

Hypomagnetic Exposure and Hemodynamic Response: Macro - To Microscale

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Abstract

This article presents the results of a study devoted to investigating the effects of hypomagnetic conditions (HMC) on macro- and microhemodynamics in humans under simulated prolonged isolation. Microcirculation parameters and autonomic regulation were assessed in a group of 6 healthy volunteers (2 males and 4 females) within the SIRIUS project, using laser Doppler flowmetry and heart rate variability analysis. HMC were simulated by reducing the geomagnetic field by a factor of 350 with specialized system “Arfa”. Under HMC, a decrease in parasympathetic activity (reduced pNN50 and MxDMn values), an increase in sympathetic activity, and elevated heart rate and blood pressure were observed. At the level of skin microcirculation an increase in the amplitude of endothelial and neurogenic oscillations was noted, alongside a decrease in the amplitude of venular and pulse oscillations. It was found that HMC trigger activation of the sympathoadrenal system and alter microcirculation regulatory mechanisms. The obtained data suggest a potential increase in oxidative stress under reduced geomagnetic field conditions, which may pose health risks during long-duration spaceflights.

Introduction

An important evolutionary and ecological aspect of the existence of all living organisms on Earth is the geomagnetic field (GMF). It forms a shield protecting ecosystems from excessive influence of the solar wind (Erdmann et al. 2021; Pan et al. 2023). In addition, animals included in various taxons (birds, fish and insects) orient themselves in space mainly by its fluctuations (Narayanan 2023).

Geomagnetic fluctuations affect both animals (Luo et al. 2020; Hu et al. 2020) and important physiological processes in the human body, affecting the functioning of both individual organs and physiological systems (Hart 2023). Functional changes caused by the reduction of GMF – hypomagnetic conditions (HMC) – are observed in the cardiovascular (CVS), central nervous (CNS), immune, and reproductive systems (Pishchalnikov et al. 2019). These changes are observed when the strength of GMP is reduced by less than 10 times (Binhi and Prato 2017; Pishchalnikov et al. 2019).

The CVS, along with the CNS, is, perhaps, the most sensitive system in the body, and HMC s can cause significant changes (Popova and Rusanov 2023; Popova et al. 2024). It has been experimentally established that a decrease in GMF s can lead to changes in heart rate variability (HRV), blood pressure, and heart rate (HR), which can result in a decrease in the efficiency of hemodynamics and overall body function (Vasin et al. 2019).

In the human circulatory system, there are two distinct levels: macrohemodynamic and microhemodynamic. As the final link, the microcirculatory bloodstream (MCB) of the CVS participates in the hemodynamic support of metabolic processes. This is due to the structural and functional organization of the smooth muscle and endothelial cells of the microcirculatory module (Fedorovich 2010).

HMC affects not only central but also peripheral hemodynamics, including capillary blood flow (Gurfinkel et al. 2014; Gurfinkel et al. 2016). The interaction of the magnetic field with ion channels in cell membranes modifies the processes of regulation of vascular permeability and smooth muscle tone (Zhang et al. 2021). In this aspect, the study of the influence of HMC on the MCB and indicators of cardiac rhythm regulation is of significant interest.

The study of macro- and microhemodynamics is one of the critical areas in modern space physiology, as the force of the HMC decreases as the distance from the Earth's surface increases, and the members of space crews will be in an evolutionally atypical HMC (Hart 2023).

It should be noted that the study of this factor of space flight (SF) in human experiments is difficult due to ethical considerations. However, such studies are necessary, and their implementation must comply with bioethical requirements.

Materials and methods

The presented study was part of a comprehensive study of the effect of simulated HMC on the physiological systems of the human body within the framework of the SIRIUS (Scientific International Research in Unique terrestrial Station) project (<http://sirius.imbp.ru/>). It involved 6 healthy volunteers (2 males and 4 females) who received approval from the medical and expert commission of the State Research Center of the Russian Federation – IBMP of the Russian Academy of Sciences. The volunteers ranged in age from 25 to 37 years. The body mass index of males was $22.13 \pm 0.57 \text{ kg/m}^2$, and that of females was $20.25 \pm 1.4 \text{ kg/m}^2$. The studies were approved by the Bioethics Commission of the State Research Center of the Russian Federation – IBMP of the Russian Academy of Sciences (Protocol No. 643 dated July 7, 2023).

