Healthy cognitive ageing

Ian Deary

The Scottish Mental Surveys of 1932 and 1947

THE SCOTTISH COUNCIL FOR RESEARCH IN EDUCATION

Scottish Mental Survey 1932

THE INTELLIGENCE OF SCOTTISH CHILDREN

A NATIONAL SURVEY OF AN AGE-GROUP

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1932 MENTAL SURVEY TEST

SUITABLE FOR PUPILS OF TEN AND ELEVEN YEARS OF AGE

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THE SCOTTISH COUNCIL FOR RESEARCH IN EDUCATION

Scottish Mental Survey 1947

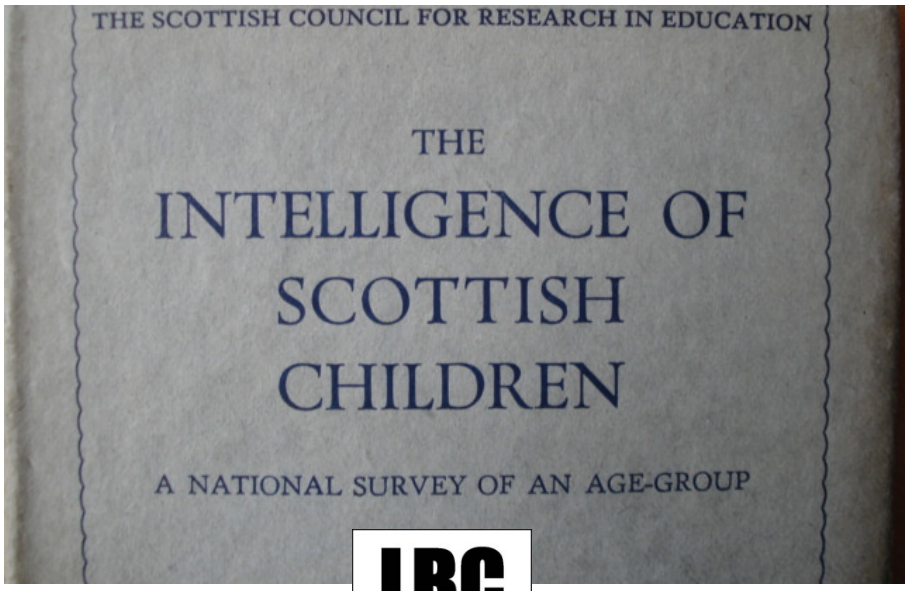
THE TREND OF SCOTTISH INTELLIGENCE

A COMPARISON OF THE
1947 AND 1932 SURVEYS OF THE INTELLIGENCE
OF ELEVEN-YEAR-OLD PUPILS

The Scottish Mental Surveys' ledgers

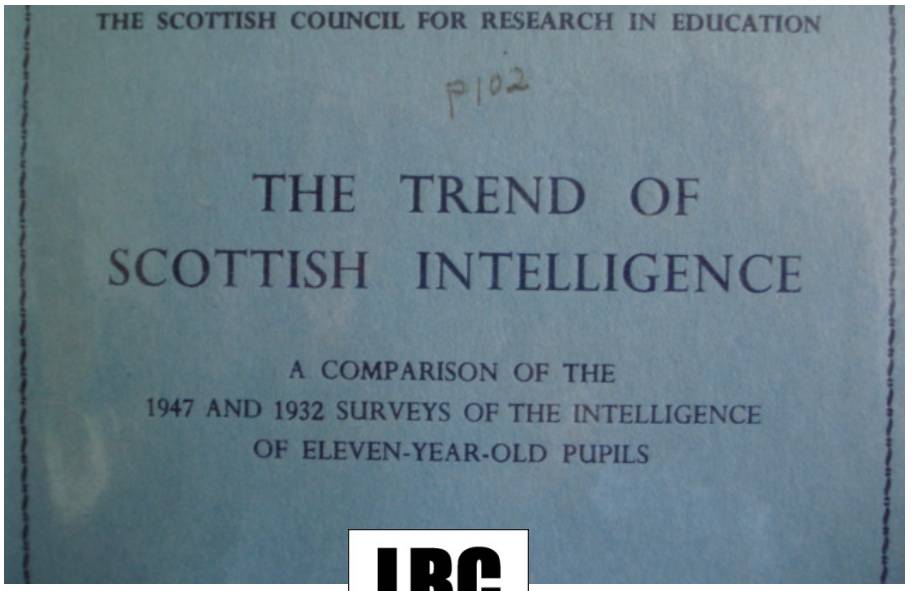
The Lothian Birth Cohorts 1921 and 1936

Scottish Mental Survey 1932

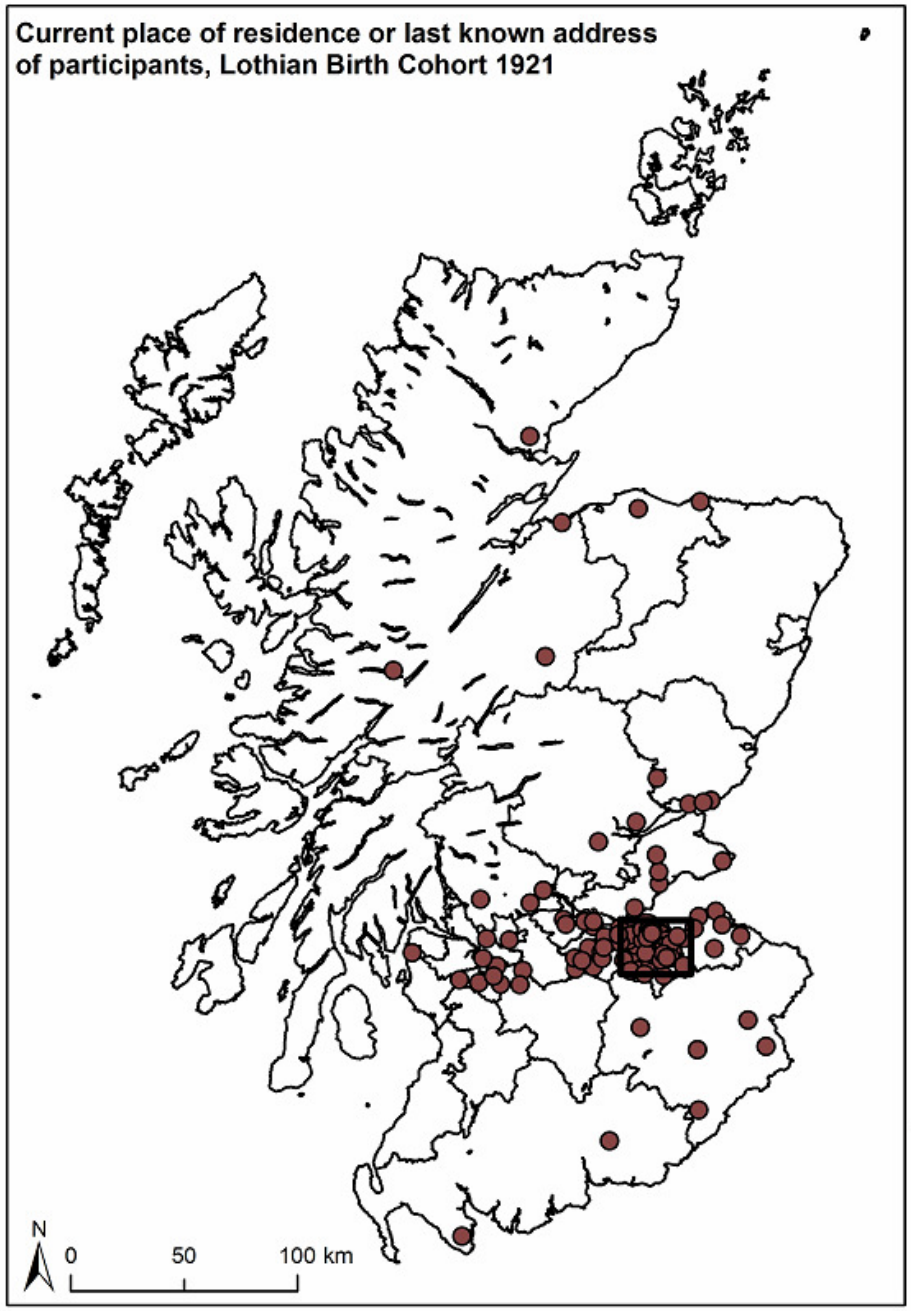


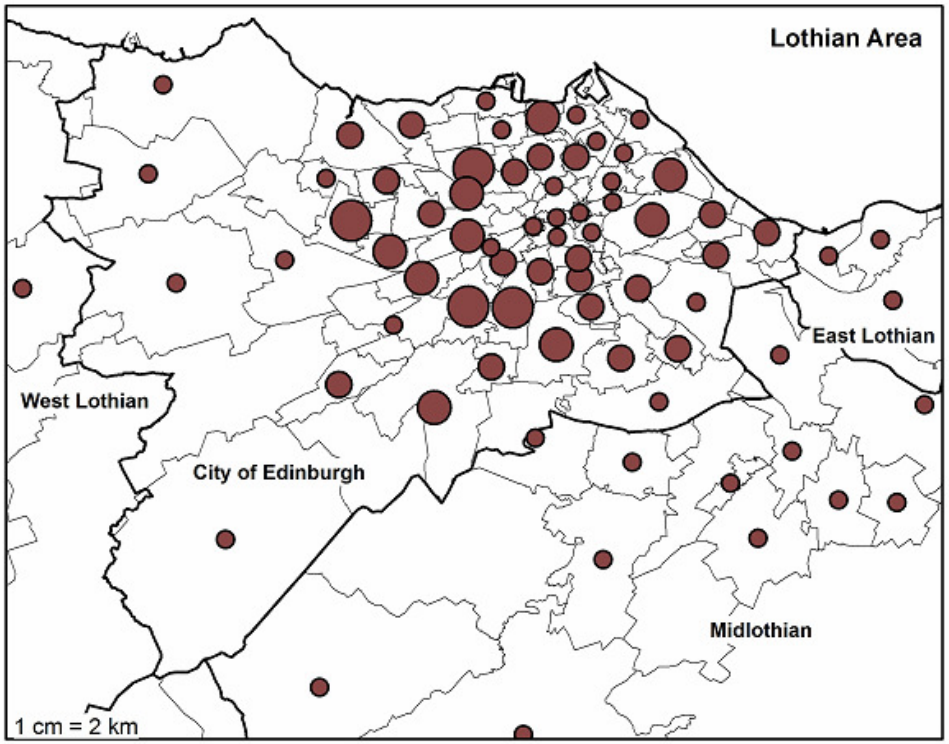
