Title: The association of birthweight, preterm birth, and foetal growth restriction on epigenetic aging across the lifespan

Authors:
Lauri A. Lavonen, Sonja Rajić, Saara Marttila, Pashupati P. Mishra, Mika Kähönen, Olli Raitakari, Terho Lehtimäki, Emma Raitoharju

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Abstract

Individuals born preterm and/or at a low birthweight are more susceptible to age-related health complications. To explore one possible mechanism for this connection, we examined how birthweight, preterm birth, and foetal growth restriction associate with the participants' biological aging in youth, adulthood, and midlife.

As indicators of biological age, we used four distinct "epigenetic clocks": DunedinPACE, PCHorvath1, PCGrimAge, and PCPhenoAge. These are computational models that form an estimate of the individual's state of biological aging based on age-related changes in DNA-methylation. We analysed whole blood DNA-methylation (Illumina array 450K and EPIC v1 and v2), registry, and survey data from the longitudinal national Young Finns Study cohort across three follow-ups: 1986 (n=274), 2011 (n=1460), and 2018-2020 (n=1114).

Our results indicate that individuals born small for their gestational age (SGA) present increased biological pace of aging in the regression models measured by DunedinPACE systematically across all follow-ups (1986: $p=0.035$, $\beta=0.036$, 2011: $p=8.5\cdot10^{-5}$, $\beta=0.033$, and 2018-2020 $p=5.8\cdot10^{-4}$, $\beta=0.036$). On the other hand, prematurely born individuals had decreased epigenetic age acceleration measured with PCHorvath1 (1986: $p=0.019$, $\beta=-1.54$, 2011: $p=0.033$, $\beta=-0.59$, and 2018-2020 $p=0.018$, $\beta=-0.93$) in all follow-ups.

Our study is the first to assess epigenetic aging from youth to midlife longitudinally in this context. In contrast to previous publications reporting an inverse linear association between birthweight and epigenetic aging, our findings show that only SGA birth advanced the epigenetic pace of aging across the lifespan. Perplexingly, being born preterm was associated with decreased age acceleration. However, this association could be explainable by survivor bias.