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Research Article

Adult Physical Function Has Roots in Early Childhood Brain Function: A Five-Decade Cohort Study

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Abstract

Objectives: Tests of physical function are often thought to measure functioning that is (1) musculoskeletal, and (2) newly declining in adult life. In contrast, this study aimed to: (1) add to evidence that physical-function tests also measure brain function, and (2) test the novel hypothesis that adult physical function is associated with brain function beginning in early childhood. We investigated early childhood brain function and midlife physical function in the Dunedin Study, a 5-decade longitudinal birth cohort (n = 1,037).

Methods: Brain function was measured at age 3 using 5 measures which formed a reliable composite (neurological examination, cognitive and motor tests, and temperament ratings). Physical function was measured at age 45 using 5 measures which formed a reliable composite (gait speed, step-in-place, chair stands, balance, and grip strength).

Results: Children with worse age-3 brain function had worse midlife physical function as measured by the age-45 composite, even after controlling for childhood socioeconomic status (β: 0.23; 95% CI: 0.16 to 0.30; $p < .001$). Worse age-3 brain function significantly predicted slower gait speed, fewer steps-in-place and chair-stands, worse balance, and weaker grip strength.

Discussion: Children with poorer brain function were more likely to have poorer physical-function scores as adults. In addition to indicating recent musculoskeletal decline, physical-function tests may also provide indications of lifelong, integrated brain–body health. By reconceptualizing the meaning of physical-function scores, clinicians can orient the use of physical-function tests in a more holistic approach to health care.

Keywords: Cognitive reserve, Life course, Neuropsychology, Physical function, Systems integrity

Physical-function tests are widely used to measure a person's physical functioning, defined as their ability to maintain independence by participating in activities of daily living (Painter et al., 1999). Various tests of strength, mobility, and balance flag signs of neuromuscular and musculoskeletal impairments that forecast when older adults are at an increased risk of falling, injury, or are too frail to live independently (Patrizio et al., 2020). A decline in physical function is associated with mortality, regardless of health, geographic area, or age (Pavasini et al., 2016). A leading view among clinicians and researchers is that physical-function tests can predict age-related health outcomes because they reflect a decline that (1) is in the musculoskeletal domain and (2) has manifested recently during adult life (Newman, 2023). However, emerging evidence is prompting a dawning awareness that this view may not capture the whole picture. In addition to describing age-related physical status, physical-function tests administered to adults may also reflect brain functions, including those that have origins in early life.

Instead of measuring only musculoskeletal health, physical-function tests may also tap into functions outside the musculoskeletal system, including brain function (defined as the central nervous system's capacity to give rise to behaviors and cognitions). Evidence that performance on physical-function tests is linked to brain function is derived from cognitive testing and MRI neuroimaging of adults. Worse physical function in adulthood is associated with worse performance and faster decline on cognitive tests in adults (De Looze et al., 2022; Jayakody et al., 2022). Worse physical function is also associated with lower brain volume, cortical thinning, higher white matter lesion volumes, and reduced surface area of certain functional networks in adults (Aribisala et al., 2013; Rasmussen et al., 2019). The connection between physical function and brain function also extends to clinical outcomes; older adults with mild cognitive impairment and dementia have poorer physical function than their unimpaired counterparts (Fujisawa et al., 2017). Taken together, findings suggest that physical-function measures are not merely tests of

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musculoskeletal function, but also indicators of central nervous system health.

Furthermore, evidence suggests that the poor adult brain functions that are associated with physical function have origins in childhood. Individual differences in cognitive performance tend to be stable from childhood to late life (Deary et al., 2013). In fact, extensive evidence shows that variation in the brain-function scores of older adults in large part reflects individual variation that has been present since early life (Walhovd et al., 2023). Moreover, early-life circumstances can have long lasting impact on later brain outcomes. Gestational exposures such as war, poor maternal nutrition, and maternal alcohol consumption are associated with smaller intracranial volumes, which indicates smaller lifetime maximal brain size (De Rooij et al., 2010). Early life factors shape the brain's cognitive reserve capacity, which is thought to buffer age-associated deterioration (De Rooij, 2022).

When brain function and physical function are both measured, researchers comment on ambiguous directionality (whether poor physical function predates cognitive decline or poor cognitive performance predates physical decline). But researchers who examine health in early life provide an alternative explanation altogether: better childhood brain function could be an indicator of a more integrated system (Deary, 2012). That integrated whole-body system would include physical function. This explanation is in line with the *early-systems integrity* theory, which states that individual differences in health are present from the beginning of life, and are consistent and persistent across the lifespan (Deary, 2012).

If adult physical-function tests share variation with adult brain function, and if adult brain function is in large part a continuation from childhood, then it is plausible that adult physical-function tests have their roots in early childhood as well. Nonetheless, we found no studies that take a life-course longitudinal approach to test this novel hypothesis of association between brain function in childhood and physical function in adulthood. At present, studies demonstrating positive associations between physical and cognitive functioning use point-in-time data, typically in older adults (Handing et al., 2020; Sprague et al., 2019). Some studies use prospective designs to show the prognostic value of physical-function tests in prediction of health outcomes, including cognitive outcomes (Hernández-Luis et al., 2018; Wang et al., 2006), but only in older adults.

To address these gaps, the present study used a prospective longitudinal design that spans five decades, studying a population-representative cohort followed from birth to midlife. Our primary aim was to quantify the association between brain function measured at age 3 and midlife physical function, measured at age 45. All analyses also controlled for childhood socioeconomic status to evaluate whether childhood-to-adulthood associations were attributable to socioeconomic resources during upbringing. We hypothesized that better brain function at age 3 would be associated with better physical function in midlife, indicating that physical-function tests index lifelong integrated health.

