# UKE Paper of the Month Dezember 2021

## Developmental decrease of entorhinal-hippocampal communication in immune-challenged DISC1 knockdown mice

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**ABSTRACT:**
The prefrontal-hippocampal dysfunction that underlies cognitive deficits in mental disorders emerges during early development. The lateral entorhinal cortex (LEC) is tightly interconnected with both prefrontal cortex (PFC) and hippocampus (HP), yet its contribution to the early dysfunction is fully unknown. Here we show that mice that mimic the dual genetic (G) -environmental (E) etiology (GE mice) of psychiatric risk have poor LEC-dependent recognition memory at pre-juvenile age and abnormal communication within LEC-HP-PFC networks throughout development. These functional and behavioral deficits relate to sparser projections from LEC to CA1 and decreased efficiency of axonal terminals to activate the hippocampal circuits in neonatal GE mice. In contrast, the direct entorhinal drive to PFC is not affected, yet the PFC is indirectly compromised, as target of the under-activated HP. Thus, the entorhinal-hippocampal circuit is already impaired from neonatal age on in GE mice.

**STATEMENT:**
*Our work identifies the lateral entorhinal cortex as developmental gatekeeper of schizophrenia-related dysfunction of prefrontal-hippocampal circuits and memory deficits.*

**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. Xiaxia Xu as well as the PhD thesis of Lingzhen Song and MD thesis of Rebecca Kringel. The project was funded by grants from European Research Council (ERC-2015-CoG 681577) and German Research Foundation (SFB 936 B5, Ha4466/11-1). The institute of Prof. Hanganu-Opatz has strong interests in understanding the development of neuronal networks in health and psychiatric disease by combining electrophysiology, optogenetics and behavior.