GROWUPGROWOLD
HUMAN DEVELOPMENT, BIRTH TO DEATH

Moffitt & Caspi
Genes Environment Health Behavior

Concept Paper Form

Provisional Paper Title: Do children who develop faster grow up to age faster in midlife?
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Today's Date: 1/16/2024

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

Objective of the study:

Development and aging have historically been conceptualized as distinct and studied separately (Feltes et al., 2015). Development is conventionally defined as growth and improvement in function during the first decades of life, whereas aging is defined as decay and decline in function later in life (Gladyshev, 2021). Accordingly, development is typically studied in samples of young people, whereas aging is studied in samples of older adults. Yet, findings from longitudinal studies have shown that aspects of child development predict aspects of adult aging. This has motivated more research to explore what sustains the link between childhood exposures and older age health outcomes over many decades of life.

Because there are few studies that follow individuals from birth to old age, the question of whether 'development' and 'aging' are linked constructs has historically remained in the philosophical realm. By contrast, our study aims to empirically examine the relationship between development and aging.

First, we will investigate whether scores on individual measures of childhood development predict the pace of biological aging at age 45. **Aim 1: To examine whether measures of childhood development predict the pace of adult aging.**

Second, we will examine whether those same individual measures of childhood development cluster together to form distinct developmental profiles. For instance, do children who have higher birth weight, also tend to have more weight gain as toddlers,

earlier growth spurt as adolescents, and earlier progression through puberty? **Aim 2: To empirically derive profiles of childhood development using biological and behavioral variables.**

Third, if profiles of childhood development emerge from these data, we will examine two competing hypotheses about the pace of childhood development as it relates to the pace of adult aging. One hypothesis states that children with the 'fast-developing' profile also go on to age faster as adults. If correct, it would suggest that "fastness" is a biological quality that unites both child development and later-life aging, in the same people. In contrast, the opposing hypothesis states that a 'slow-developing' childhood profile reflects biological inefficiency that cumulates in faster adult aging. If correct, it would suggest the possibility that unhealthy biology can manifest in slow child development, but rapid aging, over an individual's life course. **Aim 3: To examine whether profiles of childhood development differ in pace of adult aging.**

Data analysis methods:

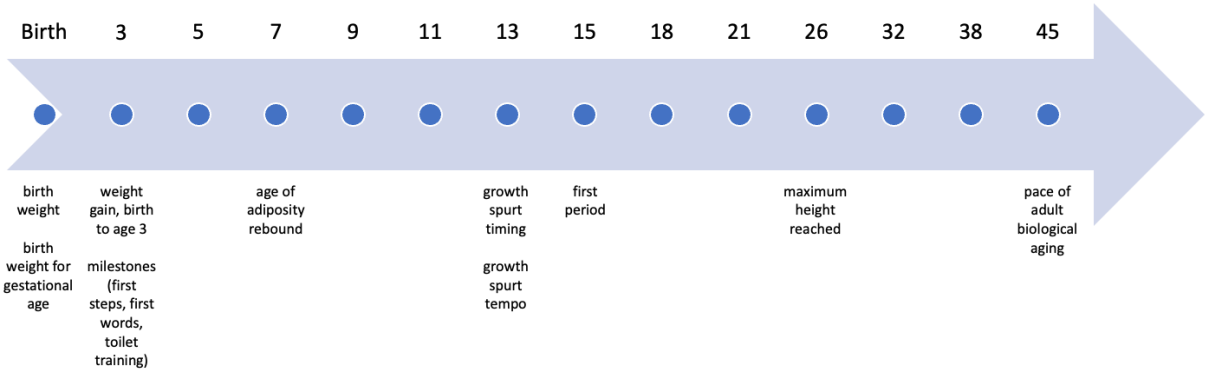

Figure 1. Timeline displaying when main analysis variables were collected. Variables of childhood development were collected between birth-Phase 26. Biological aging in adulthood is a composite variable derived from measurements at Phases 26-45.

Data preparation:

Prior to our main analyses, we will reduce the behavioral milestones into one variable. At Phase 3, Study members' parents were interviewed about when Study members reached a number of early childhood behavioral milestones (e.g., first instance of walking, talking, toilet training). We hypothesize that scores on these milestone variables will be highly intercorrelated. We will summarize these variables into a 'milestone composite' by standardizing them and deriving the mean for each Dunedin child.