In addition, we investigated whether both self-reports of physical function and objective tests of physical function were similarly related to childhood brain function. Physical-function tests are thought to improve upon traditional self-reported physical-function scales. However objective physical-function tests cannot always be used, so it is useful to determine whether self-report and objective tests are similarly related to childhood brain function (Feuering et al., 2014).

Method

A more detailed description of the study design, measures, and analyses is available in Supplementary Material.

Dunedin Study Sample

Participants are members of the Dunedin Longitudinal Study. This cohort includes all individuals born between April 1972 and March 1973 in Dunedin, New Zealand, who participated in the first follow-up assessment at age 3 (N = 1,037; 91% of those eligible; 52% male). Assessments were carried out at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and most recently 45 years, when 94% (n = 938) of the 997 Study members still alive were assessed. At each assessment, Study members were brought to the Dunedin research unit for a full day of interviews and examinations. Study member written informed consent was obtained, with study protocol approval by the New Zealand Health and Disability Ethics Committee.

The cohort is primarily New Zealand European/White; 7.5% self-identify as having Māori ethnicity (the Indigenous people of Aotearoa, New Zealand), matching the demographics of the South Island. The cohort represents the full range of socioeconomic status in the general population of New Zealand's South Island. As adults, the cohort's members match the New Zealand National Health and Nutrition Survey on key health indicators (e.g., body mass index, smoking, physical activity, and physician visits) and the New Zealand Census of citizens the same age on educational attainment (Poulton et al., 2022).

Age-3 Brain Function

At age 3 years, each child in the cohort participated in a 45-min examination that included assessments of intelligence, receptive language, motor skills, and neurologic soft signs. *Receptive language* was assessed using the Reynell Developmental Language Scales (N = 1,028; M = 34.84, standard deviation [SD] = 8.76; Reynell, 1969). *Vocabulary comprehension* was assessed with the Peabody Picture Vocabulary Test (N = 979; M = 23.52, SD = 9.57; Dunn, 1995). *Motor development* was assessed using the Bayley Motor Scales (N = 976; M = 20.56, SD = 4.38; Bayley, 1969). This assessment is used to document sequelae of brain injury in young children (Cyr et al., 2022). Each child was examined by a pediatric neurologist for *neurologic soft signs* (N = 978; M = 0.16, SD = .47). These included motility, passive movements, reflexes, facial musculature, strabismus, nystagmus, foot posture, and gait (Touwen & Prechtl, 1970). After testing, the examiner rated each child's behavior during the testing session, yielding a factor termed "*lack of control*" (N = 1,024; M = 1.29, SD = 2.27; Caspi et al., 1995). The lack of control measures characterized the child's emotional lability, restlessness, attention span, and negativism during the testing session. These five variables were significantly intercorrelated, with absolute correlations ranging from 0.13 to 0.67 (Table 1). Using these five variables, we created a summary score using confirmatory factor analysis which we termed "age-3 brain function," a global index of the child's early neurocognitive status.

The confirmatory one-factor model of age-3 brain health fit the data well, χ^2 (N = 1,035, df = 5) = 6.459, p = .2641; comparative fit index = 0.999; Tucker–Lewis index = 0.997;

Table 1. Correlations Between Age-3 Brain Function, Age-45 Physical Function, Age-45 Self-reported Physical Limitations, and Age-45 IQ

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age-3 brain function composite													
2. Age-3 Reynell receptive language	0.94												
3. Age-3 Peabody picture vocabulary	0.89	0.67											
4. Age-3 Bayley motor	0.42	0.31	0.25										
5. Age-3 neurological abnormalities	−0.19	−0.12	−0.13	−0.05									
6. Age-3 lack of control rating	−0.60	−0.44	−0.37	−0.22	0.16								
7. Age-45 physical function composite	0.28	0.24	0.25	0.15	−0.05	−0.17							
8. Age-45 gait speed	0.28	0.25	0.24	0.11	−0.06	−0.16	0.65						
9. Age-45 step-in-place	0.21	0.19	0.18	0.10	−0.02	−0.12	0.71	0.34					
10. Age-45 chair stands	0.19	0.15	0.17	0.12	−0.01	−0.13	0.86	0.34	0.45				
11. Age-45 one-leg balance	0.22	0.20	0.18	0.09	−0.04	−0.13	0.59	0.28	0.25	0.34			
12. Age-45 relative grip strength	0.09	0.08	0.08	0.09	−0.04	−0.02	0.47	0.26	0.20	0.28	0.23		
13. Age-45 SF-36 physical limitations	−0.18	−0.16	−0.16	−0.08	0.08	0.10	−0.34	−0.27	−0.23	−0.25	−0.25	−0.22	
14. Age-45 IQ	0.45	0.41	0.38	0.15	−0.11	−0.26	0.40	0.38	0.29	0.26	0.28	0.17	0.20

Notes: IQ = Intelligence Quotient; SF-36 = 36-Item Short Form Survey.
Numbers are standardized regression coefficients (β) adjusted for sex.

and root-mean-square error of approximation = 0.017. Missing data were handled using full-information maximum likelihood in MPlus Version 7. The five tests of age-3 brain had standardized factor loadings of: Reynell Developmental Language Scales = 0.86; Bayley Motor Scales = 0.44; Peabody Picture Vocabulary Test = 0.77; Neurologic soft signs = −0.22; Lack of control rating = −0.55. Factor scores were output and standardized to a mean = 0 and *SD* = 1, as previously reported (Caspi et al., 2014).