LBC 1921

Scottish Mental Survey 1947



LBC 1936





Lothian Birt Cohort 1921 (n = 552*)

Number of participants per postcode area

- 1 - 5
- 6 - 10
- 11 - 15
- 16 - 27
- Postcode area
- Council area

*Excluding 17 participants living outside Scotland.

LBC 1921

Cartography:
Centre for research on environment, society and health (CRESH)
University of Edinburgh 2012

Shapefiles provided by the Boundary Commission for Scotland 2012,
based on data from Ordenance Survey and National Records of Scotland.

Lothian Birth Cohort 1921
N = 550

Age 79 in 2000

…and 83 in 2004

…and 87 in 2008

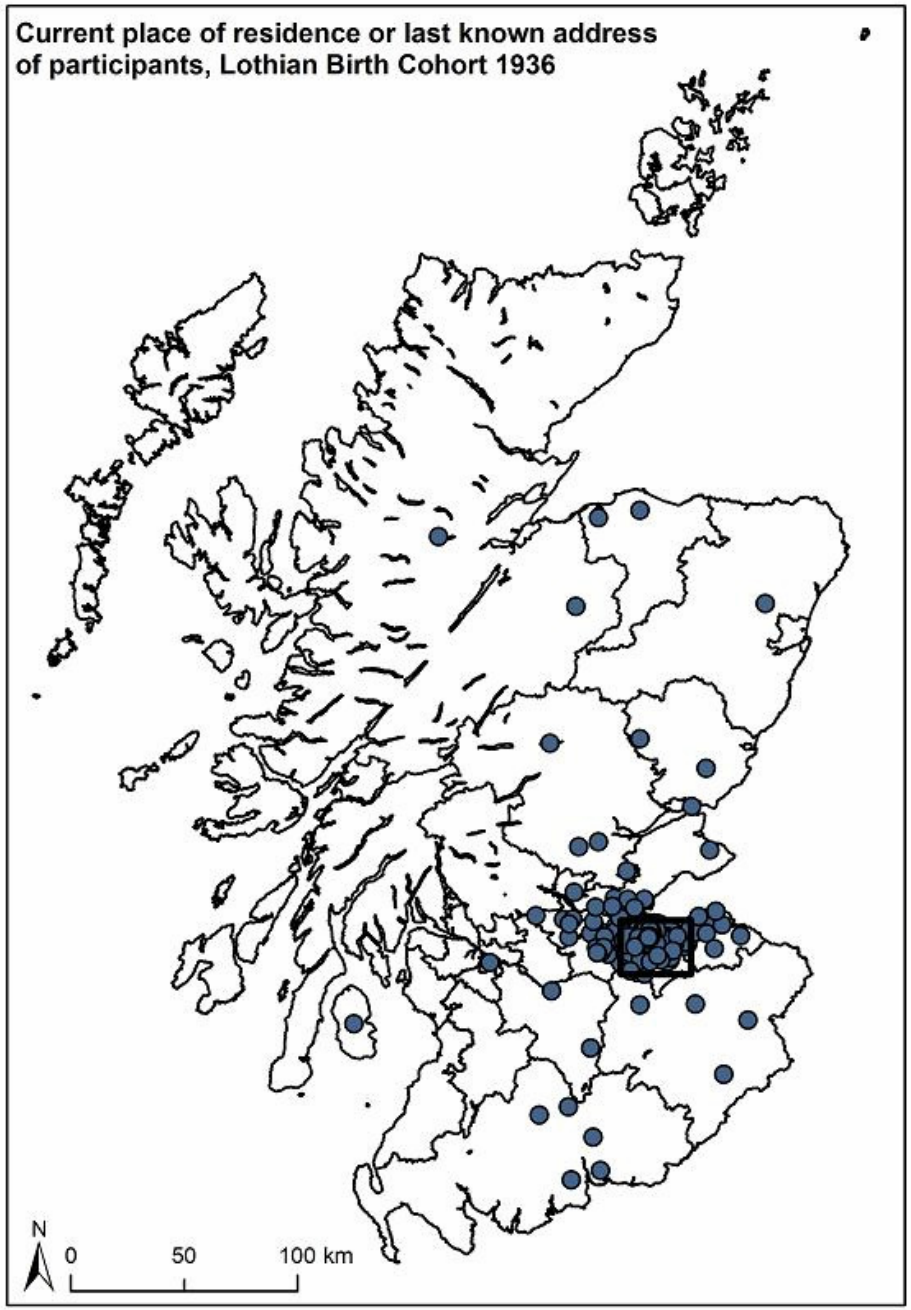
…and 90 in 2011

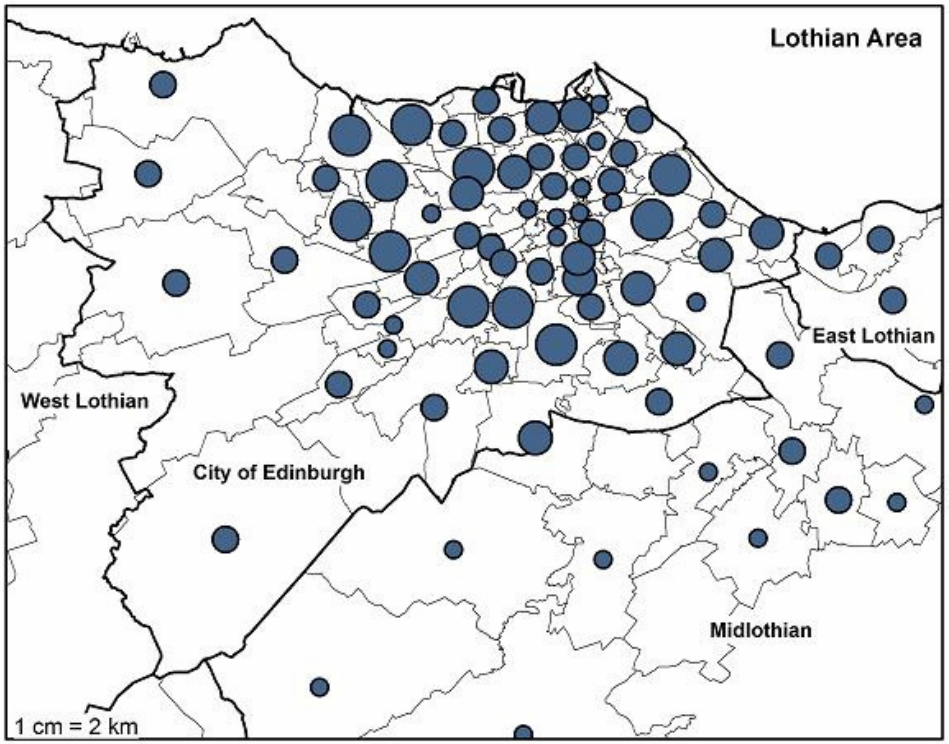
Age 11 in 1932

…and 92 in 2013

Deary et al. (2004) *Journal of Personality and Social Psychology*, *86*, 130-147.
Deary et al. (2012) *International Journal of Epidemiology*, *41*, 1576-1584.

