

Mitochondria and glutamate-induced neurodegradation, the phospholipase A₂ as a target for the prevention of the degradation

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The study of the mitochondria participation in the neurodegradation upon stimulation of brain NMDA receptors with excitatory mediator glutamate (Glu) was carried out. Overstimulation of NMDA receptors is known to result in the disorder of Ca²⁺ homeostasis and severe mitochondrial depolarization followed by cell death. It has been shown that the overload of mitochondria with Sr²⁺ leads to the release of the cation, medium alkalization, decrease of membrane potential and mitochondrial swelling, indicating a nonspecific permeabilization of the mitochondrial membrane. The permeabilization, in our opinion, is caused by the activation of Ca²⁺/Sr²⁺-dependent phospholipase A₂ (PLA₂), resulting in the formation of free palmitic and stearic acids in the mitochondrial membrane. These fatty acids bind Ca²⁺ with high affinity, and the process of binding is accompanied by the formation of a transient lipid pore – a phenomenon demonstrated earlier on both artificial and mitochondrial membranes. The inhibitors of PLA₂ have been shown to suppress permeabilization of mitochondrial membranes. In the culture of granular cerebellum neurons, the PLA₂ inhibitors prolonged the lag of the delayed Sr²⁺ disregulation and membrane depolarization. On the basis of these data – obtained on both isolated mitochondria and neurons – we suppose that the initial stages of glutamate-induced Ca²⁺ disregulation of neurons are underlain by the opening of lipid pores in brain mitochondria. A possible role of PLA₂ inhibitors as new drugs prevented the development of neurodegradative diseases is discussed.

Biography

Galina D. Mironova received Ph.D degree in Biochemistry from Alma-Ata State Medical School in 1966 and Doctor Science degree in Biophysics from Institute of Theoretical and Experimental Biophysics RAS in 1985. She is the head of laboratory of mitochondrial transport of the Institute of Theoretical and Experimental Biophysics RAS, Pushchino, Russia. She has published more than 125 papers in reputed journals. Her current research interests center on the mitochondrial ion transport, cardioprotection and neurodegradation. She is the professor in Pushchino State University and given lectures on Cytopathology.

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