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HUMAN DEVELOPMENT, BIRTH TO DEATH

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Genes Environment Health Behavior

Provisional Paper Title: Socioeconomic status and biological age across the lifespan
Proposing Author: Kyle Bourassa
Author's Email: kyle.bourassa@duke.edu
P.I. Sponsor: Terrie Moffitt and Avshalom Caspi
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Objective of the study:

We propose to study the association of socioeconomic status (SES) during childhood and adulthood with health in later life via accelerated biological aging. People who grow up in and/or experience socioeconomic disadvantage across the lifespan are less healthy than those with higher SES[1-4]. One of the ways in which socioeconomic disadvantage might translate into poorer health is by accelerating the rate at which people biologically age[5]. People who age more quickly are more likely to accumulate chronic disease, develop functional disability, and experience early mortality compared to age peers who do not evidence accelerated aging[6-8]. Several previous studies have shown that both childhood and adult SES are associated with older biological age[9-11], suggesting accelerated aging could be a mechanism linking low SES with poorer health.

Although a large body of empirical literature has supported the link between lower SES and poor health, less is known about the relative contribution of past versus current SES to health in midlife and beyond. Determining the relative influence of early life SES compared to SES in later life on biological aging would provide context as to which is more relevant to people's health across the lifespan. Several competing models have been proposed to characterize the potential associations[12].

1. Critical period models posit that experiencing low SES during certain times across the lifespan is more relevant to health than experiencing low SES at other times. For example, biological embedding models[12-13] suggest that childhood represents a critical period in which the possible health-relevant effects of low SES set people on a course of poor health across the lifespan. Alternatively, others models emphasize the important of recency, such that the SES someone experienced most recently should be the most critical to their current health.
2. Cumulative models[14-15], also known as accumulation models, emphasize that low SES is equally detrimental to health across the lifespan, such that the more life stages during which people experience low SES (i.e., the more "dosage" of low SES experienced) the poorer their health.
3. Sensitization models[16-17] suggest that lower SES in both childhood and adulthood are relevant, such that experiencing low SES as a child results in particularly poor health outcomes among people who go on to experience lower SES as an adult.
4. Social mobility models[18-20] suggest that both where people start, in terms of childhood SES, and where they end up in terms of adult SES, are relevant to health. For example, there are theories that upward social mobility can actually be harmful to health, given the stress experienced by people who do so[18-19]. Alternatively, there is a theory of downward drift, such that people who decline in social status[19] might experience declining health.

Each of these models presents potential testable models and hypotheses that are relevant to understanding the associations between health and SES across the lifespan.

Existing longitudinal cohorts that assess both biological aging and SES would allow us to test these models

across multiple populations with the power necessary to produce reliable estimates. For biological aging, a number of novel methods have been developed over the last decade to assess biological aging[21] using epigenetic methylation algorithms derived from large training datasets[21-23]. These methods are notable in that they allow for the reliable assessment of biological age at a single time point in any dataset that includes the relevant methylation data for its participants. Using aging scores derived from such methods would allow us to use biological aging data from cohorts—such as the Dunedin Study and Health and Retirement Study (HRS)—that extend across large portions of the lifespan. Both the Dunedin Study and HRS also include measures of SES in childhood and adulthood. For example, prior studies of childhood and adult SES using HRS data have utilized measures of retrospective parental educational attainment and individual educational attainment to index childhood and adult SES[24-25], respectively. The Dunedin Study has also included prospective measures of both parental and individual educational attainment that would match these measures of SES from HRS. The combination of HRS and Dunedin data would provide data measures of SES across the life course, as well as biological age in midlife and later adulthood.

For the current study, our primary aim is to test which models—critical period, cumulative, sensitization, or social mobility models—best characterize the ways in which childhood and adult SES are associated with biological age in later life. A secondary aim will be to explore whether observed associations between SES and aging are similar or different between subgroups present across the two cohorts, specifically New Zealand adults, and Black, White, and Hispanic American adults.

