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Childhood cognitive ability and age-related changes in physical capability from midlife: findings from a British birth cohort study

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Abstract

Objective: To test the hypothesis that higher childhood cognitive ability is associated with reduced risk of decline in physical capability in late midlife.

Methods: Participants were 1954 men and women from the MRC National Survey of Health and Development with complete data on cognitive ability at age 15 and measures of grip strength and chair rise speed at ages 53 and 60-64 years. Using multinomial logistic regression, associations of childhood cognitive ability with categories of change in grip strength and chair rise speed (i.e. decline; stable high; stable low; reference) were investigated. Adjustments were made for potential confounders from early life and adult mediators including health behaviours, educational level and cognitive ability at age 53.

Results: Higher childhood cognitive scores were associated with reduced risks of decline in grip strength and chair rise speed; for example, the sex-adjusted relative-risk ratio (RRR) of decline (vs reference) in grip strength per 1SD increase in childhood cognitive score was 0.82 (95% CI: 0.73, 0.92). Higher childhood cognitive scores were also associated with reduced risk of stable low and, increased likelihood of stable high chair rise speed.

Conclusions: These findings suggest that childhood cognitive ability may be related to decline in physical capability in late midlife. A number of life course pathways are implicated, including those linking childhood and adult cognitive ability. Future research aiming to identify new

opportunities to prevent or minimise age-related declines in physical capability may benefit from considering the potential role of neurodevelopmental as well as neurodegenerative pathways.

Key words: cognition; physical capability; age-related decline; neurodevelopment; life course

Abbreviations:

CI: confidence interval

CRF: clinical research facility

CSE: certificate of secondary education

FE: further education

HE: higher education

MRC: Medical Research Council

NSHD: National Survey of Health and Development

OA: osteoarthritis

RRR: relative-risk ratio

SD: standard deviation

Introduction

There is increasing research interest in the influence of neurodegeneration on age-related declines in mobility and other aspects of physical capability(1,2) and a growing body of empirical evidence highlighting its importance.(3) From a life course perspective, neurodevelopment as well as neurodegeneration may underlie this physical decline.(4,5) If so, interventions that positively affect neurodevelopmental pathways may, in addition to their benefits in earlier life, prevent, delay or minimise declines in physical capability later in life.

A few existing studies have examined associations between cognitive ability in earlier life, a commonly used marker of neurodevelopment, and objective measures of physical capability including walking speed, grip strength and chair rise time at mean ages of assessment from 50 to 79.(4,6-10) The majority of these studies present evidence of association between higher cognitive scores in earlier life and higher levels of physical capability in mid- to late adulthood. However, associations have not always been consistently found across all measures of physical capability investigated.(4,8) In addition, all previous analyses that have examined objective measures of physical capability have done so at only one time point and so cannot distinguish between the potential influences of neurodevelopment on the levels of physical capability achieved by midlife and longer term influences on subsequent age-related declines.

While it may generally be expected that early life factors will be more strongly associated with peak levels of physical capability achieved by midlife than with subsequent age-related declines, there is currently insufficient empirical evidence to formally assess this. In addition, there are reasons to expect that childhood cognitive ability may have longer term associations with age-

related changes in physical capability. Firstly, cognitive ability in childhood represents the starting point of a lifelong cognitive pathway and as higher childhood cognitive ability has been associated with reduced risk of decline in cognitive ability in midlife(11) this may have positive implications for physical capability in later life. Related to this, higher childhood cognitive ability may reflect greater levels of neurophysiological reserve.(12,13) If so, even when challenges to physical capability have accumulated across the central and peripheral nervous systems these may be less likely to reach sufficient levels to precipitate decline in those with higher childhood cognitive ability than in those with lower ability. Finally, childhood cognitive ability is associated with cumulative exposure to a number of extrinsic factors across life(13) shown to be associated with age-related declines in physical capability.(14-16)

We thus aimed to extend the existing evidence base by using data from a large nationally representative British birth cohort to test the hypothesis that higher childhood cognitive ability is associated with reduced risk of decline in objective measures of physical capability during late midlife.

Materials and methods

The Medical Research Council National Survey of Health and Development (NSHD) is a socially stratified sample of 5,362 singleton births (2547 males and 2815 females) that took place in one week of March 1946 in mainland Britain, with regular follow-up and high participation rates across life.(17,18) During two waves of data collection, in 1999 (at 53 years) and 2006-2010 (at 60-64 years), physical capability was assessed using performance-based measures.

Of the original 5362 participants, 3673 were eligible for inclusion in the data collection at age 53. Of these participants, 3035 were successfully contacted and 2984 (81%) received a home visit from a trained nurse. Of the 2327 participants not eligible for inclusion at age 53, 469 had previously died, 948 had refused to participate, 580 were living abroad and 330 could not be traced. At age 60–64, 2856 eligible participants (those known to be alive, living in England, Scotland or Wales and who had not permanently refused to participate) were invited for assessment at one of six clinical research facilities (CRFs) or to be visited by a research nurse at home of whom 2229 (78%) were assessed (1690 at a CRF and 539 at home). Of the 2506 participants not contacted at age 60-64, 778 had died (309 since age 53), 594 had refused to participate, 578 were living abroad and 556 could not be traced.

