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Childhood cardiorespiratory fitness, muscular fitness and adult measures of glucose homeostasis

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ABSTRACT

Objectives: To assess whether childhood cardiorespiratory fitness (CRF) and muscular fitness phenotypes (strength, power, endurance) predict adult glucose homeostasis measures.
Design: Prospective longitudinal study.
Methods: Study examining participants who had physical fitness measured in childhood (aged 7–15 years) and who attended follow-up clinics approximately 20 years later and provided a fasting blood sample which was tested for glucose and insulin. Physical fitness measurements included muscular strength (right and left grip, shoulder flexion, shoulder and leg extension), power (standing long jump distance) and endurance (number of push-ups in 30 s), and CRF (1.6 km run duration). In adulthood, fasting glucose and insulin levels were used to derive glucose homeostasis measures of insulin resistance (HOMA2-IR) and beta cell function (HOMA2-β).
Results: A standard deviation increase in childhood CRF or muscular strength (males) was associated with fasting glucose (CRF: $\beta = -0.06$ mmol/L), fasting insulin (CRF: $\beta = -0.73$ mU/L; strength: $\beta = -0.40$ mU/L), HOMA2-IR (CRF: $\beta = -0.06$; strength: $\beta = -0.05$) and HOMA2-β (CRF: $\beta = -3.06\%$; strength: $\beta = -2.62\%$) in adulthood, independent of the alternative fitness phenotype (all $p < 0.01$). Adjustment for childhood waist circumference reduced the effect by 17–35% for CRF and 0–15% for muscular strength (males) and statistical significance remained for all associations expect between CRF, fasting glucose and HOMA2-β ($p > 0.06$).
Conclusions: CRF and muscular fitness in childhood were inversely associated with measures of fasting insulin, insulin resistance and beta cell function in adulthood. Childhood CRF and muscular fitness could both be potential independent targets for strategies to help reduce the development of adverse glucose homeostasis.

1. Introduction

Impaired glucose homeostasis and type 2 diabetes (T2DM) are becoming increasingly prevalent[1,2] and remain a major public health concern. Efforts continue to identify effective strategies to prevent these conditions. Physical fitness, a product of both cardiorespiratory fitness (CRF) and muscular fitness, is a potential target for these prevention strategies. Associations between childhood physical fitness and adult cardiometabolic health outcomes,[3–5] including T2DM,[6] have been reported previously. These data suggest prevention strategies targeting childhood physical fitness could be fundamental in improving glucose homeostasis in later life, although further research is required.

Previous research using data from the Childhood Determinants of Adult Health (CDAH) Study has shown high childhood CRF and muscular fitness, incorporating strength, power, and endurance, to associate with decreased risk of metabolic syndrome in adulthood.[3,4] Although metabolic syndrome is a condition of clustering risk factors including high fasting glucose, more work is required to explore the association between childhood physical

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fitness and adult glucose homeostasis outcomes including fasting insulin, insulin resistance and beta cell function. These associations have been examined in part previously. Additional work using CDAH data showed a decline in CRF between childhood and adulthood (n = 647, baseline age = 9, 12, 15 years, follow-up = 20 years) to associate with increased odds of adult insulin resistance.[7] However, this study focused only on CRF and did not include muscular fitness. Furthermore, the European Youth Heart Study reported increased muscular strength and CRF in childhood (n = 317, age 15 years) to be associated with decreased insulin resistance and beta cell function 6–12 years later.[8] However, whether this longitudinal association exists between an increased range of muscular fitness phenotypes in younger children, after an extended length of follow-up, is of interest.

Therefore, using data from the CDAH Study, we aimed to determine whether CRF, muscular strength, muscular power, and muscular endurance in children aged 7–15 years independently predict adult glucose homeostasis measures 20-years later.

2. Methods

The CDAH study collected baseline data on a nationally representative sample of 8498 Australian schoolchildren in 1985. Children aged 7–15 years provided anthropometric, CRF, muscular power and muscular endurance data. Muscular strength was measured in a subset of children aged 9, 12 and 15 years. Of those who provided a measure of childhood physical fitness, 2417 participants (28.4%) had a fasting blood sample collected and tested for fasting glucose and/or insulin in adulthood, either by attending one of 34 follow-up clinics held across Australia from 2004 to 2006 or if unable to attend clinics, at remote pathology centres. Of these, 53 women were currently pregnant and excluded from analyses. See Fig. S1 for a flow chart of participation. At baseline, consent was obtained from parent and assent from child, whilst the participant provided written informed consent at follow-up. The State Directors General of Education approved the baseline study and the Southern Tasmania Health and Medical Human Research Ethics Committee approved the follow-up study.

