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Lifetime cognitive performance is associated with midlife physical performance in a prospective national birth cohort study

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Abstract

Objectives—To examine whether measures of cognitive performance across life are related to physical performance at age 53y, allowing for potential confounders.

Methods—In a large representative British birth cohort of men and women (N=2135) the associations between cognitive performance across life (i.e. standardised cognition scores at ages 15, 43 and 53y and changes in verbal memory and search speed scores between 43 and 53y) and measures of physical performance at age 53y (i.e. standing balance, chair rising and grip strength) were examined. Adjustments were made for body size, physical activity levels, health status and socioeconomic conditions at age 53y.

Results—Higher cognitive scores on all childhood and adult tests, and a slower decline in verbal memory and search speed, were associated with better standing balance. Higher verbal fluency scores and a slower decline in verbal memory and search speed were more strongly related than scores on tests of general cognitive ability to chair rising. The relationships between cognitive performance and grip strength were inconsistent and weak.

Conclusions—The differential patterns of association found are consistent with the degree to which each is dependent upon central nervous system function. Our findings suggest that initial developmental differences as well as shared ageing processes may underlie associations found between cognitive and physical performance.

Keywords

Lifetime cognition; physical performance; birth cohort; developmental differences

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Introduction

The ability to maintain independence and quality of life in later adulthood depends significantly on the maintenance of cognitive and physical performance. There are reasons to expect to find associations between cognitive and physical performance and their rate of change with age. At the simplest level, the execution of physical tasks involves the sensorimotor nervous system and requires information processing and attention. Similarly, the execution of cognitive tests may be affected by physical and sensory disabilities and evidence suggests that physical activity has a positive effect on cognitive function.(1;2) More fundamentally, both motor and cognitive systems are likely to be influenced by processes, developmental and degenerative, which regulate central nervous system (CNS) function. Consistent with the suggestion that there are developmental and ageing processes which influence both cognitive and physical performance is the evidence that both can be negatively influenced in parallel by factors such as chronic disease, sedentary lifestyles and poor socioeconomic conditions.(3–7) How the interactions between motor, cognitive and sensory systems change with age and disease has been identified as a key area for further research.(8) One of the first important steps is to establish what links exist between cognitive and physical performance independent of chronological age.

Most previous studies that have investigated the relationships between cognitive and physical performance in adulthood(9–13) have been cross sectional, heterogeneous for age, small or unrepresentative, focused on older persons, or lacking information on possible confounders. The wide age range of many study populations could have resulted in associations being found between cognitive and physical performance as an artefact of independent associations between each of these sets of variables and chronological age.(9;14) Hence there is a need to examine associations between cognitive and physical performance in narrow age cohorts.

In a large cohort of British men and women followed regularly since birth in 1946, we examine how cognitive performance and its change across life are related to different dimensions of physical performance at age 53 years, namely grip strength, standing balance and chair rising. The cognitive measures include tests of general cognitive ability taken in adolescence and adult life, tests of verbal memory and search speed administered twice in adult life, and a test of adult verbal fluency. The tests of general cognitive ability are less subject to age-associated decline than the other measures of cognitive performance.(15;16) The use of a range of different types of cognitive tests taken at different ages, some of which are stable and others which decline with age, allows us to identify whether observed relationships between physical and cognitive performance in midlife are due to initial individual differences governed by developmental processes or are due to age-related changes in adult life.

This study has several other advantages. As the cohort were all born within the same week of the same year any cross-sectional associations between cognitive and physical performance cannot be the result of confounding by chronological age. Further, subjects are in late midlife and so few have major physical, sensory or mental impairments that could interfere with the execution of the tests allowing us to rule out this explanation as the reason

for any observed relationships. Data are available on a range of potential confounders, including socioeconomic conditions, physical activity levels and health status. The cohort is large and so has good statistical power and represents the British population born in the early post war period who are tomorrow's elderly population.

Methods

The MRC National Survey of Health and Development (NSHD) is a prospective cohort study of a socially stratified sample of all the births that took place in England, Scotland and Wales during one week in March 1946. The original cohort of 5362 men and women have been followed up over 20 times, most recently when they were aged 53 years at which time 3035 were successfully contacted, 2989 of whom granted a home interview and a further 46 of whom provided information in other forms. This represents 57% of the original cohort and 70% of those still alive and resident in England, Scotland and Wales. The cohort remains nationally representative in most respects,(17) although at this age the relatively socially disadvantaged and cognitively less able were under-represented. Relevant ethical approval was received for this study.

At the most recent home visit at age 53 years, trained nurses conducted three tests of physical performance and four tests of cognitive performance using standardised protocols described in detail elsewhere.(5;15)

Physical performance at age 53y

Standing balance was measured as the longest time, up to a maximum of 30 seconds, that the cohort member could maintain a one-legged stance with their eyes closed. Censoring standing balance time at 30 seconds is unlikely to have introduced error as only 3.6% of the population achieved this maximum time. The distribution was, in fact, positively skewed and so was normalised using a natural logarithm. *Chair rising* was measured as the time taken in seconds to rise from a sitting to standing position and then sit down again ten times. In order for high scores to indicate good performance in line with the other tests, the reciprocal of the time taken was used, multiplied by 100 ($1/s \times 100$). *Grip strength* was measured in kilograms using an electronic handgrip dynamometer and the highest value out of four measures (two for each hand) was used. There were 2566 men and women who completed all three tests (85% of those successfully contacted) and 2956 who completed at least one. Most of those who did not take or complete the tests were unable to do so because of chronic disease or disability.

