THLBB2021_PUB007: Epigenetic clocks and lifespan sex differences dataset

Cohort: Twin Study
Data set accession number in THL Biobank: THLBB2021_PUB007

Publication information n

Do epigenetic clocks provide explanations for sex differences in lifespan? A cross-sectional twin study
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Published article's journal and reference information

Journals of Gerontology Series A: Biological Sciences and Medical Sciences (2021), Advance Article.
DOI: https://doi.org/10.1093/gerona/glab337

Participant and method description

Study population
The Finnish Twin Cohort (FTC) includes three large cohort studies: 1) The older FTC includes twins born before 1958, 2) Finntwin16 includes twins born in 1975-1979, and 3) Finntwin12 includes twins born in 1983-1987 (Rose et al., 2019; Kaprio et al., 2019).
The older Finnish Twin Cohort (FTC) was established 45 years ago and data collection has been extensively described recently (Kaprio et al., 2019). Finntwin16 was initiated in 1991 and to date, it includes five waves of completed data collections (Kaidesoja et al. 2019).
The main scope of the project is to identify the genetic and environmental determinants of various health-related behaviors and diseases in different stages of life. Finntwin12 is the youngest of the three FTC cohorts (Rose et al., 2019).
All eligible twins born in Finland during 1983–1987 along with their biological parents were enrolled to participate to four waves of questionnaires. Selected twins took part in laboratory studies with repeated interviews, neuropsychological tests, and collection of DNA were made as part of wave 4 in early adulthood (Kaprio et al., 2019).

Twins from all three cohorts (age range from 21 to 76 years old) who had taken part in clinical in-person studies with sampling for whole blood DNA and subsequent DNA methylation (DNAm) analyses and who had the relevant phenotype data were included to the study. The analysis sample included monozygotic (MZ) and dizygotic (DZ) same-sex twins (N = 1893, 54% MZ) as well as opposite-sex twins (347 twin individuals, 151 complete twin pairs).

DNA methylation and assessment of biological age
DNAm profiles were obtained using Illumina's Infinium HumanMethylation450 BeadChip or the Infinium MethylationEPIC BeadChip (Illumina, San Diego, CA, USA).
DNAm-based epigenetic age estimates, obtained by Horvath's (Horvath, 2013) and Hannum's clocks (Hannum et al., 2013) and by PhenoAge (Levine et al., 2018) and GrimAge (Lu et al., 2019) estimators, were calculated using a publicly available online calculator (https://dnamage.genetics.ucla.edu/new). The age acceleration (AA) of each clock was defined as the residual from regressing the estimated biological age on chronological age (AA Horvath, AA Hannum, AA PhenoAge, and AA GrimAge, respectively). The components of DNAm GrimAge (adjusted for age) were obtained as well, including

DNAm-based smoking pack-years (PACYRS) and the surrogates for plasma proteins (DNAm-based plasma proteins): DNAm adrenomedullin (ADM), DNAm beta-2-microglobulin (B2M), DNAm cystatin C, DNAm growth differentiation factor 15 (GDF15), DNAm leptin, DNAm plasminogen activator inhibitor 1 (PAI-1) and DNAm tissue inhibitor metalloproteinases 1 (TIMP-1).

Statistical analyses
Mediation models were used to test whether the association between sex and epigenetic aging (AA) is direct or mediated through lifestyle-related factors (education, body mass index, smoking, alcohol use, and physical activity) in all twins and opposite-sex twin pairs.
The single mediation models included indirect paths from sex to AA through one lifestyle factor at a time as well as the direct effect of sex on AA. Also, moderating effect of age on the associations was studied.
The multiple mediation model was fitted to assess the mediation effect of the different lifestyle factors simultaneously.
The models for the opposite-sex twin pairs were fitted using multilevel modelling, and the mediation models were specified at the within-twin pairs level. The approach controls for shared childhood environmental factors and partly for genetic factors.

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Description of THLBB2021_PUB007 dataset

The following variables are included in this dataset:

personid
familyid
zyg (1=monozygotic, 2=same-sex dizygotic, 3=opposite-sex dizygotic)
age_at_subproject (age when the twin visited for clinical measures/interviews/blood sampling etc)
education_years (U.S. years of education equivalent. variable was created by combining information about completed and ongoing studies as reported in the questionnaires)
smoking (self-reported smoking status. 0=never; 1=current; 2=former)
etoh_g_day (alcohol intake grams per day calculated from portions x 12g)
bmi (kg/m2)

DNAmAge (Horvath's epigenetic age estimate (Horvath, 2013))
DNAmAgeHannum (Hannum's epigenetic age estimate (Hannum et al., 2013))
DNAmPhenoAge (Levine's epigenetic age estimate (Levine et al., 2018))
DNAmGrimAge (Lu's epigenetic age estimate (Lu et al. 2019))
NAccDNAmRes (Epigenetic age acceleration, AA Horvath, the residual from regressing the DNAmAge on chronological age (age_at_subproject)
NAccHanRes (Epigenetic age acceleration, AA Hannum, the residual from regressing the DNAm AgeHannum on chronological age (age_at_subproject)
NAccPhenoRes (Epigenetic age acceleration, AA PhenoAge, the residual from regressing the DNAm PhenoAge on chronological age (age_at_subproject)
NAccGrimRes (Epigenetic age acceleration, AA GrimAge, the residual from regressing the DNAm GrimAge on chronological age (age_at_subproject)
Female (0=male, 1=female)
sporti (sport index, high intensity leisure-time physical activity based on Baecke's questionnaire (Baecke et al., 1982))
worki (work index, work-related physical activity based on Baecke's questionnaire (Baecke et al., 1982))
leisurei (leisure index, non-sport leisure-time physical activity based on Baecke's questionnaire (Baecke et al., 1982))
DNAmADMAdjAge (DNAm-based adrenomedullin, a component of DNAm GrimAge, adjusted for age)
DNAmB2MAdjAge (DNAm-based beta-2 microglobulin, a component of DNAm GrimAge, adjusted for age)
DNAmCystatinCAdjAge (DNAm-based cystatin C, a component of DNAm GrimAge, adjusted for age)
DNAmGDF15AdjAge (DNAm-based growth differentiation factor 15, a component of DNAm GrimAge, adjusted for age)
DNAmLeptinAdjAge (DNAm-based leptin, a component of DNAm GrimAge, adjusted for age)
DNAmPACKYRSAdjAge (DNAm-based smoking pack-years, a component of DNAm GrimAge, adjusted for age)
DNAmPAI1AdjAge (DNAm-based plasminogen activation inhibitor 1, a component of DNAm GrimAge, adjusted for age)
DNAmTIMP1AdjAge (DNAm-based tissue inhibitor metalloproteinase 1, a component of DNAm GrimAge, adjusted for age)
older (classification based on age_at_subproject: 0=21 to 42 yr-old twins, 1= over 50 yr-old twins)