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АДАПТАЦИОННЫЕ РЕАКЦИИ ГЕМОДИНАМИЧЕСКИХ СИСТЕМ НА ИСКУССТВЕННО МОДУЛИРОВАННЫЙ СТРЕСС У ЗДОРОВЫХ СУБЪЕКТОВ

© Ю.Н. Смоляков, Б.И. Кузник, С.А. Калашникова, Е.В. Федоренко, Н.А. Нольфин, М.М. Михаханов

ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия

Цель. Изучить влияние искусственного созданного стресса на показатели периферической микроциркуляторной гемодинамики (МЦГ) и вариабельность сердечного ритма у соматически здоровых молодых испытуемых.

Материалы и методы. В исследовании приняло участие 30 человек (из них 16 мужчин). Средний возраст 18,2±1,1 лет. Искусственный стресс создавался по методике Струпа. Оценка характеристик МЦГ производился методом динамического рассеяния света от эритроцитов. Сигнал интегрировался в виде трех гемодинамических индексов: HI (*Hemodynamic Indexes*). Низкочастотный индекс (HI1) определяется медленным межслоевым взаимодействием, высокочастотная область (HI3) характеризует быстрые процессы сдвига слоев. HI2 занимает промежуточное положение (прекапиллярный и капиллярный кровоток). Вариабельность выделенных из пульсовой компоненты кардиоинтервалов оценивалась методом вариационной пульсометрии (*Heart Rate Variability*, HRV).

Результаты. В ходе проведенного исследования наблюдалось повышение частоты сердечных сокращений (ЧСС) в стадию тестирования, что подтверждает высокую степень стрессовой нагрузки. В гемодинамике отмечалось перераспределение кровотока в сторону медленных скоростей сдвига (пристеночный ток крови). После прекращения стрессовой нагрузки показатели гемодинамики снижались, возвращаясь к прежним значениям. Индикаторы, характеризующие вариабельности ритма – LF (симпатический компонент), HF (вагусная активность), CVI (нелинейный парасимпатический индекс) проявляли тенденцию к росту, при этом соотношение LF/HF оставалось неизменным.

Заключение. В результате проведенного исследования удалось сформулировать многофакторную картину изменения показателей микроциркуляции и вегетативной регуляции сердечного ритма, специфичных для адаптивных реакций на индуцированный стресс. Количественные критерии полученных сдвигов могут быть интегрированы в индексы стресса и использованы в клинике. Вследствие портативности mDLS датчик, дополненный специфическими критериями оценки, может быть использован для мониторинга адаптивных реакций, вызванных стрессовыми ситуациями и принятия ранних диагностических и прогностических решений в клинике и для самоконтроля пациента.

Ключевые слова: *стресс; гемодинамика; вариабельность сердечного ритма; адаптация; микроциркуляция.*

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ADAPTATION REACTIONS OF HEMODYNAMIC SYSTEMS ON ARTIFICIALLY MODULATED STRESS IN HEALTHY INDIVIDUALS

Yu.N. Smolyakov, B.I. Kuznik, S.A. Kalashnikova, E.V. Fedorenko, N.A. Nolfin, M.M. Mikhakhanov

Chita State Medical Academy, Chita, Russia

Aim. To study the influence of artificially created stress on hemodynamic parameters of peripheral microcirculation and variability of the heart rhythm in somatically healthy young individuals.

Materials and Methods. In the study 30 individuals were involved (of them 16 men) with the mean age 18.2±1.1 years. An artificial stress was created using Stroop method. Assessment of characteristics of hemodynamics of microcirculation (HM) was performed by the method of dynamic scattering of light from erythrocytes. The signal was integrated in the form of three hemodynamic indexes: HI (*Hemodynamic Indexes*). Low frequency index (HI1) was determined by a slow interlayer interaction, high frequency area (HI3) characterized fast shearing of layers. HI2 took intermediate position (precapillary and capillary blood flow). Variability of cardiointervals isolated from pulse component, was assessed by method of variation pulsometry (*Heart Rate Variability*, HRV).

