

<https://doi.org/10.52326/ic-ecco.2022/BME.06>



Arousal from sleep, alertness induced by bimodal signals during “environment-person” communication

Anatolie Jacob Baciu^{1,3}, ORCID:
Ion Mereuta¹, ORCID:
Vasile Fedash¹, ORCID:
Lyudmila Listopadova^{2,3}, ORCID:

¹ Institute of Physiology and Sanocreatology, MD-2028, Academy str. 1, Chisinau, Republic of Moldova, anatolikbacio@gmail.com, <https://ifs.md/>

² Moldova State University, MD-2009, Alexei Mateevici str. 60, Chisinau, Republic of Moldova, <https://usm.md/>

³ Transnistria State University, MD-3300, 25th October str. 128, Tiraspol, Republic of Moldova, <http://spsu.ru/>

Abstract—An attempt to carry out a conceptual synthesis based on reviewed data and conduct experimental testing of the effects of bimodal signaling in the "environment-person" communication. It is emphasized that The environment has a very important role in the process of evolution of living beings, which, in turn, are a factor in the transformation of the environment. Bi- or multimodal signaling in the course of "environment-person" communication may be the most suitable neuromodulator and trigger of adaptive plastic remodeling in the control nerve centers. (Abstract)

Keywords—environment-person; communication; arousal; alertness

I. INTRODUCTION (HEADING 1)

The survival of the living organism to a large extent depends on the ability of the animal or human to maintain an adequate level of alertness, as well as on its ability to dynamically adjust emotional status in accordance with physiological requirements and changing environmental conditions. Wakefulness is characterized by adequate awareness of behavior, voluntary motor activity, and adequate sensitivity to environmental sensory stimuli. From the point of view of electrophysiology, the waking state is characterized by the integral activation of the cerebral cortex and the increased excitability of neurons. Despite the fact that wakefulness is often called a single state, it includes several interrelated neuropsychic components, including arousal, alertness, attention, memory, motivation, and emotions. Vigilance is determined by the general level of sensitivity of the neural centers. Often this can be measured by the degree

of stimulation required to elicit a specific response. Maintaining an adequate level of arousal essential for triggering or maintaining appropriate behavioral reactions to environmental conditions that are ultimately oriented towards the regulation of homeostatic parameters.

It is extremely important that neurons of the orexinergic activating lateral hypothalamus system have central chemosensitivity. A well-known stimulator of the activity of orexinergic neurons is: the hunger hormone ghrelin, and inhibitors: leptin and glucose, which signal satiety. The focal specific sensitivity to changes in CO₂ and H⁺ concentrations is also important for a sensitive response to hypoxic signals (lack of oxygen supply) from the external and internal environment [1, 2]. It is also important that the orexinergic activating system does not act alone, but as an integral part of a single complex system of regulatory chemosensitive centers: RTN (retrotrapezoid nucleus); the raphe nucleus, the caudal NTS (nucleus of the solitary tract), the locus coeruleus (LC), the caudal ventral medulla, the pre-Bötzing complex (the pre-Bötzing complex in the ventral respiratory center of the brainstem medulla), and the perifornical region of the lateral hypothalamus [3-9]. Along with the suprachiasmatic nucleus of the hypothalamus, the orexinergic activating center is modulated by signals of various physical modalities about the circadian cycle from the external environment. Themselves, being the drivers of the circadian rhythm, coordinate the strict internal circadian biorhythm of homeostatic processes and behavior [10-14]. Thus, the increase in hyperventilation reactions to focal acidification in the perifornical region of the lateral

hypothalamus during respiratory activity during the day is more pronounced in the waking state [15, 16]. It has long been suggested that electrical impulses from the lateral region of the hypothalamus stimulate respiration. Recent evidence suggests that orexinergic neurons project directly to the respiratory centers in the brainstem. It is important that the relationship between the orexinergic center and gas exchange is bidirectional. Therefore, the activating system is important for the daily regulation of respiration and may potentially play a role in the pathophysiology and pharmacological treatment of respiratory diseases. The indirect effect on respiration is carried out through the serotonergic (5-HT-ergic) dorsal raphe nuclei and the parasympathetic autonomic nervous system. This is how vagal neuromodulation and immunomodulation are performed, which is important for the prevention of dysfunction of the pulmonary branch of the vagus nerve and the pathogenesis of some chronic respiratory diseases, such as bronchial asthma and obstructive sleep apnea syndrome. Whereas, on the contrary, dysfunction of the central orexinergic system increases the severity of respiratory diseases [17-19]. Currently, the technological possibility of neuromodulation, accompanied by the immunomodulatory action of the parasympathetic autonomic nervous system, is of particular importance. Vagal neuromodulation is a promising alternative immunomodulatory prophylaxis for respiratory syndromes due to its potent systemic anti-inflammatory effects.

