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Aberrant neuroplasticity in aging and neurodegeneration associated with deregulation of neurogenesis and angiogenesis

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Motivation and Aim: Neuroplasticity is a common phenomenon that underlies brain's response to the changing environment. Aging is always considered as a gradual loss of brain plasticity caused by impairment of synaptogenesis and neurogenesis, mitochondrial dysfunction, accumulation of misfolded proteins, development of oxidative stress, and excessive cell death [1]. Within neurogenic niches, neurogenesis is supported by local microvessels that provide the establishment of microenvironment needed for stem and progenitor cells maintenance and recruitment. Neoangiogenesis is required for effective neurogenesis and neuroblasts migration toward the loci of neurodegeneration. Moreover, coupling of neurogenesis and angiogenesis in the adult brain contributes to the experience-driven plasticity [2] which is greatly compromised in aging and neurodegeneration, thereby leading to cognitive decline.

Methods and Algorithms: We utilized neurogenic niche *in vitro*, *ex vivo* and *in vivo* models of for the assessment of the proliferative activity of neurospheres, extracellular lactate and NAD+ levels, expression of markers of neurogenesis, angiogenesis and neuroinflammation.

Results: *In vitro* neurogenic niche model has demonstrated its functionality in the context of assessing the proliferative and differentiation potential of NSCs/NPCs, as well as *in vitro* modeling of neurodegeneration (exposure to the neurotoxic beta-amyloid Aβ1-42). We found that neurosphere-forming capacity of hippocampal stem/progenitor cells (NSCs/NPCs) *in vitro* was differently compromised in aging animals and in rodents with the model of Alzheimer's type neurodegeneration. Photoactivated ChR2-expressing astrocytes within the niche increase the proliferative activity of NSCs, change the expression of key differentiation markers. In the presence of neurospheres, there was a decrease in the number of vascular tubes formed *in vitro* from brain microvessel endothelial cells (BMECs). However, glycolytic activity of astrocytes was required for efficient angiogenesis and barriergenesis.

Conclusion: Optogenetic activation of astrocytes is effective in controlling the activity of neurogenesis and cerebral angiogenesis and might be considered as a tool for correction of aging- or neurodegeneration-associated changes in brain plasticity.

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