The volunteers were placed in an isolated ground-based experimental complex (GBEC) for 366 days. 1. This isolation experiment was the IV-th stage of the international SIRIUS project and simulated the main elements of a Lunar expedition: flight to the Lunar orbital station (days 1–4), stay at the Lunar orbital station (days 5–361), 5 Lunar surface landings by 4 crew members to perform surface operations (days 62–66, 125–129, 188–192, 251–255, 314–318), and return to Earth (days 362–366).

The GBEC is an isolated hermetic facility consisting of interconnected experimental modules with a volume of 50 m^3 , 100 m^3 , 150 m^3 and 250 m^3 with autonomous life support systems, as well as there is a lunar module for simulating extravehicular activities. The GBEC maintains a habitat with preset parameters and simulates key factors of SF – with the exception of weightlessness and radiation exposure, serving as a testing ground for technologies for missions beyond low Earth orbit (Agaptseva et al. 2024).

The complex is also equipped with first aid facilities and medical monitoring equipment, which ensured the safety of participants and helped optimize medical support programs for manned spacecraft and small groups in extreme conditions (Fedyay et al. 2023).

Prolonged human exposure to a confined environment with controlled microclimate conditions, nutrition, and regulated physical activity has a significant impact on all physiological systems of the human body, and in combination with simulated HMC, it allowed us to provoke specific changes in the volunteers' bodies and assess the effects of prolonged isolation and reduced GMF.

The analysis of the functional state of the autonomic regulation of HRV and MCB was carried out before and at the end of the isolation experiment.

The simulation of HMC was carried out using the GMF compensation method using the «Arfa» magnetic field simulation system (Kukanov et al. 2023) at the following times: 2–4 days before the volunteers were placed in the hermetic object and at the final stage of isolation (346–350 days of stay in the hermetic object). In both experimental sessions, the intensity of GMF was reduced by a factor of 350.

Modeling of HMC was performed in a limited volume by compensating the natural GMF of the Earth using a system of coaxial current-carrying windings (Helmholtz rings), whose configuration ensures that the total vector of the generated magnetic field is oriented in the opposite direction to the GMF of the Earth. By optimizing the diameter of the Helmholtz rings and their spatial arrangement within the experimental chamber, a uniform magnetic field with a uniform distribution in magnitude and direction is created. The developed system compensates for variations in the magnetic field along the vertical component, which is oriented parallel to the largest linear size of the exposure unit, allowing the magnetic field induction to be achieved in the working volume of the movable box of the exposure unit to be as low as zero and negative (with the direction of the GMF vector being inverted relative to the natural Earth's field. The magnetic field level in the “Arfa” system was monitored using a three-component magnetic sensor FL3-100 (Stefan Mayer Instruments, Germany) (Kovrov et al. 2024). The intensity of the magnetic field in the simulation of HMC was 143 ± 32 nT. The research was conducted in the lunar module during the isolation period on 346–350 mission days (2 persons per day). The frequency of the decrease in the geomagnetic field was determined as the ratio of the induction modulus of the local geomagnetic field to the decrease in the induction magnitude in the «Arfa» installation. The geomagnetic field in all modules during isolation except “Arfa” exposure sessions was not experimentally modified.

The «Arfa» magnetic field simulation system and the GBEC are shown in Fig. 1.

The study cycle is presented in Fig. 2. In the future, studies before isolation will be referred to as HMC 1, and at the end of the isolation experiment, HMC 2.

Two 4-hour exposures to HMCs were performed for each volunteer. In order to compare with the results of the exposure, background studies were performed before placing the examinees in the installation; in the figures and in the tables they are designated as “Before” (before the beginning of the volunteers' stay in the hermetic object) and “Isolation” (background studies at the final stage of isolation).

