

Difference of the status of Autonomic Nervous System in patients with chronic cerebrovascular insufficiency with Cognitive Impairment

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The aim of the study was to determine the status of the autonomic nervous system (ANS) in patients with chronic cerebrovascular insufficiency with cognitive impairment (CCICI). **Study design:** Prospective cohort study. Place and Duration of Study: Department of Neurology and Neurosurgery of the Gomel State Medical University, Neurological Department of the Gomel Regional Veterans Hospital, between September 2014 and May 2016. Methodology: 24 patients with CCICI (12 male and 12 female) and 14 volunteers (5 male and 9 female) were observed. To describe status of the ANS heart rate variability (HRV) linear parameters were used. Were analyzed using the following four parameters: SDNN (standard deviation of the normal-to-normal R-R intervals, in ms), ΔX (the difference between maximal and minimal R-R interval, in ms), Mo (mode of the duration of R-R intervals, in ms), AMo (amplitude of the R-R intervals mode, in percent). HRV linear parameters were measured at 1st day after admission. Central regulation of the autonomic nervous system: Central nervous system control of the autonomic nervous system involves several interconnected structures distributed throughout the neuraxis. The central autonomic network is organized into closely interconnected spinal, bulbopontine, pontomesencephalic, and forebrain levels. The spinal level mediates segmental sympathetic or sacral parasympathetic reflexes. The bulbopontine level is involved in the reflex control of respiration and circulation. The pontomesencephalic level controls pain modulation and integration of behavioral responses to stress. The forebrain level includes the hypothalamus and the anterior limbic circuit, which includes the insula. The forebrain is involved in goal-related autonomic and endocrine responses for homeostasis and adaptation. The insular cortex integrates visceral, pain, and temperature sensation. It is divided into an anterior and a smaller posterior part. The posterior part of the insula has a viscerotropic organization and receives input from the gustatory, visceral, muscle and skin receptors via the thalamus and projects to the right anterior insula, which integrates this input with emotional and cognitive processing to convey the conscious experience of bodily sensation. The insula carries a visceromotor function controlling sympathetic and parasympathetic outputs via a relay in the lateral hypothalamus.

The anterior cingulate cortex has extensive connections with the insula, prefrontal cortex, hypothalamus, amygdala, and brain stem and controls sympathetic and parasympathetic function. The hypothalamus is involved in homeostasis and adaptation by integrating autonomic and endocrine responses. Several brain stem areas are involved in autonomic nervous system control, including the periaqueductal gray matter of the midbrain, the parabrachial nucleus, and several parts of the medulla. The autonomic output of the CNS is divided into sympathetic and parasympathetic. In addition to thermoregulation, the sympathetic output is crucial for the maintenance of arterial pressure and regional blood flow. The sympathetic output originates from the preganglionic neurons located in the thoracolumbar spinal cord at the T1-L2 levels. These neurons are controlled by premotor neurons in the brain stem and hypothalamus to initiate appropriate responses to internal and external stressors such as

exercise and dehydration. The rostral ventrolateral medulla and lateral hypothalamic area, as well as other brain stem regions, host the main source of premotor sympathetic innervation.

The parasympathetic system output is formed by the vagal and sacral outputs and is responsible for mediating reflexes activated in an organ-specific fashion. The vagus nerve is the main parasympathetic innervation of the thoracic and abdominopelvic viscera. Eighty percent of vagal fibers are afferents with cell bodies originating from the superior and inferior vagal ganglion. The efferent fibers of the vagus nerve, preganglionic visceromotor fibers, originate from the dorsal motor nucleus of the vagus (DMV) and the nucleus ambiguus in the medulla oblongata. The nucleus of the tractus solitarius (NTS), the nucleus of the spinal tract of the trigeminal nerve, medial reticular formation of the medulla, area postrema, DMV, and the nucleus ambiguus host vagus nerve afferent projections. The vagal parasympathetic output to the heart originates primarily from the ventrolateral portion of the nucleus ambiguus via the cardiac ganglia. Output of the nucleus ambiguus is activated by the NTS during the baroreflex and inhibited during inspiration. The nucleus ambiguus output inhibits sinoatrial node automatism. The sacral parasympathetic output originates from neurons located at the S2–S4 segments of the sacral spinal cord and plays a critical role in the control of micturition, defecation, and sexual function.

The baroreflex and baroreceptors, located in the carotid sinus, aortic arch, and right atrium, are involved in blood pressure control and are activated by beat-to-beat fluctuation of systemic blood pressure. Receptors located in the carotid sinus and aortic arch are sensitive to reduction in pulse pressure, whereas receptors of the right atrium are more sensitive to alteration in blood volume. The NTS and the ventrolateral medulla receive afferents from the baroreceptors and send efferents to the insula and other autonomic centers for further processing. Brain stem and hemispheric cerebrovascular damage may affect the baroreflex causing blood pressure instability.

Results: The cluster analysis was used to determine two subgroups different in HRV parameters. The difference between them was the predominance of the sympathetic part of ANS: low SDNN ($p = 0.038$) due to sympathetic part of ANS activation (AMO, $p = 0.001$) and parasympathetic part depression (ΔX , $p = 0.02$). Mo (humoral influence on ANS status) was more in the first cluster ($p = 0.005$).

Conclusion: Significantly different for cohort of CCICI patients was found in HRV status. The first group CCICI patients was characterized by normal HRV corresponding to the values of the control group of older age. The group was characterized by sympathetic orientation of ANS and impaired humoral regulation of ANS function. The revealed difference in parameters of ANS in same clinical features indicates pathogenetic differences and further research direction.

Halinouskaya Natalia has completed his PhD at the age of 28 years from National Academy of Sciences of Belarus and postdoctoral studies from Gomel State Medical University and National Science and Practice Centre of Medical Assessment and Rehabilitation.

She is the Dean of the Postgraduates Faculty of the Gomel State Medical University, the coordinator of the Educational Program “Today and Tomorrow” for stroke patients and patients with stroke risk factors. She has published more than 150 papers in reputed journals and has been serving as an editorial board member of repute.