Relevant ethical approval was provided by the North Thames Multi-Centre Research Ethics Committee in 1999 and by the Central Manchester Local Research Ethics Committee and the Scotland A Research Ethics Committee in 2006-10. All participants provided informed consent.

Physical capability at ages 53 and 60-64

Grip strength and chair rise time were assessed at ages 53 and 60-64 by trained nurses using standardised protocols. At both ages, grip strength was measured isometrically using a Nottingham electronic handgrip dynamometer. To ensure comparability between ages, the highest value achieved of four measures recorded at age 53 (two in each hand) and the highest of the first four values (from a total of three in each hand) recorded at age 60-64 were used in analyses. At both ages chair rise time was measured, using a stopwatch, as the time taken to rise from a sitting to a standing position with straight back and legs and then sit down again ten times

as fast as possible. In order for high scores to indicate good performance, chair rise speed was calculated by dividing the number of rises (i.e. 10) by the time taken (in minutes). Nurses recorded if a study participant was unable or unwilling to perform either test and the reason for this.

In order to avoid some of the important limitations inherent in modelling change continuously when data are only available at two time points(19,20) we decided a priori to identify categories of change and to model these as our main outcomes. After careful consideration of a number of different approaches, we chose to distinguish between four groups: a group experiencing decline; a group with relatively high levels at baseline which are maintained; a group with relatively low levels at baseline who remain low; a reference group who maintain physical capability levels within a 'normal' range.(14) Participants were assigned to one of these four outcome groups for each measure based on the changes in their sex-specific standard deviation scores of grip strength and chair rise speed (categorized as: $< -1SD$; -1 to $1 SD$; $>1SD$) between ages 53 and 60-64. The groups were defined as: 1) decline (change in SD score between age 53 and 60-64 from $>1SD$ to $\leq 1SD$ or, from -1 to $1SD$ to $<-1SD$); 2) stable high (SD score >1 at both ages); 3) stable low (SD score <-1 at both ages); 4) reference (all other combinations of cross-tabulated SD scores) (see supplemental digital content table S1, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>). These categorizations were derived in the samples with valid measures at both ages. Participants with valid values at age 53 who were unable to complete the test for health reasons at age 60-64 were added to the 'decline' category and participants who were unable to complete the test for health reasons at both ages were added to the 'stable low' category.

Childhood cognitive ability

At age 15, study participants were asked to complete three cognitive tests: the Heim AH4 test, a 130-item timed test of fluid intelligence, with separate verbal and non-verbal sections;(21) the Watts-Vernon reading test, a test of reading comprehension requiring participants to select the appropriate words to complete 35 sentences;(22) and a test of mathematical ability designed specifically for the study by the National Foundation for Educational Research in England and Wales. Scores on each of these tests were standardised and then summed to derive a total score of general cognitive ability standardised (to a mean of 0 and standard deviation of 1) in the analytical sample. Where missing at age 15, values were imputed using standardised scores from similar cognitive tests undertaken at age 11 (n=103) or 8 (if missing at 15 and 11 (n=48)) based on the observation that participants in the analytical sample with cognitive test scores at more than one age in childhood maintained a similar ranking over time (Pearson correlation coefficients between the cognitive score at age 15 and those at ages 11 and 8 were 0.87 and 0.72, respectively).(23)

Covariates

Potential confounders from early life and, factors in adulthood which may mediate the main associations of interest were selected *a priori* based on previous findings in this study.(4,6,7,14,24,25) The role of educational attainment and cognitive ability at age 53, which may represent more proximal factors on a common pathway, were also investigated.(11,12,26)

Birth weight, recorded to the nearest quarter pound, was extracted from birth records and converted into kg. Paternal occupation at age 4 (or at age 11 or 15 if missing at age 4 (n=45))

was categorized using the Registrar General's Social Classification into three groups: high (I or II); middle (IIINM or IIIM); low (IV or V). Maternal educational level reported during parental interviews in childhood was categorized into four groups: secondary and further or higher education; secondary only or, primary and further or higher education; primary and further education (no qualifications attained); primary education only. Own occupation at age 53 was categorized using the Registrar General's Social Classification into the same three groups as paternal occupation. Three behavioural risk factors (overweight or obesity, physical inactivity and smoking) assessed at age 53 were combined in a cumulative behavioural risk factor score to create an ordinal scale ranging from 0 (most healthy) to 6 (least healthy). Information on the presence of four indicators of health status at age 53 (hand osteoarthritis (OA); knee OA; severe respiratory symptoms and; other disabling or life threatening conditions) were combined to create a scale ranging from 0 (no reported health problems) to 4 (all 4 indicators reported). Derivation of these scores is described in detail elsewhere.(14)

Educational level attained by age 26 was categorized into five groups: degree or higher; A levels, usually attained at age 18, or their equivalents; O levels, usually attained at age 16, or their equivalents; certificate of secondary education (CSE), clerical course or equivalent; none. Two tests of cognitive ability at age 53 were included. Verbal memory was assessed using a 15-item word learning task with a total score representing the number of words correctly recalled over three trials (maximum: 45). Search speed was assessed using a timed letter search with the score representing the number of letters scanned in one minute (maximum score: 600).

