Seminar/Talk

Glutamatergic drivers for spatial orientation and Tau propagation

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Host: Sandra Siegert

Deficits in spatial navigation and orientation are associated with early cognitive decline prior to Alzheimers disease. The apparent spread of pathological misfolded forms of the Tau protein (pTau) across different areas of the cerebral cortex correlates with cognitive decline, and this is thought to be initially driven by the spread of pTau from the entorhinal cortex to the hippocampus. The anterior thalamus acts as a relay for sensorimotor messages concerning orientation and space to reach the cortex. We observed in post-mortem human thalamus that the anterodorsal nucleus is unusually vulnerable to pTau at all stages of disease progression, even in cognitively unimpaired cases. Using double-labelling pre-embedding immunohistochemistry and electron microscopy, we discovered that large glutamatergic presynaptic terminals from the mammillary body accumulated pTau, but corticothalamic terminals did not, even at the stage before Alzheimers disease. Furthermore, we detected pTau+ filaments at both presynaptic and postsynaptic sites, suggesting a previously unrecognized subcortical route for the transsynaptic spread of Tau in the human brain. The anterodorsal nucleus contains a high density of head direction (HD) cells, but the neurochemical identity and synaptic targets of individual thalamic HD cells are unknown. We use extracellular recordings and juxtacellular labelling in awake mice to define single HD cells in order to make predictions about the consequences of their dysfunction in humans. Spatial orientation deficits, relating to activity in the anterodorsal nucleus, could be a good predictor of future cognitive impairment leading to Alzheimers disease.

Friday, July 14, 2023 03:00pm - 04:00pm

Sunstone Bldg / Ground floor / Big Seminar Room A + B (I23.EG.102)

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