Monocyte Epigenetic Age Relates to Non-Somatic Depressive Symptoms in Women With and Without HIV

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BACKGROUND

- HIV and its neuropsychiatric complications have been linked with accelerated biological aging using several DNA methylation-based **epigenetic clocks**.
- **Depression** disproportionately impacts women with HIV (WWH).
- Relationships between depression and inflammation in people with HIV (PWH) **differ by sex**[1].
- **Monocytes**, essential to the innate immune response, may contribute to depression in PWH.
- Peripheral monocytes in twins with a history of depression have **differential methylation** from non-depressed twins[2].
- Epigenetic age in monocytes has not been examined as a **biomarker** for depressive symptoms in WWH and women without HIV (WWoH).

METHODS

- Participants were obtained from the Women's Interagency Health Study (**WIHS**), a prospective observational cohort[3].
  - WWH (n=261; age=43.7±8.9 years; 38% Black; 48% Hispanic; 84% undetectable viral load); WWoH (n=179; age=39.5±10.0 years; 31% Black; 49% Hispanic).
- Age acceleration was calculated from blood using a new monocyte-based epigenetic clock, **MonoDNAmAge**[4].
  - Trained on monocytes from 1,202 relatively healthy individuals from a cardiovascular study.
  - DNA methylation profiling using Illumina methylation microarrays (BeadChip 450K or EPIC).
  - 186 cytosine-guanine (CpG) dinucleotides selected for final monocyte aging model.
  - CpG sites enriched for aging, smoking, cancer, alcohol; some mapped to pro-inflammatory genes.
  - 12.1-year MonoDNAmAge increase in WWH vs. WWoH.
- MonoDNAmAge, the non-cell-specific **Horvath clock**, and chronological age were tested for association with depressive symptoms.
- Depressive symptoms quantified with Center for Epidemiologic Studies Depression scale (**CES-D**), divided into **somatic** and **non-somatic** subscales.

Accelerated epigenetic aging in monocytes is linked with non-somatic depressive symptoms in a mixed-serostatus group of women, an effect primarily driven by women with HIV with undetectable viral load.

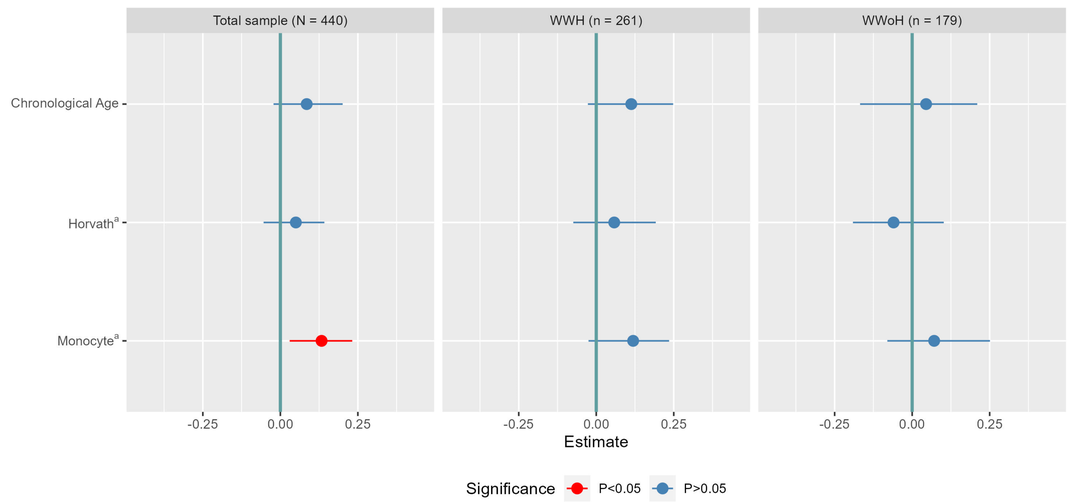


Fig. 1. Associations between biological clocks and non-somatic depressive symptoms in the total sample, WWH, and WWoH. [a]Represents biological ages (Horvath and Monocyte) after orthogonalization with respect to the chronological age. X-axis values represent estimated effect sizes per unit increase in age (years).

HYPOTHESES

- Across all participants, **accelerated aging** in monocytes will be linked with increased depressive symptoms.
- Due to the prevalence of **inflammatory depressive subtypes** in PWH, stronger associations between monocyte age and depression will be observed for WWH compared to WWoH.

RESULTS

- Monocyte age was significantly associated with **non-somatic** but not somatic depressive symptoms across all participants (p=0.02).
- Non-somatic depression mainly reflected **anhedonia**-related questionnaire items.
- This association was driven mainly by WWH with **undetectable** viral load (p=0.047).
- Somatic depressive symptoms were not linked with either clock or with chronological age.
- The non-specific Horvath clock was not associated with depressive symptoms.

CONCLUSIONS

- Biological clocks reflecting the epigenetic age of immune cells may represent **sensitive biomarkers** of non-somatic depression in women, particularly WWH.
- Relationships between other morbidity- and mortality-tuned epigenetic clocks (e.g., GrimAge, PhenoAge) and depression merit future study.

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CITATIONS

[1]Petersen, *et al.* Brain, Behavior, & Immunity 2023; [2]Zhu, *et al.* Translational Psychiatry 2019; [3]Adimora, *et al.* Int. J of Epidemiology 2018; [4]Liang, *et al.* Alcohol Clin. & Exp. Res. 2022.