GROWUPGROWOLD
HUMAN DEVELOPMENT, BIRTH TO DEATH

Moffitt & Caspi
Genes Environment Health Behavior

Provisional Paper Title: Identifying treatable pediatric health risk factors for accelerated aging
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Objective of the study:

We propose to study the developmental origins of accelerated aging to identify modifiable pediatric health conditions associated with accelerated aging in adulthood. International comparative studies have shown that the poorer health of older members of countries can largely be explained by a nation's ill health in early life[1]. Although aging is a distinct construct from physical health, people who age more quickly are also more likely to accumulate chronic disease, develop functional disability, and experience early mortality compared age peers who do not evidence accelerated aging[2-4]. The wide array of poor health outcomes associated with accelerated aging presents a critical opportunity. Although traditional biomedical models suggest targeting people who have already developed disease to improve health, biological aging is a process that accumulates across the lifespan. As a result, prevention appears to be the most effective method of intervention[5]. Intervening to slow aging in childhood and early adulthood[6] could improve people's health as they age over adulthood and into older age—reducing morbidity, disability, and mortality[7-9].

What pediatric interventions would be the most effective in preventing accelerated aging in adulthood? To answer this question, we will test the association of four common childhood health conditions—asthma, psychopathology, smoking, and obesity—with accelerated aging in midlife. These conditions have high population prevalence, high levels of chronicity, peak onset early in life, and most critically, known modifiability[10-16]. The Dunedin Study has tracked these conditions since childhood and has multiple validated methods of assessing aging in midlife, making it particularly well suited to our aims. Determining which modifiable childhood health conditions are associated with faster aging would provide empirical evidence as to which pediatric interventions might slow people's aging early in the lifespan, prior to the accumulation of health consequences in adulthood.

Data analysis methods:

Aim 1: Investigate the association of four childhood risk factors—childhood asthma, smoking, obesity, and psychopathology—with accelerated aging in midlife. Accelerated aging will be assessed using the Pace of Aging[6], facial aging[6], brain age[17], and gait speed at age 45. These variables will be used to create factor scores representing accelerated aging. We will first assess the independent association between each childhood risk factor and aging factor scores. Next, we will test the association between the childhood risk factors and accelerated aging in a combined multiple regression model. Finally, we will create a sum score using risk factors that are significantly associated with midlife aging and test the association between that risk score and accelerated aging. We predict that the four childhood risk factors will each be uniquely associated with accelerated aging.

Aim 2: We will examine the Aim 1 models while adjusting for childhood covariates—childhood health, SES,

and ACEs. The models will first assess the association between each childhood risk factor and the accelerated aging factor while adjusting for these covariates. Next, we will examine the association between the childhood risk factors and accelerated aging in a combined multiple regression model adjusting for the three covariates. We predict that the childhood risk factors will remain associated with accelerated aging.

Sensitivity analysis: We will test the association between the four childhood risk factors and the each individual indicator of the accelerated aging factor. We will test the associations independently and in a combined model. Pace of Aging results will be used to provide a metric for the size of the associations.

General analysis methods: To create the factor score, the four indicators of aging will be standardized and recoded such that higher scores represent relatively faster aging. Principal components analysis will be used to create a single factor score that will be exported and used in subsequent analyses. The models testing the childhood risk factors will use multiple regression and will adjust for sex. All models will be run in MPLUS[18] using full information maximum likelihood estimation to account for missing data[19].

Variables needed at which ages:

- Accelerated aging (factor score will be derived from four indicators of aging)
    - Pace of Aging at 45
    - Gait speed at 45
    - Brain age at 45
    - Facial age at 45
- Childhood risk factors
    - Obesity status at age 15
    - Daily smoking status at age 15
    - Asthma status at age 15
    - Mental health diagnosis at age 11, 13, or 15
        - ADHD diagnosis at age 11, 13, or 15
        - Conduct disorder diagnosis at age 11, 13, or 15
        - Anxiety disorder diagnosis at age 11, 13, or 15
        - Depressive disorder diagnosis at age 11, 13, or 15
- Childhood covariates
    - Childhood health
    - Childhood SES
    - Childhood prospective ACEs
- Demographic covariates: Sex

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

Discovering the developmental origins of accelerated aging in childhood would provide multiple avenues for future prevention efforts aiming to reduce the burden of chronic diseases, disability, and early mortality as people age. The four childhood risk factors included in this study are relatively common, chronic, have an early-peak onset, and most importantly *are modifiable*. Smoking cessation interventions, cognitive behavioral therapies, respiratory therapies, and weight loss interventions can each be used to address these common conditions. The results from these analyses would present strong empirical evidence as to the most relevant treatable pediatric health conditions that could be treated to prevent accelerated aging and would have direct clinical relevance to pediatric treatment prioritization and decision-making.

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