Childhood Socioeconomic Status

Childhood socioeconomic status was defined as the highest occupational status of either parent averaged across study assessments from the Study member's birth through 15 years (1 = *unskilled laborer*; 6 = *professional*), on New Zealand's occupational rating of the 1970s (Poulton et al., 2002).

Midlife Physical Function

At age 45 (hereafter termed midlife), physical function was assessed by five exercises that index the ability to perform everyday activities (see Figure 1 for an illustration of each test). *Gait speed* (measured in meters/s) was assessed with the 6-meter long GAITRite Electronic Walkway (CIR Systems, Inc.) with a 2-meter acceleration and a 2-meter deceleration before and after the walkway. Gait speed was assessed under three conditions: (1) usual gait speed: walk at normal pace from standing, measured as a mean of two trials; (2) maximum gait speed: walk as fast as possible, measured as a mean of three trials; and (3) dual-task gait speed: walk at a normal pace while reciting alternate letters of the alphabet out loud, starting with the letter "A," measured as the mean of two trials. Gait speed was correlated across the three conditions (r = 0.46 between usual and maximum gait speed, r = 0.75 between usual and dual-task gait speed, r = 0.45 between maximum and dual-task gait speed). To increase measurement reliability, we averaged the three walk conditions to generate our measure of composite gait speed, as previously reported (Rasmussen et al., 2019).

There were two tests of lower body strength and coordination. Study members did the *2-min step test*, which is measured as the number of times they could lift their right knee to mid-thigh height (halfway between the kneecap and the iliac crest) in 2 min, while standing, at a self-directed pace. Study members also did the *chair stand test*, measured as the number of chair stands a Study member completed in 30 s from a seated position.

Balance was assessed using the *one-legged balance test*. With arms crossed over the chest, Study members stood on their choice of leg, lifted their other leg, found their balance, and then closed their eyes. The test continued until the Study member uncrossed arms put a foot down, opened their eyes, or after 30 s had elapsed. Study members were given three attempts to reach the 30 s maximum. Otherwise, the score was recorded as the maximum time across the three trials. At age 45, a large proportion of Study members (n = 176) stood for the entire 30 s. To optimize normality, the variable was recoded into seven bins ([0,5] = 1, (5,10] = 2, (10,15] = 3, (15,20] = 4, (20,25] = 5, (25,29] = 6, (29,30] = 7). This binned balance variable was used for all analyses.

Finally, *hand-grip strength* was measured using the Jamar digital dynamometer. Because grip strength is influenced by upper extremity position, we required the elbow to be held at 90 ° and the upper arm to be tight against the trunk for a series of three

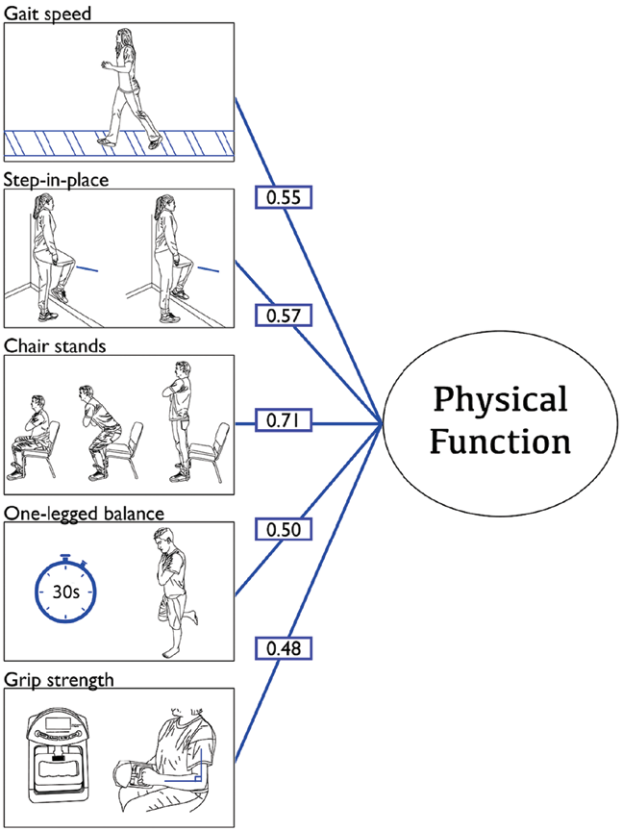

Figure 1. Confirmatory factor analysis yielded a one-factor model of midlife physical function. Numbers are factor loadings. The comparative fit index (CFI; 0.976), the Tucker–Lewis index (TLI; 0.953), and the root-mean-square error of approximation (RMSEA; 0.058) indicate that the model fits the data well. The maximum likelihood estimator and the nonlinear minimization subject to box constraints (NLMINB) optimization method were used, yielding a factor score for 922 Study members.

measurements, with brief pauses between each. The forearm was not resting on a surface during testing. Grip strength was recorded as the maximum value of the three measurements on either hand. A measure of relative grip strength normalized for each Study member's body weight was used due to the greater utility of this measure in representing sarcopenia compared to unadjusted grip strength (Peterson et al., 2023).

