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Longitudinal associations of childhood fitness and obesity profiles with midlife cognitive function: an Australian cohort study

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ABSTRACT

Objectives: Clusters of low fitness and high obesity in childhood are associated with poorer health outcomes in later life, however their relationship with cognition is unknown. Identifying such profiles may inform strategies to reduce risk of cognitive decline. This study examined whether specific profiles of childhood fitness and obesity were associated with midlife cognition.
Design: Prospective study.
Methods: In 1985, participants aged 7–15 years from the Australian Childhood Determinants of Adult Health study were assessed for fitness (cardiorespiratory, muscular power, muscular endurance) and anthropometry (waist-to-hip ratio). Participants were followed up between 2017 and 2019 (aged 39–50). Composites of psychomotor speed-attention, learning-working memory and global cognition were assessed using CogState computerised battery. Latent profile analysis was used to derive mutually exclusive profiles based on fitness and anthropometry. Linear regression analyses examined associations between childhood profile membership and midlife cognition adjusting for age, sex and education level.
Results: 1244 participants were included [age: 44.4 ± 2.6 (mean ± SD) years, 53% female]. Compared to those with the highest levels of fitness and lowest waist-to-hip ratio, three different profiles characterised by combinations of poorer cardiorespiratory fitness, muscular endurance and power were associated with lower midlife psychomotor-attention [up to −1.09 (−1.92, −0.26) SD], and lower global cognition [up to −0.71 (−1.41, −0.01) SD]. No associations were detected with learning-working memory.
Conclusions: Strategies that improve low fitness and decrease obesity levels in childhood could contribute to improvements in cognitive performance in midlife.

Practical implications

- Profiles in children with a combination of higher levels of CRF and muscular fitness and lower abdominal obesity were associated with better psychomotor-attention and global cognition at midlife.
- Activities and interventions aimed at increasing multiple areas of fitness and reducing obesity in children also should be implemented for midlife brain health, particularly those that can be maintained throughout adolescence and adulthood.
- Maintaining fitness and reducing obesity across the lifespan contributes to greater cognitive performance at midlife and beyond, and may reduce the risk of cognitive decline.

1. Introduction

Cognition incorporates a number of domains including memory, attention, and executive function, which are essential for everyday activities. The pathological processes underlying cognitive decline may begin many decades before mild symptoms or a diagnosis of dementia are clinically detected.[1] A decline in cognitive performance can begin as early as middle-age,[2] and lower midlife cognition has been associated

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with a greater likelihood of developing mild cognitive impairment and dementia in older age.[3] As such, it is important to identify factors in early life that may protect against cognitive decline during later life.

Muscular (i.e., strength, endurance and power) and cardiorespiratory fitness (CRF) in childhood are associated with later life health outcomes. For example, higher levels of childhood muscular fitness are associated with decreased risk of cardiometabolic disease in early adulthood.[4] Higher adult fitness levels are also associated with better cognitive function, potentially through reduced cardiovascular risk or protective mechanisms such as neurogenesis and angiogenesis.[5] For example, stronger grip strength at midlife is associated with better cognitive function, slower decline, and reduced risk of dementia in older age.[6] Higher CRF at midlife also confers protective effects on cognition in older age.[7] Despite this, little is known if objective measures of fitness at childhood associate with midlife cognition.

Higher CRF assessed at early adulthood (ages 18–30 years) was associated with better memory and psychomotor speed measured 25 years later.[8] Relatedly, high amounts of physical activity in childhood (6–12 years) have been linked to better reaction time at midlife.[9] However, there are no published studies examining whether muscular fitness or CRF at childhood predict midlife cognition. Obesity is also associated with higher cardiovascular risk, and central adiposity is linked to chronic inflammation and reduced insulin sensitivity,[10] both important for neuronal health and cognition. However, there is mixed evidence as to whether higher levels of obesity at childhood, adolescence or adulthood may be associated with poorer cognitive function at midlife.[11–13]

Identifying individual modifiable factors at childhood that are associated with poorer midlife cognition may inform protective interventions or strategies that attenuate the risk of cognitive decline in later life. However, clusters and combinations of childhood cardiovascular behavioural risk factors including muscular fitness and obesity, have been previously linked to worse cardiovascular and metabolic health in adulthood.[4,14] Given this, it is plausible that phenotypic profiles consisting of childhood levels of obesity, muscular and CRF may also be associated with cognitive function in later life. This is currently untested, but may add value in providing a more nuanced approach to identifying groups of children for interventions to maintain brain health later in life. Therefore, the aim of this longitudinal study was to examine the association between specific profiles of childhood fitness (CRF, two measures of muscular power and muscular endurance) and abdominal obesity with three measures of cognitive performance in midlife.

