frontiers | Frontiers in Space Technologies

TYPE Opinion
PUBLISHED 16 September 2022
DOI 10.3389/frspt.2022.998610

OPEN ACCESS

EDITED BY
Mark Sephton,
Imperial College London,
United Kingdom

REVIEWED BY
Gabriel G. De La Torre,
University of Cádiz, Spain

*CORRESPONDENCE
V. B. Rusanov,
vasilyrusanov@gmail.com

SPECIALTY SECTION
This article was submitted
to Space Exploration,
a section of the journal
Frontiers in Space Technologies

RECEIVED 20 July 2022
ACCEPTED 05 September 2022
PUBLISHED 16 September 2022

CITATION
Rusanov VB, Fomina EV and Orlov OI
(2022), Does heart rate variability reflect
brain plasticity as a likely mechanism of
adaptation to space mission?
Front. Space Technol. 3:998610.
doi: 10.3389/frspt.2022.998610

Does heart rate variability reflect brain plasticity as a likely mechanism of adaptation to space mission?

V. B. Rusanov*, E. V. Fomina and O. I. Orlov

State Scientific Center of the Russian Federation Institute of Biomedical Problems of Russian Academy of Sciences, Moscow, Russia

KEYWORDS

heart rate variability, brain plasticity, adaptation, space mission, system biology

In space medicine, the definition of "health" is considered as the ability of a crew member to carry out a high-quality space mission program and at the same time retain enough functional reserves for readaptation to earth conditions after it is completed (Baevsky et al., 2013).

Professional space crews are formed from specially selected, practically healthy people trained to work in changed conditions and under constant stress (Kovacs and Shadden, 2017). Monitoring of their functional state is based on the assessment of changes within the physiological norm, where the main ones are shifts (reorganizations) occurring in the mechanisms of regulation and developing at the information-temporal or information-energy levels of the body (Baevsky et al., 2011). In this sense, the individual approach of space medicine to health assessment can be seen as a prerequisite for modern personalized medicine (Dietrich et al., 2018; Pavez Loriè et al., 2021).

On the one hand, the structural elements of the human body are a system of independent components, on the other hand, they are characterized by complex interactions (Burggren and Monticino, 2005; Grenfell et al., 2006), therefore, the creation of a unified concept of health in space medicine is an integrative task that can be solved from the standpoint of systems biology.

The totality of space flight factors requires the human body to exert constant tension on its regulatory systems to maintain homeostasis (Baevsky et al., 2014). The complex impact of stress factors leads to the fact that ever-higher levels of control over the physiological functions of the body are involved in the adaptation process (Baevsky et al., 2007; Baevsky et al., 2009). This ensures the necessary coordination of various systems and processes within the framework of a single goal—balancing the body with the environment (Baevsky and Chernikova, 2016).

One of the characteristics of a system that ensures the quality of its functioning is plasticity, which allows it to quickly cope with the challenges of a changing environment (Goldberger, 1991; Beckers et al., 2006; McCraty et al., 2009; Smith et al., 2017). First of all, this is due to the ability of neurons, neural structures, and neural networks of the brain to dynamically change structural and functional characteristics and modify response patterns in response to changes in external conditions and afferent stimuli (Slenzka, 2003; Pearson-Fuhrhop and Crame, 2006).

In this regard, neuroimaging is an important tool for studying the plasticity of the brain in space flight, as well as the dynamic structural and functional networks that connect the body and brain in the process of adaptive changes.

Studies of structural changes in the brain after spaceflight appear compression of the gyri, narrowing of the calcarine and central sulcus, supravermian cistern, expansion of the cerebral ventricles with extensive redistribution of cerebrospinal fluid, and, in general, an upward displacement of the brain inside the skull. These changes were directly related to the duration of the mission and persisted for some time after the end of the mission (Roberts et al., 2017; Van Ombergen et al., 2018; Van Ombergen et al., 2019; Kramer et al., 2020).

In addition, microstructural changes occurring during a space mission in sensorimotor pathways, including tracts connecting the cerebellum, as well as within the corpus callosum, inferior fronto-occipital, and arcuate fascicles, may reflect various sources of space flight effects on the brain, including fluid displacement effects, structural brain changes and neuroplasticity (Doroshin et al., 2022).