Cognitive performance at age 53y

Verbal memory was assessed using a 15-item word learning task and the score represented the number of words correctly recalled over three trials (maximum score: 45). *Search speed and concentration* (henceforth search speed) was assessed by a timed letter search where the score represented the number of letters scanned in one minute (maximum score: 600).

Verbal fluency was assessed by counting the number of animals cohort members were able to name in one minute (highest score: 62). *National Adult Reading Test (NART)*, a word pronunciation test (maximum score: 50), which is highly correlated with general cognitive

ability and less subject to change with age than the other tests, was administered according to standard procedure.(18)

Cognitive performance at age 43y

Verbal memory and *search speed* were also assessed at age 43y using the same protocols. A different word list was given to each half of the cohort at 43y, and then these lists were reversed at 53y. Target letters were in different positions on the page at 43 and 53y.

Cognitive performance at age 15y

At age 15y, cohort members took the Heim AH4 test, a 130-item timed test of fluid intelligence, with separate verbal and non-verbal sections summed to yield a general ability score,(19) the Watts-Vernon reading test,(20) and a test of mathematical ability designed specifically for the study by the National Foundation for Educational Research in England and Wales. A single measure of general cognitive ability was obtained by combining the scores on each of these tests, after standardisation. This measure of cognition at age 15 years has been shown to predict declines in cognitive ability in adulthood.(15)

Potential confounders at age 53y

Body size—Height (in cm) and weight (in kg) in light clothing were measured according to standardised protocols (21).

Physical activity—*Physical activity* was assessed by the number of occasions in the previous four weeks cohort members reported taking part in sports, exercises or other physical activities in their leisure time. The categories were inactive (no occasions), mildly active (1–4 occasions) or moderately active (more than 4 occasions).

Health status—Standardised questions assessed angina (22) and respiratory problems (23) and a checklist identified other health problems. This information was used to create two binary variables identifying those in the sample with poor health status. The first of these variables identified a group with the most severe respiratory symptoms defined as the report of one or more of the following: a wheezy or whistling chest most days or nights; usually bringing up phlegm or coughing in the morning or during the day or night in winter for at least three months each year; or more than one chest illness in the last three years that kept them off work or indoors for a week or more. The second variable identified a group with other disabling or life threatening common health conditions that might affect physical or cognitive performance. These conditions were diabetes (n=79), cancer (n=95) or epilepsy (n=47) in the last ten years, or cardiovascular disease (n=177) as one or more of the following: a heart attack (n=48) or stroke (n=25) ever, aortic stenosis or valvular disease in the last 10 years (n=6), doctor diagnosed angina or Rose angina grade I or II (n=142), or intermittent claudication (n=12).

Socioeconomic conditions—*Socioeconomic conditions* were defined by the British Registrar General's classification of occupation, grouped to distinguish between the manual and non-manual social classes, and based on own occupation in adult life.

Statistical Analyses

The sample for analysis included 2135 cohort members with valid values on all three physical performance tests, the adult cognitive tests and who had information on height and weight, health status, activity levels and socioeconomic conditions at age 53 years. Those with incomplete data (n=431) were excluded from all analyses presented. Standardised scores with a mean of 0 and a standard deviation of 1 were derived for all the cognitive tests.

We first examined the relationships between each standardised cognitive test score and each of the three physical performance tests using multiple regression models. As well as examining each cognitive test score separately, we also assessed whether change in verbal memory or search speed between ages 43 and 53 years was associated with physical performance at age 53 years by running regression models including the verbal memory or search speed scores at 43 and 53 years as explanatory factors simultaneously. In this initial set of analyses, to test whether the associations between cognitive and physical performance differed by sex, interaction terms (sex by each cognitive score) were included in models. Where there was no evidence of interaction, adjustments were made in this first set of models for sex, current height and weight, and a weight by sex interaction, the latter of which was included as the adverse effects of weight on standing balance and chair rises have previously been shown to be stronger for women than men.⁽⁵⁾ Where there was evidence of interaction between the cognitive scores and sex, models were run separately for men and women with adjustments made for height and weight. Tests of deviation from linearity were performed in all models.

In a second set of models we examined whether the effects of verbal fluency at 53 years and changes in verbal memory and search speed between 43 and 53 years on physical performance were independent of general adult cognitive ability, as measured by the NART, and of physical activity, health status and adult socioeconomic conditions. In these models we were also able to assess the effects of the NART after adjustment for verbal fluency and changes in verbal memory and search speed and the other potential confounding factors.