Data analysis methods:

Aim 1: Investigate the association of lower SES—assessed using parental and current educational attainment—with more advanced biological age in middle and older age, as assessed by methylated measures of biological aging[21-23]. We predict that lower childhood and adult SES will be independently associated with accelerated biological age, in support of a cumulative/accumulation model of SES and health.

Aim 2: We will examine the Aim 1 models within different subgroups. We will first compare the results between the two cohorts to examine whether there are apparent differences between American and New Zealand participants. Second, we will examine the Aim 1 models within racial and ethnic subgroups, specifically Black, White, and Hispanic adults.

Sensitivity analysis: Dunedin includes broader measures of SES, which we will use to replicate the Aim 1 models to test whether results using educational attainment match those using a broader measure of SES.

General analysis methods: The statistical analysis will follow a systematic series of nested models testing the presence, timing, and accumulation of exposures to lower SES[26-29]. The models will use multiple regression and a series of parameters that will represent: 1.) the potential of critical periods of lower SES in either childhood or adulthood, 2.) a cumulative effect of lower SES, 3.) an interaction of lower SES in childhood with lower SES in adulthood, and 4.) social mobility from childhood to adulthood. The use of these models will allow us to test which best represent the existing data linking SES to biological age across the lifespan. All models will adjust for sex, and those run within HRS will also adjust for age. Participants will be included in the analyses if they have data on parental educational attainment, current educational attainment, and biological aging scored derived from methylation data. HRS data will be coded to match the values from Dunedin for relevant variable (i.e., educational attainment). Separate models will be run for each of the five biological age scores within Dunedin and HRS.

Variables needed from Dunedin at which ages:

- DNA-methylation measures of biological aging at age 45
    - DunedinPACE at age 45
    - Horvath at age 45
    - Hannum at age 45
    - GrimAge at age 45
    - Levine at age 45
- Measures of SES
    - Age 45 educational attainment
        - Will be assessed using three categories: less than a high school degree, a high school degree (and/or some college), and a secondary/university degree (B.A.).
    - Age 15 parent educational attainment
        - Will use the highest of the parent's education, divided into three categories: less than a high school degree, a high school degree (and/or some college), and a secondary/university degree (B.A.).
    - Childhood SES (SEschildhd)
    - Adult SES at age 45 (SESall45)
- Demographic covariates: Sex

Significance of the Study (for theory, research methods or clinical practice):

Better understanding the association between SES across the lifespan and biological aging in midlife and older age would help support intervention efforts to reduce the burden of chronic diseases, disability, and early mortality as people age. Determining whether childhood SES or adult SES is more strongly associated with biological age would provide more effective potential avenues to intervene to slow the rate at which people age, improving health in older age. The results from these analyses would present empirical evidence as to the most health-relevant period for socioeconomic disadvantage and evidence as to which models—critical period, cumulative, sensitization, or social mobility—might best represent the association between SES and aging across the life course.

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Data Security Agreement

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☒	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
☒	My project is covered by the Duke ethics committee OR I have /will obtain ethical approval from my home institution.
☒	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: a) encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) b) password-protected c) configured to lock-out after 15 minutes of inactivity AND d) has an antivirus client installed as well as being patched regularly.
☒	I will not "sync" the data to a mobile device.
☒	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Moffitt or Caspi.
☒	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
☒	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. Study participants have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to Temi or Avshalom for strategies for achieving compliance with data-sharing policies of journals.*
☒	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. This data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.

Signature: 

CONCEPT PAPER RESPONSE FORM

A.

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Proposing Author	Kyle Bourassa
Other Contributors	Terrie Moffitt, Avshalom Caspi, Dan Belsky, HonaLee Harrington, Renate Houts, Richie Poulton, Sandhya Ramrakha, Ben Williams, Karen Sugden,
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B. To be completed by potential co-authors:

☐	Approved
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Please check your contribution(s) for authorship:

☐	Conceptualizing and designing the longitudinal cohort study
☐	Conceptualizing data collection protocols and creating variables
☐	Data collection
☐	Conceptualizing and designing this specific paper project
☐	Statistical analyses and interpretation (or reproducibility check)
☐	Writing
☐	Reviewing manuscript drafts
☐	Final approval before submission for publication
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