In a study by Barisano et al. (2019) an increase in the lateral ventricles and a decrease in the subarachnoid space in the vertex region were found, which correlated with an increase in the volume of the perivascular space of the basal ganglia and the perivascular space of the white matter after space flight.

It seems to us that the plasticity of nervous structures underlies successful adaptive reactions that maintain homeostasis at an adequate level. In addition, it provides a transition between the functional states associated with autonomous control. Neuroplasticity induces adaptive changes or predisposes functional systems to adaptive plasticity.

Weightlessness, as a condition of existence atypical for an organism, models the specific relationship between the brain and the heart. This process is based on structural and functional networks dynamically changing in time and space, which provide multilevel interactions in the whole organism (Ivanov et al., 2016). The dynamic network approach to defining states has revealed new aspects of the connections between the heart and brain (Valenza et al., 2016). CAN include structures that modulate autonomic balance brain stem nuclei that directly regulate the functioning of the heart, solitary tract, hypothalamus, and amygdala, as well as areas of the prefrontal cortex (Benarroch, 1993; Beissner et al., 2013; Dampney, 2015; Shoemaker and Goswami, 2015). Piper et al. (2014) to study the dynamics of the central autonomic network (CAN), which controls the cardiovascular and cardiorespiratory systems, used time-varying coherence analysis to quantify the role of neural networks in the sympathetic control of the heart.

According to the “neurovisceral integration” model (Thayer and Lane, 2000; Thayer and Lane, 2009), CAN neural structures interact with each other as a “supersystem” that provides adaptive regulation. An integrative characteristic that reflects the level of functioning of this system is heart rate variability (HRV) since it reflects the degree of functional integration between areas of the prefrontal cortex, the brain stem, and the peripheral nervous system. The hypothesis is that HRV is not only an indicator of cardiac function but also an indicator of adaptive regulation and brain plasticity (Thayer et al., 2012). This is consistent with the concept of functional state analysis used to evaluate adaptation processes in space flight (Baevsky et al., 2011; Baevsky and Chernikova, 2016).

Neuroimaging studies have demonstrated links between HRV and specific brain regions (Thayer et al., 2012). Evidence suggests that the medial prefrontal cortex and adjacent anterior cingulate cortex are associated with HRV modulation (Sakaki et al., 2016). The dynamics of these associations are related to sex and age (Koenig and Thayer, 2016; Kumral et al., 2019).

External conditions model the dynamic relationship between the brain and the heart. In a situation of high stress, the degree of synchronization between the prefrontal cortex and the heart can change (Chand et al., 2020). This flexibility determines the transition between functional states mediated by the autonomic nervous system (Baevsky and Chernikova, 2017).

HRV may be one of the complex markers of stress, as it is associated not only with dynamic modulation of vagal control of heart rate (Author Anonymous, 1996) but also through putative connections with neural structures involved in threat and safety assessment (Sakaki et al., 2016), can characterize the level of functional state, as well as individual signs associated with physical and mental health (Holzman and Bridgett, 2017). The current theoretical foundations of HRV suggest that it reflects the ability to self-regulate (the ability to regulate behavioral, cognitive, and emotional processes) and, therefore, can be used as a biomarker of the circulatory system and complex mental and behavioral processes (Porges and Furman, 2011; Oken et al., 2015; Crestani 2016; Walker et al., 2017).

HRV gives an idea of the adaptation processes to the conditions of the space environment due to the integration of the brain and vegetative processes and the activation of higher vegetative centers, which ultimately determines the health level of a space mission participant (Baevsky et al., 2014).

To maintain cardiovascular homeostasis at an optimal level, active restructuring of regulatory mechanisms is necessary. At different stages of adaptation of the body to microgravity conditions, the degree of tension of regulatory systems and their functional reserves change, and the adaptation process itself is associated with a gradual increase in the influence of higher levels of regulation (Baevsky et al., 1998, 2013). At the same time, the reaction of regulatory mechanisms depends on individual characteristics that persist during repeated flights after several years (Baevsky et al., 2014).