Statistical analysis

Multinomial logistic regression models were used to test the associations of childhood cognitive ability with each of the different categories of change (vs the reference group) in grip strength and chair rise speed. Relative-risk ratios (RRR) were estimated for a 1SD change in the childhood cognitive score with deviations from linearity formally tested to ensure assumptions of linearity were met. Initial models were adjusted for sex, after formally testing sex interactions. Subsequent models were adjusted in turn for potential confounders from early life (birth weight, paternal occupational class and maternal educational level), potential adult mediators (own occupational class and cumulative scores of behavioural risk and health status), own educational level and cognitive ability at age 53 (verbal memory and search speed)) before all covariates were included in a fully-adjusted model. Models were run on the sample with complete data on childhood cognitive ability and change (maximum N=1954 (1811 for grip strength and 1875 for chair rise speed)). To maintain statistical power and minimize the level of bias introduced due to missing information, missing values of the covariates in this sample (birth weight (n=5), paternal occupational class (n=28), maternal educational level (n=115), own educational level (n=58), own occupational class (n=4), behavioural risk score (n=9), health indicator count (n=25), verbal memory (n=26) and search speed (n=12)) were imputed using multiple imputation chained equations implemented in Stata version 14. All analyses were run across 20 multiply imputed datasets and estimates were combined using Rubin's rules. Sensitivity analyses were performed to test the main associations in the maximum available samples with complete data (for comparison with those run on imputed datasets).

Results

One in five participants (20%) were classified as having experienced potentially meaningful decline in grip strength and in chair rise speed between ages 53 and 60-64. An additional 5% were classified as stable high and a similar proportion as stable low (Table 1). Mean levels of performance at ages 53 and 60-64 in each of these categories are shown in table S2, Supplemental Digital Content 1 (<http://links.lww.com/PSYMED/A396>). Distributions of each covariate are presented in Table 1.

Changes in grip strength

In a sex-adjusted model, higher childhood cognitive scores were associated with lower risk of decline in grip strength (RRR of decline (vs reference) per 1SD increase in cognitive ability =0.82 (95% CI: 0.73, 0.92)) (Table 2). There was no evidence of sex interaction or deviation from linearity. Adjustment for each set of covariates, except educational level attained, had an impact on this association. Consistent with the finding that higher childhood SEP (indicated by paternal occupational class and maternal educational level) and higher verbal memory scores at age 53 were associated with lower risk of decline in grip strength (table S3, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>), adjustment for these covariates had the greatest impact. In a fully adjusted model the main association was attenuated (RRR of decline (vs reference) per 1SD increase in cognitive ability=0.90 (95% CI: 0.75, 1.07)). There was no clear evidence of associations between childhood cognitive scores and likelihood of being in the stable high or stable low categories of grip strength (vs reference), although associations with stable low were in the expected direction.

Changes in chair rise speed

In a sex-adjusted model, higher childhood cognitive scores were associated with reduced risks of being in the decline and stable low categories of chair rise speed and with increased likelihood of being in the stable high category when compared with the reference category (Table 2). There was some evidence to suggest that associations with childhood cognitive scores were stronger for the stable low category (RRR=0.63 (95% CI: 0.51, 0.77)) than the decline category (RRR=0.82 (0.73, 0.92)). There was no evidence of sex interactions or deviations from linearity. Consistent with the finding that own educational level and verbal memory scores at age 53 were most strongly associated with changes in chair rise speed (table S3, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>), adjustment for these covariates had the greatest impact on the associations between childhood cognitive scores and changes in chair rise speed.

There were no differences in findings when models were rerun on the maximum available samples with complete data.

Discussion

Higher childhood cognitive scores were associated with reduced risks of decline in grip strength and chair rise speed between ages 53 and 60-64 years in a British birth cohort study. Participants with higher childhood cognitive scores were also less likely to be categorized as having stable low chair rise speed and more likely to be categorized as stable high.

The association between childhood cognitive ability and decline in grip strength was partially attenuated after adjustment for each set of covariates except educational level attained.

Conversely, adjustment for educational level attained had a greater impact on the associations of childhood cognitive ability with change in chair rise speed than adjustments for other covariates. This suggests that different pathways (outlined below) may be implicated in explaining the observed associations of childhood cognitive ability with changes in grip strength and chair rise speed.

Comparison with other studies

These new findings are consistent with those from previous studies showing links between higher cognitive ability in earlier life and better performance in different objective tests of physical capability assessed at a single time-point.(4,6-10) Our findings are also consistent with those from a recent study of Finnish males which found that higher cognitive scores at a mean age of 20.3 were associated with better self-reported physical functioning at a mean age of 71.4 via an association with better self-reported physical functioning approximately a decade earlier.(27) Our findings extend these previous analyses by demonstrating evidence of associations of childhood cognitive ability with changes in objective measures of physical capability in late midlife.