The five tests of physical function were positively correlated, with correlations ranging from 0.20 to 0.45 (Table 1). To construct a summary measure of midlife physical function, we fit a one-factor confirmatory factor model in R using the lavaan 0.6-12 package. The model fit the data well: χ^2 (df = 5) = 20.426, p = .001; comparative fit index = 0.976; Tucker–Lewis index = 0.953; and root-mean-square error of approximation = 0.058. The five physical-function tests were loaded onto a single factor with standardized factor loadings of 0.48–0.72. Figure 1 shows the structure of the physical-function composite factor analysis. The maximum likelihood estimator and the nonlinear minimization subject to box constraints optimization method were used to extract a factor score for 922 Study members. In addition to physical-function tests, we also asked Study members to report their severity of physical limitations using the 10-item physical function rating scale from the RAND 36-item Short Form Survey, with higher scores reflecting more limitations (Ware & Sherbourne, 1992).

Midlife Brain Function (WAIS-IV IQ)

Brain function at age 45 was assessed with the Wechsler Adult Intelligence Scale, 4th edition, which generates the overall full-scale Intelligence Quotient (IQ; Wechsler, 2012).

Statistical Analysis

To be included in the analyses, we required that participants have data on the age-3 brain function composite and the age-45 physical function composite, resulting in an analysis sample of N = 920.

Continuous measures are presented as mean (SD). We calculated Pearson correlation coefficients (r). We performed linear regression analyses with all variables standardized to mean = 0 and SD = 1, and we present standardized regression coefficients (β) for the associations between age-3 brain function and midlife physical-function tests using two models: (1) adjusting for sex and (2) adjusting for sex and childhood socioeconomic status. We present effect sizes (β), 95% CIs, and p values for all tests conducted.

Statistical analyses were performed in R version 4.2.2. Analyses reported here were preregistered (https://dunedinstudy.otago.ac.nz/files/1688609086_Xie.pdf) and checked for reproducibility by an independent data analyst, who used the manuscript to recreate the statistical code and applied it to a fresh copy of the data set.

Results

Of the original 1,037 Study members, 997 were still alive at age of 45 years, and 938 (94.1%) were assessed at midlife. Attrition analyses comparing the full cohort, those alive at age 45, and the study sample showed no statistically significant differences in childhood socioeconomic status or age-3 brain function, suggesting no differential drop-out over the course of the longitudinal study (Supplementary Figure 1).

Age-3 Brain Function and Midlife Physical Function

The physical-function tests were positively intercorrelated; midlife adults who performed well on one test also performed well on the other tests (Table 1). Using the physical-function composite which combined the five physical-function tests into a single factor, we found that children with worse brain function at age 3 had significantly lower scores on midlife physical function (β: 0.28; 95% CI: 0.22 to 0.35; p < .001), even after controlling for childhood socioeconomic status (β: 0.23; 95% CI: 0.16 to 0.30; p < .001; Table 2).

After additionally controlling for age-45 socioeconomic status, the association remained significant (β: 0.17; 95% CI: 0.11 to 0.24; p < .001). However, age-45 socioeconomic status could mediate the association from age-3 brain function to midlife physical function or age-45 socioeconomic status could be an outcome of poor adult physical function. Thus, this could be an overcontrol. There were no sex differences in the association between age-3 brain function and midlife physical function (Supplementary Figure 2).

To ensure that the association between age-3 brain function and midlife physical function did not unduly depend on the dual-task gait paradigm, we repeated the analyses omitting the dual-task gait paradigm, which did not significantly affect results (β: 0.29; 95% CI: 0.22 to 0.35; p < .001 without controlling for Socioeconomic Status (SES), and β: 0.23; 95% CI: 0.17 to 0.30; p < .001 after controlling for SES).

Table 2. Comparison of Associations Between Components of Age-3 Brain Function and Components of Age-45 Physical Function, Before and After Controlling for Childhood Socioeconomic Status (SES) in the Models

Age-3 brain function	Age-45 physical function															
	Physical function composite		Gait speed		Step-in-place		Chair stands		One-legged balance		Relative grip strength		Self-reported physical limitations	
	Without SES	With SES	Without SES	With SES	Without SES	With SES	Without SES	With SES	Without SES	With SES	Without SES	With SES	Without SES	With SES
Brain function composite	*.28 (.22,.35)*	*.23 (.16,.30)*	*.28 (.21,.35)*	*.23 (.16,.30)*	*.21 (.14,.28)*	*.18 (.11,.25)*	*.19 (.12,.26)*	*.15 (.08,.22)*	*.22 (.16,.29)*	*.18 (.11,.25)*	*.09 (.04,.15)*	*.07 (.01,.13)*	*-.18 (-.24, -.11)*	*-.15 (-.22, -.08)*
Reynell receptive language	*.24 (.18,.31)*	*.19 (.12,.26)*	.25 (.19,.32)	.21 (.14,.28)	.19 (.12,.26)	.15 (.08,.23)	.15 (.08,.22)	.11 (.04,.18)	.20 (.13,.27)	.16 (.09,.23)	.08 (.02,.14)	.06 (.00,.12)	-.16 (-.23, -.10)	-.13 (-.20, -.06)
Peabody picture vocabulary	*.25 (.18,.31)*	*.19 (.13,.26)*	.24 (.17,.30)	.19 (.12,.26)	.18 (.11,.25)	.15 (.07,.22)	.17 (.11,.24)	.14 (.07,.21)	.18 (.12,.25)	.14 (.07,.21)	.08 (.02,.13)	.06 (-.00,.12)	-.16 (-.22, -.09)	-.13 (-.19, -.06)
Bayley motor	*.15 (.08,.22)*	*.14 (.07,.21)*	.11 (.04,.19)	.10 (.03,.18)	.10 (.02,.17)	.09 (.01,.16)	.12 (.04,.19)	.11 (.04,.18)	.09 (.02,.17)	.08 (.01,.16)	.09 (.03,.15)	.08 (.02,.14)	-.08 (-.15, -.01)	-.07 (-.14,.00)
Neurological abnormalities	*-.05 (-.12,.02)*	*-.04 (-.11,.03)*	-.06 (-.13,.02)	-.05 (-.12,.02)	-.02 (-.09,.06)	-.01 (-.09,.06)	-.01 (-.09,.06)	-.01 (-.08,.06)	-.04 (-.11,.03)	-.03 (-.11,.04)	-.04 (-.10,.02)	-.04 (-.09,.02)	.08 (.01,.15)	.07 (.00,.14)
Lack of control rating	*-.17 (-.23, -.10)*	*-.15 (-.22, -.09)*	-.16 (-.23, -.09)	-.15 (-.21, -.08)	-.12 (-.19, -.05)	-.11 (-.18, -.04)	-.13 (-.20, -.06)	-.12 (-.19, -.05)	-.13 (-.20, -.07)	-.12 (-.19, -.06)	-.02 (-.08,.03)	-.02 (-.08,.04)	.10 (.03,.16)	.09 (.03,.16)