LBC 1921





Lothian Birth Cohort 1936 (n = 1087*)

Number of participants per postcode area

- 1 - 5
- 6 - 15
- 16 - 25
- 26 - 48
- Postcode area
- Council area

*Excluding 4 participants living outside Scotland.

LBC 1936

Cartography:
Centre for research on environment, society and health (CRESH)
University of Edinburgh 2012

Shapefiles provided by the Boundary Commission for Scotland 2012,
based on data from Ordenance Survey and National Records of Scotland.

Lothian Birth Cohort 1936
N = 1091

Age… 70 in 2006

…and 73 in 2009

…and 76 in 2012

Age 11 in 1947

Deary et al. (2007) *BMC Geriatrics*, *7*, 28.
Deary et al. (2012) *International Journal of Epidemiology*, *41*, 1576-1584.

LBC 1936

clinical
research
facility
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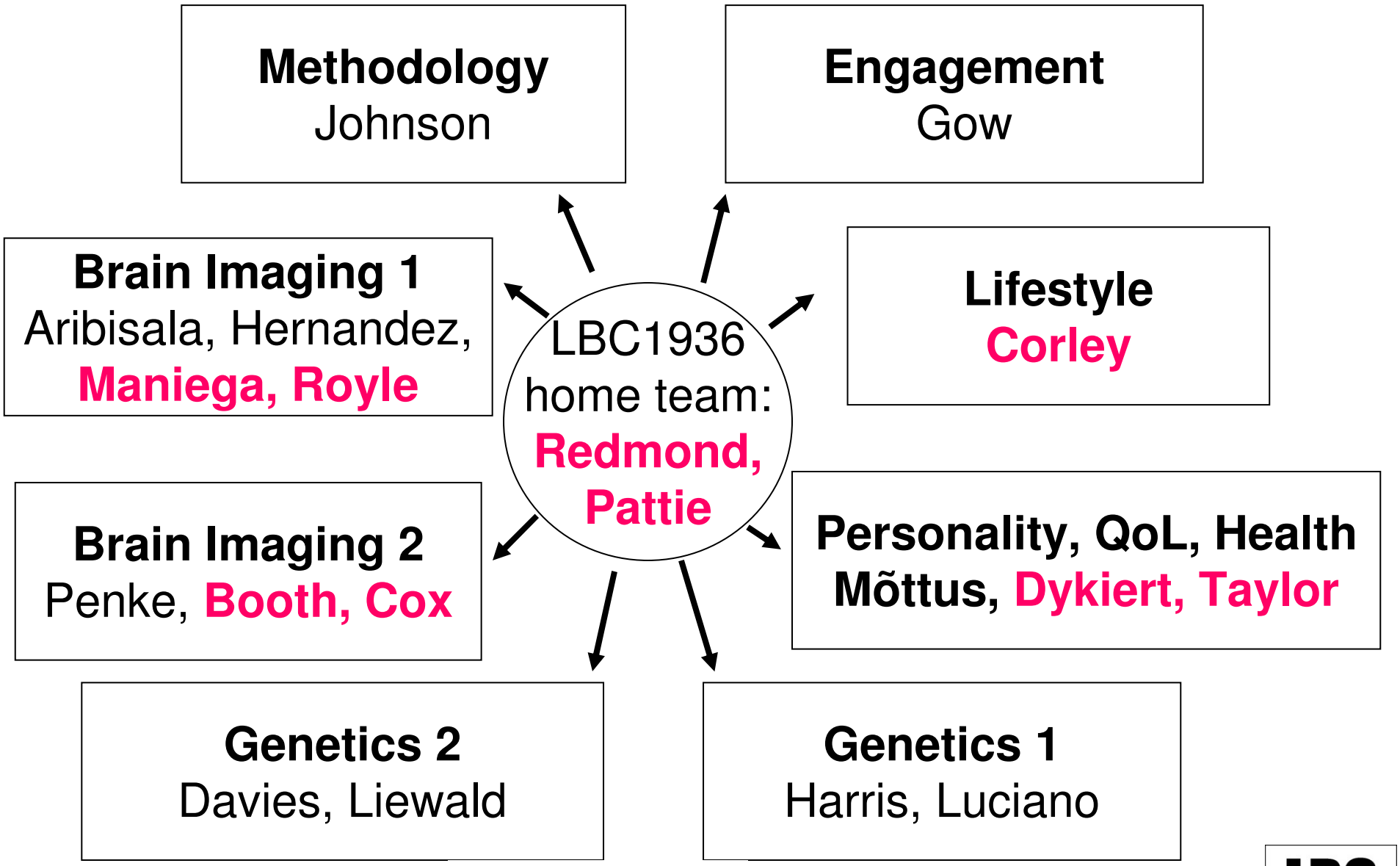

MRC Medical Research Council

Lifelong Health & Wellbeing
Research for Healthy Ageing

ageUK

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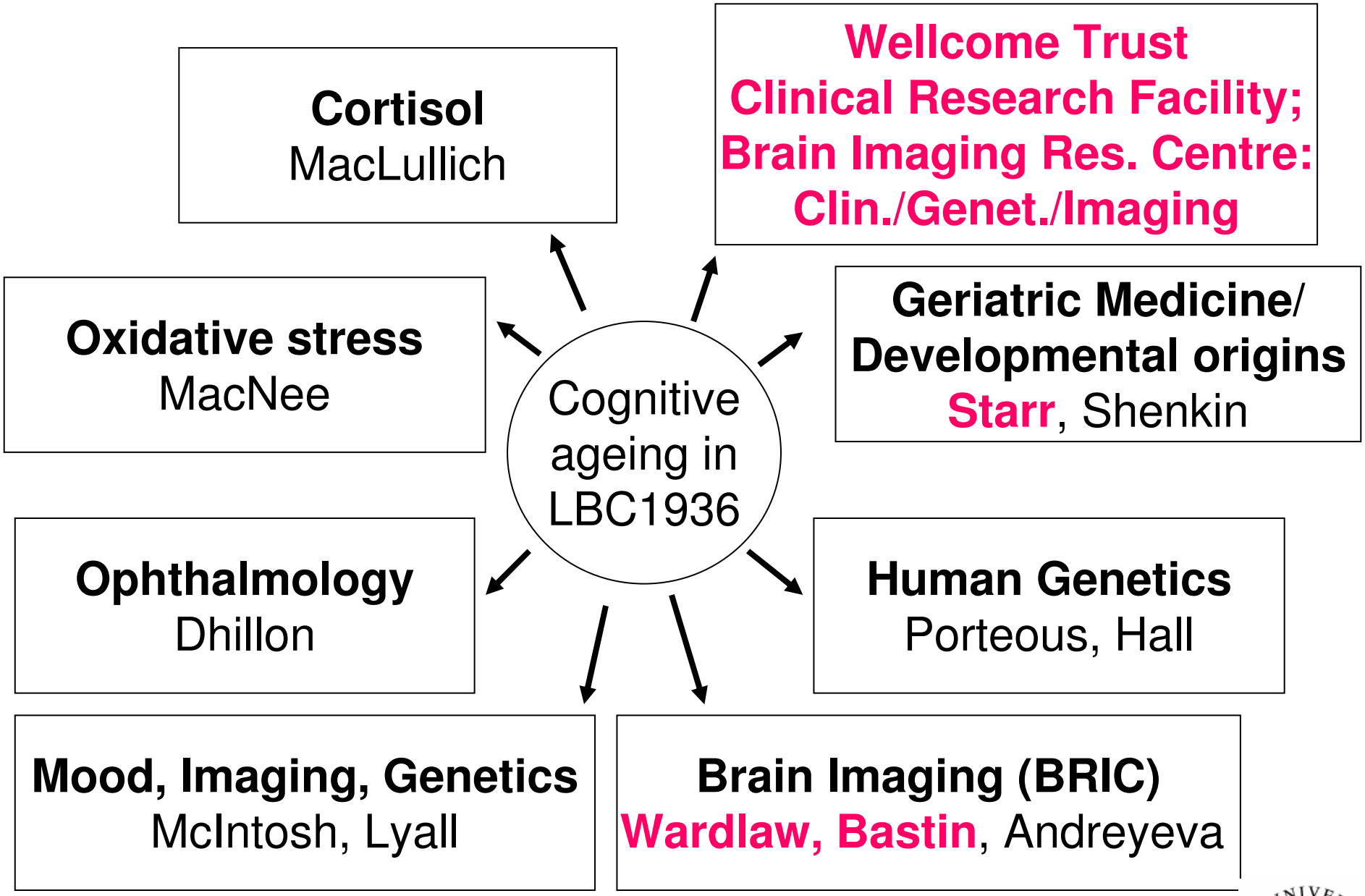