In a final stage of analysis we tested whether the effects of changes in verbal memory and search speed between 43 and 53 years, and the effects of verbal fluency at 53 years on physical performance were independent of childhood cognitive ability, and of physical activity, health status and adult socioeconomic conditions. These models also allowed us to examine whether associations between childhood cognitive ability and physical performance in midlife were independent of change in verbal memory or search speed between ages 43 and 53 or verbal fluency at age 53, physical activity, health status and adult socioeconomic conditions. The analyses including childhood cognitive ability were undertaken on the 1822 men and women with complete data on childhood cognitive ability as well as all other variables. We investigated whether there were any differences between this group and the 313 in our main sample without a childhood cognitive score.

To assess the impact of excluding those with missing data on cognitive function or any of the other covariates from the analyses described above, all analyses were repeated on imputed data sets. SAS release 9.1 was used to impute 100 data sets for each analysis using PROC MI with the method of Markov chain Monte Carlo.

Results

The results that follow are from complete case analyses as there were no differences in findings between these analyses and analyses using multiple imputation methods. Of the 2135 cohort members included in analyses 1047 (49.0%) were male (table 1). Men had higher mean grip strength and standing balance time than women. In both sexes mean search speed and verbal memory scores declined between ages 43 and 53 years. Almost one in ten (9.6%) of the sample had one or more disabling or life threatening conditions, with slightly more people (17.6%) reporting one or more severe respiratory symptoms.

In analyses adjusted for sex, height and weight, balance time at age 53 was strongly associated with all cognitive test scores at age 53, such that those who performed better on the cognitive tests also had a better balance time (table 2). These associations were linear except for the relationship with the NART that was J-shaped. Balance time was also positively associated with verbal memory and search speed at age 43 (table 2). Balance time remained independently and positively associated with verbal memory and search speed at 53 years after adjusting for the score on the same test at 43 years, indicating that a slower decline in these functions, for given scores at 43 years, was related to a better balance time (table 2). Childhood cognitive ability was also positively associated with balance time at 53. There was no evidence of gender differences in any of these associations.

Chair rising at age 53 was also positively associated with all cognitive scores at age 53 in analyses adjusted for sex, height and weight (table 2). As for balance time, chair rising was also positively associated with search speed and verbal memory at age 43y and childhood cognitive ability (table 2). Slower declines in verbal memory and search speed between 43 and 53 years were associated with better chair rising time (table 2). There was no evidence of non-linear relationships or gender differences in these associations.

Results for grip strength are presented separately by sex because of evidence that grip strength's associations with search speed and verbal memory differed by sex ($p=0.07$ for sex $\times$ search speed at 43 years interaction, $p=0.06$ for sex $\times$ verbal memory at 43 years interaction). The pattern of association between grip strength and cognitive performance in analyses adjusted for height and weight was inconsistent and weak (table 2). There was no evidence of an association between grip strength and NART, search speed at 53y, change in verbal memory, change in search speed or childhood cognitive performance in either sex. There were negative associations between verbal memory at 43y and 53y and grip strength in men but no relationship between change in verbal memory and grip strength.

In analyses which included an adjustment for the NART, the effects of decline in verbal memory on balance time attenuated slightly but remained significant (comparing coefficients in table 2 with table 3, model 1a). Estimates were attenuated further with additional adjustment for physical activity, health status and socioeconomic conditions (table 3, model 1b). Adjusting for the NART had small effects on the estimates for the decline in search speed between 43 and 53y and for verbal fluency at age 53y (comparing coefficients in table 2 with table 3, models 2a and 3a) and there was little additional confounding by physical activity, health status and socioeconomic conditions (table 3, models 2b and 3b). The non-

linear association between NART and balance time remained significant in all adjusted analyses. Replacing the NART with childhood cognitive ability in the multivariable models gave a similar pattern of results (table 4). In these models childhood cognitive ability remained significantly associated with balance time after adjustment for change in verbal memory, change in search speed or verbal fluency and physical activity, socioeconomic conditions and health status.

Adjustment for the NART did not greatly alter the size of the effects of verbal fluency or change in verbal memory or search speed on chair rising (comparing coefficients in table 2 with table 5, models 1a, 2a and 3a). Indeed, the NART had no relationship with chair rising independently of verbal fluency or change in verbal memory (table 5, models 1a and 3a). Adjusting for physical activity, health status and socioeconomic conditions reduced the size of the effects of change in verbal memory, change in search speed and verbal fluency on chair rising slightly (table 5, models 1b, 2b and 3b), but all three effects remained significant. After adjustment for these additional variables the effect of the NART on chair rising was no longer significant in any of the models (table 5, models 1b, 2b and 3b). Replacing the NART with childhood cognitive ability in the multivariable models gave a similar pattern of results (table 6). Childhood cognitive ability was no longer associated with chair rising after adjustments.

Adjusted results for grip strength are not shown as findings were similar to unadjusted results.