Notes: Bold and italicized values denote associations involving composite measures.
Numbers are standardized regression coefficients (β) and 95% confidence intervals.
All models are adjusted for sex.

Three-year-old children with worse brain function also performed more poorly on each of the five physical-function tests at midlife; associations were statistically significant even after controlling for childhood socioeconomic status (Table 2). Children with worse brain function had slower gait speed than adults (β: 0.23; 95% CI: 0.16 to 0.30; $p < .001$). They also performed worse on tests of lower body strength and coordination: the step-in-place (β: 0.18; 95% CI: 0.11 to 0.25; $p < .001$) and the chair stand tests (β: 0.15; 95% CI: 0.08 to 0.22; $p < .001$). They had worse balance on one leg with their eyes closed (β: 0.18; 95% CI: 0.11 to 0.25; $p < .001$) and weaker grip strength (β: 0.07; 95% CI: 0.01 to 0.13; $p < .05$).

The measure of age-3 brain function included five components: Reynell Receptive Language Test, Peabody Picture Vocabulary Test, Bayley Motor Scales, neurologic soft signs, and temperament lack of control during testing (see Methods for descriptions). To test whether any single component of the age-3 brain function composite accounted for associations with midlife physical function, we separately tested the association between each component and the midlife physical-function composite. Each of the five components of age-3 brain function (and importantly, not only the neurological soft signs or motor-skills measures) was significantly associated with the midlife physical function composite (Table 2).

How Big Is the Association? Midlife IQ as a Benchmark

Midlife IQ can serve as a useful benchmark for evaluating the link between age-3 brain function and midlife physical function. One would expect an association between age-3 brain function and midlife IQ (Breit et al., 2024) and between concurrent midlife IQ and physical function. Indeed, the association between age-3 brain function and the WAIS-IV IQ measured 42 years later was significant (β: 0.46; 95% CI: 0.39 to 0.52; $p < .001$), as was the association between midlife physical function and concurrent midlife IQ (β: 0.40; 95% CI: 0.34 to 0.46; $p < .001$). We hypothesized that, like the benchmark association between age-3 brain function and midlife IQ (β: 0.46; 95% CI: 0.39 to 0.52; $p < .001$), the association between age-3 brain function and midlife physical function would be moderate, positive, and significant. It was: β: 0.28; 95% CI: 0.22 to 0.35; $p < .001$.

Figure 2 shows that age-3 brain function was related to both midlife IQ and midlife physical function in a dose-response manner. Children who scored in the lowest quintile of brain function at age 3 scored 0.73 *SD* units more poorly on midlife physical-function tests (Figure 2A) and 1.19 *SD* units more poorly on midlife IQ tests (Figure 2B) compared to their counterparts in the best quintile of age-3 brain function.

Self-reported Physical Function

In many settings, it is not possible to administer objective physical-function tests. Instead, physical function is ascertained with self-report measures. Most Dunedin Study members reported few physical limitations in midlife ($M = 2.1$, $SD = 3.29$). Consistent with other research, Study members who self-reported more physical limitations performed worse on objective physical-function tests: β: −0.32; 95% CI: −0.38 to −0.26; $p < .001$, for the composite factor score, as well as with each individual test of physical function (Table 1). Crucially, age-3 brain function was similarly associated with both self-reported (β: −0.15; 95% CI: −0.22 to −0.08;