Electrocardiogram (ECG) registration with HRV analysis was performed with the Varicard 2.8 device (RAMENA LLC, Ryazan, Russia) in the second standard lead.

Blood pressure was registered by the oscillometric method using the Medisana BU 550 tonometer (Medisana GmbH, Berlin, Germany).

Skin microhemodynamics were recorded using a portable laser analyzer "LAZMA-PF" (SPE "LAZMA" Ltd, Moscow, Russia) by the method of laser Doppler flowmetry (LDF). The sensor was installed in the central part of the forehead in the area of glabella.

Physiological signals were recorded simultaneously 10 minutes before the «Arfa» was turned on, and then for 10 minutes before it was turned off.

The ECG signal was processed and HRV analysis was performed using the ISKIM-6 software (Ramena LLC, Ryazan, Russia). The obtained signal was edited using visual inspection and manual correction of individual RR intervals with classification of QRS complexes. Abnormal complexes that were not caused by sinoatrial (SA) node depolarization were excluded from the recording.

"Lazma" software (SPE "LAZMA" Ltd, Moscow, Russia) was used to calculate the MCB parameters.

The analyzed indicators of HRV include: $MxDMn$ (ms) – the difference between the maximum and minimum values of the RR interval; $pNN50(\%)$ – the number of pairs of cardiac intervals with a difference of more than 50 ms in relation to the total number of cardiac intervals; HF (ms^2) – the power of high-frequency oscillations, which represents the relative level of activity of the parasympathetic regulation system; LF (ms^2) – the power of low-frequency oscillations, which represents the relative level of activity of the sympathetic regulation system.

The analyzed indicators of the MCB are: A_E – amplitude of endothelial oscillations; A_N – amplitude of neurogenic oscillations; A_R – amplitude of venular oscillations; A_C – amplitude of pulse oscillations.

Statistical processing of the obtained data was carried out using GraphPAD Prism 9 software (GraphPad Software, USA) and STATISTICA 13.0 (IBM; USA). Using the Shapiro-Wilk test, the samples were evaluated for compliance with the normal distribution. However, due to the fact that they did not meet the conditions of normality, the nonparametric paired T-test of Wilcoxon for dependent samples was used for statistical analysis. Differences were considered statistically significant at a value of $p < 0.05$. The data in the tables are presented as the median (Me), lower (LQ), and upper (UQ) quartiles in the form of Me (LQ; UQ), and in the graphs as the median and interquartile range.

Results

The main parameters characterizing the autonomic modulatory influences on the CVS changed in the HMC as follows. The indicators $MxDMn$ (ms), $pNN50(\%)$, which reflect the processes of autonomic regulation and the state of the vagosympathetic balance, determined by the parasympathetic modulatory influences on the SA-node, decreased when in the HMC both before and after the stay in the annual isolation (Fig. 3). In addition, an increase in sympathetic modulatory influences (LF , ms^2) was

observed in the HMC. This coincided with a slight increase in HR and blood pressure (systolic (SBP) and diastolic (DBP)) (Table 1).

Table 1 Central hemodynamics in HMC and previous background studies (Me (LQ; UQ))				
HR	Before	HMC 1	Isolation	HMC 2
(bpm)	56,83 (51,60;62,92)	71,25 (66,66;74,70)*	52,11 (50,38;61,17)	69,12 (68,69;69,80)*
SBP	101	109	94	118
(mmHg)	(96;107)	(107;111)	(86;100)	(116;123)*
DBP	64	69	59	77
(mmHg)	(56;73)	(67;72)	(55;62)	(68;84)
Note: *significant difference from background studies, p < 0.05				

Analysis of experimental data reflecting MCR revealed changes in the amplitude of endothelial (A_E), neurogenic (A_N), venular (A_R), and pulse oscillations (A_C) (Fig. 4).