Discussion

Summary of findings

In this prospective birth cohort study, specific patterns of association were demonstrated between different domains of cognitive performance across the life course and physical performance at age 53 years. Balance time and chair rising at age 53 were associated with verbal fluency and with change in verbal memory and search speed between 43 and 53 years, independent of childhood or adult general cognitive ability. Additionally, balance time was associated with general cognitive ability in childhood and adult life, independently of verbal fluency or change in verbal memory or search speed. Chair rising was associated with general cognitive ability in childhood and adult life independently of change in adult search speed, but not independently of physical activity, health status and socioeconomic conditions. Otherwise, physical activity, health status and socioeconomic conditions were not major confounders or mediators of the associations between cognitive performance and balance time and chair rising. Cognitive performance did not show a strong or consistent pattern of association with grip strength.

Interpretation

Grip strength is arguably the simplest of the three physical performance measures, being under direct command from the motor cortex through motor-neurones, fine-tuned at the spinal level, and good performance is dependent mainly on muscle cross-section area. Balancing on one leg with eyes closed requires mental concentration and subtle motor

control; this involves integration by the CNS of input from the vestibular organs, muscle spindles and proprioceptive information from many sources throughout the body. Chair rising requires good balance as well as strength and speed in the extensor muscles of the lower body; it might therefore be expected to have the strongest relation with domains of cognitive performance that show age-related change. This was borne out by the results that showed that chair rising was most strongly related to verbal memory, fluency and search speed. After allowing for these effects, there was little association between chair rising and general cognitive ability in childhood or adult life, more stable measures of cognitive performance across the life course. These findings support the idea that the same CNS ageing processes underlie the links between cognition and some aspects of physical performance i.e. chair rising.

In contrast, balance time was related to general cognitive ability in both childhood and adult life as well as to measures that decline with age, and was more strongly related to the former than the latter. These findings suggest that the associations between cognition and other aspects of physical performance, i.e. standing balance, are due to initial developmental differences. Researchers studying the relations between motor and cognitive development in early life argue that motor control may be a productive model for understanding many aspects of cognitive development.(24) This is because the development of motor control involves problem solving, integration of multiple information sources, and the organisation of dynamic internal representations.

In this context we should note that complex CNS pathways that integrate motor, sensory and higher mental function are involved at this level of motor control. Two subcortical systems, the cerebellum and the basal ganglia are particularly important. The cerebellum is essential for the coordination of movement, and evidence suggests that the cerebellar cortex is adapted for combining simple elements of movement into more complex synergies.(25) Furthermore, patients with diseases confined to the cerebellum show a range of cognitive impairment, particularly in memory, visuospatial function, and executive function,(26) although it is unclear to what extent these impairments are independent of lower general cognitive ability. Consistent with this, anatomical studies show that the cerebellum has prominent connections to the prefrontal cortex,(27) an area particularly involved in the control of higher mental function.

Links between motor control and cognitive function are also suggested by the fact that the prefrontal cortex receives dopaminergic efferents from the basal ganglia, a forebrain system that is also essential for motor control. Indeed, basal ganglia diseases, such as Parkinson's disease, also involve cognitive impairment, particularly in memory, visuospatial function, and executive function.(28) As with the cerebellar syndrome, these cognitive effects may be based on gradual age-associated changes in basal ganglia function.

Our findings are consistent with evidence from other studies which have also found associations between cognitive and physical performance.(10–13;29–32) While it has been argued recently, using evidence from narrow age cohorts, that shared factors may not explain associations found between age-related declines in cognitive and sensori-motor functions(33) most existing studies cannot rule out the possibility that shared factors may be

at least partially responsible. Where our findings differ from those of other studies there are often reasonable explanations including differences in age of study participants, methods of outcome measurement and types of tests used. For example, a cohort study in Aberdeen showed no effect of childhood general cognitive ability on balance time, measured dichotomously, independently of mood or brain stem lesion.(34) These study participants were in late old age and so the effects of major and minor brain pathology, including strokes and white matter disease, may have obscured more subtle neurodevelopmental pathways to motor control. Whereas we have not found evidence of an association between cognitive function and grip strength some studies have.(13;29;35) However, we are not the only study to find no evidence of association and summaries of the effect sizes calculated in existing studies suggest that they cover a wide range.(9;10) The lack of an association in the NSHD despite the existence of associations in other studies may be because grip strength is associated with cognitive performance only through ageing processes not yet detectable in the NSHD.

It had previously been shown that childhood cognitive ability, based on tests taken at age 8y, was positively associated with chair rising and standing balance at 53y in the NSHD.(36) We have now shown associations between cognitive ability at 15 years and physical performance that are independent of adult cognitive performance. Cognitive ability at 15 years is based on a more comprehensive range of tests than cognitive ability at age 8 years. In addition, we have been able to show that the associations between declines in cognitive function and physical performance are largely independent of childhood cognitive ability, a predictor of cognitive decline in adulthood in the NSHD.(15) Our study also adds to previous research which showed that earlier age at reaching developmental milestones was associated with higher cognitive test scores in childhood and also with verbal fluency at age 53y.(37) Taken together these findings suggest the need to consider shared developmental processes as well as shared degenerative processes that may underlie associations found between adult cognitive and physical performance. The NSHD is one of the few cohorts with prospective developmental data to examine this.