2. Methods

The 1985 Australian Schools Health and Fitness Survey was a nationally representative sample of 8498 Australian children aged 7–15 years.[15] Participants have been followed up at three time points as part of the Childhood Determinants of Adult Health study (CDAH), a prospective cohort study based on the Survey participants. The current analyses included participants at the third timepoint (CDAH-3), who completed questionnaires and attended clinics between 2017 and 2019 (ages 39–50). Participants with fitness measures in childhood, and one valid measure of cognition at midlife were included in primary analysis (n = 1244). Measures of muscular strength were only collected in a subset of the original sample (n = 415 out of current sample), and therefore were not included in this analysis. For the Australian Schools Health and Fitness Survey, consent was obtained from a parent and assent obtained from children. At CDAH-3, all participants gave written informed consent. The State Directors General of Education approved the Survey, and the Southern Tasmania Health and Medical Human Research Ethics Committee approved follow-up studies.

Cardiorespiratory fitness in childhood was estimated by the duration of a 1.6 km run/walk performed over a level course. Verbal encouragement was provided.

Childhood muscular power (POWER-JUMP) was measured as the longest distance (centimetres) from two attempts at a standing long jump test. Anaerobic power (POWER-SPRINT) was measured by a 50 m sprint on a straight track. Participants were given a warm-up before testing and completed one trial, instructed to run as fast as possible. Muscular endurance (END) was estimated by the number of correctly completed inclined push-ups in 30 s. Two hands were placed on the front edge of a chair, shoulder width apart, with legs straight at a 90° angle to the body and arms fully extended. A complete push-up involved the body being lowered until their chest touched the chair and then raised by the arms fully extending.

Waist circumference at childhood and midlife was measured to the nearest 0.1 cm at the level of the umbilicus with a constant tension tape. Hip circumference was measured at the level of the greatest posterior protuberance of the buttocks. Waist-to-hip ratio (WHR) was calculated by dividing waist by hip circumference. It was used as a proxy measure of abdominal obesity rather than BMI, which does not distinguish between the opposing effects of fat mass and lean mass. WHR has also been found to be associated with brain health in older age.[16]

Cognitive function was assessed at midlife by the CogState Brief Battery (CogState Ltd., Melbourne, Australia) using four tests: 1. Detection task measuring simple reaction time (ms); 2. Identification task measuring choice reaction time (ms); 3. One Card Learning task measuring visual memory (correct responses); 4. One Back task measuring working memory (ms). Reaction times were $\log_{10}$ transformed, while the square root of the proportion of correct responses was arcsine transformed.[17] Performances failing task criteria (Supplementary Table 1) were removed. The One Card Learning task was not presented to participants at some clinics, resulting in fewer tests (n = 560). Raw scores for each task were transformed into *Z*-scores using the mean and standard deviation of the total sample. Composite domains were then created as follows, with higher scores indicating better performance.[17]

- Global cognitive function: average for all tests
- Learning-Working memory: average for One Card Learning and One Back Tasks
- Psychomotor-Attention: average for Detection and Identification Tasks

At childhood, questionnaires were only administered to 9–15 year olds. Postcodes of children aged 9–15 were used to categorise area-level socioeconomic status (SES), based on Australian Bureau of Statistics index of relative socioeconomic disadvantage derived from the 1981 census. Children aged 9–15 years completed a self-reported questionnaire for smoking, passive smoking and drinking habits. Those who didn't smoke were classified as 'non-smokers', and children regularly smoking were classified as 'smokers'. Parental smoking was considered positive if at least one parent smoked. For alcohol consumption, participants were classified as 'never', 'less than once a week', and 'more than once a week'. Scholastic level, a five level variable ('poor' to 'excellent') was assigned to each child by a representative (e.g., teacher) from each school. At midlife, self-administered questionnaires collected health and demographic data, including diagnosis of health conditions. Participants reported their highest level of education (ranging from secondary school to higher degree) and smoking status (current, ex, or non-smoker). Typical adult alcohol consumption was estimated from a food frequency questionnaire and converted to total intake per week (in grams) for analysis.

Fitness and waist-to-hip measures were standardised for age (between 7 and 15 years) and sex, against the original sample (i.e., n = 8498). Latent profile analysis (LPA) was used to identify childhood fitness and obesity profiles present (see Supplementary material and Supplementary Fig. 1 for methods). The LPA included participants with 50 m sprint time (POWER-SPRINT), 1.6 km run duration (CRF), jump distance

(POWER-JUMP), push-ups [muscular endurance (END)], WHR and sex. *Z*-scores for the 1.6 km run and 50 m sprint were reversed (i.e., negative to positive) with higher Z-scores indicating better performance. Associations between resulting profile membership and each midlife cognitive composite were assessed via linear regression. Model 1 was unadjusted, model 2 was adjusted for age at midlife, sex, and education level. We then examined the effect on coefficients when adjusting for alcohol and smoking at adulthood, and socioeconomic status, smoking status, alcohol, passive smoking and scholastic ability at childhood. As there were missing data in fitness variables and covariates, multiple imputation using chained equations was used to impute missing data at childhood and follow-up, and analyses repeated.[18] We did not adjust for medical history such as hypertension and diabetes as these variables were considered on the pathway between the fitness/obesity measures and cognition. Pregnant women were excluded from regression analyses as pregnancy is associated with lower cognitive function.[19] Residual plots were inspected for normality prior to analysis and the assumption of homoscedasticity verified. The significance level was set at $p < 0.05$. Statistical analyses were conducted using STATA 15.1 (STATA, College Station, TX, USA).

