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Adaptive lymphocyte profiles correlate to brain Aβ burden in patients with mild cognitive impairment

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Background: We previously found that subjects with amnestic mild cognitive impairment exhibit a pro-inflammatory immune profile in the cerebrospinal fluid similar to multiple sclerosis, a central nervous system autoimmune disease. We therefore hypothesized that early neuroinflammation would reflect increases in brain amyloid burden during amnestic mild cognitive impairment.

Methods: Cerebrospinal fluid and blood samples were collected from 24 participants with amnestic mild cognitive impairment (12 men, 12 women; 66±6y; 0.5 Clinical Dementia Rating) enrolled in the AETMCI study. Analyses of cerebrospinal fluid and blood included immune profiling by multi-parameter flow cytometry, genotyping for apolipoprotein (APO)ε, and quantification of cytokine and immunoglobin levels. Amyloid (A)β42 deposition was determined by 18F-florbetapir positron emission tomography. Spearman rank order correlations were performed to assess simple linear correlation for parameters including amyloid imaging, central and peripheral immune cell populations, and protein cytokine levels.

Results: There was a significant decline in solube Aβ42 in the cerebrospinal fluid as mean brain Aβ42 deposition, as well as amyloid burden in the precuneus and posterior cingulate cortices, increased. Lymphocyte profiling revealed a significant decline in T cell populations in the cerebrospinal fluid, specifically CD4+ T cells, as Aβ42 deposition in the posterior cingulate cortex increased. In contrast, increased Aβ42 burden correlated positively with increased memory B cells in the cerebrospinal fluid, which was exacerbated in APOε4 carriers. For peripheral circulating lymphocytes, only B cell populations decreased with Aβ42 deposition in the precuneus cortex, as peripheral T cell populations did not correlate with changes in brain amyloid burden.

Conclusions: Elevations in brain Aβ42 burden associate with a shift from T cells to memory B cells in the cerebrospinal fluid of subjects with amnestic mild cognitive impairment in this exploratory cohort. These data suggest the presence of cellular adaptive immune responses during Aβ accumulation, but further study needs to determine whether lymphocyte populations contribute to, or result from, Aβ dysregulation during memory decline on a larger cohort collected at multiple centers.

Speaker Biography

Ann M Stowe has completed her PhD in Molecular & Intergrative Physiology from the University of Kansas, and a Post-dotoral Fellowship fromWashington University in St. Louis. She is currently an Assistant Professor in the Dept. of Neurology at UT Southwestern Medical Center in Dallas. Her research focuses on the role of neuroinflammation in CNS injury and repair in both preclinical mouse models of stroke, as well as clinical studies involving patients with either stroke or amnestic mild cognitive impairment (aMCI).

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