Endothelial and neurogenic oscillations are active factors in the regulation of microvessels and manifest as fluctuations in blood flow in low-frequency ranges (LF, VLF). The lowest-frequency oscillations are associated with the functional activity of the endothelium – endothelial oscillations (range – 0.0095–0.021 Hz). Neurogenic oscillations are associated with the impulse activity of sympathetic nerve fibers that innervate the microcirculatory module and are in the range of 0.021–0.052 Hz. In turn, venular and pulse oscillations are passive factors in the regulation of microvessels, since they are formed outside the MCB. They are located in the high-frequency ranges (HF, CF). Venular oscillations (range – 0.145–0.6 Hz) are associated with the respiratory wave, and pulse oscillations (range – 0.6–2 Hz) are associated with the pulse wave. It has been observed that in HMC, there is an increase in the amplitude of endothelial and neurogenic oscillations, as well as a decrease in the amplitude of venular and pulse oscillations. It is worth noting that in the study, these indicators remained stable in the forehead area during the final stage of isolation (Pashkova et al. 2026).

Discussion

Since the study presented by us is one of the few ones in which the experimental influence of HMCs on the human CVS is modeled not in isolation, but in a whole body, with the participation of a small number of volunteers, it undoubtedly has a significant number of limitations. However, the results obtained by us allow us to formulate some assumptions explaining the results obtained.

As noted above, HMC led to a decrease in the pNN50(%) parameter, which is sensitive to high-frequency, respiratory fluctuations in heart rate and therefore reflects the activity of the autonomous regulatory loop

and the tone of the autonomic nervous system (Baevsky et al. 2021). On the MCB side, blood flow oscillations that are synchronized with breathing propagate into the microvessels through the blood outflow pathways, are recorded in the venules, and are referred to as venular (A_R) oscillations (Krupatkin 2014). From this perspective, we assumed that we should expect unidirectional changes in the described indicators, which is what we found. Moreover, an increase in the amplitude of venular oscillations indicates an increase in microcirculatory pressure and, as a result, a slight increase in venous outflow, which may be part of a compensatory mechanism to maintain perfusion pressure (Korneeva et al. 2024), which in turn ensures the flow of blood through the vessels. This mechanism may be related to the outflow of blood into larger vessels.

Under the conditions of HMC, the autonomic regulation system, which controls the parameters of HRV, reacted by reducing the level of parasympathetic influences on the SA-node in all volunteers. From the perspective of microhemodynamics, HMC led to the activation of neurogenic oscillations, which was expressed by the dominance of microvascular tone regulation (reflected in the spectrum power graph), and we believe that this fact indicates the predominance of the ergotropic direction of forehead skin MCB regulation (Cogliati et al. 2000).

HMC can enhance the effects of oxidative stress. This is evidenced by the results of a study (Shchegolev et al. 2022), which showed that red blood cells exposed to a weakened magnetic field produced more reactive oxygen species than red blood cells exposed to a normal magnetic field. It is known that oxidative stress is associated with the overproduction of reactive oxygen species (ROS) and can lead to changes in endothelial cell homeostasis (Vlasova et al. 2023). Additionally, it has been shown that magnetic fields can induce the production of ROS (Zhang and Tian 2020). As is known, oxygen transport is actively regulated at the microcirculatory level, both by diffusion in capillaries and by dilatation of arterioles. This function is realized through structural and metabolic interactions between neurons, endothelial cells, astrocytes, and pericytes, the building blocks of the neurovascular unit (Erdener et al. 2019). It is logical that the likely increase in ROS contributed to the activation of endothelial cells, which in turn influenced the production of NO, accompanied by an increase in the amplitude of endothelial oscillations.

In addition, an increase in the amplitude of neurogenic oscillations was observed from the side of the active mechanisms of regulation of microvascular tone. This indicates a decrease in neurogenic sympathetic tone. In turn, for areas rich in arteriovenular anastomoses (which include the skin of the forehead), such dynamics may indicate an increase in the proportion of bypass blood flow. Arteriovenular anastomoses accelerate the redistribution of blood, which, together with an increase in the amplitude of endothelial oscillations, may indicate the activation of metabolic processes.