3. Results

The flow of participants through the study is presented in Supplementary Fig. 2. Average length of follow up between childhood and midlife was 32.8 years. Participant characteristics are provided in Table 1. At midlife, 53% were female, and the average age was 44.4 ± SD 2.6 years. At childhood, participants in the study were similar to those not included (n = 7254), but a higher percentage lived in a higher socioeconomic area (28.5 vs 22.8% in highest category).

A six-profile LPA model was the most appropriate fit, in which n = 1159 were included (n = 85 did not have complete sets of all fitness measures and were not assigned to profiles). Profile 1 is small (n = 5) however in models with fewer profiles this group consistently emerged, suggesting an important and distinct phenotypic profile.

Participant characteristics at childhood for each profile are presented in Supplementary Table 2 and mean *Z*-scores of fitness and obesity measures visualised in Fig. 1. The fitness and obesity profiles were: profile 1 [↓↓↓ POWER-JUMP, ↓↓↓CRF, ↓↓↓ POWER-SPRINT, ↓ END, ↑ WHR], profile 2 [↓ POWER-JUMP, ↓↓↓ CRF, ↓ POWER-SPRINT, ↓ END, ↓ WHR], profile 3 [↓↓ POWER-JUMP, ↓ CRF, ↓↓↓ POWER-SPRINT, ↓ END, ↑ WHR], profile 4

Table 1
Participant characteristics at baseline and follow-up.

Childhood	n	All	Males	Females	n	Not in analysis
N, %		1244	586 (47%)	658 (53%)	7254	
Age (yr), n (%)		11.1 (2.5)	11.2 (2.5)	11.1 (2.5)		10.9 (2.5)
7–9		382 (31)	170 (29.0)	212 (32.2)		2527 (34.8)
10–12		438 (35)	206 (35.1)	232 (35.2)		2508 (34.6)
13–15		424 (34)	210 (35.8)	214 (32.5)		2219 (30.6)
Standing long jump (cm)	1243	146.7 (30.5)	155.6 (31.7)	138.9 (27.1)	7218	142.5 (28.6)
1.6 km run time (min)	1162	9.0 (1.8)	8.2 (1.5)	9.8 (1.7)	6714	9.3 (2.0)
50 m run time (s)	1186	9.1 (1.1)	8.8 (1.0)	9.3 (1.0)	6883	9.2 (1.1)
Push-ups in 30s (n)	1241	10.6 (6.6)	13.6 (6.2)	7.8 (5.6)	7195	10.6 (6.5)
Waist-to-hip ratio	1243	0.83 (0.06)	0.85 (0.04)	0.82 (0.06)	7246	0.84 (0.06)
Socioeconomic status, n (%)	964				5335	
Low		59 (6.1)	35 (7.9)	24 (4.7)		523 (9.8)
Medium		630 (65.4)	303 (66.2)	327 (64.6)		3597 (67.4)
High		275 (28.5)	118 (25.9)	157 (30.9)		1215 (22.8)
Smoking status, n (%)	978				5392	
Non-smoker		872 (89.2)	411 (88.6)	461 (89.7)		4620 (85.7)
Smoker		106 (10.8)	53 (11.4)	53 (10.3)		772 (14.3)
Parental smoking, n (%)	983				5390	
None		616 (62.7)	298 (63.8)	318 (61.6)		2620 (48.3)
≥1 parent		367 (37.3)	169 (36.2)	198 (38.4)		2778 (51.7)
Alcohol consumption, n (%)	985					
Never		663 (67.3)	298 (63.8)	365 (70.6)		3633 (67.1)
Less than once/week		259 (26.3)	134 (28.7)	125 (24.1)		1339 (24.7)
More than once/week		63 (6.4)	35 (7.5)	28 (5.3)		440 (8.1)
Scholastic ability, n (%)	1171				6790	
Excellent		178 (15.2)	71 (12.8)	107 (17.4)		565 (8.3)
Poor		16 (1.4)	13 (2.3)	3 (0.5)		376 (5.5)