Various physical natural environmental factors can negatively affect cognitive function. Factors that can be considered extreme, namely heat, hypoxia, and cold, can alter a person's cognitive function due to a variety of psychological and/or biological processes. It is noteworthy that acclimatization, adaptation to acceptable environmental conditions is based on a neuromodulatory effect, which can lead to impaired cognitive functions during communication. The states of activation of the cerebral cortex allow you to increase the ability to process information during communication. Whereas the activation itself may not contain specific information. Such activation states are tonic or phasic, and also relatively global or more localized. Among these states are arousal, alertness, vigilance, and attention. Sometimes these terms are not ideal to describe these states of cortical activation, as most of the terms are widely used with various associations. In general, ideal physiological markers do not exist [20].

The goal is a conceptual synthesis based on reviewed data and experimental testing of the effects of bimodal signaling during the "environment-person" communication.

II. MATERIAL AND METHOD

The Experimental models for studying the influence of the environment on neuronal and neuromuscular plasticity are urgently needed under both physiological conditions and developing pathology. At the same time, initial standardization in laboratory animal models is accompanied by parallel interpolation of data on the human body. The use of experimental models on laboratory animals allows us to fundamentally argue the revealed mechanisms of the relationship between the organism and the environment and to expand our understanding of the neuromodulatory effects of its factors, characterized by adaptive plastic remodeling of nerve centers and neuromuscular junctions. However, the "positive" effects on brain plasticity in response to an enriched and stimulating environment have only recently been investigated. An enriched environment (EE) can be simulated in rodents by placing mice in larger cages equipped with toys and nesting material to encourage sensory stimulation and wheel running to promote voluntary physical activity.

An experimental animal model was used with the inclusion in the experiment of 3 groups of laboratory animals (mature male rats): control (n=5); hypoxic/hypercapnic environmental signal during the rest period (08:00-16:00) (n=5); auditory environmental signal during the rest period (08:00-12:00 h) (n=5).

In our experimental model, we used sexually mature laboratory animals (rats) raised in a vivarium on a standard diet with free access to water and natural light. Prior to the start of the experiment, all animals underwent surgery using a stereotaxic technique under general anaesthesia by inspiration of oxygen and isoflurane (1-3%) mixture. Animals were implanted with electrodes for electrophysiological recordings. After the postoperative recovery period, an experiment on modeling hypoxic/hypercapnic environmental signal (n=5) began, in which, using a rostral mask equipped with a corrugated hose and a tap, breathing from the atmosphere through the mask and rebreather breathing (without exhalation into the atmosphere) with a closed tap were simulated. The combined effect of hypoxia/hypercapnia was dosed by varying the exposure of breathing with a closed tap (from 1 to 5 s). Polysomnographic 24-hour recording was carried out in experimental animals (n=5) by using of 6 electroencephalogram (EEG) channels, 1 electrooculogram (EOG) and 1 electromyogram (EMG) channel and was accompanied by video behavior monitoring. Arousals from slow-wave (delta) sleep and REM-sleep were evoked by auditory environmental signal application (natural threat vocalization of rat) of different intensities (50-60 dB). For arousal estimation the ratio of total power of delta-rhythm before and after stimulus application was calculated. Total power was determined

for period of ten 3-second epochs (30 seconds). In addition, the latency of arousal, duration of slow wave recovery, and magnitude of arousal induced EEG desynchronization were manually scored “Fig. 1” and “Fig. 2”.