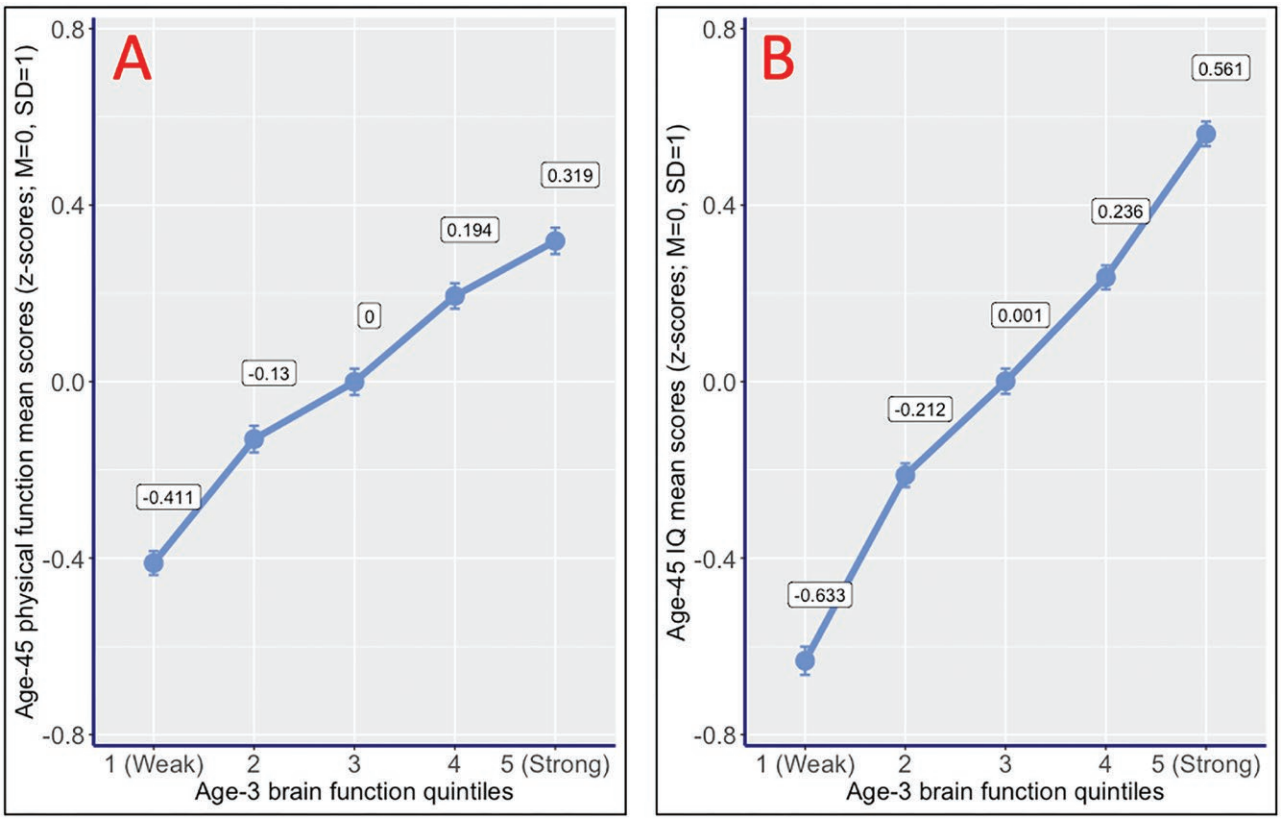

Figure 2. The association between age-3 brain function and age-45 physical function (Panel **A**) followed a dose-response pattern, as did the association between age-3 brain function and age-45 IQ (Panel **B**). Age-3 brain function was binned into quintiles for illustrative purposes. Age-45 physical function and age-45 IQ were each standardized to $M = 0$ and $SD = 1$. Panels A and B plot means and standard error bars, after controlling for sex. The association between age-3 brain function and midlife physical function (β: 0.28; 95% CI: 0.22 to 0.35; $p < .001$) was about two-thirds the size of the association between age-3 brain function and midlife IQ (β: 0.46; 95% CI: 0.39 to 0.52; $p < .001$). Three-year old children in the weakest quintile of brain function scored 0.73 *SD* more poorly on the adult physical function tests (Panel **A**) and 1.19 *SD* more poorly on the midlife IQ test (Panel **B**) compared to their counterparts in the strongest quintile of brain function.

$p < .001$) and objective measures (β: 0.23; 95% CI: 0.16 to 0.30; $p < .001$) of physical function (Figure 3).

Discussion

In the Dunedin Study cohort, brain function and physical function were correlated over four decades. Children with worse brain function at age 3 had significantly worse midlife physical function measured at age 45, even after controlling for sex and childhood socioeconomic status. Worse age-3 brain function was significantly associated with slower gait speed, fewer step-in-place and chair stands, worse balance, and weaker grip strength. This association was about two-thirds the size of the association between age-3 brain function and midlife IQ.

The present study's findings have implications for theory. Traditional theoretical views state that physical-function tests reflect musculoskeletal health (Painter et al., 1999; Patrizio et al., 2020; Pavasini et al., 2016). When physical-function tests are used in clinical geriatric practice, they are applied to detect a decline in function that is often assumed to have begun in late life (Newman, 2023). In contrast, emerging theoretical views emphasize that the individual differences in scores on tests administered to older adults reflect variation that has been present from early life and better childhood function indicates a more integrated system that persists across the life course (the *early-systems integrity* perspective; Deary, 2012).

The findings of this study are consistent with systems integrity theory, illustrating that physical-function tests tap into brain function in addition to musculoskeletal strength and integrity. First, consistent with previous research showing correlations between physical and cognitive function (Blackwood et al., 2023; Rosano et al., 2005; Sprague et al., 2019), the midlife physical-function composite was correlated with concurrent midlife IQ testing. Second, this study provides the novel finding that midlife physical function is also associated with age-3 brain function, demonstrating that the connection between physical and cognitive domains traces back to early childhood. Notably, when the age-3 brain function composite was decomposed, the midlife physical function composite was associated with all of the age-3 brain function composite's constituent tests except neurological soft signs and not just the Bayley Motor Scales. This suggests that all domains of age-3 brain function (e.g., language skills and self-control), not just motor skills, are related to midlife physical function.

