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HUMAN DEVELOPMENT, BIRTH TO DEATH | Genes Environment Health Behavior

Concept Paper template form

Provisional Paper Title: Early origins of intrinsic capacity in midlife	
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Please describe your proposal in 2-3 pages with sufficient detail for helpful review by addressing all areas outlined below.

Objective of the study:

Given the rapid global increase in the aging population, longer lifespans are often accompanied by more years lived with chronic disease. To shift the focus from treating disease to promoting healthy aging, the World Health Organization proposed the construct of intrinsic capacity, defined as the sum of an individual's total physical and mental abilities. Intrinsic capacity encompasses five domains – locomotor, cognitive, psychological, sensory, and vitality – that support independence and the ability to maintain activities of daily living. Unlike disease-centered models, intrinsic capacity emphasizes what people can do and value in their daily lives. Importantly, intrinsic capacity provides valuable information of one's subsequent functioning beyond that of age, personal factors, and multimorbidity[1], making it a promising marker of healthy aging. Despite the increase in intrinsic capacity research, most studies are restricted to older adults aged 60 and older[2]. As a result, little is known about intrinsic capacity in midlife or its developmental origins.

A life-course perspective on aging[3] provides one compelling rationale for studying intrinsic capacity earlier in the lifespan, emphasizing that early experiences and abilities shape health and functional outcomes across the lifespan. An existing body of evidence has identified four early-life factors with cascading effects on adult functioning: (1) childhood IQ (2) self-control (3) socioeconomic status and (4) exposure to early adversity[4-7]. However, past studies have typically examined each factor in relation to single domains of functioning, and few have tested how these early-life factors contribute to a multidimensional construct of functional capacity in midlife, which intrinsic capacity represents. For example, childhood self-control predicts adult physical

health[4] , yet its relevance for other components of intrinsic capacity, such as vision and hearing functions in midlife is underexplored.

The Dunedin study cohort is uniquely positioned to fill this gap. We aim to use data from birth to age 45 to investigate whether four key early-life factors, childhood IQ, self-control, socioeconomic status, and adverse childhood experiences predict intrinsic capacity in midlife – a period before the widespread onset of late-life disease. Unlike prior studies of intrinsic capacity that have relied on retrospective recall of childhood experiences[8-10], we will use prospectively assessed measures to test long-term effects with greater accuracy. Although adverse childhood experiences and low socioeconomic status may co-occur, research suggests their health relevance is distinct,[11,12] warranting separate consideration. Analyses will also extend to each of the WHO-specified domains to determine how early-life factors map onto distinct aspects of intrinsic capacity, with the sensory domain examined separately for hearing and vision. By integrating a comprehensive profile of childhood functioning with multidomain measures of intrinsic capacity in adulthood, this project provides a rare opportunity to identify the early foundations of intrinsic capacity over nearly five decades of development.

Data analysis methods:
We will conduct a series of analyses to investigate associations between early life factors: childhood IQ, self-control, socioeconomic status (SES), and adverse childhood experiences, and midlife intrinsic capacity. Consistent with published Dunedin work[4,11,13], IQ scores will be averaged into one measure and standardized; nine measures of self-control will be averaged into a composite score; SES represents the highest SES level of either parent from the participant's birth through age 15, and adverse childhood experiences will be summed to create a cumulative adverse childhood experiences score (0,1,2,3 or 4+). The Dunedin study includes repeated assessments across the WHO-specified domains of intrinsic capacity, which are currently being used to construct a composite intrinsic capacity score at age 45 described in Kathy Xie's concept paper. This measure, along with domain-level scores will be used as the outcomes in the analyses below.

1. Bivariate correlations will be used to assess individual associations of childhood IQ, self-control, socioeconomic status (SES), and adverse childhood experiences with an intrinsic capacity composite and its domains at age 45.

2. Multivariate regression models will test the contributions of all four predictors of intrinsic capacity at age 45, while adjusting for sex.

3. This model will then be repeated six times, each with an individual domain: locomotor, cognitive, psychological, sensory (hearing and vision), and vitality as the outcome, to examine domain-specific associations.

4. Apart from testing the significance of the relationship between childhood factors and intrinsic capacity, another way we can evaluate the significance of our findings is to compare them to the childhood-adult stability of the functions included in the assessment of intrinsic capacity. Specifically, we will match and correlate childhood and adult measures of IQ, balance, motor function, hearing, visual acuity, loneliness, and lung function.

If steps 1 through 3 above yield significant associations, exploratory analyses may be conducted using receiver operating characteristic (ROC) analyses to answer: *Can early-life predictors reliably distinguish between adults with higher versus lower intrinsic capacity?* This will also depend on the distribution of scores and the ability to define an empirically meaningful threshold.

<u>Variables needed at which ages:</u>
Primary Independent Variables
Childhood IQ composite (ChildIQ_chstd**;** ages 7 to 13)
Self-Control composite (Lscuw311; ages 3 to 11)
Childhood SES composite (Sesav115; birth to 15)
Adverse childhood experiences count (ProAces and ProAces_Trunc; birth to 15)
These measures have already been published and are lodged at the unit.

Additional Independent variables:
Bayley Motor Scales total and balance subtest (Bmotor3; age 3)
McCarthy Motor Scales (age 5)
Basic Motor Ability Test total and balance subtest (Xzmot7; ages 7 and 9)
Visual acuity right and left eye (ages 7, 9, 11)
Speech perception in hearing (Spin11; age 11)
Pure, tone audiometry (Pta511; ages 7, 9, 11)
FEV/VC lung function (ages 9, 11, 13, 15)
Child loneliness (Lonr511p and Lonr511t; ages 5,7, 9, 11)
These measures have already been published and are lodged at the unit.

Primary Dependent Variables
Intrinsic capacity composite at age 45
Intrinsic capacity domain scores and all variables associated with: locomotor, cognitive, psychological, sensory (hearing and vision), and vitality at age 45.
These measures are currently being constructed and have not been published yet.

Demographic covariates
Sex

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

The project will advance the development of intrinsic capacity by situating it within a life-course framework, consistent with the WHO's shift from deficit-based models of aging toward a healthy aging perspective. Rather than viewing intrinsic capacity only as a marker of capacity in older adulthood, we will test whether it reflects the accumulation of childhood abilities and experiences. This work advances theory by leveraging the Dunedin cohort's nearly five decades of rich prospective data and investigating the early origins of intrinsic capacity[14]. Clinically, identifying early-life predictors of intrinsic capacity has important preventive implications, offering opportunities to promote capacity and reduce disparities in aging before the onset of age-related disease.

How the paper will contribute to Māori health advancement and/or equitable health outcomes

This study will not include a separate analysis of specific ethnic groups, but the results are expected to be generalizable to the Māori community. By clarifying which early-life factors shape intrinsic capacity in midlife, this work can inform strategies to reduce health disparities before older adulthood.

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