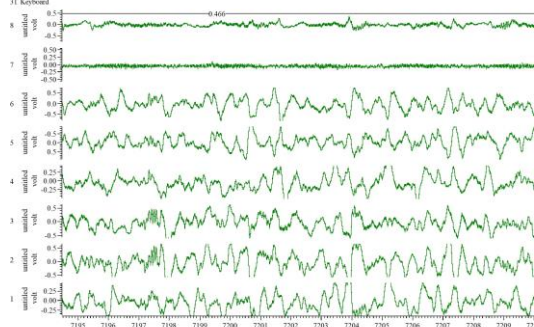


Figure 1. Appearance of electrophysiological recordings of EEG, EOG and EMG for identification of stages of sleep, awakening and alertness

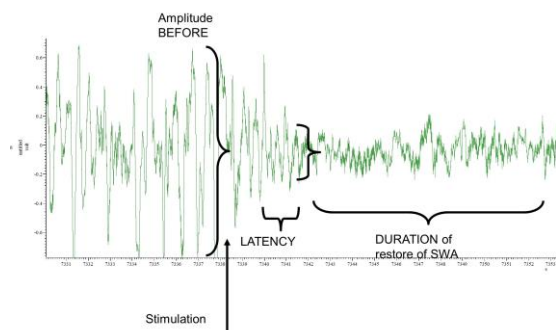


Figure 2. Maximized recording of EEG activity to measure the latent period, amplitude and duration of response to environmental bimodal signaling

Statistical analysis was realized by use of ANOVA method with Student’s t-criterion utilization.

III. RESULT AND DISCUSSION

Conceptually, strategically, we postulate some basic provisions for favoring the environment-person communication and the modulating action of natural environmental factors of various modalities induced by it. For the formation and estimation of the common indicators of healthy/unhealthy communication regarding 1) – the presence/absence of communicability that creates a state of mutual satisfaction and 2) – the presence/absence of communicative aggressiveness that creates social discomfort, it is particularly important to understand that communication is determined not only of communication between people (interpersonal), but also of communication between people and the external environment (surrounding space). In most acts of communication, an individual (person) communicates, namely, with the external environment. For the target directed study and mental health promotion we take into

account the fact that communication between the person and the environment is carried out permanently and is conditioned by evolution. Living organismal machines favorably differ from man-made machines in their abilities for self-organization, self-assembly, self-diagnosis, self-repair, structural and functional improvement. These unique advantages are determined by communication with the environment, daily activity in this environment and the success of adaptive remodeling of structures. This environment-person communication is fulfilled through the communicative channels which according to their physical nature are: visual; auditory; tactile or haptic; olfactory; biomagnetic; biochemical. It is obvious that channel identification depends on the sensory modality that ensures the perception of signals from the environment. There is already a branch of science that investigates the functioning of communication and the meaning of communicative signals, i.e. the relationships between code and message, between sign and discourse, and which is called “Semiotics”. Currently, semiotics is a research technique that explains exactly how communication and meaning work. Biosemiotics represents communication, namely, between living organisms, in general. During the millions of years of evolution in the genome of living beings, all the nuances of the organism’s communication with the environment were determined. We remind you that the environment, specified when necessary as the surrounding environment, the ambient environment or the natural environment, is a notion that refers to the totality of the natural conditions on Earth or in a region of it, in which beings or things evolve. These conditions include atmosphere, light, water, soil, relief, temperature, etc., as well as other living beings and things. The environment has a very important role in the process of evolution of living beings, which, in turn, are a factor in the transformation of the environment.

Anthropogenically, there was a danger of losing the close ties between the organism and the natural environment by means the creation of the artificial environment. According to the statistical analysis carried out, for example, in Canada, most people around 90% of the time during the circadian activity stay indoors at work, at home or even in the hospital. From this consideration, in particular, the interior must be arranged in a sanogenic way, i.e. naturally. In general, Canada has a social justice orientation and is a global leader in promoting the health of every citizen. The replacement of the natural environment, to which the organism’s adaptation is genotypically determined, with an artificial environment causes disharmony expressed, first of all, in the changes in the higher nervous activity. Communication with the environment is carried out thanks to the reception capacities, that is, the functioning of the sensory

apparatus. That's why every change in the set of communicative signals from the surrounding environment is exactly directed towards certain neural information processing centers.