Links between brain functional networks and HRV have been analyzed in studies by Otsuka et al. In one of them, the authors report that space missions lasting 6 months improve HRV (Otsuka et al., 2019). Another study documented an increase in the circadian periodicity of HRV, an improvement in sleep quality, and an increase in parasympathetic modulating influences at night (Otsuka et al., 2021). According to the authors, these data indicate an unconscious activation of the functional network of the brain during long-term space travel and contribute to slowing down the aging of regulatory mechanisms.

Changes in brain function reflected in HRV may explain the fact that the process of neural adaptation improves with the increase in the number of missions since neuroplasticity refers to the ability of the nervous system to change its activity in response to internal or external stimuli by reorganizing its structure, functions or connections (Demertzi et al., 2016; Pechenkova et al., 2019).

Perhaps the reorganization of the brain in repeated space missions is associated with countermeasures implemented on board the International Space Station (ISS). In the previously mentioned study and Barisano et al. (2019) differences in the reorganization of the brain of NASA astronauts, the European Space Agency, and Roscosmos cosmonauts were revealed. The authors have suggested that this is due to differences in the use of countermeasures and high-resistance exercise regimens, which may affect the redistribution of cerebral fluid, since age, mission duration, and environmental conditions on the ISS were identical.

Physical exercise has a positive effect on the functional connectivity of the brain and can act as neuroenhancers. In a study by Schneider et al. (2013), in a 520-day isolation experiment simulating a flight to Mars, it was shown that post-exercise cortical activity was most pronounced after endurance-oriented protocols using an active treadmill. In another analog space mission with 120-days of isolation, simulating a flight to the Moon and a stay in lunar orbit, it was demonstrated that individual aerobic running training induces responses that maintain brain plasticity (Abeln et al., 2022).

In our opinion, the study of the structural and functional effects that occur in the central nervous system in weightlessness will open up possibilities for understanding the body functions associated with the adaptation and health of space travelers. The theoretical assumption is that due to the interaction of neural networks consisting of nerve centers dynamically located at all levels of the brain and controlling HRV, it is this integral characteristic that reflects brain plasticity as a possible mechanism for adaptation to microgravity conditions. Undoubtedly, this thesis requires experimental confirmation and, nowadays has serious limitations associated with the insufficiency of repeated long-term space missions. In addition, the complexity of the mechanisms of neuronal cardiovascular integration requires their clearer differentiation, which is the subject of further research. However, understanding the impact of weightlessness on the processes of reorganization of the human brain and identifying possible markers of this process is important for developing an adequate strategy of countermeasures to maintain the health and performance of space crews, which will ultimately determine the success and safety of future long-term space missions to distant planets.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Funding

The work was carried out within the framework of the basic theme of RAS 63.1 and 64.1 for 2013–2023.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

Abeln, V., Fomina, E., Popova, J., Braunsmann, L., Koschate, J., Möller, F., et al. (2022). Chronic, acute and protocol-dependent effects of exercise on psycho-physiological health during long-term isolation and confinement. *BMC Neurosci.* 23, 41. doi:10.1186/s12868-022-00723-x

Author Anonymous (1996). Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task force of the European society of cardiology and the north American society of pacing and electrophysiology (membership of the task force listed in the appendix). *Eur. Heart J.* 17, 354–381. doi:10.1016/j.neubiorev.2016.03.007

Baevsky, R. M., Baranov, V. M., Funtova, I. I., Pashenko, A. V., Chernikova, A. G., Jordan, J., et al. (2007). Autonomic cardiovascular and respiratory control during prolonged spaceflights aboard the international space station. *J. Appl. Physiol.* 103 (1), 156–161. doi:10.1152/japplphysiol.00137.2007

Baevsky, R. M., and Chernikova, A. G. (2016). Assessment of adaptation risk in individual prenosological monitoring system. *Neurosci. Behav. Physiol.* 46 (4), 437–445. doi:10.1007/s1105

Baevsky, R. M., Chernikova, A. G., Funtova, I. I., and Tank, J. (2011). Assessment of individual adaptation to microgravity during long term space flight based on stepwise discriminant analysis of heart rate variability parameters. *Acta Astronaut.* 69, 1148–1152. doi:10.1016/j.actaastro.2011.07.011

