Links between Oral Health, Cognition, and Epigenetic Age Acceleration in People Living with and without HIV

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Background: People living with HIV (PWH) on antiretroviral therapy (ART) typically experience advanced biological aging, potentially driven by chronic immune activation and inflammation. Epigenetic clocks derived from DNA methylation (DNAm) provide quantitative measures of biological aging, yet current evidence has not focused on older populations. This study investigates the links between oral health, neurocognitive outcomes, and biological aging in PWH and people without HIV (PWoH)

Methods: Eighty-four participants (53 PWH, 31 PWoH) were enrolled. DNAm was generated from peripheral blood using the Illumina EPIC v2 array; beta values were processed in minfi with functional normalization (preprocessNoob) and mapped to the genome (mapToGenome). Second-generation epigenetic clocks (PhenoAge, DunedinPACE) were used to estimate EAA. Stimulated and unstimulated saliva were collected under standardized protocols, and periodontal and dental examinations were performed by trained hygienists. Neurocognition was assessed with the Brain Baseline Assessment of Cognition and Everyday Functioning (BRACE), capturing psychomotor speed, processing speed, and visuospatial learning and memory. Multivariable linear regressions evaluated relationships between EAA, neurocognitive function, and oral health outcomes.

Results: HIV serostatus was significantly associated with EAA, with PWH exhibiting a mean 3.52-year increase in PhenoAge relative to PWoH ($p=.008$), with a similar trend observed for DunedinPACE ($p<0.1$). Among PWH, subjective xerostomia was positively associated with PhenoAge EAA ($p=.091$), while smoking was positively associated with DunedinPACE EAA ($p=.045$). Stroop speed was associated with EAA in both PWH and PWoH ($p=.039$, $p=.095$, respectively), whereas faster finger-tapping was associated with lower EAA among PWH ($p=.018$).

Conclusions: HIV is associated with epigenetic age acceleration, particularly using inflammation-sensitive epigenetic measures. Xerostomia may represent a novel oral marker of systemic aging, and neurocognitive performance is linked to EAA processes. Together, these findings support a multi-system model in which oral, behavioral, neurological, and systemic domains are interconnected manifestations of biological aging in HIV.