Pulse oscillations in the microvasculature occur due to the propagation of a pulse wave. This wave represents the spread of increased pressure from the aorta to the arteries and smaller vessels. It is caused by the left ventricle ejecting blood into the vascular system during systole (contraction of the heart muscle). When the pulse wave passes through the arterial part of the microvasculature, it briefly

dilates a section of the vascular wall. This dilation can be detected as a pulse wave. The first peak on the pulse wave graph is formed by the direct (systolic) wave, which occurs when blood is ejected from the heart. The second peak is formed by the reflected wave. This wave occurs when the volume of blood that moves through the aorta and major arteries towards the lower extremities is partially reflected and sent back to the ascending aorta. It is believed that the intensity of this reflection depends on the tone of the small muscular arteries, where the main processes of wave reflection occur. In addition, since the pulse wave can be associated with HR (Tan et al. 2016; Bikia et al. 2020), an increase in this parameter may indicate an increase in the intensity of the pulse wave, which leads to a decrease in the amplitude of pulse oscillations at the microcirculatory level, as an increase in the intensity of the pulse wave causes an increase in vascular tone. These changes indicate a decrease in the flow of arterial blood to the capillaries, which is likely due to the activation of the sympathoadrenal system, as evidenced by the observed increase in BP.

The proposed mechanism of response to HMCs in terms of heart rate regulation and microcirculation is presented in Fig. 5.

Conclusion

Thus, it can be assumed that in the conditions of HMC, there is probably a modification of the mechanisms of regulation of the CVS - in particular, the activation of the sympathoadrenal system, as well as the dominance of the neurogenic circuit of regulation of microvascular tone. In addition, it is worth noting that HMC can enhance the effects of oxidative stress, which also represents a potential risk in the case of a significant decrease in GMF.

Declarations

Compliance with ethical standards.

All studies were conducted in accordance with the principles of biomedical ethics outlined in the 1964 Helsinki Declaration and its subsequent amendments. They were also approved by the Biomedical Ethics Committee of the Institute of Biomedical Problems of the Russian Academy of Sciences (Moscow), Protocol No. 643 dated July 7, 2023. Each participant provided voluntary written informed consent after receiving explanations about the potential risks and benefits, as well as the nature of the upcoming study.

Clinical Trial

Number Not applicable.

Consent to Publish

All study participants provided their voluntary written informed consent, which they signed after potential risks and benefits, as well as the nature of the upcoming study, were explained to them.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Competing Interest

The authors declare no competing interests.

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Author Contribution

OO, RV conceived and designed research; PO and PD collected data; PO, PD analyzed data; PO, PD, RV interpreted the results; RV, PO, PD, PJ drafted manuscript. All authors approved the final manuscript.

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to the organizers of the SIRIUS project; all volunteers participated in this study; SIRIUS-23 crew members for conducting techniques in isolation.

Data Availability

No datasets were generated or analysed during the current study.

Code Availability

The underlying code for this study is not publicly available for proprietary reasons.

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Figures

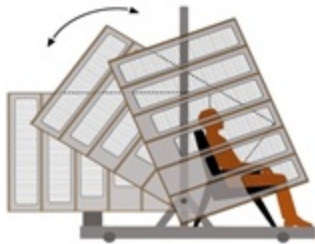
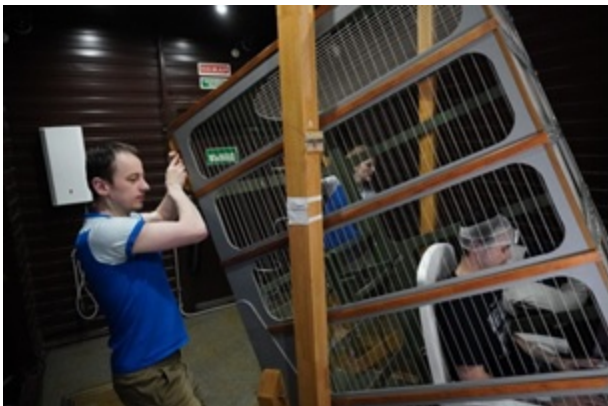


Figure 1

The «Arfa» magnetic field simulation system and the isolated ground-based experimental complex