Midlife	n	All	Males	Females	n	Not in analysis
Age (yr)	1244	44.4 (2.6)	44.5 (2.6)	44.4 (2.6)	323	42.1 (3.3)
Waist-to-hip ratio	1237	0.85 (0.09)	0.91 (0.07)	0.80 (0.07)	318	0.83 (0.09)
Education, n (%)	1244				305	
Higher degree, post-graduate diploma		662 (53.2)	287 (49.0)	375 (57)		171 (56.1)
Undergraduate diploma, apprenticeship		417 (33.5)	216 (36.9)	201 (30.6)		96 (31.5)
School only		165 (13.3)	83 (14.2)	82 (12.5)		37 (12.1)
Smoking status, n (%)	1166				308	
Non-smoker		751 (64.4)	357 (65.4)	394 (63.6)		179 (58.1)
Ex-smoker		318 (27.3)	139 (25.5)	179 (28.9)		94 (30.5)
Smoker		97 (8.3)	50 (9.1)	47 (7.6)		35 (11.3)
Alcohol consumption (gm/week)	1232	65.8 (110.9)	84.2 (139.9)	49.7 (73.1)	313	60.1 (94.5)
Diagnosis of:						
Hypertension, n (%)	1236	194 (15.7)	108 (18.6)	86 (13.1)	317	40 (12.6)
Diabetes, n (%)	1235	60 (4.9)	9 (1.6)	51 (7.8)	317	19 (6.0)
Cardiovascular episode, n (%)	1236	12 (1.0)	6 (1.0)	6 (0.9)	317	3 (0.9)
Depression, lifetime, n (%)	1239	228 (18.4)	84 (14.4)	144 (21.9)	259	61 (23.6)
Anxiety/phobia, lifetime, n (%)	1238	264 (21.3)	75 (12.9)	189 (28.8)	259	52 (20.1)

Values are mean ± SD, or n, percentage of participants in category. Cardiovascular episodes represent previous occurrence of angina, stroke, heart attack. Childhood-not in analysis: participants who did not provide valid cognitive assessment data at clinic visits at midlife. Midlife- not in analysis: participants who attended clinic visits for CDAH-3 but did not provide valid cognitive assessment data.

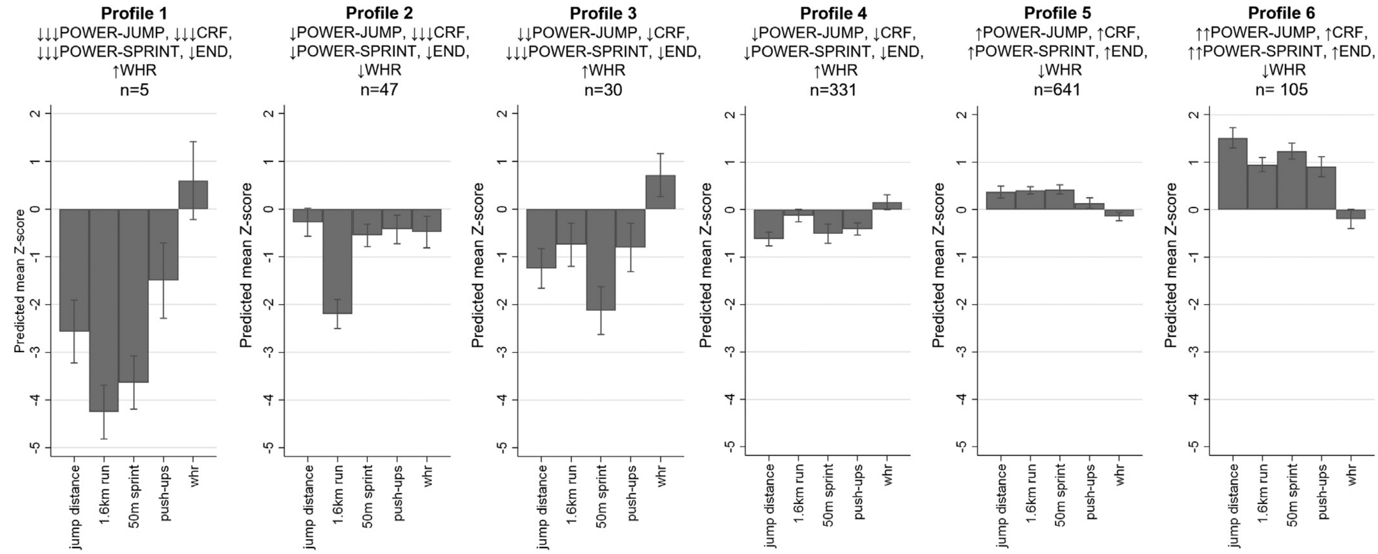

Fig. 1. Mean age and sex adjusted Z-scores for each latent profile (n = 1159).
Values are mean Z-scores ±95% CI. A higher Z-score for WHR is a worse outcome, for all other variables a higher Z-score equates to greater performance. CRF: cardiorespiratory fitness (1.6 km run), END: muscular endurance (push-ups completed in 30 s), POWER: anaerobic and muscular power (50 m sprint and standing long jump), WHR: waist-to-hip ratio. Z-scores were ↑: above average for childhood variable0–1 SD above average for variable; ↑↑: >1 SD above average for variable); ↓: 0–1 SD below average;below average; ↓↓: 1–2 SD below average; ↓↓↓:: >2 SD below average.

