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Original article

Longitudinal telomere length shortening and cognitive and physical decline in later life: The Lothian Birth Cohorts 1936 and 1921

Sarah E. Harris[a,b,*], Riccardo E. Marioni[a,b,c], Carmen Martin-Ruiz[d], Alison Pattie[e], Alan J. Gow[a,f], Simon R. Cox[a,e], Janie Corley[e], Thomas von Zglinicki[d], John M. Starr[a,g], Ian J. Deary[a,e]

[a] Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, 7 George Square, Edinburgh EH8 9JZ, UK
[b] Medical Genetics Section, University of Edinburgh Centre for Genomic and Experimental Medicine and MRC Institute of Genetics and Molecular Medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK
[c] Queensland Brain Institute, The University of Queensland, Brisbane 4072, QLD, Australia
[d] Institute for Ageing, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL, UK
[e] Department of Psychology, University of Edinburgh, 7 George Square, Edinburgh EH8 9JZ, UK
[f] Department of Psychology, School of Life Sciences, Heriot-Watt University, Edinburgh EH14 4AS, UK
[g] Alzheimer Scotland Dementia Research Centre, University of Edinburgh, 7 George Square, Edinburgh EH8 9JZ, UK

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ABSTRACT

Telomere length is hypothesised to be a biological marker of both cognitive and physical ageing. Here we measure telomere length, and cognitive and physical abilities at mean ages 70, 73 and 76 years in the Lothian Birth Cohort 1936 (LBC1936), and at mean ages 79, 87, 90 and 92 years in the Lothian Birth Cohort 1921 (LBC1921). We investigate whether telomere length change predicts change in cognitive and physical abilities. In LBC1936 telomere length decreased by an average of 65 base pairs per year and in LBC1921 by 69 base pairs per year. However, change in telomere length did not predict change in cognitive or physical abilities. This study shows that, although cognitive ability, walking speed, lung function and grip strength all decline with age, they do so independently of telomere length shortening.

1. Introduction

Determining the biological factors that influence both cognitive and physical decline in later life is an important challenge facing researchers today (Blazer et al., 2015; den Ouden et al., 2011). Telomeres are nucleo-protein complexes at the end of eukaryotic chromosomes. They protect the ends of chromosomes, but shorten each time a somatic cell replicates (Harley et al., 1990; Lindsey et al., 1991). Environmental factors also contribute to accelerated decline in telomere length. These include low socio-economic status, smoking, oxidative stress, and psychological stress (Valdes et al., 2005; von Zglinicki, 2002; Robertson et al., 2013). Telomere length decreases with age and a systematic review determined that the correlation between telomere length and chronological age is about −0.3 (Muezzinler et al., 2013). Leukocyte telomere length has previously been associated with a number of traits and diseases in older age including cognitive abilities (Harris et al., 2006, 2012; Yaffe et al., 2009; Der et al., 2012; Ma et al., 2013), dementia (Grodstein et al., 2008; Martin-Ruiz et al., 2006; Panossian et al., 2003; von Zglinicki et al., 2000), physical health (Gardner et al., 2013; Woo et al., 2014; Masi et al., 2014; Baylis et al., 2014) and obesity (Valdes et al., 2005; Njajou et al., 2012), and has been hypothesised to be a biological marker of ageing (von Zglinicki and Martin-Ruiz, 2005). However, a systematic review concluded that current results were equivocal and that more studies, including longitudinal studies, were required that assessed telomere length and ageing-related functional measures (Mather et al., 2011). Longitudinal studies have the potential to measure age-related decline in telomere length, and cognitive and physical abilities more accurately than cross-sectional studies and also allow the investigation of the change of multiple variables in parallel with each other.

There are many studies that show lower childhood cognitive ability is associated with poorer health and more illness in adulthood and older age, and to earlier mortality from all causes and from several specific causes, such as cardiovascular disease (Deary et al.,

* Corresponding author at: University of Edinburgh, Centre for Cognitive Ageing and Cognitive Epidemiology, 7 George Square, Edinburgh EH8 9JZ, UK. Fax: +44 131 651 1771.
E-mail address: Sarah.Harris@igmm.ed.ac.uk (S.E. Harris).

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Table 1
Summary descriptive data for LBC1936. g_f = general cognitive ability, FEV_1 = forced expiratory volume in one second.

