

## Are age-related biomarkers of dementia risk accelerated by low educational attainment?

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Background: Low education significantly elevates dementia risk but it is not clear whether this is through chronic systemic inflammation, early-onset dementia pathology, or other factors. This project compares biomarkers of inflammation and dementia pathology in a young-old and older cohort. Due to significantly lower education in the young-old cohort, we hypothesized evidence of similar or higher biomarker levels in the young-old cohort compared to the older cohort.

Methods: Blood samples were used to measure pro-inflammatory cytokines (C-reactive protein (CRP), tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-6, and IL-1 $\beta$  anti-inflammatory cytokines (IL-10 and IL-1RA), and the brain biomarkers phosphorylated tau (p-tau) and neurofilament light (NfL). Inflammatory markers were measured at the Considine Lab at the Indiana University School of Medicine using ELISA assays while p-tau and NfL were measured with Simoa assays at the Quanterix lab in Massachusetts. We used the natural logarithm of all biomarker variables to address skewed data. Linear regression was used to investigate race- and gender-adjusted differences in the biomarkers.

Results: The young-old cohort (N=42) has a mean age of 62.4, 69.1% are female, and 78.6% are non-Hispanic black (NHB), while the older cohort (N=60) has a mean age of 80.3, 60% are female, and 20% are NHB. Median education in the young-old cohort is 12 vs 16 in the older cohort. Adjusted models showed higher mean CRP (p=0.004) and lower mean IL-10 (p<0.001) in the young-old cohort. TNF- $\alpha$  (p <0.001), IL-6 (p=0.021), and IL-1 $\beta$  (p=0.017), P-tau (p=0.003), and NfL (p<0.001) were all higher in the older cohort.

Conclusion: We found partial support of our hypothesis in that the younger, low education cohort had higher mean CRP and lower mean IL-10 (anti-inflammatory). However, brain biomarkers were higher in the older cohort. More research will be needed to determine if and how low education elevates ADRD risk through systemic inflammation.