Baevsky, R. M., Funtova, I. I., Chernikova, A. G., Baranov, V. M., Tank, J., Diedrich, A., et al. (2009). Autonomic function testing aboard the iss using "Pneumocard. *Acta Astronaut.* 65, 930–932. doi:10.1016/j.actaastro.2009.03.029

Baevsky, R. M., Luchitskaya, E. S., Funtova, I. I., and Chernikova, A. G. (2013). Study of the autonomic regulation of blood circulation during a long-term space flight. *Hum. Physiol.* 39, 486–495. doi:10.1134/S0362119713050046

Baevsky, R. M., Moser, M., Nikulina, G. A., Polyakov, V. V., FuntovaII, and Chernikova, A. G. (1998). Autonomic regulation of circulation and cardiac contractility during a 14-month space flight. *Acta Astronaut.* 42, 159–173. doi:10.1016/s0094-5765(98)00114-3

Baevsky, R. M., and Chernikova, A. G. (2017). Heart rate variability analysis: Physiological foundations and main methods. *Cardiometry* 10, 66–76. doi:10.12710/cardiometry.2017.10.6676

Baevsky, R. M., Funtova, I. I., Luchitskaya, E. S., and Chernikova, A. G. (2014). The effects of longterm microgravity on autonomic regulation of blood circulation in crewmembers of the International Space Station. *Cardiometry* 5, 35–49. doi:10.12710/cardiometry.2014.5.3549

Barisano, G., Sepehrband, F., Collins, H. R., Jillings, S., Jeurissen, B., Taylor, J. A., et al. (2019). The effect of prolonged spaceflight on cerebrospinal fluid and perivascular spaces of astronauts and cosmonauts. *Proc. Natl. Acad. Sci. U. S. A.* 119 (17), e2120439119. doi:10.1073/pnas.2120439119

Beckers, F., Verheyden, B., and Aubert, A. E. (2006). Aging and nonlinear heart rate control in a healthy population. *Am. J. Physiology-Heart Circulatory Physiology* 290, H2560–H2570. doi:10.1152/ajpheart.00903.2005

Beissner, F., Meissner, K., Bär, K. J., and Napadow, V. (2013). The autonomic brain: An activation likelihood estimation meta-analysis for central processing of autonomic function. *J. Neurosci.* 33, 10503–10511. doi:10.1523/JNEUROSCI.1103-13.2013

Benarroch, E. E. (1993). The central autonomic network: Functional organization, dysfunction, and perspective. *Mayo Clin. Proc.* 68, 988–1001. doi:10.1016/s0025-6196(12)62272-1

Burggren, W. W., and Monticino, M. G. (2005). Assessing physiological complexity. *J. Exp. Biol.* 208 (17), 3221–3232. doi:10.1242/jeb.01762

Chand, T., Li, M., Jamalabadi, H., Wagner, G., Lord, A., Alizadeh, S., et al. (2020). Heart rate variability as an index of differential brain dynamics at rest and after acute stress induction. *Front. Neurosci.* 14, 645. doi:10.3389/fnins.2020.00645

Crestani, C. C. (2016). Emotional stress and cardiovascular complications in animal models: A review of the influence of stress type. *Front. Physiol.* 7, 251. doi:10.3389/fphys.2016.00251

Dampney, R. A. L. (2015). Central mechanisms regulating coordinated cardiovascular and respiratory function during stress and arousal. *Am. J. Physiology-Regulatory Integr. Comp. Physiology* 309, R429–R443. doi:10.1152/ajpregu.00051.2015

Demertzi, A., Van Ombergen, A., Tomilovskaya, E., Jeurissen, B., Pechenkova, E., Di Perri, C., et al. (2016). Cortical reorganization in an astronaut's brain after long-duration spaceflight. *Brain Struct. Funct.* 221, 2873–2876. doi:10.1007/s00429-015-1054-3

Dietrich, D., Dekova, R., Davy, S., Fahrni, G., and Geissbühler, A. (2018). Applications of space Technologies to global health: Scoping review. *J. Med. Internet Res.* 20 (6), e230. doi:10.2196/jmir.9458