Childhood development variables:

After reducing the behavioral milestones into one variable, we will select a set of seven (7) childhood development variables to include in main analyses.

Height and weight were measured at birth through age 26 years to estimate (1) birth weight, (2) weight change from birth to age 3, (3) timing of toddler adiposity rebound, (4) timing of adolescent growth spurt and (5) tempo of adolescent growth spurt. (6) Early childhood behavioral milestones were reported during interviews with parents of Study members. For girls, (7) age at first menstrual period was self-reported.

Midlife biological aging variable:

For our midlife biological aging variable, we will use the Pace of Aging score at Phase 45, a composite score of physiological deterioration across organ systems derived from 19 biomarker measurements repeated at Phases 26, 32, 38, and 45.

General analysis methods:

Linear regressions controlling for sex and SES will be conducted for Aim 1, to examine if scores on our seven (7) childhood development variables predict pace of adult aging.

For Aim 2, we will use the child development variables as indicators in a latent profile analysis. We will estimate a model to enumerate profiles which characterize pace of childhood development. Once the model is fit, we will estimate if profile membership predicts midlife biological aging as a distal outcome for Aim 3.

Full information maximum likelihood will be used to estimate parameters when there are missing data. Models will be run in R and MPlus.

Variables needed at which ages:

Category	Variable Description	Variable Name
Anthropometric (height and weight) measurements	Birth weight	wt00
	Birth weight for gestational age	bwga
Variables derived from anthropometric measurements	Change in weight from birth to age 3 years, with imputed values (Belsky et al., 2012)	growthB3i
	Adiposity rebound age; age at nadir of BMI growth curve (Belsky et al., 2012)	AdipRbndAge
	Adiposity rebound BMI; BMI at nadir of BMI growth curve (Belsky et al., 2012)	AdipRbndBMI
	Maximum height ages 3-26 years; upper asymptote of height growth curve	grwth_upper_asym
	Adolescent growth rate; tempo, with respect to age, at which	grwthrateHT

	Study member progressed from lower to upper asymptote in height growth curve	
	Adolescent growth timing; age at which Study member was halfway between the lower and upper asymptotes in height growth curve	grwthrateTiming
Self- and informant-reported developmental milestones	Age of first smile, months	ms_smile
	Age of sitting up, months	ms_situp
	Age of first steps, months	ms_walk
	Age of feeding self without assistance, months	ms_feed
	Age of first words, months	ms_talk
	Age of communicating in sentences, months	ms_sentences
	Age of completed toilet training during daytime, months	ms_dryday
	Age of completed toilet training during nighttime, months	ms_drynight
	Age of first menstrual period, months	FstPeriod
Midlife biological aging measurement	Composite score of physiological deterioration across organ systems, measured at ages 26, 32, 38, and 45 years	PaceOfAgingP45
Background and control variables	Participant ID number	snum
	Participant sex	sex
	Childhood SES	SESchildhd

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

This study evaluates two competing hypotheses of lifespan development. These hypotheses operate under a conventional assumption where faster development is seen as positive and precocious, whereas faster aging is seen as negative and deleterious.

If children who develop faster go on to age faster as adults, findings would support the *antagonistic pleiotropic theory*, which states that some molecular mechanisms that are beneficial to young organisms can be deleterious in later life, leading to age-related phenotypes (Williams, 1957). This may also be compatible with *life history theory* in evolutionary biology, which posits that variation in human traits is geared towards attaining reproductive advantage; thus, developing faster would mean a higher

likelihood of successful reproduction and survival, but the tradeoff might be faster senescence and decline (Nettle & Frankenhuis, 2020).

By contrast, if children who have a comparatively weaker, slower start to life go on to age faster as adults, findings would support the *developmental origins of health and disease* perspective, which states that insults in early life (i.e., when developing tissue is most susceptible to external harm) increase the risk of disease in later life (Langley-Evans, 2006).

Direction notwithstanding, any observed association between developmental profiles and biological aging would support further use of longitudinal methods to study 'development' and 'aging' as a continuous process. Lifespan developmental psychologists have argued for the use of this continuous research paradigm, where both 'development' and 'aging' refer to selective age-appropriate changes in adaptive capacity (Baltes et al., 1999). The necessary birth-to-late-life studies are very rare, making this project in the five-decade Dunedin Study an important first step in understanding the relation between child development and aging.

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