The hippocampus and entorhinal cortex (EC), the earliest affected areas, are considered relative to early memory loss in Alzheimer's disease (AD). The hippocampus is composed of heterogeneous subfields that are affected in a different order and varying degrees during Alzheimer's disease pathogenesis. Gao et al. conducted a comprehensive proteomics analysis of the hippocampal subfields and EC region in human postmortem specimens obtained from the Chinese human brain bank. Bioinformatics analysis identified region-consistent differentially expressed proteins (DEPs) which associated with astrocytes, and region-specific DEPs which associated with oligodendrocytes and the myelin sheath. Further analysis illuminated that the region-consistent DEPs functioned as connection of region-specific DEPs. Moreover, in region-consistent DEPs, the expression level of S100A10, a marker of protective astrocytes, was increased in both aging and AD patients. Immunohistochemical analysis confirmed an increase in the number of S100A10-positive astrocytes in all hippocampal subfields and the EC region of AD patients. Dual immunofluorescence results further showed that S100A10-positive astrocytes contained apoptotic neuron debris in AD patients, suggesting that S100A10-positive astrocytes may protect brain through phagocytosis of neuronal apoptosis. In region-specific DEPs, the proteome showed a specific reduction of oligodendrocytes and myelin markers in CA1, CA3, and EC regions of AD patients. Immunohistochemical analysis confirmed the loss of myelin in EC region. Above all, these results highlight the role of the glial cells in AD and provide new insights into the pathogenesis of AD and potential therapeutic strategies [1)].

1)
Gao Y, Liu J, Wang J, Liu Y, Zeng LH, Ge W, Ma C. Proteomic analysis of human hippocampal subfields provides new insights into the pathogenesis of Alzheimer's disease and the role of glial cells. Brain Pathol. 2022 Jan 11:e13047. doi: 10.1111/bpa.13047. Epub ahead of print. PMID: 35016256.