Anatomy of the whole neurogenic system in adulthood, connection with fractones, meninges, choroid plexus, and a functional test for investigating relevance to neural stem cell fate decision*

Frederic Mercier, Deep Matrix Microsystems, Manoir de Keryvoas, Kerlouan
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Numerous scientific investigators consider as granted that several neurogenic zones exist in the adult brain. Here, we used dual immunohistochemistry for heparan sulfate proteoglycans (HSPG) and Bromodeoxyuridine on serial sections throughout the whole brain of the adult mouse to investigate neurogenesis anatomy. We show that neurogenesis occurs in a continuous single axis that comprises the subventricular zone (SVZ) of the caudate nucleus, of the amydala, the rostral migratory stream, the olfactive bulb and the sub-callosal zone. We counted more than 30,000 proliferating cells through the neurogenic axis in all three mice, and counted the relative numbers of proliferating cells along the neural structures. Moreover, HSPG immunoreactivity demonstrated the trajectory of the whole neurogenicaxis, and the dual presence of fractones -the punctate extracellular matrix structures that bind and activate neurogenic growth factors- and the vascular niche that comprise the caudate artery and can be traced downstream up to the Circle of Willis. Moreover, HSPG immunoreactivity revealed associated structures, meninges and choroid plexus. Multiple mmunoreactivity for gap junction connexin 26 (Cx26), CX43 and S100beta further revealed a meningeal fibroblast network that connect to the neurogenic axis. To determine whether this meningeal network is functionally implicated in the regulation of neurogenesis, we used 6 hydroxydopamin (6OHDA) supplemented with a neuroprotectant to focally induce the death of fibroblasts far away at the surface of the brain while assessing the effect of this treatment on cell proliferation in the neurogenic axis. We show that neurogenesis is significantly increased in the SVZ when the path of the meningeal network is chemically cut at the surface of the falx cerebri, while there is no effect of killing fibroblasts in other meningeal zones of the dorsal brain surface, This suggests the presence of sub-networks of fibroblasts involved in stem cell fate decision. Our results show that adult neurogenesis occurs in a single axis in the adult mouse. Our results also demonstrate the existence of a system of connection with the meninges. We anticipate that neurogenesis functions via a ubiquitous biological unit system, which operates through a long distance intercellular communication meningeal network, but locally acts through a series of fractones in the neurogenic axis to control the production of new neurons and glia throughout adulthood.