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Stimulation of glutamatergic neuronal activity in the striatum enhances neurogenesis in the sub-ventricular zone of normal and stroke mice

Shan Ping Yu

Emory University, USA

Neurogenesis in the sub-ventricular zone (SVZ) of the adult brain may contribute to tissue repair after brain injuries. Although the regulation of neurogenesis by molecular genes and signal pathways has been extensively investigated, especially in the dentate gyrus (DG) of the hippocampus, whether SVZ neurogenesis can be regulated by neuronal activities is not well defined. Using the spatial and cell type specific optogenetic technique combined with multiple approaches of *in vitro*, *ex vivo* and *in vivo* examinations, we showed morphological and functional evidence of a novel neuronal link between the striatum and SVZ. Transgenic mice expressing the light-gated channelrhodopsin-2 (ChR2) channel in glutamatergic neurons, optogenetic stimulation of the glutamatergic activity in the striatum triggered glutamate release that consequently evoked membrane currents, Ca²⁺ influx and increased proliferation of SVZ neural stem cells, mediated by AMPA receptor activation. In ChR2 transgenic mice subjected to focal ischemic stroke, optogenetic stimuli to the striatum not only promoted cell proliferation but also the migration of neuroblasts into the peri-infarct cortex with increased neuronal differentiation and improved long-term functional recovery. These data provide the first morphological and functional evidence showing a unique striatum-SVZ connection that up-regulates SVZ neurogenesis and may be a therapeutic target for promoting adult neurogenesis and brain tissue repair.

Biography

Shan Ping Yu has received his PhD from Stony Brook University and Post-doctoral training in Neuroscience from the Howard Hughes Medical Institute. He is currently the O Wayne Rollins Endowed Chair Professor at Emory University. He has published more than 120 peer-reviewed papers in reputed journals such as *Science*, *PNAS*, *Journal of Neuroscience*, *FASEB Journal*, *Journal of Cerebral Blood Flow and Metabolism*, *Cell Death and Differentiation* and *Neurobiology of Diseases and Stroke*. He has been serving as an Editorial Board Member of more than 10 scientific journals.

ingrid.lang@medunigraz.at

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