Cortisol
MacLullich
Wellcome Trust
Clinical Research Facility;
Brain Imaging Res. Centre:
Clin./Genet./Imaging
Oxidative stress
MacNee
Geriatric Medicine/
Developmental origins
Starr, Shenkin
Cognitive ageing in LBC1936
Ophthalmology
Dhillon
Human Genetics
Porteous, Hall
Mood, Imaging, Genetics
McIntosh, Lyall
Brain Imaging (BRIC)
Wardlaw, Bastin, Andreyeva

Brain cortical thickness
Evans/Karama: Montreal

Diet & nutrition
McNeill: Aberdeen

GWAS
Visscher: Brisbane

Cognitive ageing in LBC1936

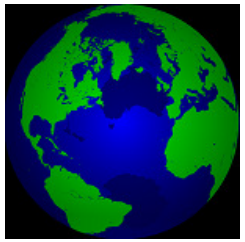
Biomarkers
Sattar: Glasgow

Proteomics
Mischak: Glasgow

Blood brain barrier
Abbott: KC London

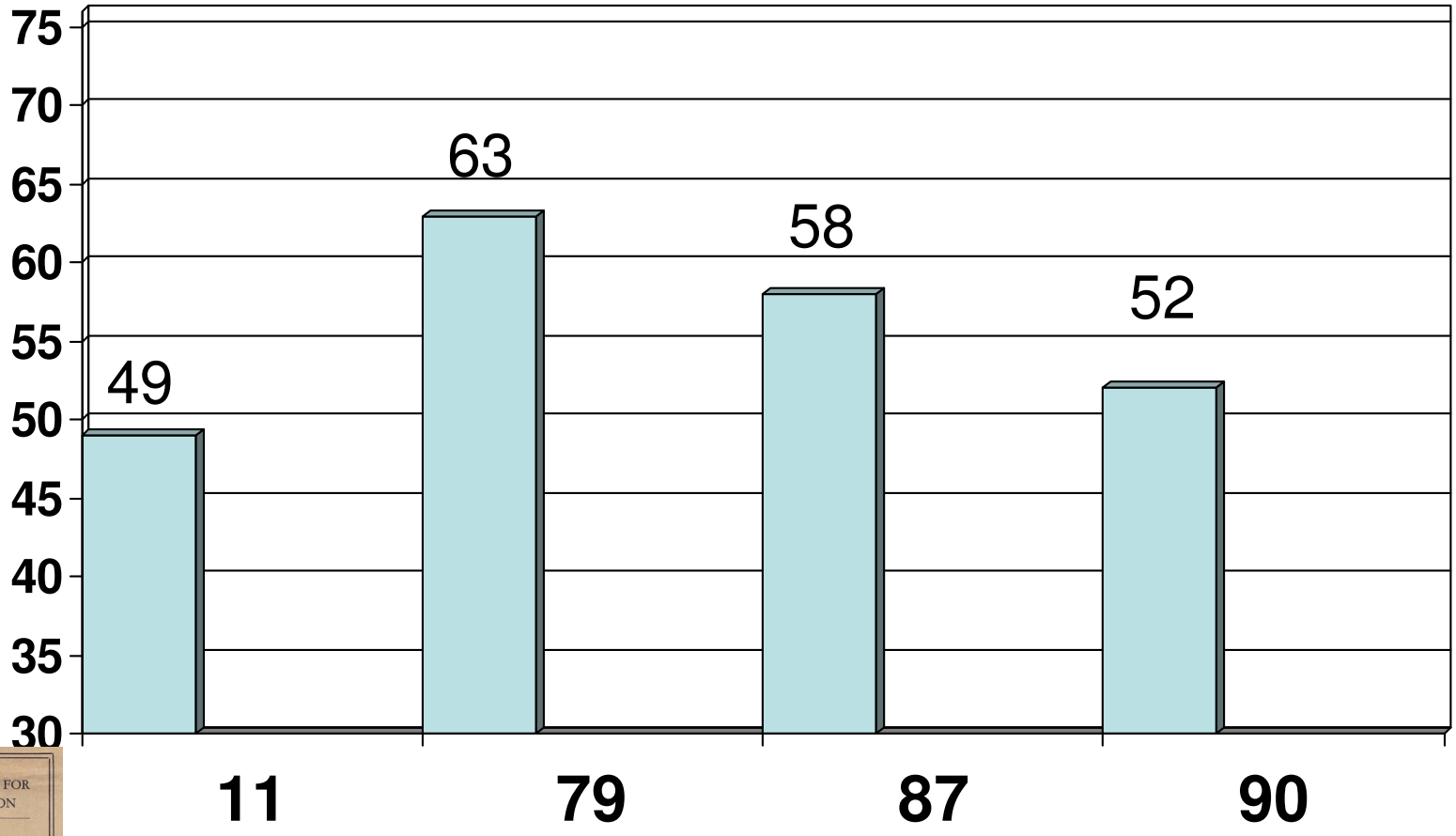
Immunology
Moss: Birmingham

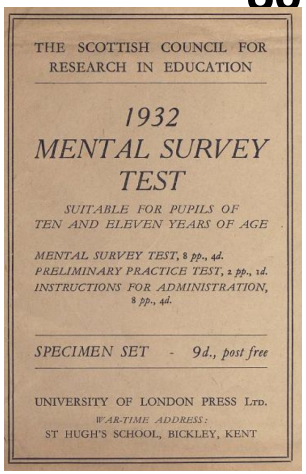
Telomeres
Von Zglinicki: Newcastle



Finding factors that influence cognitive ageing

Mean Moray House Test scores in Lothian Birth Cohort 1921

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1932
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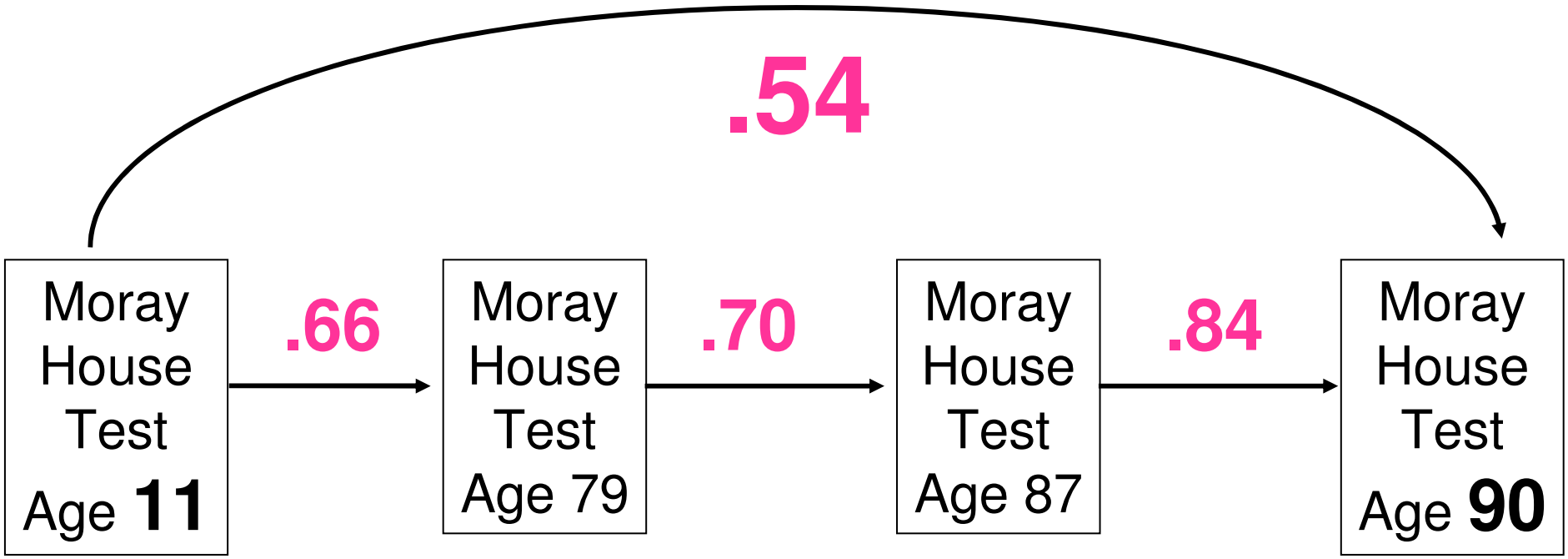
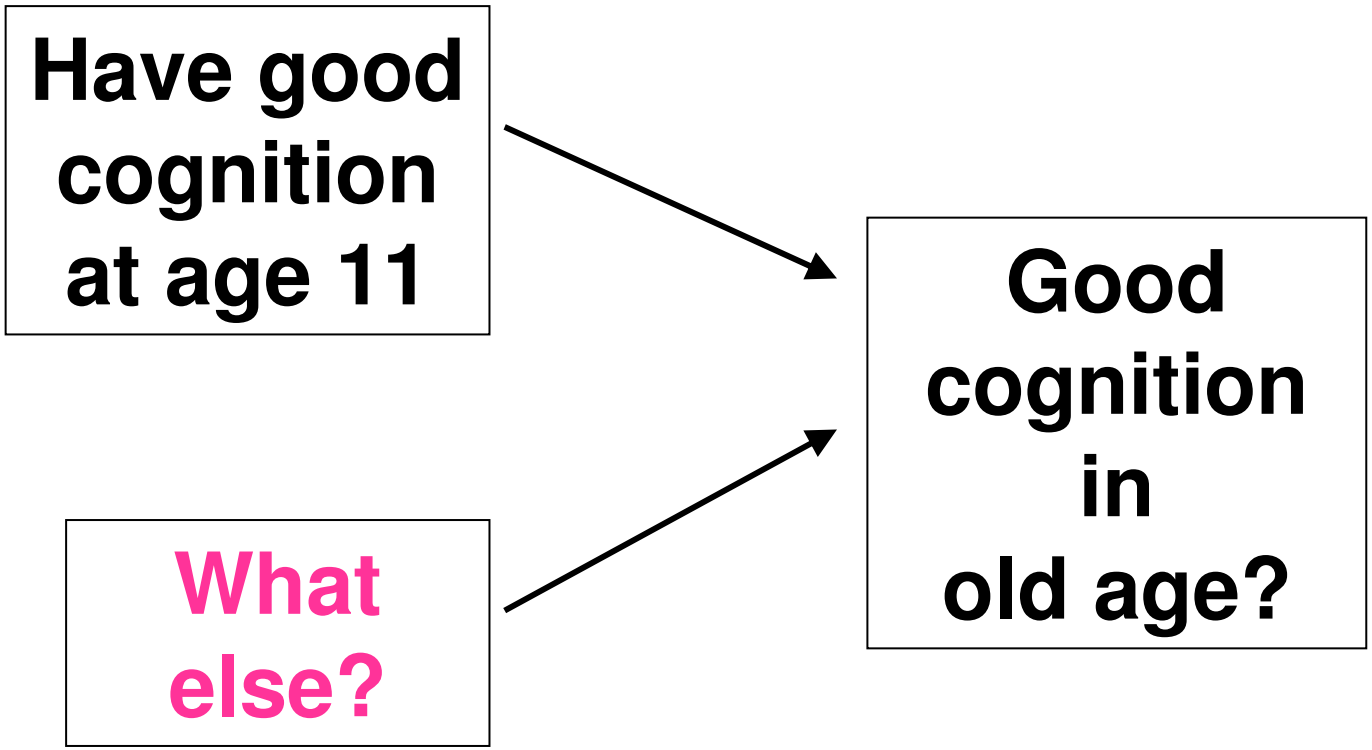
LBC
1921



Deary et al. (2004) *Journal of Personality and Social Psychology*, *86*, 130-147.