We are confident that the associations observed between cognitive and physical performance do not simply reflect an inability to follow instructions in this midlife sample. Grip strength showed much less association with cognitive performance than chair rise or balance times, despite instructions for this test requiring at least as much processing as instructions for the other tests. At this age, few study members had functional limitations that might interfere with the execution of these tests. If the associations were due to the existence of a subgroup with chronic conditions that impair physical and cognitive performance we might have expected that physical performance would be most strongly related with cognitive performance at lower scores, but level off with increasing cognitive performance. Instead we found that associations were linear across all cognitive scores, or for the NART were strongest at higher values. Finally, the test of search speed requires a certain level of manual dexterity; but further analyses (not shown) indicated that the associations we observed between search speed and physical performance remained even after adjusting for scores on a specific test of manual dexterity (a pegboard test (38)) taken at age 43.

The main limitation of this study is the absence of any measures of change in physical performance. We therefore could not test the “common cause” hypothesis(39;40) which proposes that common ageing processes underlie the associations between age-related declines in cognition and sensori-motor systems whereby age-related decline in physical and cognitive performance would occur in parallel. An additional limitation is the loss to follow-up of some cohort members and the exclusion from analyses of those with missing data in complete case analyses. Those who were interviewed at age 53y but did not complete all three physical performance tests (n=423) and so were excluded from analyses were more likely than those who completed all the tests to suffer from respiratory problems or other chronic conditions, be inactive, come from the manual social classes and have lower cognitive test scores which may affect the generalizability of our findings. There was also weak evidence that those without a childhood cognitive score (n=313), who were therefore excluded from analyses of childhood cognition, had slightly higher adult cognitive function than those with a score (the strongest effect was seen for the NART, $p=0.04$), however, they did not differ in their physical performance. Further, analyses using multiple imputations to allow for missing data on cognitive function and covariates produced very similar results to those from complete case analyses demonstrating that our conclusions are robust. In addition, despite losses to follow-up it has been shown that the cohort remained nationally representative in most respects at age 53y.(17) The use of self-reported information on physical activity and health status could also be considered a limitation of our study. However, a benefit of our study is that all the main explanatory and outcome variables of interest were recorded by trained health professionals using standardised protocols.

Conclusions

Among men and women from a large, representative British birth cohort, better cognitive performance across the life course was related to physical performance at age 53y. Standing balance had the strongest relationship with general cognitive ability in childhood and adult life, measures that show less age-associated change over time. Chair rising was strongly related to verbal fluency and measures of change in verbal memory and search speed over the previous ten years, measures that show more age-associated decline. Grip strength had the least association with cognitive performance. Shared risk factors, such as inactivity, health problems and poor socioeconomic conditions generally explained only a small part of the observed associations. Our findings support the idea that adult physical and cognitive performance are influenced by the same underlying developmental and ageing processes.

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Acronyms

CNS   central nervous system

MRC	Medical Research Council
NSHD	National Survey of Health and Development
NART	National Adult Reading Test

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Table 1

Characteristics of the study sample with complete data on physical performance, adult cognitive test scores and all potential confounders (N=2135)

	Mean (standard deviation) or N(%)		
	Total	Men	Women
N	2135	1047	1088
Physical performance at 53y			
Grip strength (kg)	38.0 (14.1)	48.1 (11.8)	28.2 (8.0)
Chair rise time *	5.2 (1.7)	5.4 (1.8)	5.1 (1.6)
Standing balance time †	5.1 (2.2)	5.7 (2.3)	4.6 (2.1)
Cognitive test scores			
Search speed ‡:			
43y	342.8 (75.7)	329.0 (76.5)	356.2 (72.6)
53y	283.2 (74.6)	273.5 (73.9)	292.6 (74.1)
Verbal memory §:			
43y	25.5 (6.0)	24.7 (5.8)	26.1 (6.2)
53y	24.6 (6.1)	23.6 (6.1)	25.5 (5.9)
Verbal fluency ** at 53y	24.1 (6.9)	24.2 (6.6)	23.9 (7.1)
NART †† at 53y	34.8 (9.3)	35.0 (9.4)	34.7 (9.2)
Other characteristics at age 53y			
Height (m)	1.7 (0.1)	1.8 (0.1)	1.6 (0.1)
Weight (kg)	77.2 (14.8)	83.2 (13.1)	71.3 (13.9)
Occupational class			
Non-manual	1472 (68.9)	675 (64.5)	797 (73.3)
Manual	663 (31.1)	372 (35.5)	291 (26.7)
Physical activity levels			
None	964 (45.2)	455 (43.5)	509 (46.8)
1–4 times per month	421 (19.7)	224 (21.4)	197 (18.1)
> 4 times per month	750 (35.1)	368 (35.1)	382 (35.1)
Disabling and/or life threatening health conditions ‡‡			
None	1930 (90.4)	943 (90.1)	987 (90.7)
1	205 (9.6)	104 (9.9)	101 (9.3)
Severe respiratory symptoms §§			
None	1759 (82.4)	862 (82.3)	897 (82.4)
1	376 (17.6)	185 (17.7)	191 (17.6)