[↓ POWER-JUMP, ↓ CRF, ↓ POWER-SPRINT, ↓ END, ↑WHR], profile 5 [↑ POWER-JUMP, ↑ CRF, ↑ POWER-SPRINT, ↑ END, ↓ WHR], profile 6 [↑↑ POWER-JUMP, ↑ CRF, ↑↑ POWER-SPRINT, ↑ END, ↓WHR]. Where *Z*-scores were; ↑: 0–1 SD above average for variable; ↑↑: >1 SD above average; ↓: 0–1 SD below average;; ↓↓: >1–2 SD below average; ↓↓↓:: >2 SD below average. Overall, profile 1 possessed the lowest levels of each fitness variable (lowest fitness), while profile 6 possessed the highest levels of fitness, and was categorised as the 'fittest' profile and used as the reference.

After adjusting for age, sex and education, compared to profile 6 (the highest fitness profile), profile 1 ($p = 0.009$), profile 2 ($p = 0.002$), and profile 4 ($p = 0.011$) had lower estimated scores for the psychomotor-attention composite, and lower scores for the global cognition composite (profile 1: $p = 0.046$, profile 2: $p = 0.028$, and profile 4: $p = 0.023$) (Table 2). There were no interactions between profile and sex. There were no significant associations with learning-working memory.

When including participants with all adult and childhood covariates (n = 791) β coefficients were between 0.01 and 0.09 SD (3–7%) higher in model 2 (adjusted for age, sex and education level), compared to the model adjusted for all covariates (model 3; Supplementary Table 3). Imputing missing data did not substantially affect predicted profile membership, with 85% of participants displaying stability across 10 imputed iterations, compared to original profile membership. After imputing missing data for fitness, obesity and covariates, β-coefficients for profile 2 with global cognition and the psychomotor-attention composite decreased by 0.12–0.22 SD (40–43%) (Supplementary Table 4).

4. Discussion

In this longitudinal study, profiles of fitness and obesity were created using childhood data and associations examined with cognitive performance measured in midlife. Compared to membership in the 'fittest'

Table 2
Associations between childhood fitness and obesity profiles and midlife cognitive performance (*Z*-scores).

	Global cognition β-value (95% CI)		Learning-working memory β-value (95% CI)		Psychomotor-attention β-value (95% CI)	
Reference Profile 6 [↑↑ POWER-JUMP, ↑ CRF, ↑↑ POWER-SPRINT, ↑ END, ↓WHR]	0.14	(−0.003, 0.29)	0.06	(−0.13, 0.25)	0.18	(0.01, 0.35)
Model 1		n = 1154		n = 926		n = 1148
Profile 1 [↓↓↓POWER-JUMP, ↓↓↓CRF, ↓↓↓POWER-SPRINT, ↓END, ↑WHR]	**−0.81**	**(−1.52, −0.11)**	−0.13	(−1.01, 0.75)	**−1.18**	**(−2.02, −0.35)**
Profile 2 [↓POWER-JUMP, ↓↓↓CRF, ↓POWER-SPRINT, ↓END, ↓WHR]	**−0.30**	**(−0.57, −0.03)**	−0.06	(−0.40, 0.27)	**−0.50**	**(−0.82, −0.18)**
Profile 3 [↓↓POWER-JUMP, ↓CRF, ↓↓↓POWER-SPRINT, ↓END, ↑WHR]	−0.12	(−0.44, 0.20)	−0.20	(−0.59, 0.19)	−0.12	(−0.49, 0.26)
Profile 4 [↓POWER-JUMP, ↓CRF, ↓POWER-SPRINT, ↓END, ↑WHR]	**−0.21**	**(−0.38, −0.04)**	−0.02	(−0.24, 0.20)	**−0.27**	**(−0.47, −0.07)**
Profile 5 [↑POWER-JUMP, ↑CRF, ↑POWER-SPRINT, ↑END, ↓WHR]	−0.15	(−0.31, 0.01)	−0.07	(−0.28, 0.13)	−0.18	(−0.37, 0.01)
Model 2		n = 1154		n = 926		n = 1148
Profile 1 [↓↓↓POWER-JUMP, ↓↓↓CRF, ↓↓↓POWER-SPRINT, ↓END, ↑WHR]	**−0.71**	**(−1.40, −0.01)**	−0.03	(−0.91, 0.85)	**−1.09**	**(−1.92, −0.27)**
Profile 2 [↓POWER-JUMP, ↓↓↓CRF, ↓POWER-SPRINT, ↓END, ↓WHR]	**−0.30**	**(−0.57, −0.03)**	−0.02	(−0.36, 0.32)	**−0.51**	**(−0.83, −0.19)**
Profile 3 [↓↓POWER-JUMP, ↓CRF, ↓↓↓POWER-SPRINT, ↓END, ↑WHR]	−0.14	(−0.45, 0.18)	−0.19	(−0.58, 0.20)	−0.14	(−0.52, 0.23)
Profile 4 [↓POWER-JUMP, ↓CRF, ↓POWER-SPRINT, ↓END, ↑WHR]	**−0.20**	**(−0.37, −0.03)**	−0.01	(−0.21, 0.23)	**−0.26**	**(−0.47, −0.06)**
Profile 5 [↑POWER-JUMP, ↑CRF, ↑POWER-SPRINT, ↑END, ↓WHR]	−0.13	(−0.29, 0.03)	−0.05	(−0.26, 0.15)	−0.17	(−0.36, 0.02)