Finally, the findings of this study support the theoretical construct of *cognitive reserve*, which proposes that there exist individual differences in brain resilience that allow some people to cope with brain changes better than others (Stern, 2009). These individual differences can be detected through neurological exams and through tests of cognitive function

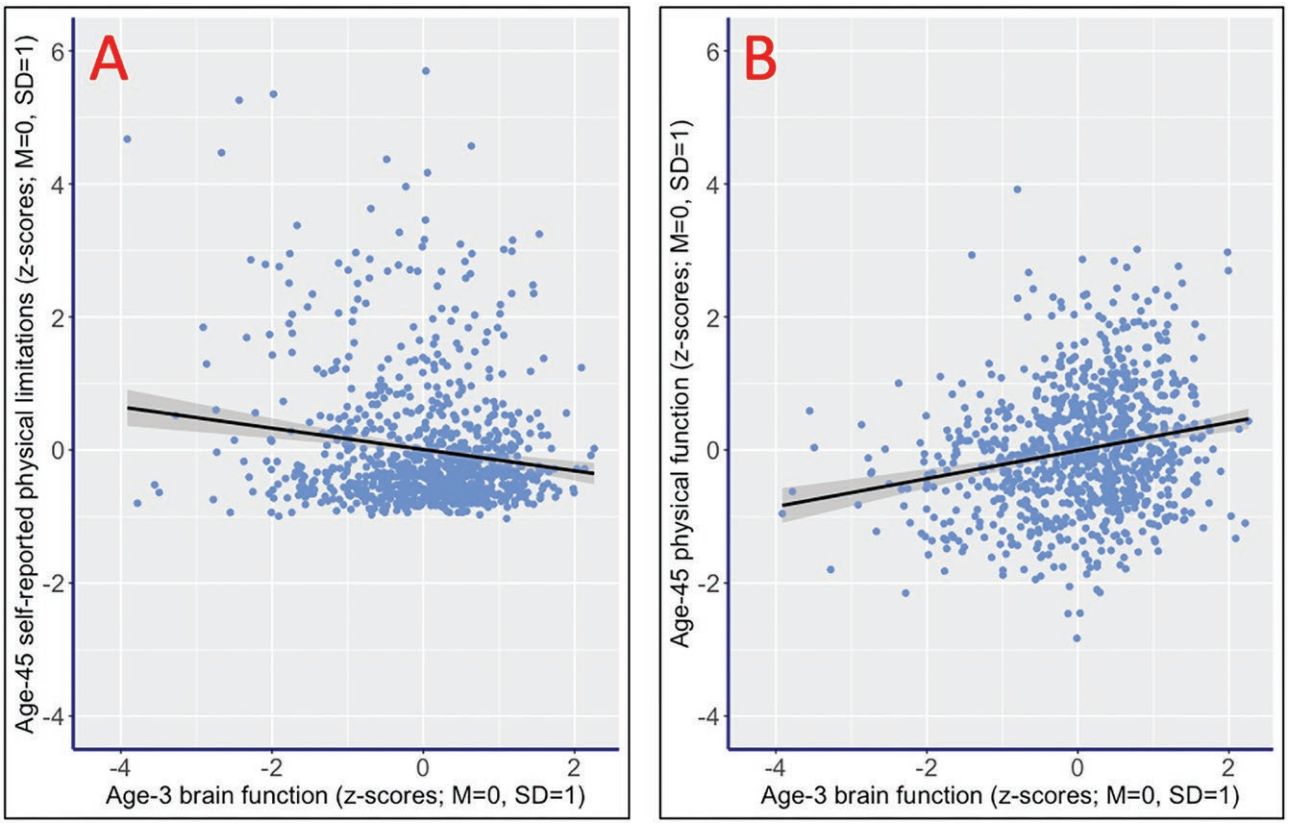

Figure 3. Age-3 brain function was significantly associated with both self-reported physical limitations (Panel **A**) and objective physical function test performance (Panel **B**) at age 45. Self-reported physical limitations (Panel **A**) are responses on the SF-36 questionnaire at age 45. Physical function (Panel **B**) reflects scores on the age-45 physical function composite. Both scores were standardized to $M = 0$ and $SD = 1$; models controlled for sex and childhood socioeconomic status. Age-3 brain function was similarly associated with self-reported physical limitations (β: −0.15; 95% CI: −0.22 to −0.08; $p < .001$) as with the objective measures of physical function (β: 0.23; 95% CI: 0.16 to 0.30; $p < .001$). Study members who reported more physical limitations in midlife performed more poorly on the objective physical function tests (β: −0.32; 95% CI: −0.38 to −0.26; $p < .001$). Reanalysis of Panel A without outliers (Study members with SF-36 scores 4 *SD* above the mean) also yielded a significant association between age-3 brain function and age-45 self-reported physical limitations (β: −0.11; 95% CI: −0.17 to −0.05; $p = .001$).

that reveal efficiency or flexibility in task performance (Stern, 2009). To that end, our assessment of age-3 brain function has components that measure both neurologic soft signs and cognitive capacity (e.g., intelligence assessments and lack of control). Better age-3 brain function may help individuals cope with brain changes throughout life, the effects of which may be reflected in physical-function test performance in midlife.

It is striking that an association between age-3 brain function and midlife physical function has emerged from data spanning four decades. Yet, the effect size is not so large that it implies that children who have low brain function are doomed to a lifelong trajectory culminating in poor physical function. Rather, this finding highlights the importance of additional supports (e.g., special health and education programs) to bolster resources for children whose brain health may deem them at risk.