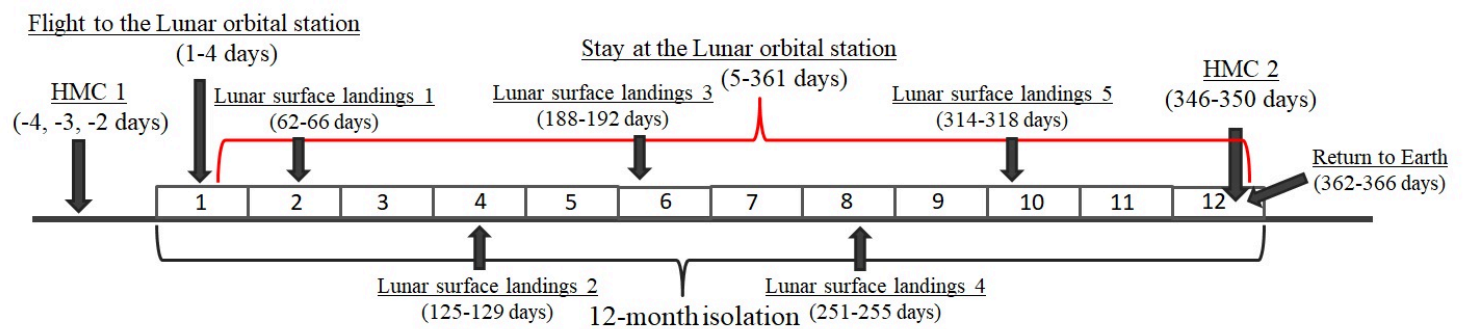


Figure 2

Research cyclogram

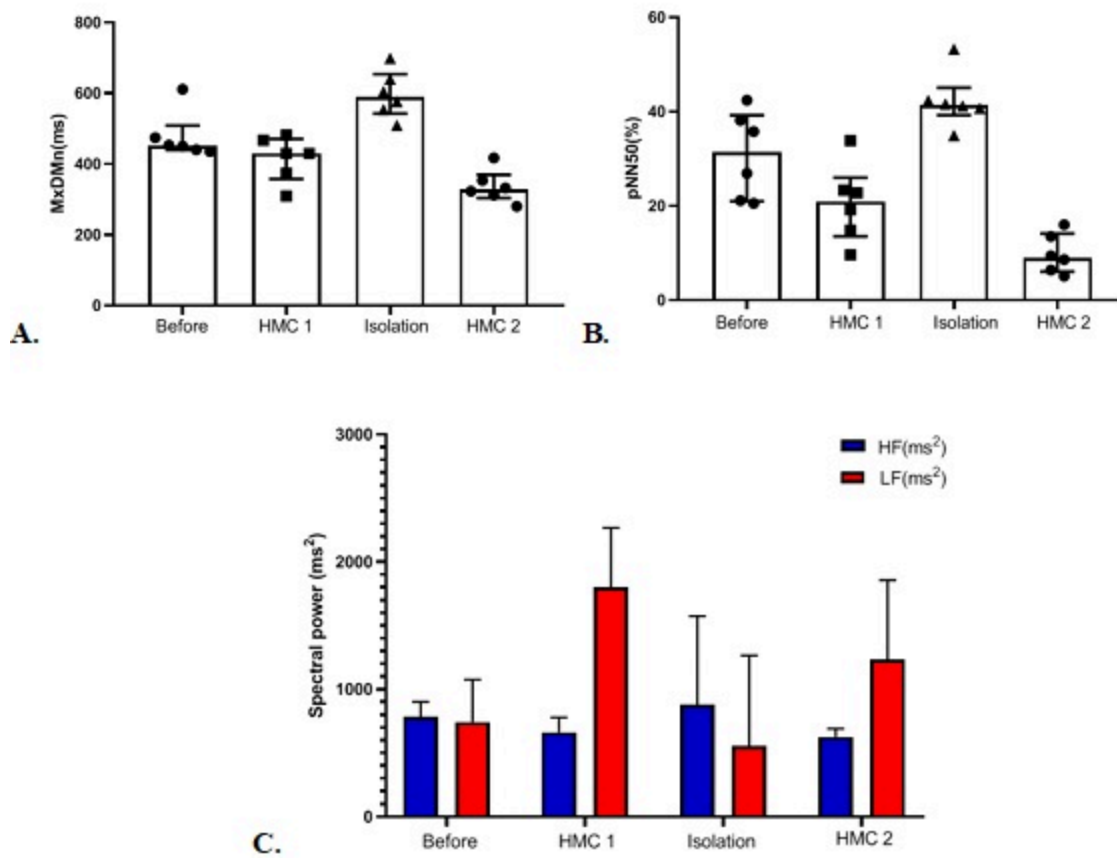


Figure 3

Dynamics of **A.**- MxDMn (ms), **B.** -pNN50 (%) and **C.**-spectrum power indicators

