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Neurotransmitter reorganization of cognitive functions as the basis of brain adaptation under chronic hypoperfusion, dopaminergic and cholinergic systems

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Neurotransmitter organization of cognitive functions under chronic cerebral hypoperfusion (carotid ligation, 2VO model) can differ from norm and its own pharmacotherapy is required to treat delayed cognitive dysfunctions. In rats, the dopaminergic (DA) and cholinergic (ACh) mechanisms of rapid one-trial, working long-term memories and learning were studied on 2VO model. 6-7 days (7d) or 1 month (1M) after carotid ligation, rats were trained on the spatial contextual model in the Morris water maze and taken to a neurochemical experiment 2-3 days after the end of training. In synaptosomal subfractions of the cortex and hippocampus, the activity of the DA and ACh neurons markers, respectively, of tyrosine hydroxylase and choline acetyltransferase was estimated. The rats of control group (sham operated, SO) were divided into an upper quartile (the most capable rats); lower quartile (the incapable rats) and two middle quartiles according to their cognitive abilities. SO rats in each quartile had its own specificity of DA-ACh synaptic links (correlations) with cognitive functions, including also the same and differently directed links (positive-negative correlations). In the 7D group, the learning-memory was significantly impaired and the lower quartile rats dominated; DA influences on the functions completely disappeared, ACh influences significantly reduced or emerged new ones. In the 1M group, the functions were restored, but the level of upper quartile was reached only for long-term memory; only a few DA or ACh synaptic links were restored; new, including nonDA and nonACh links, dominated. DA and ACh reorganization of functions in 2VO rats was the result of degeneration or synaptogenesis of corresponding synaptic populations. A working hypothesis is that the neurotransmitter reorganization of cognitive functions is an obligatory consequence of the brain adaptation to hypoperfusion and altered blood supply of the brain. Such studies are required to determine the pharmacotherapy of delayed disturbance of cognitions.

Recent Publications

1. Liu Y, Dong YH Lyu PY, Chen WH and Li R (2018) Hypertension-induced cerebral small vessel disease leading to cognitive impairment. Chin Med J (Engl). 131:615-619.
2. Miyanohara J, Kakae M, Nagayasu K, Nakagawa T, Mori Y, Arai K, Shirakawa H and Kaneko S (2018) TRPM2 channel aggravates CNS inflammation and cognitive impairment via activation of microglia in chronic cerebral hypoperfusion. J Neurosci pii 2451-2417.
3. Duncombe J, Kitamura A, Hase Y, Ihara M, Kalaria RN and Horsburgh K (2017) Chronic cerebral hypoperfusion: a key mechanism leading to vascular cognitive impairment and dementia. Closing the translational gap between rodent models and human vascular cognitive impairment and dementia. Clin Sci (Lond) 131:2451-2468.
4. Du SQ, Wang XR, Xiao LY, Tu JF, Zhu W, He T and Liu CZ (2017) Molecular mechanisms of vascular dementia: what can be learned from animal models of chronic cerebral hypoperfusion? Mol Neurobiol 54:3670-3682.
5. Jayant S and Sharma B (2016) Selective modulator of cannabinoid receptor type 2 reduces memory impairment and infarct size during cerebral hypoperfusion and vascular dementia. Curr Neurovasc Res 13:289-302.

Biography

Elena I Zakharova is a Specialist in Neurophysiology and Neurochemistry. Using the original method of synaptic fractionation, she previously participated in studies that revealed a different cholinergic synaptic organization of cognitive functions in the brain of intact animals with different cognitive abilities. Under the leadership of MD Alexander Dudchenko (hypoxia, ischemia, biochemistry, molecular biology) and together with PhD Zinaida Storozheva (neurophysiology, neurodegenerative diseases, learning models) and PhD Mikhail Monakov (cerebral hypoperfusion, ischemia, surgery), she revealed a significant cholinergic reorganization of learning and memory under cerebral hypoperfusion in rats on the 2VO model. This suggested that the neurotransmitter reorganization of functions can play an important role in brain adaptation in these pathological conditions and that the new influences of neurotransmitters can maintain the damaged cognition. It was necessary to investigate other neurotransmitter systems and in more detail in the same pathological conditions.

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