Inflammatory Biomarkers Aid in Diagnosis of Dementia

Erik B. Erhardt, [1] John C. Adair, [2,3] Janice E. Knoefel, [2,3] Arvind Caprihan, [4] Jillian Prestopnik, [3] Jeffrey Thompson, [3] Sasha Hobson, [3] David Siegel, [5] and Gary A. Rosenberg [2,3,*]

Abstract

Dual pathology of Alzheimer's disease (AD) and vascular cognitive impairment and dementia (VCID) commonly are found together at autopsy, but mixed dementia (MX) is difficult to diagnose during life. Biological criteria to diagnose AD have been defined, but are not available for vascular disease. We used the biological criteria for AD and white matter injury based on MRI to diagnose MX. Then we measured multiple biomarkers in CSF and blood with multiplex biomarker kits for proteases, angiogenic factors, and cytokines to explore pathophysiology in each group. Finally, we used machine learning with the Random forest algorithm to select the biomarkers of maximal importance; that analysis identified three proteases, matrix metalloproteinase-10 (MMP-10), MMP-3 and MMP-1; three angiogenic factors, VEGF-C, Tie-2 and PLGF, and three cytokines interleukin-2 (IL-2), IL-6, IL-13. To confirm the clinical importance of the variables, we showed that they correlated with results of neuropsychological testing.

Keywords: Alzheimer's disease, vascular cognitive impairment and dementia, inflammation, diffusion tensor imaging, cerebrospinal fluid, white matter disease, machine learning

Highlights