Gow et al. (2011) *Psychology and Aging*, *26*, 232-240.
Deary et al. (in press) *Psychological Science*.

LBC 1921


Have good cognition at age 11
What else?
Good cognition in old age?

Social and lifestyle factors

- Alcohol*
- Caffeine*
- Other dietary intakes*…

- Body mass index*
- Smoking
- Cholesterol

- Activities/engagement*
- Occupation
- Education
- Bilingualism

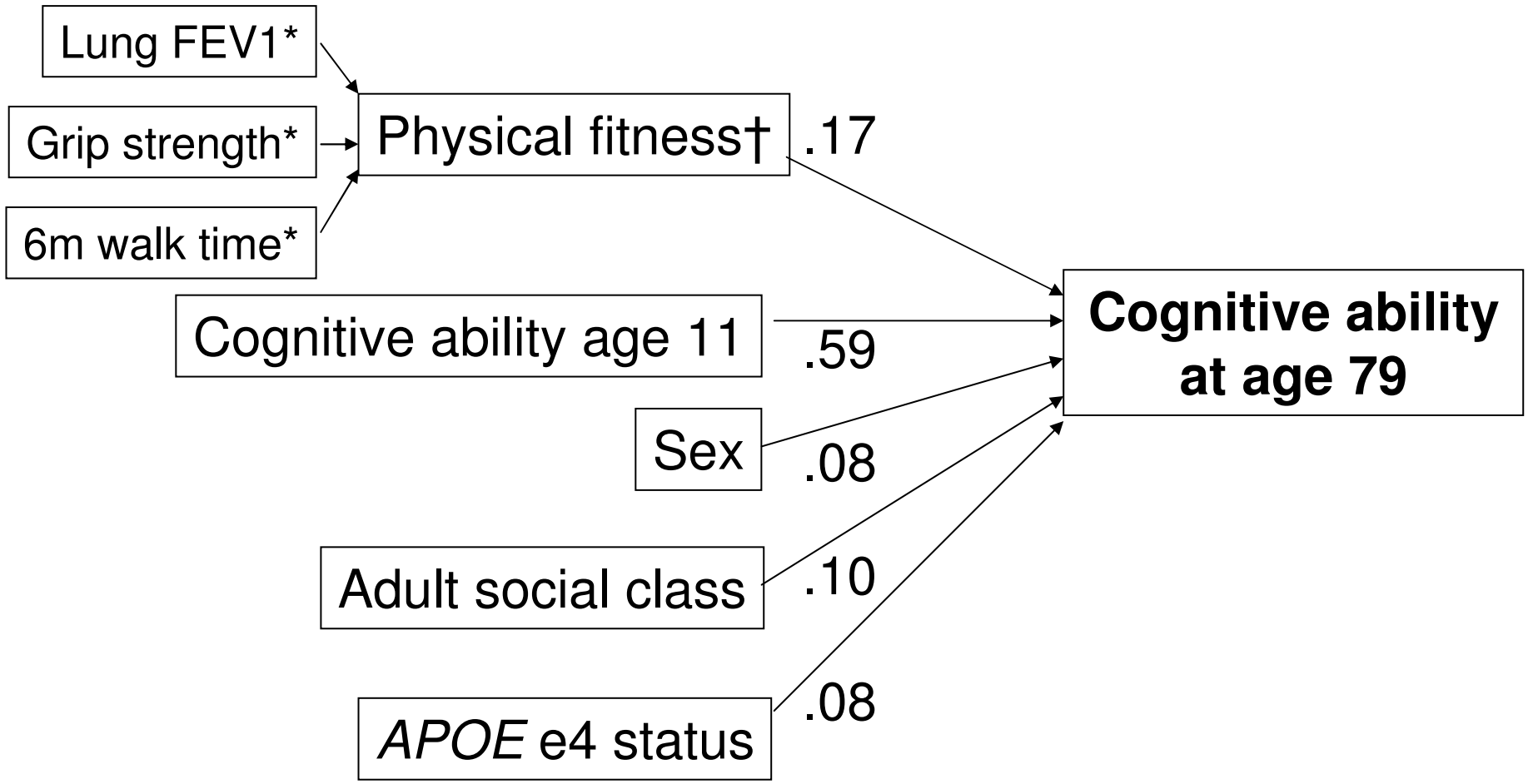
- Etc.

Physical fitness and lifetime cognitive change

Ian J. Deary, PhD; Lawrence J. Whalley, MD; G. David Batty, PhD; and John M. Starr, MD

Abstract—*Objective:* To test the hypothesis that physical fitness is associated with more successful cognitive aging. *Methods:* Surviving participants (N = 460) of the Scottish Mental Survey of 1932 were tested on the same general

Deary et al. (2006) *Neurology*, *67*, 1195-1200.



Deary et al. (2006) *Neurology*, *67*, 1195-1200.

LBC 1921

Alcohol and cognitive ageing

	eta^2	eta^2: adjusted for age 11 MHT	eta^2: adjusted for adult social class
General fluid cognition	**.021***	**.005**	**.008**
Processing speed	**.017***	**.007**	**.008**
Memory	**.034***	**.012***	**.021***

Corley et al. (2011) *Neuropsychology, 25*, 166-175.

