Astrocyte Biomarkers in Alzheimer's Disease

Astrocytic contributions to Alzheimer's disease (AD) progression were, until recently, largely overlooked. Astrocytes are integral to normal brain function and astrocyte reactivity is an early feature of Alzheimer's disease, potentially providing a promising target for preclinical Alzheimer's Disease diagnosis and Alzheimer's Disease treatment. Several in vivo Alzheimer's Disease biomarkers already exist, but presently there is a paucity of specific and sensitive in vivo astrocyte biomarkers that can accurately measure preclinical AD. Measuring monoamine oxidase-B with neuroimaging and glial fibrillary acidic protein from bodily fluids are biomarkers that are currently available. Developing novel, more specific, and sensitive astrocyte biomarkers will make it possible to pharmaceutically target chemical pathways that preserve beneficial astrocytic functions in response to AD pathology [1)]

A meta-analysis demonstrated that astrocyte biomarkers are consistently altered in AD and supports further investigation for their inclusion in the AD clinical research framework for observational and interventional studies [2)]

Ferrari-Souza et al. assessed 121 individuals across the aging and Alzheimer's disease clinical spectrum with positron emission tomography (PET) brain imaging for Aβ ([18F]AZD4694) and tau ([18F]MK-6240), as well as CSF GFAP and YKL-40 measures. They observed that higher CSF GFAP levels were associated with elevated Aβ-PET but not tau-PET load. By contrast, higher CSF YKL-40 levels were associated with elevated tau-PET but not Aβ-PET burden. Structural equation modeling revealed that CSF GFAP and YKL-40 mediate the effects of Aβ and tau, respectively, on hippocampal atrophy, which was further associated with cognitive impairment. The results suggest the existence of distinct astrocyte biomarker signatures in response to brain Aβ and tau accumulation, which may contribute to the understanding of the complex link between reactive astrogliosis heterogeneity and Alzheimer's Disease progression [3)].

1)
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2)
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3)
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