When lifetime cognitive performance was related to grip strength and chair rise speed at age 53 in the NSHD, no clear patterns of association were found with grip strength.(4) As associations had been shown in older study populations, it was proposed that our null findings might be explained by an influence of ageing processes not yet detectable at age 53; our new findings support this. This also explains why associations were found with risk of decline but not with either of the other outcomes (i.e. stable low or high, associations which would be driven by an

influence on baseline levels at age 53). As associations with cognitive ability at age 15 were found with chair rise speed at age 53,(4) our finding of associations with all three categories of change is therefore consistent. At age 53, associations of chair rise speed with markers of adult fluid ability (assessed by verbal memory and search speed tests) were stronger than those with markers of general cognitive ability (including the measure at age 15) which is consistent with our finding of an attenuation of effect after adjustment for verbal memory.

Explanation of findings

The generation of maximal muscle force and chair rising performance both have a neurocognitive component; good performance on these tests, and the maintenance of this performance over time, depends to a certain extent on the healthy functioning of the central and peripheral nervous systems and the sensori-motor system.(28-30) Measures that capture the functioning of particular aspects of these systems, such as cognitive tests, would therefore be expected to be associated with tests of physical capability, when measured contemporaneously. However, why these associations extend across life requires further explanation as follows.

A number of pathways linking childhood cognitive ability to later health outcomes have been proposed,(13) some of which may contribute to explaining our observed associations with age-related declines in physical capability. For example, it has been suggested that childhood cognitive ability may predict health behaviours, health literacy and entry into safe environments in adulthood. This is consistent with the partial attenuation of our observed associations after adjustment for behavioural risk factors and occupational class. That educational level attained attenuated associations between childhood cognitive ability and chair rise speed could be

explained by education acting in concert with cognition on these extrinsic pathways. In previous analyses these pathways have been shown to be more strongly related to chair rise speed than grip strength in midlife(31,32) which may explain the differences in the impact of these adjustments between outcomes.

It has also been suggested that childhood cognitive ability may be associated with later life outcomes because it acts as a marker of relevant underlying neurophysiological processes. Recent empirical evidence of associations between the development and subsequent degeneration of specific brain structures(33) and, the finding that cross-sectional associations between cognitive ability and brain cortical thickness in old age were largely explained by childhood cognitive ability when this was taken into account(34) both lend support to the suggestion that these processes are lifelong. Related to which are systematic review findings confirming a link between whole brain volume and white matter volume and measures of physical capability.(35)

Evidence suggests that higher childhood cognitive ability and greater educational attainment promote better midlife cognitive function.(12) This may then confer benefits on physical capability as well as cognitive outcomes in later life. For example, in a French study of adults aged 65-85, associations between white matter lesions and slower walking speed were only found among participants with lower levels of education.(36) The attenuation of our associations after adjustment for verbal memory at age 53 suggests that pathways linking childhood and adult cognition are likely to be important in explaining associations between childhood cognitive ability and age-related changes in physical capability, as found for mortality.(26)

Methodological considerations

Key strengths of our analyses include availability of prospectively ascertained data on childhood cognitive ability, captured prior to pre-morbid decline, and on change in two objective measures of physical capability, which are components of common age-related disorders including frailty and sarcopenia and, have been related to risk of premature mortality, mobility disability and chronic disease.(37-39) Analyses also benefited from the prospective ascertainment of a range of covariates. However, including factors such as education and adult cognitive ability could be viewed as an over-adjustment.

Our method of analysing change in physical capability was chosen with the aim of avoiding some of the limitations associated with modelling change continuously when data are only available at two time points, including regression to the mean, measurement error and practice effects.(19) We acknowledge that this chosen method also has important limitations and so our results need to be interpreted with caution; for example, there is heterogeneity between individuals within each of the four outcome groups for both measures (see table S4, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>), especially the reference categories which include relatively sizeable groups who appear to have improved over time (see table S1, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>) and the ‘stable’ groups where declines in means were observed (see supplemental digital content tables S2 and S4, <http://links.lww.com/PSYMED/A396>). However, by choosing to analyse four outcome groups rather than using one of the established methods of creating binary categorizations of change scores,(40) we hope to have taken greater account of the observed heterogeneity in intra-individual change.(14) We have also identified different groups likely to be meaningful in the

context of healthy ageing similar to those identified in other recent studies using alternative approaches.(41) While the validity of our approach has not been formally assessed, there are clear differences in the levels of change in mean grip strength and chair rise speed observed in these groups between ages 53 and 60-64 (see supplemental digital content tables S2 and S4, <http://links.lww.com/PSYMED/A396>). Further, additional analyses confirm that the four categories of change in grip strength and chair rise speed distinguish between groups of individuals with different health and disability prospects (see table S5, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A396>).

