Role of GABAergic Interneurons in Mediating Early Life Experiences and Implications in Psychiatric Illnesses

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Neural circuits are shaped by experience during critical periods of development, allowing individuals to uniquely adapt their behaviors to the surrounding environment. As such, early life experiences exert profound long-term effects on the susceptibility to mood disorders in adolescents and adults. The developing mouse somatosensory cortex receives an array of sensory stimuli at a time when neural networks are dominated by intrinsically generated synchronous activity. This provides an excellent model for studying how experience interacts with intrinsic programs to shape the representation of the external world in the brain. To determine the network activity of distinct neuronal populations, we developed a longitudinal *in vivo* two-photon calcium imaging preparation in neonatal mice that allows them to be imaged into adulthood. Using this technique combined with electrophysiology, rabies synaptic tracing and genetic approaches, we established the functional significance of early network activities in two interneuron subtypes: the layer-1 (L1) reelin-expressing (Re) interneurons and the medial ganglionic eminence (MGE)-derived interneurons including parvalbumin (Pv) and somatostatin (Sst) interneurons. The L1 Re interneurons restrict spontaneous L2/3 excitatory neurons activation to promote sensory map formation; the MGE-derived interneurons, on the other hand, co-activate with excitatory neurons in spatially segregated assemblies. This unique assembly pattern is a critical determinant of interneuron apoptosis, fundamental for balancing the circuit E/I ratio. These findings put forth the concept that the population specificity and pattern of network activity have significant functional consequences on circuit maturation. We are currently expanding our efforts to understand how different types of early life experiences, such as social bonding and stress, impact circuit assembly and mature function.

1. Che A, De Marco García NV. An in vivo calcium Imaging approach for the identification of cell-type specific patterns in the developing cortex. **Front Neural Circuits** 15, 747724 (2021).
2. Duan ZS*, Che A*, Chu P* et al. GABAergic Restriction of Network Dynamics Regulates Interneuron Survival in the Developing Cortex. **Neuron** 105, 1-13 (2020). * Equal contribution.
3. Che A et al. Layer I interneurons sharpen sensory maps during neonatal development. **Neuron** 99, 98-116 (2018).