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Abstracts

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spinogenesis and also cognitive impairment. It is currently hypothesized that proliferative and differentiation alterations in neural progenitor cells (NPC) may contribute to DS pathophysiology. Previous studies have demonstrated that astrocytes and NPC can influence each other, but, at present, the potential contribution of dysfunctional astroglia in DS neuropathology is largely unexplored. Recently, through a proteomic approach, we could identify several novel astrocyte-derived proteins with a modulatory role on NPC proliferation and differentiation (Cvijetic S. et al., Glia, 2017, 65(1):169-181). Based on these initial findings, we decided to investigate whether astrocyte-NPC cross talk could be dysregulated in DS. To this aim, we generated primary astrocytes and NPC from the subventricular zone and hippocampus of Ts65Dn (Trisomic, TS) and euploid (EU) neonatal mice and evaluated the proliferation rate and differentiation potential of TS and EU NPC in presence of TS/EU astroglial-conditioned media (ACM). We could demonstrate that EU NPC were responding to soluble astrocytic signals, whereas TS NPC were generally unresponsive to them. Moreover, TS ACM, but not EU ACM, significantly reduced neuronal differentiation of EU NPC. All together these data suggested that in DS astrocyte-NPC communication may be dysregulated due to both cell autonomous and non-cell autonomous defects. By a proteomic analysis we could finally identify several soluble factors which were differentially released by TS/EU astrocytes and we now propose that specific signaling pathways involved in astroglia-NPC cross-talk are altered in DS.

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Astrocyte-generated neuroblasts functionally integrate in the QA-lesioned striatum

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After Quinolinic Acid lesion subsets of striatal astrocytes undergo a spontaneous neurogenic activation leading to the local generation of a large amount of neuroblasts up to at least months post-lesion. Yet the fate and the occurrence of functional integration of these newborn cells remain essentially unexplored. Fate mapping and 3D reconstruction analysis show that neuroblasts undergo a maturation process in which initially, they organize in cluster, subsequently disperse as individual cells, and gradually attain complex morphologies often showing dendritic spines. Yet, similar to other models of physiological and lesion-induced striatal neurogenesis, striatal newborn neurons live transiently and fail to express typical markers of striatal neurons. Nonetheless, monosynaptic rabies virus-based tracing technique revealed that neuroblasts receive local inputs from striatal projection neurons and interneurons as well as long-range inputs from Electrophysiological recordings confirmed the neuronal nature of these cells and their synaptic integration. Further, we found that some individual neuroblasts receive excitatory inputs, while others, likely consistent with a more mature status, become also able to receive inhibitory inputs and to fire trains of action potentials when subjected to depolarizing current steps.
These results indicate that striatal neuroblasts functionally interact with pre-existing circuits, thus potentially taking part in post-lesion network plasticity supporting functional recovery after damage.