Model 1: unadjusted; Model 2: age at assessment, sex, and education level; CRF: cardiorespiratory fitness (1.6 km run), END: muscular endurance (push-ups completed in 30 s), POWER-JUMP: muscular power (standing long jump), POWER-SPRINT: anaerobic power (50 m sprint), WHR: waist-to-hip ratio. Where *Z*-scores were; ↑: 0–1 SD above average for variable; ↑↑: >1 SD above average; ↓: 0–1 SD below average;; ↓↓: >1–2 SD below average; ↓↓↓:: >2 SD below average.
Bold denotes significant findings.

profile, three profiles of poorer fitness and obesity were associated with lower scores in composites assessing psychomotor-attention and global cognition. These associations were independent of potential confounders including educational attainment, smoking and alcohol consumption at midlife and scholastic ability and socioeconomic status at childhood. No associations were found with a learning-working memory composite. Our findings suggest that improving fitness and obesity levels at childhood may be an important strategy for maintaining psychomotor attention and global cognition at midlife.

To our knowledge, this is the first study demonstrating a relationship between phenotypic profiles of objectively measured fitness and obesity measures at childhood, with midlife cognition. We used a data-driven approach to discover latent profiles, and analysed real-world co-occurrence of factors rather than estimating independent associations. Our findings extend evidence that clusters and combinations of childhood muscular fitness and obesity measures are linked to worse cardiovascular and metabolic health in adulthood.[4,14] They also support previous studies where factors established in childhood, such as a higher number of cardiovascular risk factors (e.g., physical inactivity and obesity),[14,20] and obesity alone,[12] were associated with poorer midlife cognition.

Members of the “fittest” profile (9% of sample) had, on average, scores up to 1.09 SD higher in psychomotor-attention, and 0.71 SD higher in global cognition, compared to the “poorest” fitness and obesity profile (profile 1). Profile 2 had the second lowest CRF and was also associated with both poorer psychomotor-attention and global cognitive function, despite having lower abdominal obesity. Our findings imply a protective effect of relatively higher levels of CRF in childhood for midlife cognition. This supports a prior prospective study with older participants (aged 18–30 years; $n = 2747$), where higher maximal CRF was associated with better performance in verbal memory and psychomotor speed assessed 25 years later.[8] In a study with a shorter follow-up period, higher CRF in adolescents aged 15 years predicted cognitive advantages up to three years later.[21] Our findings suggest that higher CRF levels may provide benefits over longer time periods. Higher CRF has been associated with greater hippocampal and cortical volume in adults, increased cerebral blood flow and synaptic plasticity which augments and maintains cognition, and a reduction in peripheral risk factors (e.g., hyperlipidaemia, inflammation) which are linked to worse cognitive performance, decline and dementia.[22] Taken together, high CRF seems to be particularly important for cognitive function.

There was evidence that a marker of abdominal obesity was also important for cognitive function, as profiles 1 and 4 had higher WHR and were associated with poorer psychomotor-attention and global cognition. A higher BMI in adolescence has been associated with poorer midlife global cognition, but only in those with low childhood socioeconomic position.[11] Our findings support previous research where children with a combination of low levels of obesity and higher CRF, had a reduced risk of metabolic syndrome at adulthood.[23] Childhood and adolescent obesity are important predictors of adult obesity, which may adversely impact cognition through associations with vascular disease.[10] Therefore minimising obesity in childhood, or buffering its impact through improving levels of muscular or CRF, should be encouraged through adherence to World Health Organisation physical activity guidelines[24] to preserve later life cognition.