Doroshin, A., Jillings, S., Jeurissen, B., Tomilovskaya, E., Pechenkova, E., Nosikova, I., et al. (2022). Brain connectometry changes in space travelers after long-duration spaceflight. *Front. Neural Circuits* 16, 815838. doi:10.3389/fncir.2022.815838

Goldberger, A. L. (1991). Is the normal heartbeat chaotic or homeostatic? *Physiology* 6, 87–91. doi:10.1152/physiologyonline.1991.6.2.87

Grenfell, B. T., Williams, C. S., Bjornstad, O. N., and Banavar, J. R. (2006). Simplifying biological complexity. *Nat. Phys.* 2 (4), 212–214. doi:10.1038/nphys231

Holzman, J. B., and Bridgett, D. J. (2017). Heart rate variability indices as biomarkers of top-down self-regulatory mechanisms: A meta-analytic review. *Neurosci. Biobehav. Rev.* 74, 233–255. doi:10.1016/j.neubiorev.2016.12.032

Ivanov, P. Ch., Liu, K. K. L., and Bartsch, R. P. (2016). Focus on the emerging new fields of network physiology and network medicine. *New J. Phys.* 18, 100201. doi:10.1088/1367-2630/18/10/100201

Kramer, L. A., Hasan, K. M., Stenger, M. B., Sargsyan, A., Laurie, S. S., Otto, C., et al. (2020). Intracranial effects of microgravity: a Prospective Longitudinal MRI Study. *Radiology* 295, 640–648. doi:10.1148/radiol.2020191413

Koenig, J., and Thayer, J. F. (2016). Sex differences in healthy human heart rate variability: A meta-analysis. *Neurosci. Biobehav. Rev.* 64, 288–310. doi:10.1016/j.neubiorev.2016.03.007

Kovacs, G., and Shadden, M. (2017). Analysis of age as a factor in NASA astronaut selection and career landmarks. *PLoS ONE* 12, e0181381. doi:10.1371/journal.pone.0181381

Kumral, D., Schaare, H. L., Beyer, F., Reinelt, J., Uhlig, M., Liem, F., et al. (2019). The age-dependent relationship between resting heart rate variability and functional brain connectivity. *Neuroimage* 185, 521–533. doi:10.1016/j.neuroimage.2018.10.027

McCraty, R., Atkinson, M., Tomasino, D., and Bradley, R. T. (2009). The coherent heart heart–brain interactions. Psychophysiological coherence, and the emergence of system-wide order. *Int. Rev.* 5, 10–115.

Oken, B. S., Chamine, I., and Wakeland, W. (2015). A systems approach to stress, stressors and resilience in humans. *Behav. Brain Res.* 282, 144–154. doi:10.1016/j.bbr.2014.12.047

Otsuka, K., Cornelissen, G., Furukawa, S., Kubo, Y., Shibata, K., Mizuno, K., et al. (2021). Astronauts' well-being and possibly anti-aging improved during long-duration spaceflight. *Sci. Rep.* 11, 14907. doi:10.1038/s41598-021-94478-w

Otsuka, K., Cornelissen, G., Kubo, Y., Shibata, K., Mizuno, K., Ohshima, H., et al. (2019). Anti-aging effects of long-term space missions, estimated by heart rate variability. *Sci. Rep.* 9, 8995. doi:10.1038/s41598-019-45387-6

Pavez Loriè, E., Baatout, S., Choukér, A., Buchheim, J-I., Baselet, B., Dello Russo, C., et al. (2021). The future of personalized medicine in space: From observations to countermeasures. *Front. Bioeng. Biotechnol.* 9, 739747. doi:10.3389/fbioe.2021.739747

Pearson-Fuhrhop, K. M., and Crame, S. C. (2010). Genetic influences on neural plasticity. *PM&R* 2 (12), S227–S240. doi:10.1016/j.pmrj.2010.09.011

Pechenkova, E., Nosikova, I., Rumshiskaya, A., Litvinova, L., Rukavishnikov, I., Mershina, E., et al. (2019). Alterations of functional brain connectivity after long-duration spaceflight as revealed by fMRI. *Front. Physiol.* 10, 761. doi:10.3389/fphys.2019.00761