Using isometric dynamometers (Smedley's Dynamometer, TTM, Tokyo, Japan), childhood muscular strength was measured as maximum voluntary contractile force of right and left grip, shoulder flexion and extension, and leg. Right and left grip strength was measured by gripping the dynamometer with maximum force with one hand. Shoulder flexion and extension strength was measured by participants holding the dynamometer in front of their chest with both hands parallel to the ground and then either pulling (extension) or pushing (flexion) with maximum effort. Leg strength was measured as participants stood on a leg-back dynamometer with flat feet, a straight back and with their body flat against a wall behind them. Participants held a bar with an overhand grip, whilst they flexed their knees until reaching an angle of 115° at which point a chain was attached from the dynamometer to the bar. Participants then pulled the bar as far upwards as possible by sliding their body up the wall. The maximum of two attempts at each strength measure was used in analyses, with the exception of grip strength where only one attempt for each hand was allowed. A combined muscular strength score was obtained via principal component analysis and estimating the first principal component of each of the five muscular strength measures.[9] Muscular power was measured as the best resulting distance in centimetres from two attempts at a standing long jump, with each jump requiring a two-footed take-off. Muscular endurance was estimated by the number of correctly completed inclined push-ups in 30 s. Participants started by placing their hands shoulder width apart on the front edge of a chair, arms fully extended at a 90° angle to the body and with their legs straight. A correct push up was defined when participants' bodies were lowered until their chests touched the chair and then raised until their arms were fully extended. Additional methodology detail is reported elsewhere.[3,10] To create measures of muscular fitness not attributable to body weight, body weight was regressed on each phenotype and the residuals were used.[9] All muscular fitness phenotypes were standardised for age and sex (see Table S1 for summary statistics). Previous systematic reviews have highlighted the reliability of these muscular fitness measures.[11,12] In childhood, non-significant test-retest differences have been shown for grip strength (males: 0.3 ± 2.5 kg; females: 0.0 ± 1.8 kg) and standing long jump distance (males: -0.3 ± 12.9 cm; females: 0.3 ± 9.0 cm),[13] and high intraclass reliability estimates have been presented for one version of the push up test (R = 0.98 (0.97, 0.99)).[14]

Childhood CRF was estimated by the duration of a 1.6 km run performed over a level, marked course. Verbal support was provided to encourage maximum effort. The reliability of the 1.6 km run test has been reported previously (males: intraclass correlation coefficient (ICC) = 0.80 (0.70, 0.86); females: ICC = 0.87 (0.78, 0.92)).[15] The duration of the 1.6 km run strongly correlates with maximal oxygen consumption (VO_2 max) (−0.85 to −0.73).[16] To assist with interpretation, 1.6 km run duration was used to estimate VO_2 max using the equation by Cureton et al.[17] Estimated VO_2 max was standardised for age and sex (summary statistics shown in Table S1).

In childhood, a constant-tension tape was used to measure waist circumference at the level of the umbilicus, to the nearest 0.1 cm. Using regularly calibrated scales, body mass was measured to the nearest 0.5 kg, whilst a Kawe height tape was used to measure height to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters squared).

In adulthood, fasting status was enquired from participants. Fasting glucose and insulin levels were measured using blood samples collected from those who observed a 12 h fast. An Olympus AU5400 automated analyser (Olympus Optical, Tokyo, Japan) was used to enzymatically measure fasting glucose, whilst a microparticle enzyme immunoassay kit (AxSYM; Abbot Laboratories, Abbot Park, IL) or an electrochemiluminescence immunoassay (Elecsys Modular Analytics E170; Roche Diagnostics, Mannheim, Switzerland) with interassay standardisation was used to measure fasting insulin.[7]

Adult glucose homeostasis measures included insulin resistance (HOMA2-IR) and beta cell function (HOMA2-β).[18,19] These measures were calculated by a homeostasis model assessment (HOMA2) calculator (version 2.2.3 available from http://www.dtu.ox.ac.uk/homacalculator) using fasting glucose and fasting insulin.[20] Participants with fasting glucose levels outside the range 3.5–25 mmol/L (n = 0) and fasting insulin levels outside the range 2.88–57.60 mU/L (20–400 pmol/L) (n = 167) were excluded from HOMA2 calculations as these values were outside the range of clinically realistic fasting values accepted by the calculator.[20]

All statistical analyses were performed using Stata (Version 15.0, StataCorp, College Station, Texas). Participant baseline and follow-up characteristics are stratified by sex and summarised as mean and standard deviation (SD) for normally distributed data or median and interquartile range for skewed data.

Linear regression was used to estimate associations between childhood physical fitness phenotypes and adult glucose homeostasis measures. Where necessary, outcome variables were transformed (e.g. by taking logarithms) prior to analysis to remove skewness. Inverse probability weighting was used to account for missing data at follow-up, with multiple imputation of incomplete baseline data, following the approach of Seaman et al.[21] Three multivariable models with successive adjustment were considered for each association. Model one adjusted for childhood age, sex and

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