To our knowledge, no prior studies have attempted to link childhood levels of muscular power and endurance with midlife cognition. Profiles with low levels of muscular power and endurance (1,2, and 4) were associated with poorer psychomotor-attention and global cognition, compared to the “fittest” profile. The mechanisms underpinning these associations are unclear, and it is not known whether our findings were driven by high CRF levels. However, higher levels of muscular power and endurance individually, and within phenotypes at childhood, are linked to lower central adiposity and better metabolic profiles at childhood and midlife,[4,25] which may directly or indirectly mediate the benefits for midlife cognition we observed in the fittest profile. Furthermore, evidence is mixed for a positive association between muscular fitness (strength, power and endurance) and academic achievement in childhood and adolescence,[25,26] and these benefits may endure to adulthood. Still, it possible that muscular fitness levels may cluster with CRF levels in childhood, as demonstrated in our profiles, but have little effect, independently, on cognition.[27] It is also possible that fitness and obesity are both associated with total physical activity and hence cognitive function.[28] Therefore, strategies that improve and maintain muscular fitness levels in childhood, encourage physical activity, and promote an active lifestyle, should be promoted both at home and in school curricula, particularly those which prevent obesity and reinforce lasting positive health behaviours.

Several factors may explain why learning-working memory did not differ between fitness profiles. Processing speed improves during the first three decades of life before linearly declining at an estimated rate of 0.02 SD per year,[29] whereas working memory especially declines in the seventh decade. Thus, in 39–50 year-olds, psychomotor speed and attention may already be exhibiting subclinical changes, while working memory is intact. Mixed evidence for an association between a greater number of early life CVD risk factors (e.g., elevated lipids, BMI) and poorer working memory at midlife has been reported.[13,20] However, apart from the measures of working memory assessed, these studies differed to ours with wider age ranges at baseline (i.e. 6–24 years),[13] which may explain our null findings.

Limitations of our study were that although the sample was demographically balanced at recruitment, there was an 85% loss at follow-up over, on average, 33 years. Second, in those who attended CDAH-3 there was missing data in some of the childhood fitness, obesity and covariate data. We attempted to account for this data through multiple imputation. Third, as cognitive function was not assessed at childhood, we could not determine its potential intermediary role. Childhood cognition can extend into midlife, and lead to a lifestyle of healthier behaviours.[30] Our study also had several strengths. To our knowledge, this is the first study to evaluate the associations of data-driven profiles of childhood fitness and obesity with cognitive function at midlife. It included a long follow-up (≥30 years) of a large, well-characterised national sample with baseline ages younger than past studies, and collected multiple objective measures rather than retrospective or self-reported fitness data.

5. Conclusion

In summary, a profile of children with the highest levels of CRF and muscular fitness and below average WHR had higher midlife scores in composites of psychomotor function and attention, and global cognition, compared to childhood profiles with lower CRF and muscular fitness and typically higher WHR. These findings suggest that factors influencing midlife cognition may already be present at childhood. Strategies aimed at improving low fitness and high abdominal obesity in childhood could contribute to improvements in cognitive performance in midlife.

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Confirmation of Ethical Compliance

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Australian Schools Health and Fitness Survey was approved by the State Directors General of Education, and CDAH was approved by the Southern Tasmania Health and Medical Human Research Ethics Committee and Tasmania Health and Medical Human Research Ethics Committee.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

The authors affirm that human research participants provided informed consent for publication of the results to the journal.

CRediT authorship contribution statement

JLT contributed to the conceptualization of the paper, analysed data and wrote the manuscript, TAC provided general and statistical advice, assisted with interpretation, and critically reviewed the manuscript, SLG (data curation, methodology) critically reviewed the manuscript, VKS and CM contributed to the conceptualization of the paper and critically reviewed the manuscript, CGM, TD, BJF and AJV participated in the study design, acquired funding for the project, and critically reviewed the manuscript. MLC contributed to the conceptualization of the paper and wrote the manuscript. Each of the authors have read and approved the final manuscript.

The authors declare that the manuscript has not been published elsewhere and is not being considered for publication elsewhere. The research reported will not be submitted for publication elsewhere until a final decision has been made as to its acceptability by the Journal.

