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MSB 160

Division of Medical Sciences Seminar Series 2023 – 2024

Astroglia in ageing in neurodegeneration: Challenging "inflammageing" of the brain: glial paralysis, rather than reactivity defines brain ageing and opens the gate for neurodegeneration

Ageing is associated with morphological and functional remodelling of astrocytes with a prevalence of morphological atrophy and loss of function, not of the widely popularised 'inflammation'. In particular ageing is associated with (i) decrease in astroglial synaptic coverage; (ii) deficits in glutamate and potassium clearance; (iii) reduced astroglial synthesis of synaptogenic factors such as cholesterol; (iv) decrease in aquaporin 4 channels in astroglial endfeet with subsequent decline in the glymphatic clearance; (v) decrease in astroglial metabolic support through the lactate shuttle; (vi) adult neurogenesis resulting from diminished decreased proliferative capacity of radial stem astrocytes; (vii) decline in the astroglial-vascular coupling and deficient blood-brain barrier and (viii) decrease in astroglial ability to mount reactive astrogliosis. Decrease in reactive capabilities of astroglia as well as degeneration off dystrophy of microglia are permissive for age-dependent neurodegenerative diseases. Neuroglial morphology and function can be influenced and improved by lifestyle interventions such as intellectual engagement, social interactions physical exercise, caloric restriction, and healthy diet. These modifications of lifestyle are paramount for cognitive longevity.