ARTICLE IN PRESS

Intelligence xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Intelligence

journal homepage: www.elsevier.com/locate/intell

Reaction time, cardiorespiratory fitness and mortality in UK Biobank: An observational study

Thomas Yates[a,b,*], Kishan Bakrania[a], Francesco Zaccardi[a], Nafeesa N. Dhalwani[a,d], Mark Hamer[b,c], Melanie J. Davies[a,b], Kamlesh Khunti[a,d]

[a] Diabetes Research Centre, College of Medicine, Biological Sciences and Psychology, University of Leicester, Leicester LE5 4PW, UK
[b] NIHR Leicester Biomedical Research Centre, University of Leicester & Loughboorugh University, Leicestershire, UK
[c] School of Sport, Exercise and Health Sciences, Loughborough University, Loughborough, UK
[d] NIHR Collaboration for Leadership in Applied Health Research and Care – East Midlands, UK

A R T I C L E I N F O

Keywords:
Cardiorespiratory fitness
Intelligence, mortality
Reaction time

A B S T R A C T

Intelligence has previously been associated with mortality, although it is unclear whether the inverse association is independent of other related cognitive factors, such as information processing, or of measures related to physical health, such as cardiorespiratory fitness. We investigate whether fluid intelligence, reaction time and cardiorespiratory fitness are independently associated with mortality within the general population. UK Biobank recruited adults across England, Scotland and Wales, between March 2006 and July 2010: 54,019 participants (women 52%) with complete data were included in the analysis. Those who died in the first year of follow-up (n = 58) were excluded. Fluid intelligence was measured as the number of correct answers during a two minute logic/reasoning-test, reaction time was measured as average time taken to respond to matching symbols on a computer screen and cardiorespiratory fitness was measured through a sub-maximal exercise test. Associations with mortality were assessed by Cox-proportional hazard models adjusted for age, sex, ethnicity, social deprivation, cancer and non-cancer illnesses, medications, employment, education, smoking, BMI, diet, sleep, and physical activity. Over 5.8 years of follow-up, there were 779 deaths. Higher intelligence (hazard ratio [HR] per SD = 0.91; 95% CI 0.84, 0.99), faster reaction time (HR per SD = 0.92; 0.85, 0.98) and higher fitness (HR per SD = 0.85; 0.78, 0.93) were associated with a lower risk of mortality after adjustment for each other and other covariates. No interaction was observed between fluid intelligence and reaction time (p = 0.147) or between fluid intelligence and cardiorespiratory fitness (p = 0.238). In conclusion, fluid intelligence, reaction time and cardiorespiratory fitness were independently associated with mortality.

1. Introduction

Higher levels of intelligence have consistently been associated with a lower risk of mortality across different populations and age groups (Batterham, Christensen, & Mackinnon, 2009; Calvin et al., 2010; Christensen, Mortensen, Christensen, & Osler, 2016; Iveson, Čukić, Der, Batty, & Deary, 2017). However, mechanisms supporting these associations have not been well elucidated and confounding or reverse causality remains a possibility. One suggested hypothesis is that higher intelligence might reflect greater 'system integrity' resulting in an organism that can respond more robustly to environmental stressors (Deary, 2008). This hypothesis has been explored in several small studies through the use of reaction time, which is as a measure of the brain's information processing efficiency whilst also acting as a wider marker of cognitive function and whole body systems integrity (Batterham, Bunce, Mackinnon, & Christensen, 2014; Deary, 2012; Deary & Der, 2005; Hagger-Johnson, Deary, Davies, Weiss, & Batty, 2014; Nissan, Liewald, & Deary, 2013; Roberts, Der, Deary, & Batty, 2009; Shipley, Der, Taylor, & Deary, 2006). For example, a small epidemiological study (n = 898) found that the association between intelligence and mortality was attenuated after adjusting for reaction time, whilst another investigation found that the association between brain white matter integrity and general intelligence was mediated through measures of reaction time (Deary & Der, 2005; Penke et al., 2012). Taken together, these studies suggest whole body system integrity may support higher order manifestations of cognitive function such as general intelligence whilst acting as the fundamental determinant of health status. However, these studies have not been replicated within a contemporary population and it remains uncertain whether measures of information processing or whole body system integrity help

* Corresponding author at: Leicester Diabetes Centre, Leicester General Hospital, Gwendolen Rd, Leicester LE5 4PW, UK.
E-mail address: Ty20@le.ac.uk (T. Yates).

https://doi.org/10.1016/j.intell.2017.11.006
Received 27 June 2017; Received in revised form 15 November 2017; Accepted 15 November 2017
0160-2896/

explain the association between general intelligence and health or whether these exposures are independently associated with health.

Another hypothesis is that, along with reflecting greater socioeconomic status, those with higher intelligence are more likely to engage in healthy lifestyle behaviours and thus have better underlying physical health (Deary, 2008). Cardiorespiratory fitness is one of the most robust measures of physical health status and as such is considered a cardiovascular clinical vital sign (Kodama et al., 2009; Ross et al., 2016). Importantly, cardiorespiratory fitness, physical activity and sedentary behaviour are also associated with cognitive function (Bakrania et al., 2017; Barnes, Yaffe, Satariano, & Tager, 2003; Freudenberger et al., 2016; Hillman, Erickson, & Kramer, 2008; McAuley et al., 2011; Sabia et al., 2010). Cardiorespiratory fitness has been associated with brain function and structure whilst exercise training interventions have been shown to reduce reaction time, increase brain volume and improve cognitive functioning (Barnes et al., 2003; Colcombe et al., 2004; Colcombe et al., 2006; Erickson et al., 2011; Freudenberger et al., 2016; Ponce-Bravo, Ponce, Feriche, & Padial, 2015; Predovan, Fraser, Renaud, & Bherer, 2012; Rooks, Kiel, Parsons, & Hayes, 1997). Thus, it is possible that the association between intelligence and mortality are confounded by cardiorespiratory fitness or vice-versa. Alternatively, cardiorespiratory fitness and intelligence may be correlated through sharing some environmental (i.e. exercise) or genetic determinants but reflect largely different systems of overall health and therefore act as independent predictors of mortality.

