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 AD progression [1].

Alzheimer disease (AD)-related pathology was assessed in cortical biopsy samples of 111 patients with idiopathic normal pressure hydrocephalus. Alzheimer disease hallmark lesions-amyloid beta (Aβ) and hyperphosphorylated tau (HPtau)-were observed in 47% of subjects, a percentage consistent with that for whole-brain assessment reported postmortem in unselected cohorts. Higher-immunostained area fraction of AD pathology corresponded with lower preoperative mini-mental state examination scores. Concomitant Aβ and HPtau pathology, reminiscent of that observed in patients with AD, was observed in 22% of study subjects. There was a significant correlation between Aβ-immunostained area fraction in tissue and Aβ42 (42-amino-acid form of Aβ) in cerebrospinal fluid (CSF). Levels of Aβ42 were significantly lower in CSF in subjects with concomitant Aβ and HPtau pathology compared with subjects lacking pathology. Moreover, a significant correlation between HPtau-immunostained area fraction and HPtau in CSF was noted. Both HPtau and total tau were significantly higher in CSF in subjects with concomitant Aβ and HPtau pathology compared with subjects lacking pathology. The 42-amino-acid form of Aβ (Aβ42) and HPtau in CSF were the most significant predictors of the presence of AD pathology in cortical biopsies. Long-term follow-up studies are warranted to assess whether all patients with idiopathic normal-pressure hydrocephalus with AD pathology progress to AD and to determine the pathologic substrate of idiopathic normal-pressure hydrocephalus [2].

1)
Ferrari-Souza JP, Ferreira PCL, Bellaver B, Tissot C, Wang YT, Leffa DT, Brum WS, Benedet AL, Ashton NJ, De Bastiani MA, Rocha A, Therriault J, Lussier FZ, Chamoun M, Servaes S, Bezgin G, Kang MS, Stevenson J, Rahmouni N, Pallen V, Poltronetti NM, Klunk WE, Tudorascu DL, Cohen AD, Villemagne VL, Gauthier S, Blennow K, Zetterberg H, Souza DO, Karikari TK, Zimmer ER, Rosa-Neto P, Pascoal TA. Astrocyte biomarker signatures of amyloid-β and tau pathologies in Alzheimer's disease. Mol Psychiatry. 2022 Aug 10. doi: 10.1038/s41380-022-01716-2. Epub ahead of print. PMID: 35948658.
2)
Elobeid A, Laurell K, Cesarini KG, Alafuzoff I. Correlations Between Mini-Mental State Examination Score, Cerebrospinal Fluid Biomarkers, and Pathology Observed in Brain Biopsies of Patients With Normal-Pressure Hydrocephalus. J Neuropathol Exp Neurol. 2015 May;74(5):470-479. PubMed PMID: 25868149.