UKE Paper of the Month November 2022

ΔFosB accumulation in hippocampal granule cells drives cFos pattern separation during spatial learning

Lamothe-Molina PJ, Franzelin A, Beck L, Li D, Auksutat L, Fieblinger T, Laprell L, Ahlbeck J, Gee CE, Kneussel M, Engel AK, Hilgetag CC, Morellini F, Oertner TG.

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ABSTRACT:

Mice display signs of fear when neurons that express cFos during fear conditioning are artificially reactivated. This finding gave rise to the notion that cFos marks neurons that encode specific memories. Here we show that cFos expression patterns in the mouse dentate gyrus (DG) change dramatically from day to day in a water maze spatial learning paradigm, regardless of training level. Optogenetic inhibition of neurons that expressed cFos on the first training day affected performance days later, suggesting that these neurons continue to be important for spatial memory recall. The mechanism preventing repeated cFos expression in DG granule cells involves accumulation of ΔFosB, a long-lived splice variant of FosB. CA1 neurons, in contrast, repeatedly expressed cFos. Thus, cFos-expressing granule cells may encode new features being added to the internal representation during the last training session. This form of timestamping is thought to be required for the formation of episodic memories.

STATEMENT:

The paper is one of the first studies using optogenetic manipulation in the water maze. It revealed a form of epigenetic repression that was not previously reported in the hippocampus. It provides a new concept about the representation of time in the brain, particularly during spatial learning.

BACKGROUND:

This work is a collaboration between the research groups of Thomas Oertner, Fabio Morellini, Claus Hilgetag, Matthias Kneussel and Andreas Engel, who share a common interest in unravelling the mechanisms of learning and memory on the cellular and molecular level. The work was generously funded by the DFG trough SFB 936 (Project B7) and FOR 2419.