UKE Paper of the Month November 2019

Resolving and Rescuing Developmental Miswiring in a Mouse Model of Cognitive Impairment

Chini M, Pöpplau JA, Lindemann C, Carol-Perdiguer L, Hnida M, Oberländer V, Xu X, Ahlbeck J, Bitzenhofer SH, Mulert C, Hanganu-Opatz IL

Neuron

ABSTRACT:

Cognitive deficits, core features of mental illness, largely result from dysfunction of prefrontal networks. This dysfunction emerges during early development, before a detectable behavioral readout, yet the cellular elements controlling the abnormal maturation are still unknown. Here, we address this open question by combining in vivo electrophysiology, optogenetics, neuroanatomy, and behavioral assays during development in mice mimicking the dual genetic-environmental etiology of psychiatric disorders. We report that pyramidal neurons in superficial layers of the prefrontal cortex are key elements causing disorganized oscillatory entrainment of local circuits in beta-gamma frequencies. Their abnormal firing rate and timing relate to sparser dendritic arborization and lower spine density. Administration of minocycline during the first postnatal week, potentially acting via microglial cells, rescues the neuronal deficits and restores pre-juvenile cognitive abilities. Elucidation of the cellular substrate of developmental miswiring causing later cognitive deficits opens new perspectives for identification of neurobiological targets amenable to therapies.

STATEMENT:

In a mouse model of mental disorders, Chini et al. dissect an early-emerging prefrontal network dysfunction that subsequently gives rise to cognitive deficits. We show that this deficiency can be rescued by minocycline administration, thus identifying a potential biomarker amenable for future therapies.

BACKGROUND:

This work was performed at the group Developmental Neurophysiology (head: Prof. Dr. Ileana Hanganu-Opatz), Institute of Neuroanatomy, in collaboration with the Psychiatry Neuroimaging Branch, Department of Psychiatry and Psychotherapy (Prof. Dr. Christoph Mulert). It is part of the PhD thesis of Mattia Chini. The project was funded by the ERC (Consolidator Grant 681577 “Psychocell” to I. Hanganu-Opatz) and DFG (SPP 1665, SFB 936 and FOR 2419). The group of Prof. Hanganu-Opatz has strong interests in understanding the development of neuronal networks by combining electrophysiology, optogenetics and behavior.