UKE Paper of the Month November 2018

Arc/Arg3.1 mediates a critical period for spatial learning and hippocampal networks

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ABSTRACT: During early postnatal development sensory regions of the brain undergo periods of heightened plasticity which sculpt neural networks and lay the foundation for adult sensory perception. Such critical periods were also postulated for learning and memory, but remain elusive and poorly understood. Here we present evidence that the activity regulated and memory-linked gene Arc/Arg3.1 is transiently up-regulated in the hippocampus during the first postnatal month. Conditional removal of Arc/Arg3.1 during this period permanently alters hippocampal oscillations and diminishes spatial learning capacity throughout adulthood. In contrast, removal of Arc/Arg3.1 post-developmentally leaves learning and network activity patterns intact. Long-term memory storage continues to rely on Arc/Arg3.1 expression throughout life. These results demonstrate that Arc/Arg3.1 mediates a critical period for spatial learning, during which Arc/Arg3.1 fosters maturation of hippocampal network activity necessary for future learning and memory storage.

STATEMENT: *The study by Gao et al., in the interdisciplinary journal PNAS addresses the long debated question: Do critical periods exist for learning and memory? Using genetically-engineered mouse models, biochemical and molecular tools, behavior analysis, and in vivo electrophysiology, the study shows, for the first time, that this is indeed the case. During a critical period in the development of the brain, the plasticity- and memory-linked Arc/Arg3.1 gene is activated and is responsible for establishing neuronal networks, which are required later for complex learning in adulthood.*

These findings will pave the way to understand how regulation of Arc/Arg3.1 by genetic, environmental factors, as well as experience during childhood can determine adult cognitive capacity. The ultimate goal will be to provide optimal environments for child-raising and better treatments for neuropsychiatric conditions in which brain development was disturbed. This study has drawn much public attention and was featured in the media including Die Welt, Süddeutsche Zeitung, Die Zeit, Focus, Bild and many others.

BACKGROUND: This study was conducted in the Institute for Molecular and Cellular Cognition of the ZMNH and directed by Professor Dietmar Kuhl and Dr. Ora Ohana. The first authors: Xiaoyan Gao, Sergio Castro-Gomez and Jasper Grendel performed the research work during their Ph.D. and postdoctorate, they put a great amount of work, knowledge, talent, and enthusiasm into this project. *In vivo* brain recordings were established and performed in close collaboration with Professor Dirk Isbrandt in Hamburg and later in Cologne. Funding was provided by a DFG grant to SFB 936 Project B4 and by the Landesforschungsförderung Molekulare Mechanismen der Netzwerkmodifizierung.