The present study's findings also have implications for future research. Historically, the concepts of early-life development and aging have been treated as distinct and studied separately (Schreck, 2014). Our findings fit an alternative life-course developmental perspective that development and aging exist along the same conceptual path, requiring that they are studied together (Mikkola et al., 2023). Researchers interested in aging should look beyond only studying older adults and use longitudinal cohorts to investigate the mechanisms through which early-life development is linked to later-life aging. We propose two nonexhaustive hypotheses for future research about the link between early childhood brain function and adult physical function.

The first hypothesis is that common genes may affect both childhood brain function and adult physical function. Although there have been increasingly large investigations of the genetics of intelligence (Savage et al., 2018; Sniekers et al., 2017) and of physical function (Garatachea & Lucia, 2013), to our knowledge, there are no studies that identify genetic factors implicated in both cognitive and physical function. Genes that contribute to intelligence are predominantly enriched in brain tissue (Savage et al., 2018), while those contributing to physical function are enriched in skeletal, muscular, and inflammation-related processes (Garatachea & Lucia, 2013). However there is suggestive evidence of genetic correlations between physical-function measures and brain function. For example, genes associated with gait speed are also involved in synaptic function and neuronal development pathways (Ben-Avraham et al., 2017), and genes associated with grip strength are also implicated in neuronal maintenance (Willems et al., 2017).

The second hypothesis for future research is that the impacts of social determinants of health and related lifestyle factors accumulate over time in children with worse brain function,

leading to poorer adult physical function (Belsky et al., 2015; Lioret et al., 2020). Perhaps there is an occupational mediator as well, wherein people with poorer brain function do worse in school and are more likely to attain jobs in industries involving physical labor, which erode musculoskeletal health over time. Children with poorer brain function may also be less likely to access medical attention if they become unwell as adults, given that lower childhood IQ is associated with less knowledge about health in adulthood (Murray et al., 2011).

Last, the present study's findings have implications for clinical practice. The association between age-3 brain function and midlife physical function remained robust when the physical-function composite was decomposed into its five constituent tests. Despite measuring slightly different aspects of physical function (e.g., upper body vs lower body strength), the five physical-function tests are all associated with brain function in a way that extends back to early childhood. This is a useful insight, given that the five physical-function tests used in this study are among the most commonly used in clinical practice (Patrizio et al., 2020). We also note that age-3 brain function was similarly associated with objective and self-reported measures of physical function. In situations where it is not possible to administer a battery of physical-function tests, self-report physical-function scales may be a useful substitute.

With evidence that physical-function tests tap into lifelong integrated health that includes brain function, we can reconceptualize their meaning in clinical settings. Clinicians can orient the use of these tests in a more holistic approach to health care, beginning earlier in life. Findings from the present study show that there is already appreciable variation in physical function in midlife, supporting the wider use of physical-function tests in primary-care settings. Most importantly, findings show that poor physical function indicates more than just musculoskeletal weakness; rather, it reflects a lifelong deficit in central nervous system health. This suggests that physical-function tests, while simple, consistently predict later mortality because they tap into brain functioning along with physical strength and integrity.

This study offers several strengths. First, the Dunedin Study is a population-representative birth cohort with minimal attrition throughout its 45 years of investigation which gave us the rare opportunity to study how early childhood relates to health status in midlife in the same sample. For early childhood exposures, we were able to use direct measurements from participants instead of retrospective life history surveys, and analyses were not hampered by survivor bias. Second, childhood brain function is an important predictor of health and mortality across the lifespan (Calvin et al., 2011) and our measure of age-3 brain function probes the construct holistically and in a sensitive period. Given that education is the most lasting and robust intervention for improving cognitive function (Ritchie & Tucker-Drob, 2018), early childhood (i.e., before children start schooling) is a particularly appropriate time for risk factor identification. Third, midlife physical function is important to study given that age-related disease processes begin in midlife (Infurna et al., 2020; Moffitt et al., 2017). Midlife physical-function measurement allows more opportunity for intervention (e.g., physical therapy) that may slow the progression of physical decline, compared to measurement in old age.

This study has limitations. First, Dunedin Study members represent one country and are mainly White. The current results should be replicated in samples with different ancestral backgrounds to determine whether findings generalize. Second, the Dunedin Study did not employ all of the same physical-function tests before age 45 and the sample has not yet reached older age. As a result, we are only able to examine physical function as a point-in-time outcome and cannot comment on change over time. There is evidence that change in gait speed is more predictive of cognitive decline in older age than a point-in-time gait speed measure (White et al., 2013). In the future, it will be important to probe the predictive properties of age-3 brain function with regards to change trajectories of physical-function measures brought on by advanced age.

Age-3 brain function and midlife physical function were correlated in a population-representative study spanning five decades. This association remained robust after controlling for sex and childhood socioeconomic status. These findings support the theories of systems integrity and cognitive reserve and support the more extensive use of physical-function tests in midlife as a window into holistic health. More research is needed about the 2nd to 4th decades of life to investigate what sustains the connection between age-3 brain function and midlife physical function.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* online.

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Conflict of Interest

None.

Data Availability

Data sets are available from the data owners. Data from the Dunedin Study can be accessed through agreement with the Study investigators. Analyses reported here were preregistered (https://dunedinstudy.otago.ac.nz/files/1688609086_Xie.pdf) and checked for reproducibility by an independent data analyst, who used the manuscript to recreate the statistical code and applied it to a fresh copy of the data set.

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Ethical Approval

The Dunedin Study was approved by the University of Otago Ethics Committee. Participants gave written informed consent before participating.

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