Results. In the course of study, increase in the heart rate (HR) in the stage of testing was observed that confirms a high extent of stress load. In hemodynamics, redistribution of blood flow was noted toward slow shear velocities (near-wall blood flow). After cessation of stress load, hemodynamic parameters declined and returned to previous values. Parameters characterizing variability of rhythm – LF (sympathetic component), HF (vagal activity), CVI (non-linear parasympathetic index) showed a tendency to growth; here, LF/HF ratio did not change.

Conclusion. In result of the carried out study it was possible to formulate a multifactor picture of variation of parameters of microcirculation and of autonomic regulation of cardiac rhythm specific of reactions of adaptation to induced stress. The quantitative criteria of the obtained shears may be integrated into stress indexes to be used in clinical practice. A portable mDLS sensor may be supplemented with specific assessment criteria and used for monitoring of adaptive reactions induced by stressful situations, and for taking early diagnostic and prognostic decisions in the clinical practice, and for self-control of a patient.

Keywords: *stress; hemodynamics; heart rate variability; adaptation; microcirculation.*

The concept of stress includes a complex of non-specific adaptation changes in an organism in response to external and internal factors (stressors). The most prominent response of an individual to stress is considered to be reactions on the part of the nervous system and, as a consequence, of the cardiovascular system; complex measurement of these reactions becomes one of criteria for assessment of adaptation status of an organism. Mechanism of primary (early) reactions to stress studied on healthy individuals, provides the basis for its comparison with similar responses in patients with different pathologies, and as a consequence, the possibility for taking early diagnostic and prognostic decisions.

Aim – to study the influence of stimulated psychoemotional stress on the hemody-

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namic parameters of the peripheral microcirculation in somatically healthy young individuals.

Materials and Methods

In the experiment 30 somatically healthy individuals (16 men and 14 women) participated. The mean age was 18.2±1.1 years. The study was conducted in compliance with the ethical principles of World Medical Association Declaration of Helsinki (1964, 2013); National Standard of the RF "Good Clinical Practice" (GOST P 52379-2005). All individuals included into the study, gave voluntary informed consent. The protocol of study was approved by Local ethical committee of Chita State Medical Academy (Protocol № 86 of 01.11.2017).

Experiment was conducted in three stages each lasting 5 minutes:

T1 – resting state,

T2 – modulated stress,

T3 – recovery of resting state.

Each stage was conducted with measurement of parameters of hemodynamics and with assessment of heart rate variability. Stress was created by a color test based on Stroop's effect. This method was designed to assess establishment of association links between cortical zones responsible for perception of color and of letter form. A mismatch between the color and the meaning of the words leads to conflict of perception and, as a result, to stress.

A sensor of dynamic scattering of light mDLS (miniaturized Dynamic Light Scattering, Elfi-Tech, Rehovot, Israel) senses photons reflected from erythrocytes moving in the neighboring blood flow laminae (shear velocity, or lateral velocity gradient). The sensor was positioned on the index finger on the palm side of the hand. The signal was integrated in the form of three hemodynamic indexes HI. Fast Fourier transform (FFT) was used for spectral decomposition of the signal to frequency components associated with hemodynamic sources of different shear velocity of laminae. Low-frequency (1-300 Hz) index (HI1) was determined by slow interlaminar coupling, high-frequency (3000-24000 Hz) region (HI3) characterized fast interlaminar shear processes. HI2 takes intermediate position (precapillary and capillary blood flow). For assessment of redistribution tendency of the blood flow between fast and slow processes, HI1/HI3 ratio was introduced.