The whole ensemble of communicative sensory signals is received through the prism of Security, Reproduction and Nutrition. Because of this, any threat signal leads to anxiety, fear or aggression. Conversely, the lack of threat, pacifying conditions initiates a relaxed and comforting disposition. The presence of foods with a hedonic character that brings pleasure or to the sexual partner triggers a series of sensory, affective, cognitive and somato-vegetative reactions closely related to the activity of the central activation and reward systems.

We are already developing communication laboratory experimental models that accurately model healthy and unhealthy environmental conditions.

The First Step that is strictly necessary for mental health promotion is the direct or indirect (virtual) contact of the individual with Living Nature, the more this contact is limited, the further the mental health is far from the ideal. Unbridled urbanization and rural design characterized by an aggressive environment, the isolation and fragmentation of the natural landscape face this strict condition "Fig. 3".



Figure 3. Comparison of the communication of individuals with the natural (A) and artificial (B) environments: A – example of a sanogenic environment (promotion of mental health and harmony); B – example of dissanogenic environment (causing mental disorders).

The Second Step consists in the absence of threats to destroy the body or the environment. Otherwise, anxiety, depression or a host of disorders related to exaggerated

aggression develop. An individual who has been brought up and constantly communicates with the psychologically dissonant environment can represent a danger to civil society. We do not have the bioethical and social right to carry out a social experiment as a result of which a psychopath develops.

For application in practical The Health Creation Program we propose tests based on natural or virtual immersion of the individuals in the modeled environment and synchronous recording of the psycho-somatic and/or psycho-vegetative reactivity that expresses through the language of the face (facial muscles activity) and body language (gesture), as well as through fluctuations in the activity of the breathing systems and blood circulation. Such experiments were carried out by the imitation of the sanogenic and dissanogenic environment accompanied by the psychosomatic reactions recordings. We applied a method of estimation through video monitoring of individual psychomotor reactions to the experimental simulation of threatening, gratifying and neutral environmental conditions. Imitation of the flow of communicative signaling with a negative, positive and neutral content was achieved by applying the video presentation.

Obtained data of experimental testing manifest that arousal during deep slow wave (delta) sleep, and REM-sleep is symmetrical and more pronounced, but arousal is regionally different, i.e. asymmetrical, during superficial slow wave (delta) sleep "Fig. 4".

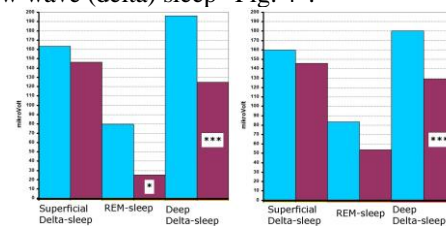


Figure 4. Average amplitude of the delta range of EEG-activity at different stages of sleep during arousal hyperventilation due to hypoxic/hypercapnic environmental signaling

The expression of EEG-arousal is characterized by the decrease in frontal-parietal-occipital direction. It is for interest that arousal threshold is higher during REM-sleep in comparison with superficial and even deep slow wave (delta) sleep in the same hemisphere. Latency shows lengthening, but the duration of alertness, on the contrary, is reduced during deep slow wave sleep "Fig. 5".

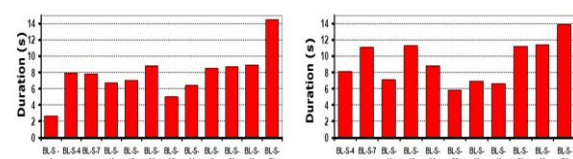


Figure 5. The duration of arousal and the state of alertness after the application of environmental auditory signaling until the restoration of delta waves in the EEG (in dependence on signal intensity).

These findings suggest that sensory inhibition is more pronounced during REM-sleep and deep slow wave sleep.

IV. CONCLUSION

Bi- or multimodal signaling in the course of "environment-person" communication may be the most suitable neuromodulator and trigger of adaptive plastic remodeling in the control nerve centers.