The NSHD was selected at birth to be nationally representative and at ages 53 and 60-64 years remained so in many respects.(42,43) However, only those participants who were assessed at ages 53 and 60-64 could be included in our analyses and so losses to follow-up before age 53 are a potential source of bias in our analyses. Further bias may have been introduced by excluding participants assessed at age 53 who subsequently died; those participants in the NSHD who had weaker grip strength and slower chair rise speed at 53 had higher rates of all-cause mortality when followed up to age 66 years.(44) However, in a Finnish study which examined the impact of right censoring due to death there was little evidence that estimates of annual change in grip strength before age 65 were altered(45) suggesting that any bias introduced by this in our analyses is likely to be minimal. Bias may also have been introduced by the exclusion of participants with missing data on childhood cognitive ability. However, there were no significant differences in the patterns of change when those participants with missing data on childhood cognitive ability were compared with those included in analyses. Implementing multiple imputation for missing data on covariates minimised another potential source of bias.

Conclusions

Higher childhood cognitive ability was associated with reduced risks of decline in grip strength and chair rise speed during midlife. This suggests that additional insights may be provided by considering neurodevelopmental as well as neurodegenerative pathways when future research is undertaken to identify opportunities to prevent or minimise age-related declines in physical capability.

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Data used in this publication are available to bona fide researchers upon request to the NSHD

Data Sharing Committee via a standard application procedure. Further details can be found at

<http://www.nshd.mrc.ac.uk/data> doi: 10.5522/NSHD/Q101; doi: 10.5522/NSHD/Q102

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Table 1: Characteristics of the MRC National Survey of Health and Development

	Men		Women	
	N ^a	% or Mean (SD)	N ^a	% or Mean (SD)
<i>Categories of change in physical capability</i>				
<i>between ages 53 and 60-64</i>				
Grip strength^b				
Reference	609	70.7	637	67.1
Decline	155	18.0	214	22.6
Stable high	51	5.9	50	5.3
Stable low	47	5.5	48	5.1
Chair rise speed^b				
Reference	607	68.4	714	72.3
Decline	189	21.3	189	19.2
Stable high	49	5.5	33	3.3
Stable low	43	4.8	51	5.2
<i>Physical capability at ages 53 and 60-64^c</i>				
Grip strength (kg) at age: 53	851	47.9 (12.2)	917	28.2 (7.9)
60-64	851	44.8 (11.6)	917	26.0 (7.4)
Chair rise speed (stands/min) at age: 53	837	32.2 (10.1)	921	31.2 (9.3)
60-64	837	26.5 (7.3)	921	25.6 (7.9)
<i>Covariates</i>				
Birthweight (kg)	922	3.5 (0.5)	1027	3.3 (0.5)
Paternal occupational class (age 4)				
High (I or II)	227	25.0	255	25.1

Middle (IIINM or IIIM)	440	48.4	513	50.4
Low (IV or V)	242	26.6	249	24.5
Maternal educational level (age 6)				
Secondary & FE or HE	120	13.8	124	12.8
Secondary only or, primary and FE or HE	113	13.0	115	11.8
Primary and FE (no qualifications)	147	16.9	142	14.6
Primary only	488	56.2	590	60.8
Own occupational class (age 53)				
High (I or II)	507	55.1	395	38.4
Middle (IIINM or IIIM)	322	35.0	448	43.5
Low (IV or V)	92	10.0	186	18.1
Behavioural risk factor score (age 53)	921	2.9 (1.3)	1024	2.8 (1.5)
(range 0 – 6)				
Health indicator count (age 53)	913	0.5 (0.7)	1016	0.7 (0.8)
(range 0 – 4)				
≥ 1 health indicator reported		40.9		51.3
Own educational level (age 26)				
Degree or higher	152	17.1	60	6.0
A levels, or their equivalents	273	30.6	268	26.7
O levels, or their equivalents	131	14.7	267	26.6
CSE, clerical course or equivalent	48	5.4	97	9.7
None	287	32.2	313	31.1
Verbal memory score (age 53)	909	23.5 (6.1)	1019	25.4 (6.0)
Search speed score (age 53)	920	276.4 (73.7)	1022	290.4 (73.7)

Note: sample restricted to those NSHD participants with data on childhood cognitive ability and change in grip strength and/or chair rise speed (maximum N=1954)

FE = further education; HE=higher education

Distribution of cognitive ability at age 15 not presented as this has been standardised (to a mean of 0 and SD of 1)

a. Total Ns vary due to missing data

b. For mean levels of grip strength and chair rise speed at ages 53 and 60-64 in each category see supplemental digital content table S2

c. Overall means and SDs presented for sample with data on childhood cognitive ability and valid measures of grip strength/chair rise speed at both ages. Please note, total Ns for categories of change are higher due to inclusion of: (1) participants with valid values at 53 who were unable to complete the test for health reasons at 60-64 years in the 'decline' category (n=38 for grip strength (11 men, 27 women), n=84 for chair rise speed (37 men, 47 women)) and; (2) participants who were unable to complete the test for health reasons at both ages in the 'stable low' category (n=5 for grip strength (0 men, 5 women), n=33 for chair rise speed (14 men, 19 women))

Table 2: Associations of childhood cognitive ability with changes in grip strength and chair rise speed between ages 53 and 60-64 years

