Concept Paper

Provisional Paper Title: Rethinking Gait: Gait Speed in the First Five Decades of Life

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P.I. Sponsor: Terrie Moffitt & Avshalom Caspi

Today's Date: 14 December 2018

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

Objective of the study:

Gait speed is associated with morbidity and mortality[1] and is commonly used in geriatric settings as a quick, simple, and reliable measure of patients' functional capacity. The ability to walk and the resulting gait speed depends on the function and interplay of multiple physiological systems, including vision, central and peripheral nervous systems, perception, aerobic capacity, cardiorespiratory fitness, musculoskeletal system, and energy production and delivery[2,3]. Reduced gait speed is a sign of advancing age; it is associated with poor general health lower functional capacity, lowered response to rehabilitation, functional dependence, frailty, mobility disability, falls, institutionalization, hospitalization, cardiovascular-related events, and mortality[1,4–6]. It is also associated with cognitive decline[7].

Whereas much is known about the influence of reduced gait speed on health and behavior in later life, little is known about the life-course trajectories of gait speed and whether early-life factors influence gait speed later in life. Gait speed has largely been viewed as a measure of age-associated functional decline, but is it possible that gait speed captures brain dysfunction already in childhood?

Here, we aim to investigate 1) whether gait speed is a useful measure for describing variation in aging already at midlife, 2) whether gait speed captures brain dysfunction, and 3) whether gait speed trajectories are laid out already in early childhood.

Data analysis methods:

To address each our aims, we wish to conduct the following analyses:

1. **Is gait speed a useful measure for describing variation in aging already at midlife?**
   We will compute the distribution of gait speed at midlife to test if there is any variation in gait speed between individuals at age 45.

   Next, we will investigate whether the clinical correlates of gait speed at midlife are similar to those in aging populations, by analyzing sex-adjusted correlations between gait speed and various clinical measures, including measures that are commonly used in geriatric research:
   - Measures of functional capacity:
     - Handgrip strength
     - Balance
     - Chair stand test
     - Step-in-place
     - Grooved pegboard
     - Dexa scan (@Kim: Do you recommend any work-horse variable here?)
     - SF36
   - Measures of accelerated aging:

    - Biological Age
    - Pace of Aging
    - Facial aging

2. **Does gait speed capture brain dysfunction?**
   To investigate whether gait speed is "a brain issue", we will use correlation analyses to test if lowered gait speed is a function of reduced neurological and cognitive function, by testing the associations between imaging variables and variables of the neuropsychological test battery for cognitive function:
   - Neuroimaging:
     - Cortical thickness/surface area (total and region-specific)
     - Subcortical volumes
     - Cerebellar gray matter volume
     - White matter hyperintensities
   - Cognitive function:
     - Trail-making test
     - Animal naming
     - Wechsler memory test of mental control
     - Rey Auditory Verbal Learning Test, learning and recall
     - Processing speed
     - Working memory
     - Perceptual reasoning
     - Verbal comprehension
     - Total IQ (age 45)

3. **Are gait speed trajectories laid out in early childhood?**
   Finally, we will investigate whether gait speed is a developmental issue by testing whether the trajectory of gait begins in early life, using correlation analyses adjusted for childhood socioeconomic status to test for associations between gait speed and:
   - Childhood IQ
   - Change in IQ (Are the people with the largest decrease in IQ the ones with the lowest midlife gait speed?)
   - Age 3 brain integrity

<u>Variables needed at which ages:</u>

Childhood variables:
- Brain integrity (age 3)
- Components of brain integrity:
  - Motor: Bayley motor scale
  - Language: Reynell receptive language scale
  - Intelligence: Peabody picture vocabulary test
  - Neurological signs
  - Behavioral under control
- Childhood IQ (average across ages 7, 9, 11, 13)
- Childhood SES
- Zmotor3-9 or childhood balance

Age 45 variables:
- Average gait speed
- Individual gait speed components: walk, fast, cognitive walk
- Handgrip strength
- One-legged balance
- Grooved pegboard
- Chair stand test

- Step-in-place
- Muscle mass
- Bone density
- SF36
- Biological Age
- Pace of Aging
- Facial Aging
- Neuropsychological tests:
    - Trail-making test
    - Animal naming
    - Wechsler memory test of mental control
    - Rey Auditory Verbal Learning Test, learning and recall
    - Processing speed
    - Working memory
    - Perceptual reasoning
    - Verbal Fluency
    - IQ
- Neuroimaging:
    - Cortical thickness (total + regional)
    - Cortical surface area (total + regional)
    - Cerebellar gray matter volume
    - White matter hyperintensities

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

This study will extend our understanding of gait speed—a tool commonly used in clinical practice in the assessment of geriatric patients—and provide new information about the trajectories of gait speed as well as the functional deficits captured by reduced gait speed.

References cited:

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2. Fritz, S. & Lusardi, M. White Paper: "Walking Speed: the Sixth Vital Sign". *J. Geriatr. Phys. Ther.* **32,** 2–5 (2009).
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4. Middleton, A., Fritz, S. L. & Lusardi, M. Walking speed : The functional vital sign predictive capabilities of walking speed responsiveness of walking speed. *J. Aging Phys. Act.* **23,** 314–322 (2015).
5. Cesari, M. *et al.* Prognostic value of usual gait speed in well-functioning older people - Results from the health, aging and body composition study. *J. Am. Geriatr. Soc.* **53,** 1675–1680 (2005).
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Proposing Author	Line Jee Hartmann
Today's Date	14 December 2018

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LJHR	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
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LJHR	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.
LJHR	I will not "sync" the data to a mobile device.
LJHR	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Professor Moffitt or Caspi. (919-684-6758, tem11@duke.edu, ac115@duke.edu)
LJHR	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
LJHR	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. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to Terrie or Avshalom for strategies for achieving compliance with data-sharing policies of journals.*
LJHR	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. The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.

Signature: _____

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Comments:

Please check your contribution(s) for authorship:

	Conceptualizing and designing the longitudinal study
	Conceptualizing and collecting one or more variables
	Data collection
	Conceptualizing and designing this specific paper project
	Statistical analyses
	Writing
	Reviewing manuscript drafts
	Final approval before submission for publication
	Acknowledgment only, I will not be a co-author

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