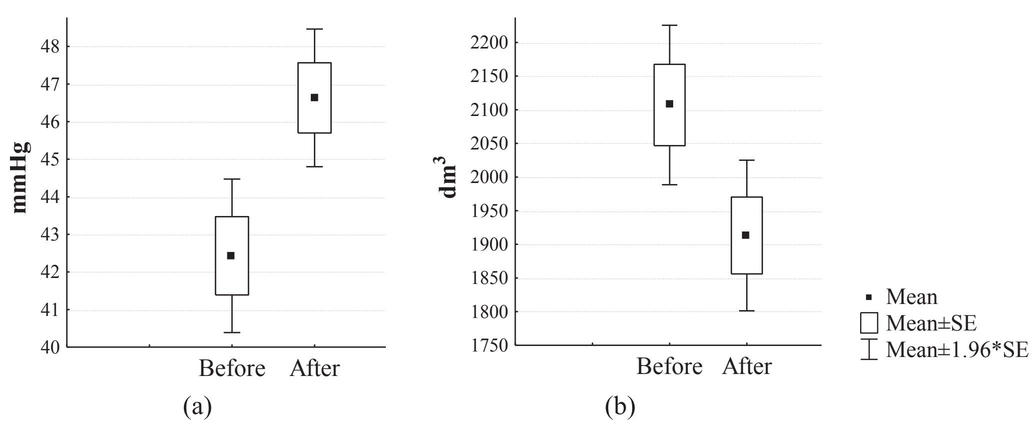

FIGURE 5. Pulse Pressure Level (a) and FVC (b) before and after the examination (SE - Standard error)

As an example, the impact of examinations on Pulse Pressure and FVC changes was analyzed (Fig. 5). It was found that after the session FVC value in the study group became lower (p <0,0003), while the pulse pressure was higher (p <0,001) than before the session.

From these results, it would be possible to conclude that examination stress leads to a reduction in FVC values and to the increase in PP for the students. However, the direction and magnitude of changes in FVC and PP in different initial ranges showed ambiguity of alterations depending on the initial values. As follows from the results obtained, in this case as a whole there kept the tendency of dependence of parameters change on their initial values (Fig. 6, 7)

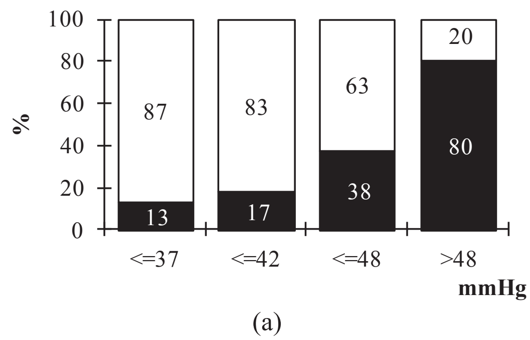

FIGURE 6. Percentage of positive (white bars) and negative (black bars) shifts of physiological parameters according to their initial value. Note: a – Pulse Pressure, b – FVC; (the y-axis – ranges of initial values, the x-axis is the proportion of occurrence of the events in%)

Consequently, analysis of generalized experimental data allowed concluding that stress reduces FVC level, while the analysis which considers the indicators initial values leads to the conclusions, demonstrating not only a decrease, but also an increase in the parameter depending on its initial value. FVC rhythmic changes recording allowed finding out that in a situation of stress, the "optimum dynamic" registration point shifts from the sub-band 2.0-2.4 dm towards the lower values of 2.0-1.6 dm.

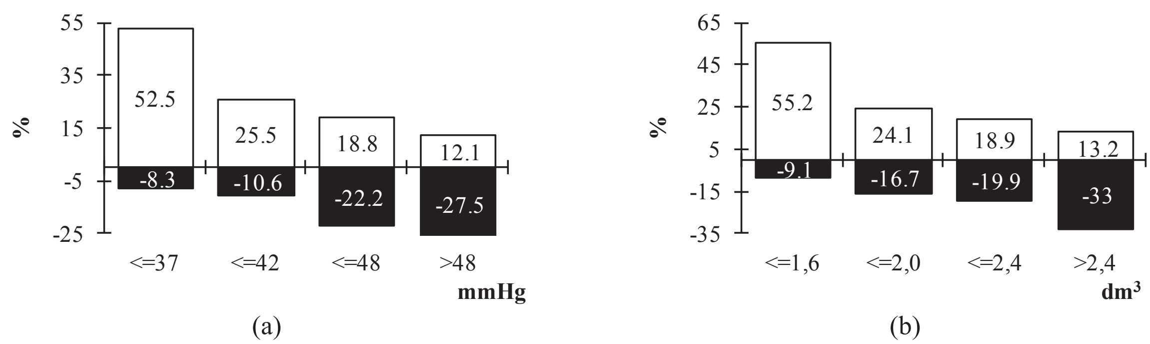

FIGURE 7. The relative magnitudes of the positive (white bars) and negative (black bars) changes in physiological parameters depending on the initial values of the parameters; Note: a – Pulse Pressure; b – FVC (y-axis - ranges of the initial values, x-axis – the value of relative change in %)

Similar to the written above, the definite conclusion regarding the increase of PP under the influence of examinations has also been criticized in the evaluation of individuals with different initial value of this indicator. So, some persons whose PP dynamics differed from the general trend were found in study group.

After the stress the individuals with higher values of PP (> 48 mm Hg) demonstrated the decline in indicator values with the same probability and at the same extent as in ordinary conditions (Fig. 6a). However, after examination stress, the magnitude of changes in the PP values in the original range ≤ 40 mm Hg increased greater than in the control group (Fig. 4c, 7a). The "optimum dynamic" point moved to PP ≤ 49 mm Hg baseline. On this basis, it is more optimal to conclude in respect of PP that stress shifted the point of change of the sign of the most probable PP dynamics to higher values, which in turn led to an increase in PP in the study group.

The obtained results showed the necessity and the possibility of taking into account the rhythmic organization of physiological processes in the analysis of non-chronobiological studies data. It seems that this approach is optimal for the individual diagnostic techniques, for the optimisation of the effectiveness of corrective actions, etc.

In conclusion, while interpreting the findings, the "law of initial values" revealed by J. Wilder in the first half of the last century (4) cannot be ignored. According to this law, the change of any parameter (the difference between the final and the initial values) is as follows: the greater is the initial value, the lower the change is; in other words, initial index increase leads to the reduction of the opportunities of further function stimulation. However, in this study, opposite changes in repeated measurements in both the presence and lack of incentives, is linked not to the "intensity" of functional systems, but to the presence of endogenous rhythms. In addition, the "law of initial values" does not consider the cases of opposite effects, but the present study shows that the baseline indicator estimates the direction and magnitude of its changes with a high probability.

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