Model (covariates included)	Relative-risk ratios (95% CI) of being in specified category of change relative to reference category per 1SD increase in childhood cognitive score		
	Stable high	Stable low	Decline
Grip strength (Total N=1811^a)	N=101	N=95	N=369
1 (sex)	1.12 (0.90, 1.38)	0.84 (0.68, 1.03)	0.82 (0.73, 0.92)
2 (sex + potential confounders from early life)	0.98 (0.77, 1.24)	0.94 (0.75, 1.18)	0.87 (0.76, 0.99)
3 (sex + potential adult mediators)	0.99 (0.79, 1.26)	0.92 (0.72, 1.16)	0.86 (0.76, 0.98)
4 (sex + own educational level)	0.89 (0.67, 1.18)	0.78 (0.59, 1.03)	0.80 (0.69, 0.94)
5 (sex + adult cognitive ability)	1.22 (0.94, 1.57)	0.89 (0.69, 1.15)	0.88 (0.76, 1.02)
6 (all covariates)	0.91 (0.66, 1.25)	0.90 (0.66, 1.24)	0.90 (0.75, 1.07)
Chair rise speed (Total N=1875^b)	N=82	N=94	N=378
1 (sex)	1.35 (1.06, 1.71)	0.63 (0.51, 0.77)	0.82 (0.73, 0.92)
2 (sex + potential confounders from early life)	1.22 (0.93, 1.59)	0.64 (0.51, 0.80)	0.81 (0.71, 0.92)
3 (sex + potential adult mediators)	1.16 (0.89, 1.52)	0.76 (0.60, 0.97)	0.85 (0.75, 0.97)
4 (sex + own educational level)	1.06 (0.77, 1.47)	0.71 (0.53, 0.94)	0.93 (0.80, 1.09)
5 (sex + adult cognitive ability)	1.15 (0.86, 1.53)	0.82 (0.63, 1.06)	0.88 (0.77, 1.02)
6 (all covariates)	0.91 (0.64, 1.31)	0.90 (0.65, 1.24)	0.96 (0.80, 1.14)

a Sample restricted to those with complete data on childhood cognitive ability and change in grip strength (reference category, N=1246)

b Sample restricted to those with complete data on childhood cognitive ability and change in chair rise speed (reference category, N=1321)

Model adjustments:

1: sex (no evidence of sex interactions ($p=0.29$ and 0.87 for grip strength and chair rise speed, respectively) or deviations from linearity ($p>0.56$ and >0.12 for quadratic terms tested in association with each of the 3 outcome groups vs. reference for grip strength and chair rise speed, respectively))

2: sex, birth weight, paternal occupational class and maternal educational level

3: sex, own occupational class and cumulative scores of behavioural risk and health status at age 53

4: sex and own educational level

5: sex, verbal memory and search speed at age 53

6: all covariates

All analyses run across 20 imputed datasets and results combined using Rubin's rules.

Supplemental digital content

Table S1: Cross-tabulation of sex-specific standard deviation scores for grip strength and chair rise speed at ages 53 and 60-64 years used to identify four main outcome groups for each measure

Grip strength (G)/chair rise speed (C) SD score at age:	60-64 years			
	53 years	< - 1SD	-1 SD to 1 SD	> 1SD
< - 1SD		4. Stable low G:90; C:61	1. Reference G:156; C:147	1. Reference G:23; C:8
-1 SD to 1 SD		2. Decline G:180; C:146	1. Reference G:906; C:1039	1. Reference G:161; C:127
> 1SD		2. Decline G:14; C:5	2. Decline G:137; C:143	3. Stable high G:101; C:82

Note: G and C are the number of participants in each cell when the categorised sex-specific standard deviation scores for grip strength (G) and chair rise speed (C) at ages 53 and 60-64 years are cross-tabulated among the sample with data on childhood cognitive ability

Total Ns used in analyses are higher than those presented in table S1 due to additional inclusion of: (1) participants with valid values at 53 who were unable to complete the test for health reasons at 60-64 years in the 'decline' category (n=38 for grip strength, n=84 for chair rise speed) and; (2) participants who were unable to complete the test for health reasons at both ages in the 'stable low' category (n=5 for grip strength, n=33 for chair rise speed)

Table S2: Mean levels of grip strength and chair rise speed at ages 53 and 60-64 years in each category of change in the MRC National Survey of Health and Development (sample restricted to those with data on childhood cognitive ability)

	Men			Women		
	N ^a (%)	Mean (SD)		N ^a (%)	Mean (SD)	
		at 53y	at 60-64y		at 53y	at 60-64y
Grip strength (kg)						
Reference	609	46.1 (9.7)	46.5 (8.4)	637 (67.1)	26.6 (5.9)	27.3 (5.7)
Decline	(70.7)	53.7 (12.1)	36.0 (11.6)	214 (22.6)	31.5 (8.4)	20.3 (6.6)
Stable high	155	68.2 (6.6)	64.8 (7.3)	50 (5.3)	42.2 (8.7)	39.1 (4.1)
Stable low	(18.0)	28.7 (6.4)	27.4 (4.3)	48 (5.1)	16.7 (2.5)	15.6 (2.6)
	51 (5.9)					
	47 (5.5)					
Chair rise speed (stands/min)						
Reference	607	29.8 (6.1)	26.9 (5.4)	714 (72.3)	29.1 (6.0)	26.1 (6.7)
Decline	(68.4)	36.5 (13.6)	21.5 (5.8)	189 (19.2)	36.1 (12.9)	21.5 (6.9)
Stable high	189	51.0 (7.8)	42.3 (6.4)	33 (3.3)	50.5 (7.9)	42.5 (8.6)
Stable low	(21.3)	18.8 (2.4)	16.6 (2.0)	51 (5.2)	17.9 (2.9)	15.2 (2.5)
	49 (5.5)					
	43 (4.8)					

