Myelination of parvalbumin interneurons shapes cortical inhibition

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Oligodendrocyte precursor cells (OPCs) represent the only non-neuronal cells that receive *bona fid*e synapses from neurons in the CNS. The function of these synapses remains poorly understood. We previously showed that OPCs in the cerebral cortex are primarily and transiently innervated by fast-spiking parvalbumin-expressing (PV) interneurons. Interestingly, PV interneurons represent the largest proportion of cortical myelinated GABAergic neurons. To investigate the role of PV interneuron-OPC synapses, we genetically inactivated γ2-mediated GABAergic synaptic signaling in OPCs. This inactivation does not affect OPC proliferation and differentiation or the cortical developmental myelination pattern. However, the disruption of GABAergic synaptic signaling of OPCs prior to myelination onset resulted in severe PV interneuron myelination defects characterized by longer internodes and nodes and a proximal axon malformation. Consequently, high-frequency PV interneuron discharges as well as PV interneuron-dependent postsynaptic latencies and strengths of excitatory neurons were reduced during postnatal development. These dysfunctions generated a strong excitation-inhibition imbalance that was associated with whisker-dependent texture discrimination impairments. We concluded that, during cortical development, the inactivation of γ2-mediated OPC synapses have profound consequences in the myelination of PV interneurons, affecting the function of mature cortical inhibitory circuits. PV interneuron-OPC synaptic activity during postnatal development constitute a key step in the construction of cortical circuits involved in rapid and strong inhibition during sensory processing.