Duke UNIVERSITY
DEPARTMENT OF PSYCHOLOGY & NEUROSCIENCE

TITLE: Association of Neurocognitive and Physical Function With Gait Speed in Midlife

A research team led by Line Rasmussen and Terrie Moffitt at Duke University reports that gait speed (how fast you walk) is not only an indicator of your physical well-being but also an index of the health of your brain. These findings are based on a study that followed a birth cohort of 1,000 children, born in the early 1970s and followed to age 45 years.

We tested gait speed in 45-year old participants from the population-representative Dunedin Study in New Zealand. Alongside gait speed, we also tested the participants' physical and cognitive functioning, and we imaged their brains in an MRI scanner. When they were young children, these study participants had their neurocognitive functions tested, so we could test the link between childhood brain health with gait speed at midlife.

We found that how fast people are walking in midlife tells us a lot about how much their bodies and brains have aged over time. Midlife adults with slower gait speed showed evidence of accelerated biological aging and greater declines in their cognitive functioning from childhood to midlife. A most remarkable finding was that we could predict how fast they walked at midlife by a childhood assessment of their neurocognitive functions at age 3. There was a difference of 12 IQ points on average between children who grew up to be the slowest (mean gait speed 1.21 meters per second) and fastest (mean gait speed 1.75 meters per second) walkers four decades later. Gait speed is not only an indicator of aging, but also an indicator of lifelong brain health.

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FINDINGS:
We studied a cohort of 1037 individuals who were born in 1972-73 and followed up until they were 45 years old. At age 45 years, we measured the research participants' gait speed by having them walk on a special 20-foot long pad equipped with sensors that measured their gait.

There was large variation in how fast people walked.

Midlife adults with slower gait showed indications of accelerated aging across multiple organ systems; their lung function, their dental health, their immune system had all deteriorated more rapidly since they were young adults, and their faces were rated as looking much older.

Midlife adults with slower gait had more physical limitations, more generally. They had weaker hand strength, they could not balance on one leg for a long time, and they had more difficulties rising rapidly from a chair. These are things that make every-day activities harder to perform.

All this may not surprise, but what was surprising was that they also showed brain changes. Those who walked more slowly had smaller brains, their brain cortex was thinner, and they had more white matter

hyperintensities. White matter hyperintensities are lesions of the white matter in the brain that are usually seen in much older adults.

In addition to these brain differences, midlife adults with slower gait also had a hard time performing on cognitive tests of memory, executive functions, processing speed, and perceptual reasoning.

Because we studied these people when they were children, we were able to show that those who walked the slowest also showed deteriorating performance from childhood to adulthood on these cognitive tests.

WHY ARE THESE FINDINGS IMPORTANT?

1. We found that the very simple test of measuring the speed at which people walk tells us a lot, not only about how the body is aging, but also how the brain is aging.

2. Gait speed is commonly used to predict risk of functional decline and mortality in geriatric and elderly populations. In a meta-analysis of 34,485 older adults (65+ years), slow gait speed was associated with earlier death (12% higher chance of survival per 0.1 meters per seconds faster gait speed; Studenski, S. et al., JAMA 2011;305(1):50-58). But why is gait speed such a good predictor? Our findings suggest that one of the reasons that gait can be such a powerful predictor of disability and death is that it indexes lifelong vulnerability in both the body and the brain.

3. Measuring gait speed may be an effective way to evaluate new clinical trials that aim to slow aging. A variety of treatments to slow human aging—ranging from low calorie diets to taking the drug metformin—are being tested. It might be easier to prevent aging-associated organ damage than to reverse it after it happens, suggesting that the effect of treatments to slow aging may work better if they were applied while people are still young and healthy. Gait speed could be used to measure the effect of such treatments on aging: the gait speed test is cheap, safe, easy to test repeatedly, and feasible to use among people in their 40s.

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UNIVERSITIES INVOLVED:

Duke University, USA; Copenhagen University Hospital Amager and Hvidovre, Hvidovre, Denmark; King's College London, United Kingdom; University of Otago, New Zealand; Durham VA Medical Center, North Carolina; University of North Carolina at Chapel Hill, USA.

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SUPPORTING DETAILS:

Participants: Participants were members of the Dunedin Longitudinal Study, an investigation of health and behavior in a representative birth cohort. The 1,037 participants were all individuals born between April 1972 and March 1973 in Dunedin, New Zealand. This birth cohort's childhood families represented the full range of socioeconomic status in the general population. Follow-ups have been carried out at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and most recently 45, when 94% of the living cohort members took part.

Measuring gait speed: Gait speed at age 45 years was measured under three walking conditions: normal walking; walking while doing another task (in our case, reciting every other letter of the alphabet); and, and maximum gait speed.

Measuring physical function: Physical function at age 45 was assessed by several brief exercises that index the ability to perform everyday activities: handgrip strength, one-legged balance, visual-motor coordination, chair-stand test, and 2-min step test.

Measuring accelerated aging: Accelerated aging was assessed by two measures: Pace of Aging and Facial Aging.

(1) Pace of Aging was measured for each participant with repeated assessments of a panel of 19 biomarkers taken at ages 26, 32, 38, and 45 years. The 19 biomarkers were: body mass index, waist-hip ratio, glycated hemoglobin (HbA1C), leptin, blood pressure (mean arterial pressure), cardiorespiratory fitness (VO_2Max), forced expiratory volume in one second (FEV_1), FEV_1 to forced vital capacity ratio (FEV_1/FVC), total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, apolipoprotein B100/A1 ratio, lipoprotein(a), creatinine clearance, urea nitrogen, C-reactive protein, white blood cell count, gum health, and caries-affected tooth surfaces. Change over time in each biomarker was modeled, and these rates of change were combined into a single Pace of Aging-index scaled in years of physiological change occurring per one chronological year.

(2) Facial Aging was based on ratings by an independent panel of 8 raters of photographs of each participant's face made during their age-45 assessment.

Measuring brain structure: At age 45, participants' brains were scanned with MRI to detect structural age-related features of the brain. High-resolution structural images were used to measure brain volume, average cortical thickness, total surface area, and white matter hyperintensities (lesions of the white matter in the brain).

Measuring neurocognitive function: Neurocognitive function at age 45 was assessed with the Wechsler Adult Intelligence Scale-IV (WAIS-IV), which generates the overall full-scale IQ, as well as measures of processing speed, working memory, perceptual reasoning, and verbal comprehension.

Measuring childhood neurocognitive function: At age 3, each child participated in a 45-minute examination that included assessments by a pediatric neurologist, standardized tests of intelligence, receptive language, and motor skills, and examiner ratings of each child's emotional and behavioral regulation. Child-to-adult cognitive decline was calculated by measuring the difference between scores on the Wechsler Adult Intelligence Scales (administered at age 45 years) and the Wechsler Intelligence Scale for Children–Revised (administered when the children were 7, 9, and 11 years old).