Piper, D., Schiecke, K., Pester, B., Benninger, F., Feucht, M., and Witte, H. (2014). Time-variant coherence between heart rate variability and EEG activity in epileptic patients: An advanced coupling analysis between physiological networks. *New J. Phys.* 16, 115012. doi:10.1088/1367-2630/16/11/115012

Porges, S. W., and Furman, S. A. (2011). The early development of the autonomic nervous system provides a neural platform for social behaviour: A polyvagal perspective. *Infant Child. Dev.* 20 (1), 106–118. doi:10.1002/icd.688

Roberts, D. R., Albrecht, M. H., Collins, H. R., Asemani, D., Chatterjee, A. R., Spampinato, M. V., et al. (2017). Effects of spaceflight on astronaut brain structure as indicated on MRI. *N. Engl. J. Med. Overseas. Ed.* 377, 1746–1753. doi:10.1056/NEJMoa1705129

Sakaki, M., Yoo, H. J., Nga, L., Lee, T.-H., Thayer, J. F., and Mather, M. (2016). Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults. *Neuroimage* 139, 44–52. doi:10.1016/j.neuroimage.2016.05.076

Schneider, S., Abeln, V., Popova, J., Fomina, E., Jacubowski, A., Meeusen, R., et al. (2013). The influence of exercise on prefrontal cortex activity and cognitive performance during a simulated space flight to Mars (MARS500). *Behav. Brain Res.* 236 (1), 1–7. doi:10.1016/j.bbr.2012.08.022

Shoemaker, J. K., and Goswami, R. (2015). Forebrain neurocircuitry associated with human reflex cardiovascular control. *Front. Physiol.* 6, 240. doi:10.3389/fphys.2015.00240

Slenzka, K. (2003). Neuroplasticity changes during space flight. *Adv. Space Res.* 31, 1595–1604. doi:10.1016/s0273-1177(03)00011-5

Smith, R., Thayer, J. F., Khalsa, S. S., and Lane, R. D. (2017). The hierarchical basis of neurovisceral integration. *Neurosci. Biobehav. Rev.* 75, 274–296. doi:10.1016/j.neubiorev.2017.02.003

Thayer, F., and Lane, R. D. (2009). Claude bernard and the heart–brain connection: Further elaboration of a model of neurovisceral integration. *Neurosci. Biobehav. Rev.* 33, 81–88. doi:10.1016/j.neubiorev.2008.08.004

Thayer, J. F., Ahs, F., Fredrickson, M., Sollers, J. J., III, and Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neurosci. Biobehav. Rev.* 36, 747–756. doi:10.1016/j.neubiorev.2011.11.009

Thayer, J. F., and Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *J. Affect. Disord.* 61, 201–216. doi:10.1016/S0165-0327(00)00338-4

Valenza, G., Toschi, N., and Barbieri, R. (2016). Uncovering brain–heart information through advanced signal and image processing. *Phil. Trans. R. Soc. A* 374 (2067), 20160020. doi:10.1098/rsta.2016.0020

Van Ombergen, A., Jillings, S., Jeurissen, B., Tomilovskaya, E., Rühl, R. M., Rumshiskaya, A., et al. (2018). Brain tissue–volume changes in cosmonauts. *N. Engl. J. Med. Overseas. Ed.* 379, 1678–1680. doi:10.1056/NEJMc1809011

Van Ombergen, A., Jillings, S., Jeurissen, B., Tomilovskaya, E., Rumshiskaya, A., Litvinova, L., et al. (2019). Brain ventricular volume changes induced by long-duration spaceflight. *Proc. Natl. Acad. Sci. U. S. A.* 116, 10531–10536. doi:10.1073/pnas.1820354116

Walker, F. R., Pfingst, K., Carnevali, L., Sgoifo, A., and Nalivaiko, E. (2017). In the search for integrative biomarker of resilience to psychological stress. *Neurosci. Biobehav. Rev.* 74, 310–320. doi:10.1016/j.neubiorev.2016.05.003