UKE Paper of the Month Mai 2021

A transient developmental increase of prefrontal activity alters network maturation and causes cognitive dysfunction in adult mice

Sebastian H. Bitzenhofer, Jastyn A. Pöpplau, Mattia Chini, Annette Marquardt & Ileana L. Hanganu-Opatz

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ABSTRACT:
Disturbed neuronal activity in neuropsychiatric pathologies emerges during development and might cause multifold neuronal dysfunction by interfering with apoptosis, dendritic growth, and synapse formation. However, how altered electrical activity early in life impacts neuronal function and behavior of adults is unknown. Here, we address this question by transiently increasing the coordinated activity of layer 2/3 pyramidal neurons in the medial prefrontal cortex of neonatal mice and monitoring long-term functional and behavioral consequences. We show that increased activity during early development causes premature maturation of pyramidal neurons and affects interneuronal density. Consequently, altered inhibitory feedback by fast-spiking interneurons and excitation/inhibition imbalance in prefrontal circuits of young adults result in weaker evoked synchronization in gamma frequency. These structural and functional changes ultimately lead to poorer mnemonic and social abilities. Thus, prefrontal activity during early development actively controls the cognitive performance of adults and might be critical for cognitive symptoms in neuropsychiatric diseases.

STATEMENT:
Our work provides the first proof that early brain activity matters. Bitzenhofer, Pöpplau et al. manipulate the early activity in the prefrontal cortex of neonatal mice, resulting in disruption of coordinated patterns of electrical activity, excitation-inhibition imbalance and impaired cognitive abilities at adult age. Thus, prefrontal activity during development is critical for the adult network function and behavioral performance.

BACKGROUND:
This work was performed at the Institute of Developmental Neurophysiology (Director: Prof. Dr. Ileana L. Hanganu-Opatz). It is part of the postdoc project of Dr. Sebastian H. Bitzenhofer and the PhD thesis of Jastyn A. Pöpplau who share the first authorship. The project was funded by the ERC (2015-CoG 681577 to I. L. Hanganu-Opatz) and DFG (Ha 4466/10-1, Ha4466/11-1, Ha4466/12-1, SPP 1665 and SFB 936 B5 to I. L. Hanganu-Opatz). The group of Prof. Hanganu-Opatz has strong interests in understanding the development of neuronal networks by combining electrophysiology, optogenetics and behavior.