Variability of cardiointervals isolated from pulse component was assessed by pulsometry method (*Heart Rate Variability,* HRV). The following parameters were used: SDNN – Standard Deviation of NN Intervals – standard deviation of all RR intervals (reflects all long-term components and circadian rhythms responsible for variability); LF – power in the low frequency range (0.04-0.15 Hz) defined by the activity of sympathetic division and characterizing delay in baroreflex realization; HF – power in the high frequency range (0.16-0.5 Hz) associated with respiratory movements and mostly provided by vagal activity; LF/HF – ratio of powers indicating the general sympathovagal balance; CVI – Cardiac Vagal Index, non-linear parasympathetic index; CSI – Cardiac Sympathetic Index, non-linear sympathetic index.

Statistical analysis and visualization were implemented in R language (http://cran.r-project.org), 3.4.4 version. Reliability of pair differences of all parameters between stages (T1, T2, T3) was assessed by Wilcoxon test. Hommel correction was used for multiple comparison. Decision on statistical significance of hypotheses was taken at the level of $p<0.05$. Quantitative presentation of parameters in the tables was implemented in M±SD format (mean value + standard deviation).

Results and Discussion

During the test all participants exhibited a significant increase in pulse, and its complete recovery to the initial values (T3) (Figure 1).

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Hemodynamic indexes also exhibited significant changes in response to stress stimulation (Table 1). In the second period (T2) there was a noticeable increase in HI1 index (associated with slow shear velocities and near-wall processes in vessels). In the third period (T3) the index returned to the initial values (Figure 2). We think that increase in HI1 may be attributed to both activation of near-wall processes and dilatation of vessels (increase in the diameter of vessel reduces shear velocity).

From this a significant increase in HI1/HI3 ratio follows characterizing the balance of distribution of interlaminar velocities. In stage T3 a tendency emerged for this index to return to the initial values, but this process lacks statistical confirmation.

Simultaneously, increase in parameters of the total variability was observed (Table 2) characterizing the general tone of the autonomic nervous system. After the test both the high-frequency component HF associated with breathing and provided by the vagal activity, and low-frequency component LF characterizing sympathetic activity and reflecting delay in the baroreflex, considerably increased.

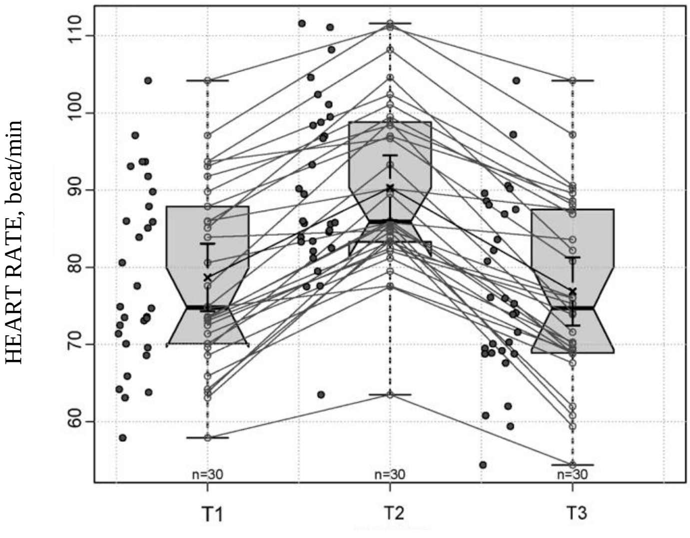

Fig. 1. Dynamics of heart rate
Note: additional lines connecting pairs of values are introduces

Table 1

Parameters of Microcirculation Hemodynamics in Response to Stress Stimulation in Somatically Healthy Young Individuals

Parameter	T1	T2	T3	p1	p2	p3
HR, beat/minute	78.7±11.7	90.3±11.2	76.9±11.9	<0.0001	0.013	<0.0001
HI1	158.0±26.4	172.0±25.4	163.0±22.5	0.007	0.070	0.015
HI2	460±166	480±154	460±153	0.61	0.98	0.68
HI3	255±109	246±103	243±98.7	0.64	0.79	0.79
HI1/HI3	0.676±0.270	0.773±0.264	0.752±0.322	0.011	0.096	0.67