a. Total N in each category. Ns for presented means in some categories vary due to inclusion of: (1) participants with valid values at 53 who were unable to complete the test for health reasons at 60-64 years in the 'decline' category (n=38 for grip strength (11 men, 27 women), n=84 for chair rise speed (37 men, 47 women)) and; (2) participants who were unable to complete the test for health reasons at both ages in the 'stable low' category (n=5 for grip strength (0 men, 5 women), n=33 for chair rise speed (14 men, 19 women))

For mean values of grip strength and chair rise speed in each category estimated using the maximum available samples, please see Cooper et al 2016(1)

Table S3: Sex-adjusted associations* of each covariate with categories of change in grip strength and chair rise speed in the MRC National Survey of Health and Development (sample restricted to those with complete data on childhood cognitive ability and change (Max N=1811 for grip strength and 1875 for chair rise speed) though Ns vary due to missing data on covariates)

		Relative-risk ratios (95% CI) of being in specified category of change relative to reference category					
		Grip strength			Chair rise speed		
		Stable high	Stable low	Decline	Stable high	Stable low	Decline
Birth weight	<i>per 1kg increase</i>	1.75 (1.16, 2.64)	0.50 (0.33, 0.76)	1.03 (0.81, 1.30)	0.98 (0.62, 1.55)	1.12 (0.73, 1.72)	1.03 (0.81, 1.30)
Paternal occupational class	<i>I or II</i>	1.00	1.00	1.00	1.00	1.00	1.00
	<i>III</i>	0.85 (0.53, 1.35)	1.37 (0.79, 2.37)	1.38 (1.01, 1.86)	0.42 (0.25, 0.70)	1.56 (0.89, 2.75)	1.20 (0.91, 1.60)
	<i>IV or V</i>	0.60 (0.33, 1.10)	1.66 (0.91, 3.04)	1.70 (1.21, 2.38)	0.37 (0.20, 0.70)	1.43 (0.76, 2.70)	0.96 (0.68, 1.34)
	<i>per category change</i>	0.78 (0.58, 1.05)	1.28 (0.95, 1.73)	1.30 (1.10, 1.54)	0.56 (0.40, 0.77)	1.17 (0.87, 1.58)	0.98 (0.83, 1.15)
Maternal educational level							
	<i>Secondary & FE or HE</i>	1.00	1.00	1.00	1.00	1.00	1.00
	<i>Secondary only or, primary and FE or HE</i>	0.60 (0.29, 1.25)	1.82 (0.65, 5.14)	1.53 (0.92, 2.57)	0.84 (0.36, 1.98)	1.73 (0.65, 4.57)	0.97 (0.60, 1.58)
	<i>Primary and FE (no qualifications)</i>	0.83 (0.43, 1.58)	2.23 (0.84, 5.93)	1.75 (1.07, 2.87)	1.22 (0.57, 2.58)	1.34 (0.50, 3.60)	1.17 (0.75, 1.83)
	<i>Primary only</i>	0.48 (0.28, 0.83)	2.55 (1.08, 6.00)	1.85 (1.22, 2.80)	0.65 (0.34, 1.26)	2.14 (0.96, 4.76)	1.23 (0.85, 1.76)
	<i>per category change</i>	0.80 (0.68, 0.96)	1.29 (1.03, 1.61)	1.18 (1.05, 1.32)	0.87 (0.71, 1.06)	1.24 (1.00, 1.55)	1.08 (0.97, 1.21)
Own occupational class	<i>I or II</i>	1.00	1.00	1.00	1.00	1.00	1.00
	<i>III</i>	0.55 (0.34, 0.88)	1.28 (0.80, 2.03)	1.40 (1.08, 1.81)	0.79 (0.49, 1.26)	1.46 (0.90, 2.37)	1.02 (0.80, 1.32)
	<i>IV or V</i>	0.69 (0.36, 1.33)	1.50 (0.81, 2.77)	1.38 (0.97, 1.97)	0.33 (0.12, 0.93)	2.51 (1.41, 4.47)	1.32 (0.94, 1.86)
	<i>per category change</i>	0.73 (0.53, 1.00)	1.24 (0.92, 1.66)	1.22 (1.03, 1.44)	0.68 (0.47, 0.97)	1.57 (1.18, 2.09)	1.12 (0.95, 1.32)
Own educational level	<i>Degree or higher</i>	1.00	1.00	1.00	1.00	1.00	1.00
	<i>A levels, or their equivalents</i>	1.10 (0.58, 2.08)	1.02 (0.47, 2.21)	1.42 (0.89, 2.27)	0.73 (0.39, 1.35)	0.99 (0.38, 2.61)	1.21 (0.77, 1.90)
	<i>O levels, or their equivalents</i>	0.80 (0.39, 1.63)	1.42 (0.65, 3.13)	1.48 (0.91, 2.41)	0.52 (0.25, 1.07)	1.73 (0.67, 4.50)	1.19 (0.74, 1.92)
	<i>CSE, clerical course or equivalent</i>	0.34 (0.09, 1.22)	1.40 (0.53, 3.74)	1.94 (1.10, 3.43)	0.21 (0.05, 0.92)	3.58 (1.30, 9.87)	1.63 (0.92, 2.88)
	<i>None</i>	0.62 (0.31, 1.23)	1.08 (0.50, 2.30)	1.64 (1.04, 2.59)	0.37 (0.18, 0.76)	2.69 (1.11, 6.53)	1.93 (1.25, 2.99)
	<i>per category change</i>	0.84 (0.72, 0.98)	1.02 (0.88, 1.19)	1.09 (1.00, 1.19)	0.77 (0.64, 0.91)	1.34 (1.15, 1.57)	1.18 (1.09, 1.28)
Verbal memory at age 53	<i>per 1SD increase</i>	0.95 (0.78, 1.17)	0.85 (0.69, 1.05)	0.80 (0.71, 0.91)	1.36 (1.07, 1.73)	0.57 (0.46, 0.71)	0.82 (0.73, 0.92)
Search speed at age 53	<i>per 1SD increase</i>	1.08 (0.89, 1.32)	1.03 (0.84, 1.27)	1.01 (0.90, 1.13)	1.34 (1.09, 1.64)	0.72 (0.57, 0.91)	0.96 (0.85, 1.08)