The aim of this paper is to investigate whether intelligence, reaction time and cardiorespiratory fitness are independently associated with all-cause mortality within the general population.

2. Methods

2.1. UK Biobank

UK Biobank recruited 502,639 individuals living within 25 miles of the 22 study assessment centres located throughout England, Scotland and Wales between March 2006 and July 2010; the aims, methods and assessed outcomes have been reported previously (UK Biobank, 2007). In brief, UK Biobank is a large prospective cohort of middle-aged adults designed to support biomedical research focused on improving the prevention, diagnosis and treatment of chronic disease. Recruited individuals provided comprehensive data on a broad range of biological, demographic, health, lifestyle, mental, social and well-being outcomes. All participants provided written informed consent and the study was approved by the NHS National Research Ethics Service (Ref: 11/NW/0382). This study is part of UK Biobank application number 10813.

2.2. Cardiorespiratory fitness

UK Biobank introduced an electrocardiogram (ECG) monitored submaximal exercise test into their suite of physical assessments in each assessment centre towards the end of recruitment. Those with high blood pressure (systolic blood pressure ≥ 180 bpm or diastolic blood pressure ≥ 110 bpm), chest pain, or pregnant women were excluded from the test. The test was terminated if 75% of age-predicted maximum heart rate was reached. The test involved 2 min at a constant workload followed by 4 min of a linearly increasing workload. The start and end workload of the graded exercise test were standardised according to age, height, weight, resting heart rate and sex to ensure a similar relative intensity across the population. Heart rate was monitored before, during, and after the exercise test via a 4-lead ECG. Maximal cardiorespiratory fitness was estimated using previous published criteria (Celis-Morales et al., 2017), involving: 1) Fitting a linear regression line between heart rate and power output between the pre-exercise (rest) and final stage; 2) Extrapolating the regression line to the age-predicted maximal heart rate with the formula: 208–0.7 × age; 3) Using the regression equation for the relationship between work rate (power) and oxygen uptake (oxygen uptake [$\text{ml kg}^{-1}\text{min}^{-1}$] = 7 + (10.8 × work rate [Watts])/body mass [kg]) to estimate maximal oxygen uptake. Metabolic equivalents (METs) were calculated through dividing maximal oxygen update by 3.5.

2.3. Fluid intelligence

Fluid intelligence was assessed through 13 questions using verbal and numeric reasoning/logic delivered over a two minute period. Each question had five possible responses in addition to "do not know" and "prefer not to answer"; participants were asked to select the correct response via a touch screen computer. Participants were instructed as follows: "In this next test you will have a maximum of two minutes to answer as many questions as possible. Don't spend too long on any one question and you can skip any question if you wish". Each question used in the test is available through the UK Biobank website (UK Biobank, 2017). The number of correct responses was used as the outcome measure. This measure of fluid intelligence employed in UK Biobank has been shown to have good reliability when repeated after a mean of 4 years (Intraclass Correlation Coefficient = 0.65; $p < 0.001$) (Lyall et al., 2016).

2.4. Reaction time

Simple reaction time was assessed with a timed test of symbol matching conducted on a touch screen computer, similar to the card game snap. Two card shapes with symbols were displayed on a computer screen with participants asked to press a red button with their dominant hand if the two cards had matching symbols. Participants undertook the test seated with the red button placed on a desk in front of them. Ten symbols with simple non-complex shapes were used (equals sign, fir tree, hollow circle, hollow square, H, smiley face, solid circle, solid square, triangle, cross). Participants completed 12 rounds, of which the first 5 were considered training rounds and removed from the analysis. Of the remaining rounds, matched cards were shown in rounds 6, 8, 11 and 12. Reaction time was calculated as the average time taken to correctly identify a match. Times under 50 ms were considered to be due to anticipation rather than reaction and removed from the analysis. Participants were allowed 2000 ms to react to each round.

2.5. Anthropometric, demographic, health and lifestyle data

This study utilised the following covariate data within UK Biobank: anthropometric (body mass index (BMI); demographic (age, sex, ethnicity, social deprivation [Townsend index], employment status and education level); health status (prevalent cancer, number of prevalent non-cancer illnesses, and number of prescribed medications); and lifestyle (smoking [never, past, current], alcohol, fresh fruit [pieces per day], raw vegetables or salad [portion per day], cooked vegetable [portion per day], sleep [hours per night], TV viewing time [hours per day], and physical activity [weekly frequency of any walking, moderate-, or vigorous-intensity physical activity undertaken lasting at least 10 min]). Alcohol was assessed through a frequency questionnaire ranging from never to daily or almost daily. Further details for each measure are available elsewhere (UK Biobank, 2007).

2.6. Assessment of mortality status and data inclusion

UK Biobank undertook comprehensive data linkage for mortality status using national records in England, Wales and Scotland. Using a unique identifier collected at baseline (e.g. NHS number), information about mortality status, date of death and causes of death were obtained from National Health Service (NHS) Information Centre for participants from England and Wales, and from the NHS Central Register, for participants from Scotland. Linkage captured all deaths occurring until