* Reciprocal of time taken (s) for 10 chair rises × 100

† Geometric mean

‡ Number of letters scanned in one minute (maximum score: 600)

§ Number of words correctly recalled over three trials of a 15-item word learning task (maximum score: 45)

**
Number of animals named in one minute

††
National Adult Reading Test score (maximum score: 50)

††
diabetes, cancer or epilepsy in the last ten years, or cardiovascular disease (defined as one or more of the following: heart attack or stroke ever, aortic stenosis or valvular disease in the last 10 years, doctor diagnosed angina or Rose angina grade I or II, or intermittent claudication)

§§
a wheezy or whistling chest most days or nights; usually bringing up phlegm or coughing in the morning or during the day or night in winter for at least three months each year; or more than one chest illness in the last three years that kept them off work or indoors for a week or more

Table 2

Differences in mean balance time (Ln seconds, maximum 30s), chair rising (1/s $\times$ 100) and grip strength (kg) at age 53 years per one standard deviation change in cognitive score.

Cognitive Performance (z-score)	Balance time (n=2135)	Chair rising (n=2135)	Grip strength			
			(Men n=1047)		(Women n=1088)	
	Regression coefficient ¹ (95% CI)	p-value	Regression coefficient ² (95% CI)	p-value	Regression coefficient ² (95% CI)	p-value
National Adult Reading Test (53y)						
Linear term	0.16 (0.12,0.19)	<.001	0.11 (0.03,0.18)	.004	-0.51 (-1.22,0.20)	.16
Quadratic term	0.04 (0.02,0.07)	.002	-	-	-	-
Verbal fluency (53y)						
	0.10 (0.07,0.14)	<.001	0.25 (0.18,0.32)	<.001	0.58 (-0.15,1.32)	.12
Verbal memory (43y)						
	0.12 (0.09,0.15)	<.001	0.12 (0.05,0.19)	.001	-0.92 (-1.65,-0.18)	.01
Verbal memory (53y)						
	0.13 (0.09,0.16)	<.001	0.19 (0.12,0.26)	<.001	-0.95 (-1.65,-0.24)	.01
Search speed (43 y)						
	0.07 (0.04,0.10)	<.001	0.08 (0.004,0.15)	.04	-0.03 (-0.73,0.67)	.93
Search speed (53y)						
	0.08 (0.04,0.11)	<.001	0.18 (0.11,0.25)	<.001	-0.02 (-0.69,0.73)	.96
Change in verbal memory (43-53y)³						
	0.09 (0.04,0.13)	<.001	0.18 (0.09,0.27)	<.001	-0.65 (-1.54,0.23)	.15
Change in search speed (43-53y)³						
	0.05 (0.02,0.09)	.01	0.20 (0.11,0.28)	<.001	0.05 (-0.81,0.92)	.90
Childhood cognitive ability (15y)⁴						
	0.15 (0.11,0.18)	<.001	0.13 (0.05,0.21)	<.001	-0.52 (-1.29,0.24)	.18

¹ Adjusted for sex, height and weight, and sex by weight.

² Adjusted for height and weight

³ The effect of verbal memory or search speed at age 53 after adjusting additionally for the score on the same test at age 43

⁴ N=1822 (898 men and 924 women)

Table 3

mean balance time (Ln seconds) per one standard deviation change in adult cognitive performance score, with adjustments for confounders.