Note: Hemodynamic indexes are dimensionless values. HR – heart rate. Statistical significance of comparison of groups by paired Wilcoxon test: p1 – T1 and T2, p2 – T1 and T3, p3 – T2 and T3

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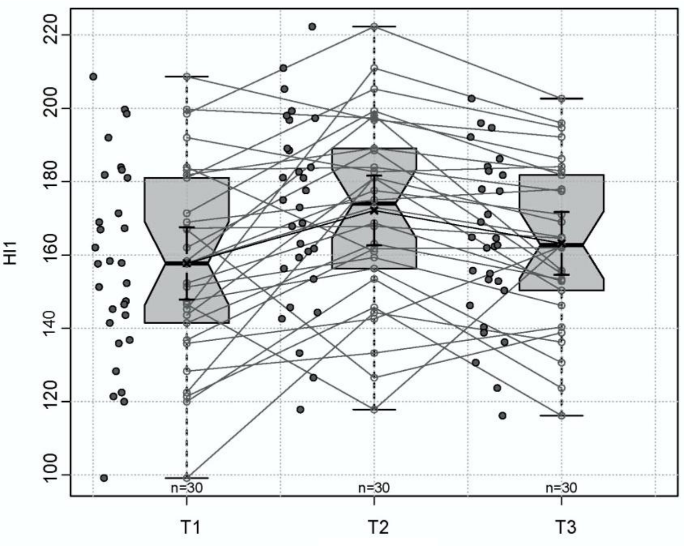

Fig. 2. Dynamics of HI1 hemodynamic index
Note: additional lines connecting pairs of values are introduces

It is known that activation of parasympathetic nervous system in stress reaction is a mechanism of protection against side effects. In our research no significant change in the balance of frequency distribution (LF/HF) was observed. Most significant growth was observed in the non-linear parasympathetic index CVI (Figure 3, Table 2) while non-linear sympathetic index (CSI) remained unchanged (Table 2).

Thus, on the one hand, the results of research once again confirm the role of Stroop effect in modulation of stress condition described earlier and manifested in our work by increase in the heart rate with return to the initial values after cancellation of stimulus.

Table 2

Changes of Parameters of Heart Rhythm Variability and of Condition of Autonomic Nervous System

Parameter	T1	T2	T3	p1	p2	p3
SDNN, msec	68.8±22.5	87.2±26.4	71.5±24.2	0.003	0.45	0.018
LF, msec ^{2}	1090 ± 628	1390 ± 681	1080±630	0.028	0.94	0.070
HF, msec ^{2}	732±458	1130±713	740±460	0.021	0.93	0.045
LF/HF	1.62±0.89	1.54±0.77	1.49±0.76	0.96	0.96	0.96
CSI	1.73±0.46	1.79±0.53	1.75±0.53	0.84	0.84	0.84
CVI	4.76±0.31	4.96±0.31	4.8±0.30	0.008	0.47	0.039

Note: statistical significance of comparison of groups by paired Wilcoxon test: p1 – T1 and T2, p2 – T1 and T3, p3 – T2 and T3

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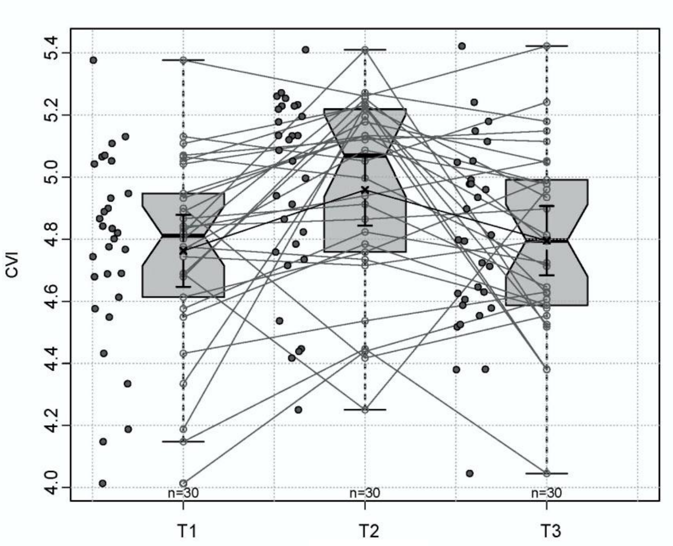