* No evidence of interactions with sex when formally tested (Grip strength: birth weight $p=0.90$; father's occupational class $p=0.94$; maternal educational level $p=0.39$; own educational level $p=0.73$; own occupational class $p=0.91$; verbal memory $p=0.79$; search speed $p=0.41$; Chair rise speed: birth weight $p=0.26$; father's occupational class $p=0.84$; maternal educational level $p=0.34$; own educational level $p=0.31$; own occupational class $p=0.60$; verbal memory $p=0.55$; search speed $p=0.09$)
Deviations from linearity also formally tested but no evidence of this found.

Note: estimates for behavioural risk and health indicator count not shown as these have previously been reported in Cooper et al, 2016(1)

Table S4: Mean (SD) and inter-quartile range (IQR) of change scores in each outcome category of grip strength and chair rise speed

	Men		Women	
	Mean (SD)	IQR	Mean (SD)	IQR
Grip strength (kg)				
Reference	0.4 (11.1)	-6.9 to 7.0	0.7 (7.6)	-4.5 to 4.8
Decline	-18.7 (8.5)	-22.8 to -13.1	-12.4 (5.8)	-15.8 to -8.1
Stable high	-3.4 (8.6)	-8.9 to -1.0	-3.1 (8.5)	-4.6 to 1.3
Stable low	-1.2 (7.0)	-4.8 to 2.7	-1.2 (3.8)	-3.0 to 1.9
Chair rise speed (stands/min)				
Reference	-2.9 (7.1)	-7.8 to 1.8	-3.0 (7.9)	-7.8 to 1.1
Decline	-16.6 (11.0)	-21.1 to -9.6	-18.4 (8.4)	-22.3 to -13.5
Stable high	-8.7 (10.9)	-13.5 to -1.6	-8.0 (9.7)	-11.8 to -3.6
Stable low	-2.2 (2.9)	-4.0 to -0.1	-2.7 (3.2)	-4.6 to -0.3

Note: Sample restricted to those with complete data on childhood cognitive ability and change. For Ns in each category please see table S2

Change scores calculated by subtracting value of grip strength (kg)/chair rise speed (stands/minute) achieved at 53 from value achieved at 60-64 whereby negative values reflect a decline with age.

Table S5: Proportion of study participants in each category of change in grip strength and chair rise speed who: 1) reported a long-term limiting illness, health problem or disability at age 60-64; 2) reported difficulty walking at age 60-64; 3) died between assessment at age 60-64 and age 70

	% reporting long-term limiting illness, health problem or disability at age 60-64	% with self-reported difficulty walking at age 60-64	% who had died by age 70
Grip strength			
Reference	21	8	3
Decline	34	18	5
Stable high	20	5	1
Stable low	32	21	7
<i>p-value^a</i>	<i><0.001</i>	<i><0.001</i>	<i>0.004</i>
Chair rise speed			
Reference	18	5	3
Decline	39	25	4
Stable high	16	0	4
Stable low	66	48	5
<i>p-value^a</i>	<i><0.001</i>	<i><0.001</i>	<i>0.57</i>

^a p-values from chi-squared tests

Note: Sample restricted to those with complete data on childhood cognitive ability and change (N=1811 for grip strength and 1875 for chair rise speed). For Ns in each category please see table S2

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