Outcome (z-score)	Model 1a			Model 1b			Model 2a			Model 2b			Model 3a			Model 3b		
	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	Regression coefficient (95%CI)	p-value	
memory (43–49)	0.06 (0.01,0.10)	.01	0.04 (0.00,0.09)		.05													
speed (43–49)				0.04 (0.003,0.08)	.04	0.04 (–0.003,0.07)		.07										
3y																		
Reading Test																		
	0.10 (0.06,0.15)	<.001	0.08 (0.04,0.13)	0.14 (0.11,0.18)	<.001	0.11 (0.07,0.15)	0.13 (0.09,0.17)	<.01	0.10 (0.05,0.14)	0.10 (0.05,0.14)	<.001	0.10 (0.05,0.14)	0.10 (0.05,0.14)	<.001	0.10 (0.05,0.14)	0.10 (0.05,0.14)	<.001	
	0.04 (0.01,0.07)	.003	0.04 (0.01,0.06)	0.04 (0.01,0.06)	.005	0.03 (0.01,0.06)	0.04 (0.01,0.07)	.01	0.04 (0.01,0.06)	0.04 (0.01,0.06)	.002	0.04 (0.01,0.06)	0.04 (0.01,0.06)	.005	0.04 (0.01,0.06)	0.04 (0.01,0.06)	.005	
	–0.24 (–0.31,–0.18)	<.001	–0.24 (–0.31,–0.18)	–0.23 (–0.30,–0.17)	<.001	–0.24 (–0.30,–0.17)	–0.21 (–0.27,–0.15)	<.001	–0.22 (–0.28,–0.15)	–0.22 (–0.28,–0.15)	<.001	–0.22 (–0.28,–0.15)	–0.22 (–0.28,–0.15)	<.001	–0.22 (–0.28,–0.15)	–0.22 (–0.28,–0.15)	<.001	
	0.01 (0.001, 0.01)	.02	0.005 (–0.001,0.01)	0.01 (0.001, 0.01)	.10	0.005 (–0.001,0.01)	0.01 (0.001,0.01)	.09	0.01 (–0.001,0.01)	0.01 (–0.001,0.01)	.01	0.01 (–0.001,0.01)	0.01 (–0.001,0.01)	.08	0.01 (–0.001,0.01)	0.01 (–0.001,0.01)	.08	
	–0.01 (–0.01,–0.003)	<.001	–0.01 (–0.01,–0.003)	–0.01 (–0.01,–0.003)	<.001	–0.01 (–0.01,–0.003)	–0.01 (–0.01,–0.004)	<.001	–0.01 (–0.01,–0.003)	–0.01 (–0.01,–0.003)	<.001	–0.01 (–0.01,–0.003)	–0.01 (–0.01,–0.003)	<.001	–0.01 (–0.01,–0.003)	–0.01 (–0.01,–0.003)	<.001	
	–0.04 (–0.01,0.001)	.08	–0.004 (–0.01,0.001)	–0.004 (–0.01,0.0005)	.13	–0.004 (–0.01,0.001)	–0.004 (–0.01,0.001)	.14	–0.003 (–0.01,0.001)	–0.003 (–0.01,0.001)	.10	–0.003 (–0.01,0.001)	–0.003 (–0.01,0.001)	.16	–0.003 (–0.01,0.001)	–0.003 (–0.01,0.001)	.16	
	–		–0.09 (–0.14,–0.04)	–	<.001	–0.10 (–0.14,–0.05)	–	<.001	–0.09 (–0.13,–0.04)	–0.09 (–0.13,–0.04)	<.001	–0.09 (–0.13,–0.04)	–0.09 (–0.13,–0.04)	<.001	–0.09 (–0.13,–0.04)	–0.09 (–0.13,–0.04)	<.001	
symptoms	–		–0.05 (–0.14,0.03)	–	.22	–0.05 (–0.14,0.03)	–	.21	–0.06 (–0.15,0.03)	–0.06 (–0.15,0.03)	.17	–0.06 (–0.15,0.03)	–0.06 (–0.15,0.03)	.17	–0.06 (–0.15,0.03)	–0.06 (–0.15,0.03)	.17	
anxiety	–		–0.12 (–0.23,–0.01)	–	.03	–0.11 (–0.22,–0.004)	–	.04	–0.12 (–0.23,–0.01)	–0.12 (–0.23,–0.01)	.03	–0.12 (–0.23,–0.01)	–0.12 (–0.23,–0.01)	.03	–0.12 (–0.23,–0.01)	–0.12 (–0.23,–0.01)	.03	
depression	–		–0.09 (–0.17,–0.01)	–	.02	–0.11 (–0.19,–0.04)	–	.004	–0.11 (–0.19,–0.04)	–0.11 (–0.19,–0.04)	.004	–0.11 (–0.19,–0.04)	–0.11 (–0.19,–0.04)	.004	–0.11 (–0.19,–0.04)	–0.11 (–0.19,–0.04)	.004	
	0.09	0.10	0.06			0.10	0.09		0.10			0.10			0.10			

il memory or search speed at age 53 after adjusting additionally for the score on the same test at age 43

for NART or change in verbal memory as appropriate and also height, weight, sex, and sex by weight

., adjusted additionally for current physical activity, health status and socioeconomic conditions

for NART or change in search speed as appropriate and also height, weight, sex, and sex by weight

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Model 2b: model 2a, adjusted additionally for current physical activity, health status and socioeconomic conditions
 Model 3a: adjusted for NART or verbal fluency at 53y as appropriate and also height, weight, sex, and sex by weight
 Model 3b: model 3a, adjusted additionally for current physical activity, health status and socioeconomic conditions

Table 4

Standard deviation change in childhood and adult cognitive performance scores, with adjustments

