

Concept Paper Form

Provisional Paper Title: Victimization and the Pace of Biological Aging During Adolescence
Proposing Author: Ruhsar Varlioglu (J.C. Barnes' student)
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P.I. Sponsor: Terrie Moffitt with J.C. Barnes serving as an advisor (if the proposing author is a student or colleague of an original PI)
Today's Date: 10/28/2021

Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

Exposure to victimization is a public health concern because victims are more likely to develop health and adjustment problems in later life.^{1,2,3} Studies show that victimization experiences, especially bullying victimization in childhood and adolescence, lead to poor general health^{2,4} as well as mental health problems.^{1,3,4} The mechanisms that underlie these relationships, however, are not well understood. In this study, we propose that biological aging is one mechanism that explains how victimization experiences lead to health problems in later life.

Biological aging is a plausible mechanism because it represents the overall level of system integrity in the body. As we age, system integrity breaks down and, as such, biological age predicts morbidity, disability, and mortality risk.^{5,6,7} Exposure to chronic stress and an unhealthy lifestyle are known to be associated with advanced biological aging.^{5,8,9} Research demonstrates that the pace of biological aging can be viewed as a marker of general well-being for adults as well as for adolescents.^{5,6,10} To the extent that victimization experiences are internalized, it is likely that individuals who have experienced victimization in their past will present with more advanced biological ages.

This study will explore whether victimization generally—and bullying victimization specifically—is a risk factor for accelerated biological aging among a representative birth cohort of British adolescents. More specifically, we will examine: 1) whether adolescents who experience victimization exhibit a faster pace of aging compared to those who do not; 2) whether there is a sensitive period for this relationship (i.e., we will separately assess the role of age 12 and age 18 victimization); and 3) the extent to which family-level characteristics (e.g., sibling support) promote resilience to victimization's impact on the pace of aging.

Data analysis plan:

Drawing on data from the Environmental Risk Longitudinal Twin Study ($N = 2,232$), we will assess the impact of victimization on the pace of biological aging among a sample of 18-year-olds. We will capitalize on the twin-structure of the data to estimate this association after adjustment for shared genetic and environmental factors while also adjusting for early childhood adverse experiences, tobacco use, BMI, and pubertal onset.

The analysis plan will unfold in four steps.

First, we will conduct linear regression analyses to test for an association between victimization experiences and biological aging. The pace of biological aging will be used as the dependent variable, and it will be measured using the DunedinPACE DNA methylation algorithm.¹¹ We will employ two strategies for assessing victimization experiences: 1) utilizing a general measure of exposure to any type of victimization and 2) performing separate analyses for each of the different types of victimization represented in the data. For example, we plan to assess the influence of exposure to bullying victimization separately from other types of victimization. All regression models (including those outlined below) will adjust for the influence of observed confounding variables, including early childhood adverse experiences, tobacco use, BMI, pubertal onset, and sex.

Second, we will conduct linear regression analyses by employing DunedinPACE as the outcome and considering both phase 12 and phase 18 victimization experiences. The goal here is to examine whether earlier (i.e., phase 12) victimization experiences are more or less influential than later (i.e., phase 18) victimization experiences.

Third, we will conduct linear regression analyses to explore the extent to which family-level factors (e.g., sibling warmth and atmosphere at home) promote resilience to the impact of victimization on the pace of aging. To do so, we will assess whether the coefficient estimate for the effect of victimization on the pace of aging varies as a function of the family-level variables. These analyses will be performed with multiplicative interaction terms (e.g., *early childhood adverse experiences* \times *victimization*) or by model stratification (i.e., separately estimate the effect of victimization across levels of the other variables) with appropriate post-hoc statistical significance tests (e.g., the z -test for coefficient comparisons).

Fourth, we will repeat all analyses from steps 1 to 3, this time taking into account the data's twin-structure. More specifically, we will rely on twin-difference models (e.g., twin fixed effects) that allow twins to serve as the counterfactual estimate for their co-twin.¹² Twin-difference models are robust because they allow for the adjustment of unobserved confounding due to influences from the shared environment as well as genetic influences.

Proposed variables:

Phase	Variable label	Variable description
Covariates		
	Early childhood adverse experiences (ACEs)	
	Smoking frequency (all available ages)	
	BMI	
	Age of pubertal onset	
	Sex	
	Socioeconomic Status	
	Cognitive Ability phase 12	workhorse variable from Motz et al. (2020)
	Low self-control	workhorse variable from Motz et al. (2020)
	Educational achievement phase 18	workhorse variable from Motz et al. (2020)
	Externalizing behavior problems	workhorse variable from Motz et al. (2020)
	Delinquency phase 12, 18	
Age 12 focal variables		
	Victimization (summed)	An overall “frequency of victimization” measure
	Individual Victimization Experiences	The constituent items that were used to create the above summed scale
Age 18 focal variables		
	DunedinPACE	
	Victimization (summed)	An overall “frequency of victimization” measure
	Individual Victimization Experiences	The constituent items that were used to create the above summed scale

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

Victimization, especially bullying victimization, is a topic of concern for youths, parents, educators, and mental health practitioners. Adolescents who have been victimized show signs of distress and adjustment problems^{1,2} and are at greater risk for poor social, economic, and health outcomes.^{1,9} Previous studies have suggested that biological aging can be viewed as a predictor of general well-being.⁵ Individuals' bodies age at different rates, and age-related biological changes that increase the risk of morbidity and diseases^{5,13} progress more rapidly in some individuals.⁵ In this sense, a better understanding of the variability in the pace of biological aging among adolescents has implications not only for public health officials but also for educators. Interventions designed to reduce victimization risk in adolescence and improve social support mechanisms following victimization may minimize the long-term adverse effects of victimization that have been observed in prior work.^{1,14} The present study, therefore, will provide insight into the potential for policy to impact early adulthood health and well-being by focusing on adolescents' victimization experiences.

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Data Security Agreement

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<input checked="" type="checkbox"/>	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
<input checked="" type="checkbox"/>	My project is covered by the Duke ethics committee OR I have /will obtain ethical approval from my home institution.
<input checked="" type="checkbox"/>	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.
<input checked="" type="checkbox"/>	I will not "sync" the data to a mobile device.
<input checked="" type="checkbox"/>	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Moffitt or Caspi.
<input checked="" type="checkbox"/>	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
<input checked="" type="checkbox"/>	I will not post data online or submit the data file to a journal for them to post. <i>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>
<input checked="" type="checkbox"/>	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.
<input checked="" type="checkbox"/>	I have read the Data Use Guidelines and agree to follow the instructions.

Signature: Ruhsar Varlioglu