	Age 70						Age 73				Age 76	
	All		Age 73 completers		Age 76 completers		All		Age 76 completers		All	
	N	Mean (SD, range)	N	Mean (SD, range)	N	Mean (SD, range)	N	Mean (SD, range)	N	Mean (SD, range)	N	Mean (SD, range)
Age (years)	1091	69.5 (0.8, 67.6–71.3)	866	69.5 (0.8, 67.6–71.3)	697	69.5 (0.8, 67.6–71.3)	866	72.5 (0.7, 70.9–74.2)	697	72.5 (0.7, 70.9–74.2)	697	76.2 (0.7, 74.6–77.7)
Telomere length (kb)	1070	4.2 (0.6, 2.7–7.1)	855	4.2 (0.6, 2.7–7.1)	691	4.2 (0.6, 2.7–7.1)	844	4.0 (0.7, 1.9–9.4)	678	4.0 (0.7, 1.9–9.4)	689	3.7 (0.7, 1.9–7.2)
g_f	1072	0.04 (1.0, −3.5–3.0)	853	0.12 (1.0, −3.5–3.0)	687	0.19 (1.0, −3.5–3.0)	856	0.02 (0.98, −3.4–3.1)	690	0.11 (0.96, −2.7–3.1)	668	−0.08 (1.0, −3.0–3.1)
6 m walk time (s)	1085	3.9 (1.2, 1.1–14.7)	863	3.8 (1.1, 1.1–14.7)	695	3.7 (1.0, 1.1–14.7)	860	4.4 (1.3, 1.6–16.0)	692	4.2 (1.1, 1.6–16.0)	692	4.7 (0.5, 1.5–15.3)
FEV_1 (L)	1085	2.4 (0.7, 0.5–5.1)	863	2.4 (0.7, 0.7–5.1)	695	2.4 (0.7, 0.7–5.1)	856	2.3 (0.7, 0.4–5.2)	692	2.3 (0.7, 0.4–5.2)	690	2.1 (0.6, 0.6–4.1)
Grip strength (Kg)	1086	29.6 (10.2, 6.0–60.0)	864	30.1 (10.0, 6.0–60.0)	696	30.4 (10.1, 6.0–60.0)	865	29.1 (9.5, 2.0–59.0)	696	29.4 (9.5, 2.0–59.0)	691	27.9 (9.6, 1.0–55.0)

2010). Early life IQ has previously been associated with telomere length in midlife (Schaefer et al., 2015). The mechanism of the childhood cognition-illness/death association is not understood, but it is possible that telomeres might provide a biomarker of how lifestyle has affected the body.

We previously reported mostly-null cross-sectional associations between telomere length and cognitive function, walking speed, lung function, and grip strength in the Lothian Birth Cohorts of 1921 and 1936 (LBC1921 and LBC1936) (Harris et al., 2006, 2012). More recently, we showed that the same cognitive and physical abilities decline on average between ages 70 and 76 years in LBC1936 (Marioni et al., 2015). Here, we report longitudinal analyses investigating whether decline in telomere length predicts cognitive and physical decline in the Lothian Birth Cohorts. We also investigate whether baseline telomere length influences subsequent decline in cognitive and physical abilities. Finally, we test whether cognitive ability measured in childhood is related to telomere length decline in later life.

2. Materials and methods

2.1. Lothian Birth Cohort 1936 (LBC1936)

LBC1936 consists of 1091 (548 men and 543 women) surviving members of the Scottish Mental Survey of 1947 (Scottish Council for Research in Education, 1949). At approximately age 11 years most took a valid mental ability test, the Moray House Test version 12 (MHT). At a mean age of 69.5 years (SD 0.8) they were recruited to a study to determine influences on cognitive ageing (Deary et al., 2007, 2012a). They underwent a series of cognitive and physical tests. Two further waves of cognitive and physical tests have occurred at mean ages 73 and 76 years. DNA was extracted from peripheral blood leukocytes at ages 70, 73 and 76 years from which telomere length was measured. Cognitive tests taken at each of the three waves included six Wechsler Adult Intelligence Scale-IIIUK (WAIS-III) (Wechsler, 1998) non-verbal subtests (matrix reasoning, letter number sequencing, block design, symbol search, digit symbol, and digit span backward). From these six cognitive tests a general fluid cognitive factor (g_f) was derived. The scores from the first unrotated component of a principal components analysis were extracted and labelled as g_f. This component explained 52% of the variance, with individual test loadings ranging between 0.65 and 0.72. Physical trait measures included time taken to walk six metres at normal pace, grip strength measured with a Jamar Hydraulic Hand Dynamometer (all subjects had three trials with the dominant hand; the best of the three trials was used), and forced expiratory volume from the lungs in one second (FEV_1) measured using a microspirometer (the best of the three trials was used).

2.2. Lothian Birth Cohort 1921 (LBC1921)

LBC1921 consists of 550 (234 men and 316 women) surviving members of the Scottish Mental Survey of 1932 (Scottish Council for Research in Education, 1933). At approximately age 11 years most took a valid mental ability test, the MHT. At a mean age of 79.1 years (SD 0.6) they were recruited to a study to determine influences on cognitive ageing (Deary et al., 2004, 2012b). They underwent a series of cognitive and physical tests. Four further waves of cognitive and physical tests have occurred at mean ages 83, 87, 90 and 92 years. DNA was extracted from peripheral blood leukocytes at ages 79, 87, 90 and 92 years from which telomere length was measured. Cognitive tests taken at each of these four waves included Raven's Progressive Matrices (Raven et al., 1977), Verbal Fluency (Lezak, 1995) and Logical Memory (Wechsler, 1987). From these three cognitive tests a general fluid cognitive factor (g_f) was derived