LBC 1936

Bio-medical factors

- **Cytomegalovirus infection***
- **C-reactive protein*, etc.**
- **Telomere length**
- **Oxidative stress**
- **S100β**
- **Retinal vessel topography**
- **Carotid artery stenosis**
- **Atherosclerotic indices**
- **Several others…**

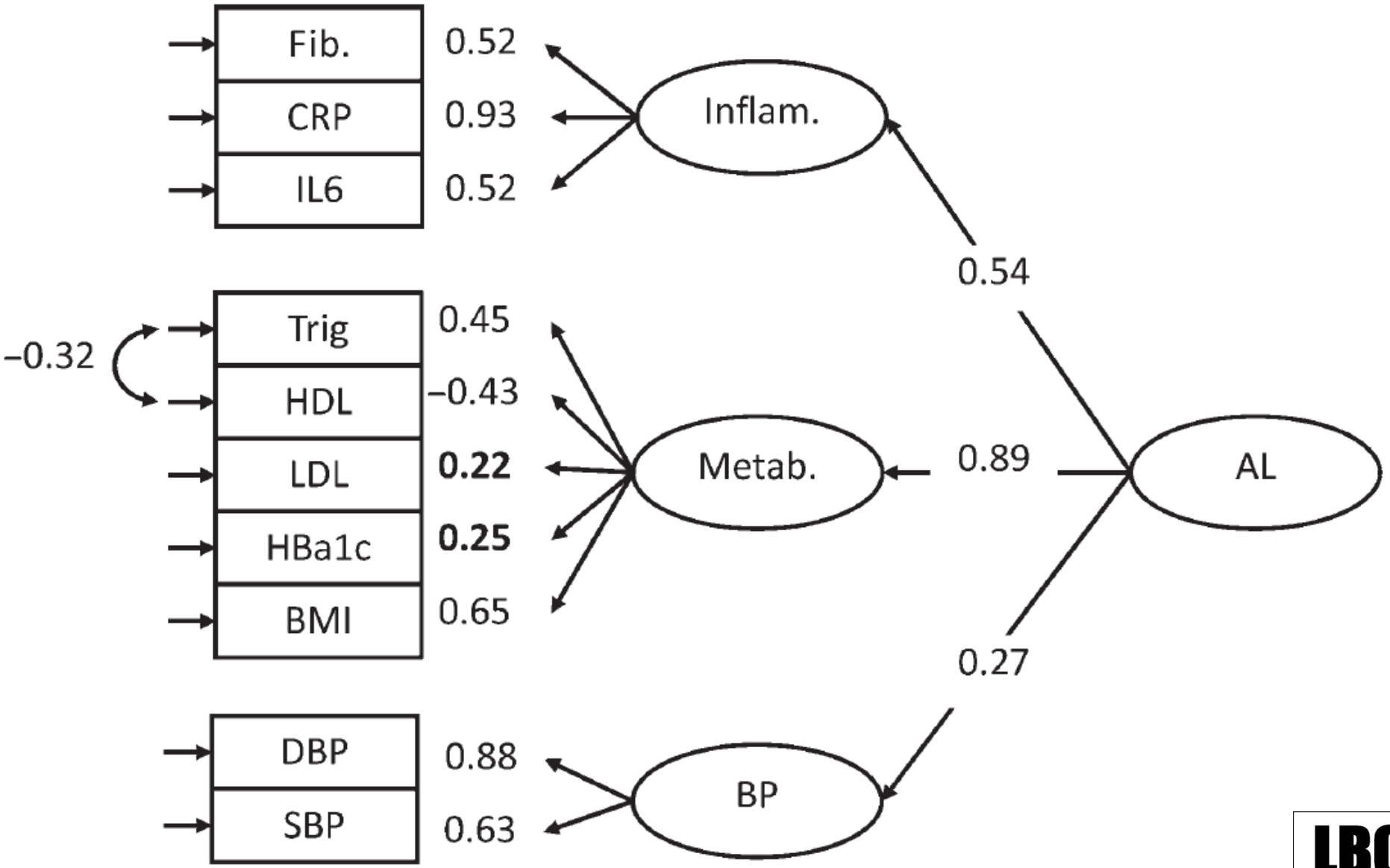
Cytomegalovirus infection (yes/no) and cognitive ageing

	eta^2	eta^2: adjusted for childhood overcrowding	eta^2: adjusted for age 11 IQ
General fluid cognition	**.012***	**.004***	.003
Processing speed	.003	.000	.000
Memory	**.004***	.001	.000

Gow et al. (2013) *Neurobiology of Aging*, *34*, 1846-1852.

LBC 1936

Allostatic load in the Lothian Birth Cohort 1936

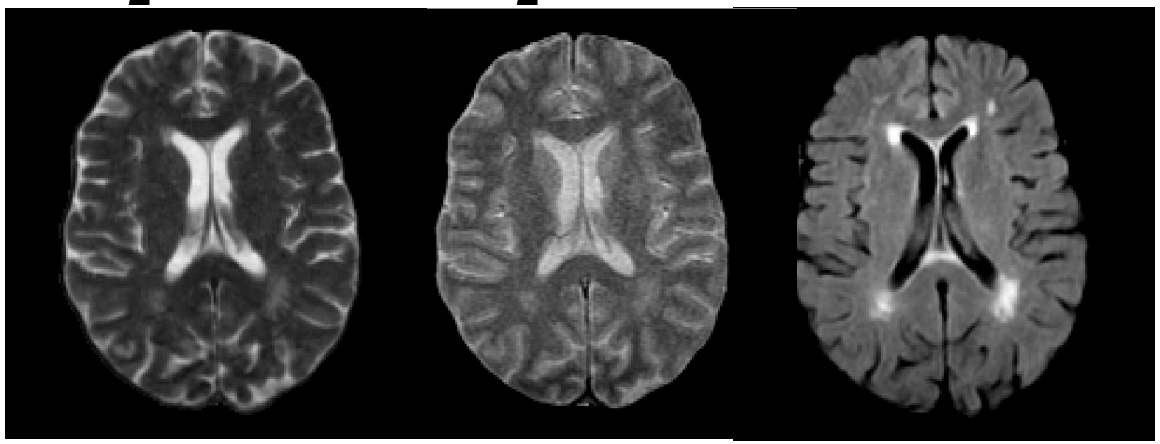


Booth et al. (2013) *American Journal of Human Biology*, *25*, 538-543.