Fig. 3. Dynamics of non-linear parasympathetic index CVI
Note: additional lines connecting pairs of values are introduces

On the other hand, parameters of the interlaminar flow dynamics obtained by method of laser speckle-interferometry, demonstrated a reliable reaction to the stimulated stress in the slow HI1 (near-wall) component, and incomplete recovery in the early period after cancellation of the stimulus. Autonomic regulation of hemodynamics was manifested by increase in the activity of the parasympathetic influence.

Unique character of the research consists in complex assessment of the reaction to stress both in terms of distribution of the interlaminar hemodynamic processes in the microcirculation using non-invasive method of laser speckles, and in terms of the autonomic regulation by analysis of heart rate variability isolated from the pulse component of speckle-signal.

Conclusion

The conducted research permitted to obtain a multifactor picture of changes in the microcirculation parameters and of the autonomic regulation of the heart rhythm specific to adaptive reactions to induced stress.

Hemodynamics is characterized by increase in the cross section (diameter of vessels) of the microcirculatory bed, and, probably, by activation of parietal adhesion processes. Autonomic nervous regulation is characterized by preservation of the balance with simultaneous activation of sympathetic and parasympathetic divisions.

Quantitative criteria of the obtained shifts may be integrated to stress indexes and used in clinical practice. A portable mDLS sensor may be supplemented with specific assessment criteria and used for monitoring of adaptive reactions induced by stressful situations, and for taking early diagnostic and prognostic decisions in the clinical practice, and for self-control of a patient.

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Дополнительная информация [Additional Info]

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Информация об авторах [**Authors Info**]

***Смоляков Юрий Николаевич** – к.м.н., доцент, зав. кафедрой медицинской физики и информатики, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Yuri N. Smolyakov** – MD, PhD, Associate Professor, Head of the Department of Medical Physics and Informatics, Chita State Medical Academy, Chita, Russia.]
SPIN: 7440-6632, ORCID ID: 0000-0001-7920-7642, Researcher ID: R-5740-2017. E-mail: smolyakov@rambler.ru

Кузник Борис Ильич – д.м.н., проф., профессор кафедры нормальной физиологии, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Boris I. Kuznik –** MD, PhD, Professor, Professor of the Department of Normal Physiology, Chita State Medical Academy, Chita, Russia.]
SPIN: 5807-7229, ORCID ID: 0000-0002-2502-9411, Researcher ID: D-2743-2018.

Калашникова Светлана Анатольевна – старший преподаватель, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Svetlana A. Kalashnikova –** Senior Lecturer, Chita State Medical Academy, Chita, Russia.]
SPIN: 4030-5496, ORCID ID: 0000-0001-8360-4624.

Федоренко Екатерина Викторовна – студент, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Ekaterina V. Fedorenko –** Student, Chita State Medical Academy, Chita, Russia.]
SPIN: 4711-2143, ORCID ID: 0000-0003-0600-7708.

Нольфин Николай Алексеевич – студент, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Nikolay A. Nolfin –** Student, Chita State Medical Academy, Chita, Russia.]
SPIN: 5376-8731, ODCID ID: 0000-0003-2570-4293.

Михаханов Манхар Михайлович – студент, ФГБОУ ВО Читинская государственная медицинская академия Минздрава России, Чита, Россия. [**Manhar M. Mikhakhanov –** Student, Chita State Medical Academy, Chita, Russia.]
SPIN: 6393-8086, ORCID ID: 0000-0002-0620-2047.

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