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Revisiting tau involvement in complex neural network remodelling through the analysis of extra-cellular neuronal activity exhibited by organotypic brain slice co-cultures

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State of the art: Considering the involvement of tau in tauopathies and the protective effect of its ablation in epilepsy due to hyperexcitability/hypersynchrony inhibition, deciphering tau functions in brain networks is paramount. However, tau functions are difficult to highlight as brain networks from tauKO (Mapt-/-) mice exhibit only elusive phenotypes. This study aimed to further explore the physiological role of tau in network remodelling.
Methodology: The impact of tau ablation was investigated in hippocampal/entorhinal slice co-cultures. We recorded spontaneous extracellular neuronal activity over two weeks from single-slice cultures and slice co-cultures established from control and tauKO animals. We compared bursting activity features and applied concepts and analytical tools intended for the study of network synchrony and connectivity.
Results: Comparison of control and tauKO co-cultures revealed that tau ablation had an anti-synchrony effect on hippocampal-entorhinal two-slice networks at late stages of co-culture, in line with literature. Focusing on the differences between single- and co-culture paradigms demonstrated tau ablation led to differential, even opposite, effects at the sub-network scale. Tau ablation induced an anti-synchrony effect likely due to an excitation/inhibition ratio reduction within the hippocampal slice throughout the co-culture. Conversely, tau ablation led to increased synchrony likely due to homogenization of the connectivity distribution within the entorhinal slice at early stages.
Conclusion: The new methodology we presented here has been proven successful to investigate the role of tau in the remodelling of complex brain-derived networks as it demonstrated, for the first time, this role is multifaceted and dependent of the sub-network nature.

Conflicts of interest

N/A