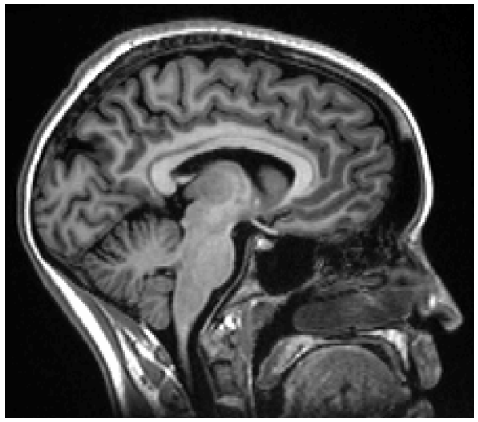
LBC 1936

Brain imaging, especially white matter integrity

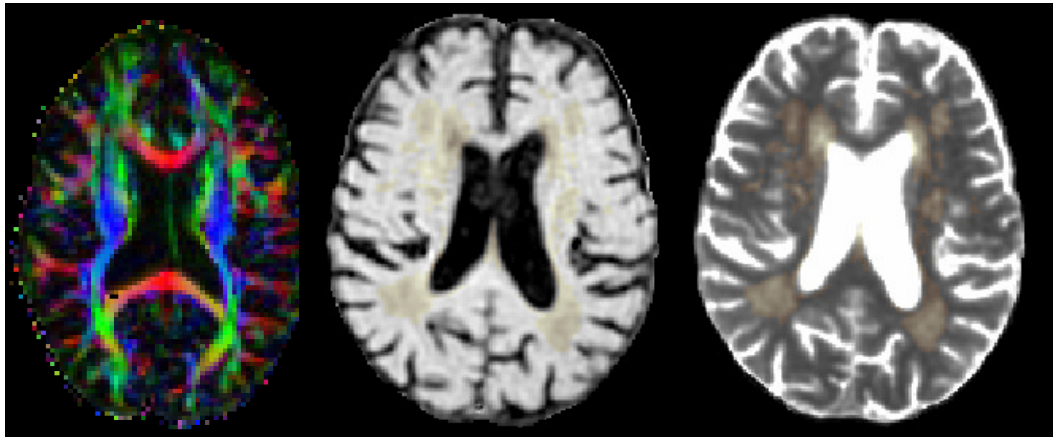
T_2W T_2*W FLAIR



T_1W volume



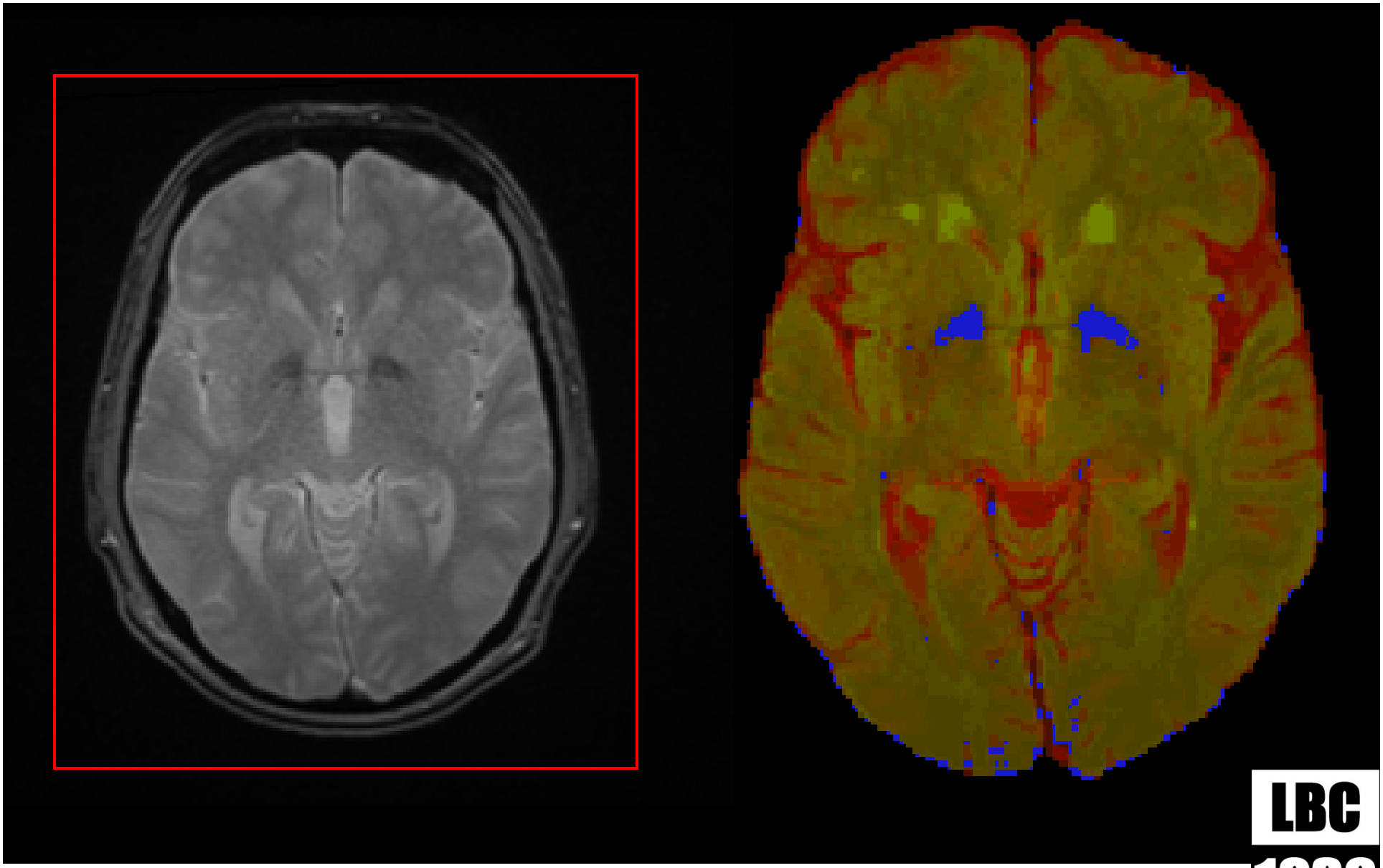
DTI MTI T_1-mapping



Wardlaw et al. (2011) *International Journal of Stroke*, *6*, 547-559.

LBC 1936

Brain iron deposits

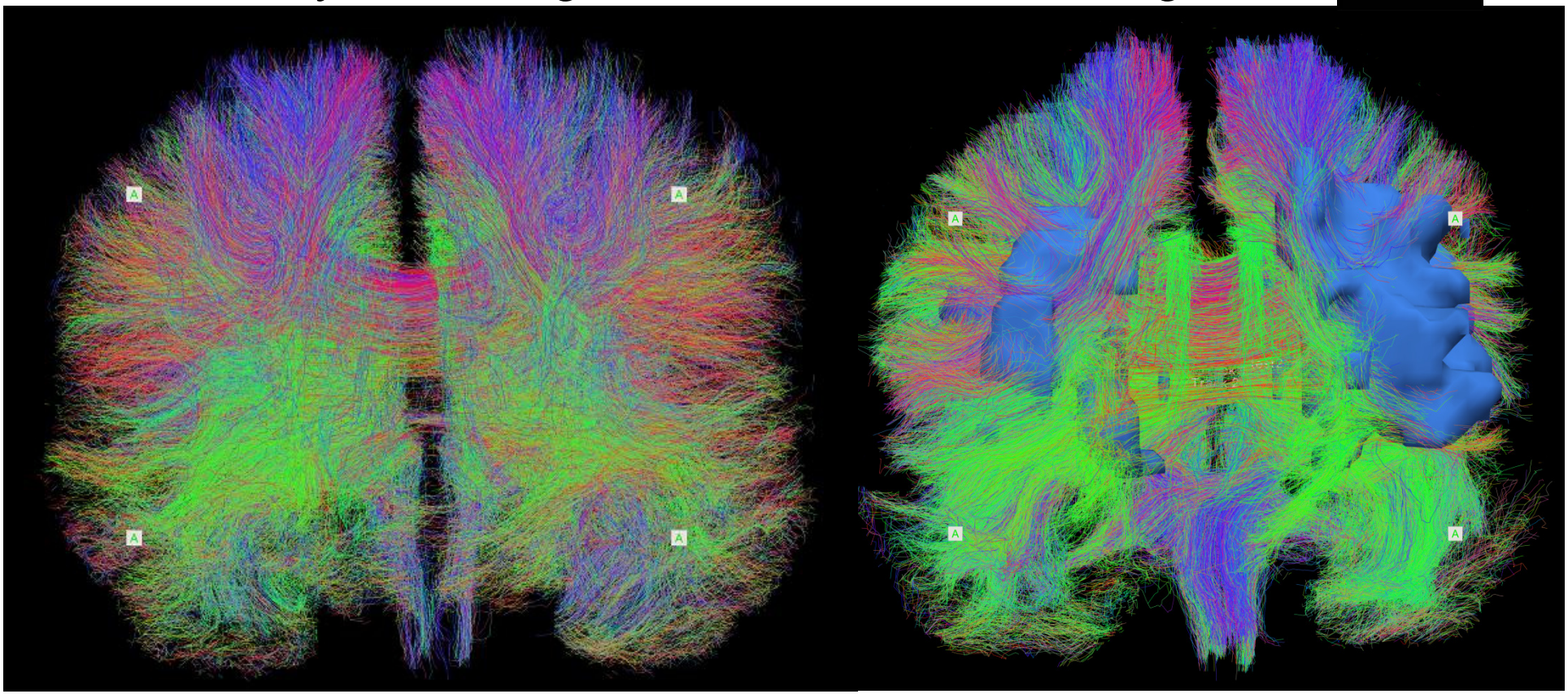


Penke, Valdes Hernandez et al. (2012) *Neurobiology of Aging*, *33*, 510-517.

Early middle age

Age 73

LBC 1936



Images courtesy of Mark Bastin.