REFERENCES

- [1] E. Nattie, and A. Li, "Respiration and Autonomic Regulation and Orexin," *Prog Brain Res.* 2012, vol. 198, pp. 25–46.
- [2] R.H. Williams, L.T. Jensen, A. Verkhatsky, L. Fugger, D. Burdakov, "Control of hypothalamic orexin neurons by acid and CO₂," *Proceedings of the National Academy of Sciences of the United States of America.* 2007, vol. 104: pp. 10685–10690.
- [3] G.S. da Silva, A. Li, E. Nattie, "High CO₂/H⁺ dialysis in the caudal ventrolateral medulla (Loeschcke's area) increases ventilation in wakefulness," *Respiratory physiology & neurobiology.* 2010, vol. 171: pp. 46–53.
- [4] M.R. Hodges, L. Klum, T. Leekley, D.T. Brozoski, J. Bastasic, S. Davis, J.M. Wenninger, T.R. Feroah, L.G. Pan, H.V. Forster, "Effects on breathing in awake and sleeping goats of focal acidosis in the medullary raphe," *J Appl Physiol.* 2004a, vol. 96: pp. 1815–1824.
- [5] M.R. Hodges, P. Martino, S. Davis, C. Opansky, L.G. Pan, H.V. Forster, "Effects on breathing of focal acidosis at multiple medullary raphe sites in awake goats," *J Appl Physiol.* 2004b, vol. 97: pp. 2303–2309.
- [6] E. Nattie, and A. Li, "Central chemoreception is a complex system function that involves multiple brain stem sites," *J Appl Physiol.* 2009, vol. 106: pp. 1464–1466.
- [7] E. Nattie, and A. Li, "Central chemoreception in wakefulness and sleep: evidence for a distributed network and a role for orexin," *J Appl Physiol.* 2010, vol. 108: pp. 1417–1424.
- [8] I.C. Solomon, N.H. Edelman, M.H. O'Neal, "3rd CO₂/H⁺ chemoreception in the cat pre-Botzinger complex in vivo," *J Appl Physiol.* 2000, vol. 88: pp. 1996–2007.
- [9] C. Yonghua, G. Yuhong, Y. Xianxia, Z. Ming, C. Hong, Q. Dongying, and W. Jijiang, "Orexin-A Excites Airway Vagal Preganglionic Neurons via Activation of Orexin Receptor Type 1 and Type 2 in Rats," *Front Cell Neurosci.* 2019, vol. 13: p. 478.
- [10] H.R. Williams, and D. Burdakov, "Hypothalamic orexins/hypocretins as regulators of breathing," *Expert Rev Mol Med.* 2008, vol. 10: e28.
- [11] I.V. Estabrooke, et al., "Fos expression in orexin neurons varies with behavioral state," *J Neurosci.* 2001, vol. 21: pp. 1656–1662.
- [12] L.I. Kiyashchenko, et al., "Release of hypocretin (orexin) during waking and sleep states," *J Neurosci.* 2002, vol. 22: pp. 5282–5286.
- [13] M.G. Lee, O.K. Hassani, B.E. Jones, "Discharge of identified orexin/hypocretin neurons across the sleep-waking cycle," *J Neurosci.* 2005, vol. 25: pp. 6716–6720.
- [14] B.Y. Mileykovskiy, L.I. Kiyashchenko, J.M. Siegel, "Behavioral correlates of activity in identified hypocretin/orexin neurons," *Neuron.* 2005, vol. 46: pp. 787–798.
- [15] C.B. Saper, T.E. Scammell, J. Lu, "Hypothalamic regulation of sleep and circadian rhythms," *Nature.* 2005, vol. 437: pp. 1257–1263.
- [16] G.J. Morton, et al., "Central nervous system control of food intake and body weight," *Nature.* 2006, vol. 443: pp. 289–295.
- [17] W. Lutz, and W.J. Sulkowski, "Vagus nerve participates in regulation of the airways: inflammatory response and hyperreactivity induced by occupational asthmogens," *Int. J. Occup. Med. Environ. Health.* 2004, vol. 17, pp. 417–431.
- [18] V.J. Lewis, A.L. Short, and K.E. Lewis, "Autonomic nervous system control of the cardiovascular and respiratory systems in asthma," *Respir. Med.* 2006, vol. 100, pp. 1688–1705.
- [19] R.S. Leung, "Sleep-disordered breathing: autonomic mechanisms and arrhythmias," *Prog. Cardiovasc Dis.* 2009, vol. 51, pp. 324–338.
- [20] L. Taylor, S.L. Watkins, H. Marshall, B.J. Dascombe, and J. Foster, "The Impact of Different Environmental Conditions on Cognitive Function: A Focused Review," *Front Physiol.* 2015, vol. 6: p. 372.