Reversible loss of neuronal function in a mouse model of demyelination/remyelination

Das et al.

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Objective

Multiple sclerosis (MS) is an inflammation-mediated demyelinating disease of the central nervous system, which affects the lives of more than two million patients worldwide. MS was traditionally thought to affect mainly the white matter of the brain, but today it is accepted that it also significantly impacts gray matter physiology. Current technologies for recording brain activity in MS animal models are informative, but can only detect changes over scales of several millimeters or larger. Thus these methods are unable to identify changes in axons, dendrites, individual neurons, or local circuits.

Methods

In this study, we used a cuprizone-based mouse model of demyelination to study cellular-resolution changes in hippocampal activity over more than 100 days using two-photon imaging of the fluorescence signal from a genetically-encoded calcium indicator.

Results

We show that cuprizone-induced demyelination of the hippocampus is correlated with a significant decrease in the activity of CA1 and dentate gyrus neurons. This reduction in hippocampal activity also correlated with spatial-memory deficits identified in these mice. Upon the termination of cuprizone diet, we identified a partial recovery of the hippocampal activity within several days.

Conclusion

Therefore, this work demonstrates long-term recording of demyelination- and remyelination-induced modulations of the brain activity patterns, which underlies some of the MS-like deficits identified in these mice.