	Model 1b		Model 2a		Model 2b		Model 3a		Model 3b	
	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value
	0.05 (0.004, 0.10)	.03								
			0.02 (−0.02, 0.06)	.40	0.01 (−0.03, 0.05)	.56				
							0.06 (0.02, 0.10)	.001	0.05 (0.02, 0.09)	.005
1	0.07 (0.02, 0.11)	.004	0.14 (0.10, 0.17)	<.001	0.09 (0.06, 0.13)	<.001	0.12 (0.09, 0.16)	<.001	0.09 (0.04, 0.13)	<.001
1	−0.26(−0.33, −0.19)	<.001	−0.24(−0.31, −0.17)	<.001	−0.26(−0.33, −0.18)	<.001	−0.22(−0.29, −0.15)	<.001	−0.23(−0.30, −0.16)	<.001
	0.003(−0.003, 0.01)	.33	0.005(−0.002, 0.01)	.15	0.003(−0.004, 0.01)	.39	0.01(−0.001, 0.01)	.11	0.003(−0.003, 0.01)	.32
1	−0.01(−0.01, −0.003)	.001	−0.01(−0.01, −0.003)	<.001	−0.01(−0.01, −0.003)	.001	−0.01(−0.01, −0.003)	<.001	−0.01(−0.01, −0.003)	.001
	−0.003(−0.01, 0.002)	.28	−0.004(−0.01, 0.002)	.18	−0.003(−0.01, 0.002)	.30	−0.003(−0.01, 0.002)	.22	−0.003(−0.01, 0.003)	.34
	−0.08(−0.13, −0.03)	<.001	−		−0.09(−0.14, −0.04)	<.001	−		−0.08(−0.13, −0.03)	<.001
	−0.06(−0.15, 0.03)	.20	−		−0.06(−0.15, 0.03)	.18	−		−0.07(−0.16, 0.02)	.15
	−0.15(−0.27, −0.03)	.01	−		−0.15(−0.26, −0.03)	.02	−		−0.15(−0.27, −0.04)	.01
	−0.12(−0.21, −0.03)	.004	−		−0.14(−0.22, −0.06)	.001	−		−0.14(−0.22, −0.06)	.001
	0.11		0.09		0.11		0.09		0.11	

ally for the score on the same test at age 43

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Variable	Model 1b			Model 2a			Model 2b			Model 3a			Model 3b		
	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value			
1	0.14 (0.04,0.23)	.01													
			0.19 (0.10,0.27)	<.001	0.17 (0.09,0.25)	<.001									
							0.24 (0.17,0.32)	<.001	0.21 (0.13,0.28)	<.001				<.001	
2	-0.03 (-0.12,0.06)	.52	0.08 (0.01,0.16)	.02	0.01 (-0.07,0.09)	.78	0.03 (-0.05,0.10)	.51	-0.04 (-0.12,0.05)	.34					
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Table 6

Standard deviation change in childhood and adult cognitive performance scores, with adjustment for

	Model 1b			Model 2a			Model 2b			Model 3a			Model 3b		
Variable	Regression coefficient (95%CI)	p-value		Regression coefficient (95%CI)	p-value		Regression coefficient (95%CI)	p-value		Regression coefficient (95%CI)	p-value		Regression coefficient (95%CI)	p-value	
Age	0.15 (0.05,0.26)	.004													
Sex															
Female				0.18 (0.08,0.27)	<.001		0.16 (0.07,0.25)	<.001		0.22 (0.14,0.30)	<.001		0.20 (0.11,0.28)	<.001	
Male															
Height															
Height at age 43	0.01 (-0.10,0.11)	0.90		0.11 (0.03,0.19)	.01		0.05 (-0.04,0.13)	.28		0.05 (-0.03,0.13)	.25		-0.01 (-0.10,0.08)	.91	
Weight															
Weight at age 43	-0.39(-0.55,-0.23)	<.001		-0.36(-0.51,-0.20)	<.001		-0.37(-0.53,-0.21)	<.001		-0.33(-0.48,-0.18)	<.001		-0.35(-0.50,-0.20)	<.001	
Weight at age 23	-0.02(-0.03,-0.005)	.01		-0.01(-0.03,-0.001)	.04		-0.02(-0.03,-0.004)	.01		-0.01(-0.03,-0.001)	.04		-0.02(-0.03,-0.004)	.01	
Weight at age 11	-0.01(-0.02,0.003)	.14		-0.01(-0.02,0.001)	.07		-0.01(-0.02,0.002)	.13		-0.01(-0.02,0.0002)	.06		-0.01(-0.02,0.001)	.10	
Weight at age 5	-0.02(-0.03,-0.004)	.01		-0.02(-0.03,-0.005)	.01		-0.01(-0.03,-0.003)	.01		-0.01(-0.03,-0.004)	.01		-0.01(-0.03,-0.003)	.01	
Height and weight	-0.20(-0.31,-0.09)	<.001		-			-0.21(-0.32,-0.10)	<.001		-			-0.19(-0.29,-0.08)	<.001	
Height and weight at age 43	-0.25(-0.45,-0.06)	.01		-			-0.25(-0.45,-0.06)	.01		-			-0.27(-0.47,-0.07)	.01	
Height and weight at age 23	-0.30(-0.55,-0.05)	.02		-			-0.29(-0.55,-0.04)	.02		-			-0.31(-0.57,-0.05)	.02	
Height and weight at age 11	-0.07(-0.25,0.11)	.45		-			-0.09(-0.27,0.09)	.31		-			-0.10(-0.28,0.08)	.28	
Height and weight at age 5				0.05			0.07			0.06			0.08		

Results for the score on the same test at age 43

Height and weight at age 43, weight, sex, and sex by weight

Height and socioeconomic conditions

Height and also height, weight, sex, and sex by weight

Height and socioeconomic conditions

Height and also height, weight, sex, and sex by weight

Height and socioeconomic conditions