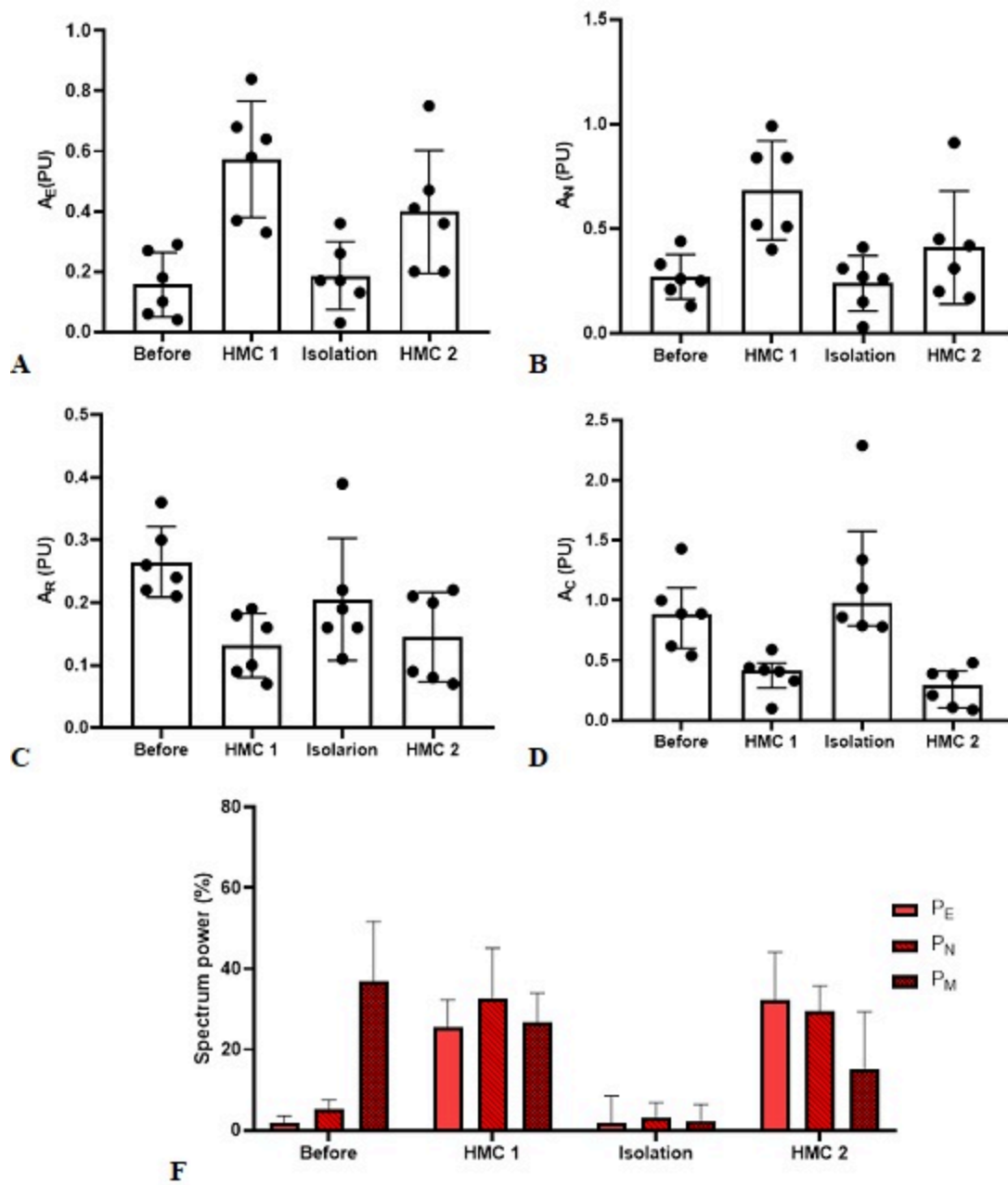


Figure 4

Dynamics indicator **A.**- A_E (PU), **B.**- A_N (PU), **C.**- A_R (PU), **D.**- A_C (PU), **F.**-spectrum power of endothelial - P_E , neurogenic - P_N , and myogenic oscillations - P_M (%) (F)

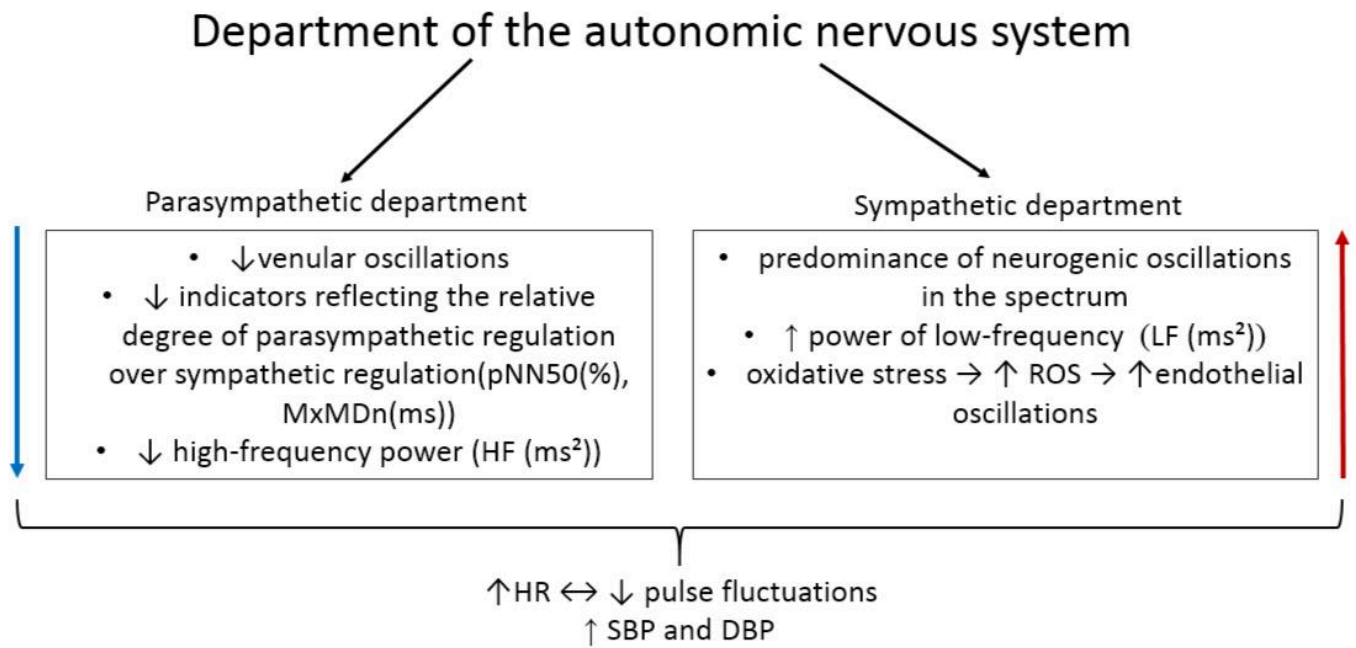


Figure 5

Mechanism of cardiac rhythm regulation in conditions of reduced GMF by a factor of 350