Declaration of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

1. Jack Jr CR, Knopman DS, Jagust WJ et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *Lancet Neurol* 2013;12(2):207-216.
2. Rovio SP, Pahkala K, Nevalainen J et al. Cognitive performance in young adulthood and midlife: relations with age, sex, and education—the cardiovascular risk in young Finns study. *Neuropsychology* 2016;30(5):532.
3. Knopman DS, Gottesman RF, Sharrett AR et al. Midlife vascular risk factors and midlife cognitive status in relation to prevalence of mild cognitive impairment and dementia in later life: the Atherosclerosis Risk in Communities Study. *Alzheimers Dement* 2018;14(11):1406-1415.
4. Fraser BJ, Huynh QL, Schmidt MD et al. Childhood muscular fitness phenotypes and adult metabolic syndrome. *Med Sci Sports Exerc* 2016;48(9).
5. Brown B, Peiffer J, Martins R. Multiple effects of physical activity on molecular and cognitive signs of brain aging: can exercise slow neurodegeneration and delay Alzheimer's disease? *Mol Psychiatry* 2013;18(8):864-874.
6. Cui M, Zhang S, Liu Y et al. Grip strength and the risk of cognitive decline and dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Front Aging Neurosci* 2021;13:1.
7. DeFina LF, Willis BL, Radford NB et al. The association between midlife cardiorespiratory fitness levels and later-life dementia: a cohort study. *Ann Intern Med* 2013;158(3):162-168.
8. Zhu N, Jacobs DR, Schreiner PJ et al. Cardiorespiratory fitness and cognitive function in middle age: the CARDIA study. *Neurology* 2014;82(15):1339-1346.
9. Hakala JO, Rovio SP, Pahkala K et al. Physical activity from childhood to adulthood and cognitive performance in midlife. *Med Sci Sports Exerc* 2019;51(5).
10. Farruggia MC, Small DM. Effects of adiposity and metabolic dysfunction on cognition: a review. *Physiol Behav* 2019;208:112578.
11. Cohen-Manheim I, Doniger GM, Sinnreich R et al. Body mass index, height and socioeconomic position in adolescence, their trajectories into adulthood, and cognitive function in midlife. *J Alzheimers Dis* 2017;55(3):1207-1221.
12. Hakala JO, Pahkala K, Juonala M et al. Cardiovascular risk factor trajectories since childhood and cognitive performance in midlife: the cardiovascular risk in young Finns study. *Circulation* 2021;143(20):1949-1961.
13. Rovio SP, Pahkala K, Nevalainen J et al. Cardiovascular risk factors from childhood and midlife cognitive performance: the Young Finns Study. *J Am Coll Cardiol* 2017;69(18):2279-2289.
14. Patterson KA, Ferrar K, Gall SL et al. Cluster patterns of behavioural risk factors among children: longitudinal associations with adult cardio-metabolic risk factors. *Prev Med* 2020;130:105861.
15. Dwyer T, Gibbons L. The Australian schools health and fitness survey. Physical fitness related to blood pressure but not lipoproteins. *Circulation* 1994;89(4):1539-1544.
16. Climie RE, Moran C, Callisaya M et al. Abdominal obesity and brain atrophy in type 2 diabetes mellitus. *PloS one* 2015;10(11):e0142589.
17. Lim YY, Pietrzak RH, Bourgeat P et al. Relationships between performance on the Cogstate Brief Battery, neurodegeneration, and Abeta accumulation in cognitively normal older adults and adults with MCI. *Arch Clin Neuropsychol* 2015;30(1):49-58.
18. Lee KJ, Carlin JB. Multiple imputation for missing data: fully conditional specification versus multivariate normal imputation. *Am J Epidemiol* 2010;171(5):624-632.
19. Davies SJ, Lum JA, Skouteris H et al. Cognitive impairment during pregnancy: a meta-analysis. *Med J Aust* 2018;208(1):35-40.
20. Reis JP, Loria CM, Launer LJ et al. Cardiovascular health through young adulthood and cognitive functioning in midlife. *Ann Neurol* 2013;73(2):170-179.
21. Åberg MA, Pedersen NL, Torén K et al. Cardiovascular fitness is associated with cognition in young adulthood. 2009;106(49):20906-20911.
22. Beydoun MA, Beydoun HA, Gamaldo AA et al. Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis. *BMC Public Health* 2014;14:643.
23. Schmidt M, Magnussen C, Rees E et al. Childhood fitness reduces the long-term cardiometabolic risks associated with childhood obesity. *Int J Obes (Lond)* 2016;40(7):1134-1140.
24. World Health Organization. *WHO guidelines on physical activity and sedentary behaviour*, 2020.
25. Smith JJ, Eather N, Morgan PJ et al. The health benefits of muscular fitness for children and adolescents: a systematic review and meta-analysis. *Sports Med* 2014;44(9):1209-1223.
26. Dwyer T, Sallis JF, Blizzard L et al. Relation of academic performance to physical activity and fitness in children. *Pediatr Exerc Sci* 2001;13(3):225-237.
27. Shigeta TT, Leahy AA, Smith JJ et al. Cardiorespiratory and muscular fitness associations with older adolescent cognitive control. *J Sport Health Sci* 2021;10(1):82-90.
28. Erickson KI, Hillman C, Stillman CM et al. Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Med Sci Sports Exerc* 2019;51(6):1242.
29. Salthouse T. Consequences of age-related cognitive declines. *Annu Rev Psychol* 2012;63:201-226.
30. Deary IJ, Whiteman MC, Starr JM et al. The impact of childhood intelligence on later life: following up the Scottish mental surveys of 1932 and 1947. *J Pers Soc Psychol* 2004;86(1):130-147.