“Interactions between Interneurons and Oligodendrocyte Precursors during Cortical Development”

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The fast conduction velocity of action potentials in the central nervous system (CNS) depends on myelin sheaths that enwrap neuronal axons. Myelin in the CNS is produced by a glial cell type named oligodendrocytes (OLs). During development, oligodendrocyte precursor cells (OPCs) constitute the major source of myelinating OLs. Interestingly, these progenitors are the only nonneuronal cells receiving synaptic inputs from neurons in the CNS. However, the operating modes and functions of these neuron-glia synapses are still poorly understood. Our team described a transient synaptic connectivity between GABAergic interneurons and OPCs in the developing neocortex (Velez-Fort et al., 2010, J Neurosci). We have examined the properties of individual interneuron-OPC synapses from the subcellular to the network level during the critical period for oligodendrogenesis. We have used paired recordings, holographic photolysis for circuit mapping and immunohistochemistry. Our findings have shown that the GABAergic innervation of OPCs form a structured synaptic network that is temporally and spatially regulated in coordination with the onset of oligodendrogenesis (Orduz et al., 2015, eLife). In a more recent study, we also showed that a subpopulation of embryonic OPCs survives in the mouse postnatal neocortex and forms functional cell clusters with GABAergic interneurons arisen from the same embryonic origin (Orduz et al., submitted). However, GABAergic synapses do not seem to play a major role in OPC proliferation and differentiation. Indeed, we genetically inactivated a specific GABAergic synapse of OPCs by deleting the 2 subunit of postsynaptic GABA-A receptors in oligodendroglia and did not obseve changes in the proliferative OPC fraction or OPC differentiation into myelinating OLs (Balia et al., 2015, Cerb Cortex ; Balia et al., 2017, Glia). Nevertheless, this inactivation causes a progressive and specific depletion of the OPC pool that lacks 2-mediated synaptic activity without affecting the OL production. In conclusion, the GABAergic synaptic connectivity of OPCs is highly regulated in time and space during cortical development. Our results also suggest that these synapses finely tune OPC selfmaintenance capacity and open the interesting possibility that a particular synaptic signaling onto OPCs plays a specific role in OPC function according to the neurotransmitter released, the identity of presynaptic neurons or the postsynaptic receptors involved.