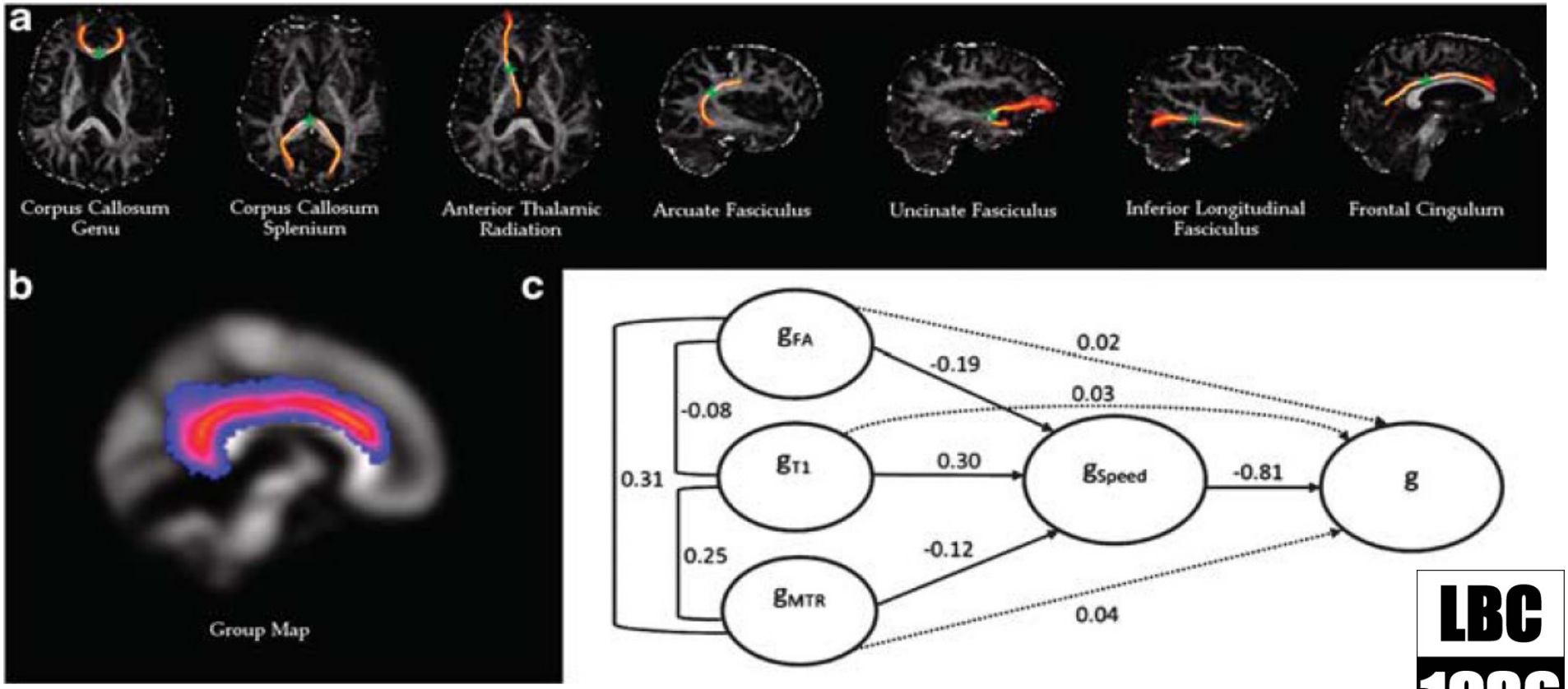
BRAIN RESEARCH IMAGING CENTRE Edinburgh

ORIGINAL ARTICLE

Brain white matter tract integrity as a neural foundation for general intelligence

L Penke[1,2,3], S Muñoz Maniega[1,3,4], ME Bastin[1,3,4,5], MC Valdés Hernández[1,3,4], C Murray[2], NA Royle[1,3,4], JM Starr[1,6], JM Wardlaw[1,3,4] and IJ Deary[1,2,3]

General intelligence is a robust predictor of important life outcomes, including educational and occupational attainment, successfully managing everyday life situations, good health and longevity. Some neuronal correlates of intelligence have been



Penke et al. (2012) *Molecular Psychiatry*, *17*, 1026-1030.

LBC 1936

Psychology and Aging
2012, Vol. 27, No. 1, 250–255

© 2011 American Psychol
0882-7974/11/$12.00 DOI: 1

Gow et al. (2012) *Psychology & Aging*, *27*, 250-255.

BRIEF REPORT

Reverse Causation in Activity-Cognitive Ability Associations: The Lothian Birth Cohort 1936

Alan J. Gow, Janie Corley, John M. Starr, and Ian J. Deary
University of Edinburgh

Active lifestyles might protect cognitive abilities; however, studies rarely consider the reverse causal direction. Activity-cognition associations might reflect stable intelligence differences rather than a protective effect of activity. The Lothian Birth Cohort 1936 (n = 1091) completed cognitive tests aged 70, having taken an intelligence test aged 11. Activity (assessed by participation in 15 activities that produced a socio-intellectual activity factor, and by physical activity) was positively associated with cognition (r = .08 to .32, $p \leq .05$). When age-11 IQ and adult social class were controlled, only physical activity remained significantly associated with general cognitive ability and processing speed.

Keywords: prior cognitive ability, cognitive ability, activity participation, physical activity, reverse causation

Neuroprotective lifestyles and the aging brain

Activity, atrophy, and white matter integrity

Gow et al. (2012) *Neurology*, *79*, 1802-1808.

A AMERICAN ACADEMY OF NEUROLOGY®

LBC 1936

Reported physical activity and brain ageing

	Standard β	β adjusted for age 11 IQ	β adjusted for age 11 IQ, class, disease
Brain white matter integrity	**.10***	**.10***	.07
Brain atrophy	**-.11***	**-.11***	**-.09***

Gow et al. (2012) *Neurology, 79*, 1802-1808.

LBC 1936

Molecular Psychiatry (2013), 1–5
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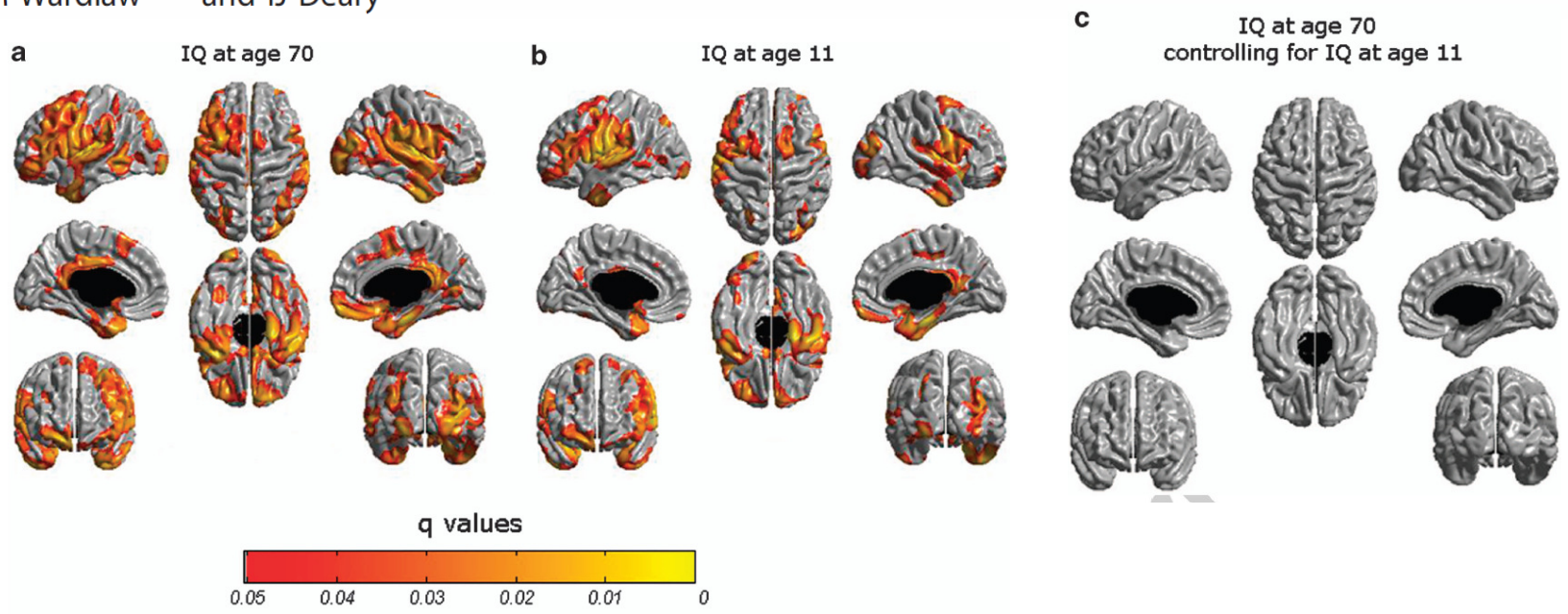
www.nature.com/mp

ORIGINAL ARTICLE

Childhood cognitive ability explains associations between cognitive ability and brain cortical thickness in old age

S Karama[1,2], ME Bastin[3,4,5], C Murray[6], NA Royle[3,4,5], L Penke[4,5,6], SM Maniega[3,4,5], AJ Gow[4,6], J Corley[6], Mdel CV Hernández[3,4,5], JD Lewis[1], M-É Rousseau[1], C Lepage[1], V Fonov[1], DL Collins[1], T Booth[4,6], P Rioux[1], T Sherif[1], R Adalat[1], JM Starr[4,7], AC Evans[1], JM Wardlaw[3,4,5] and IJ Deary[4,6]

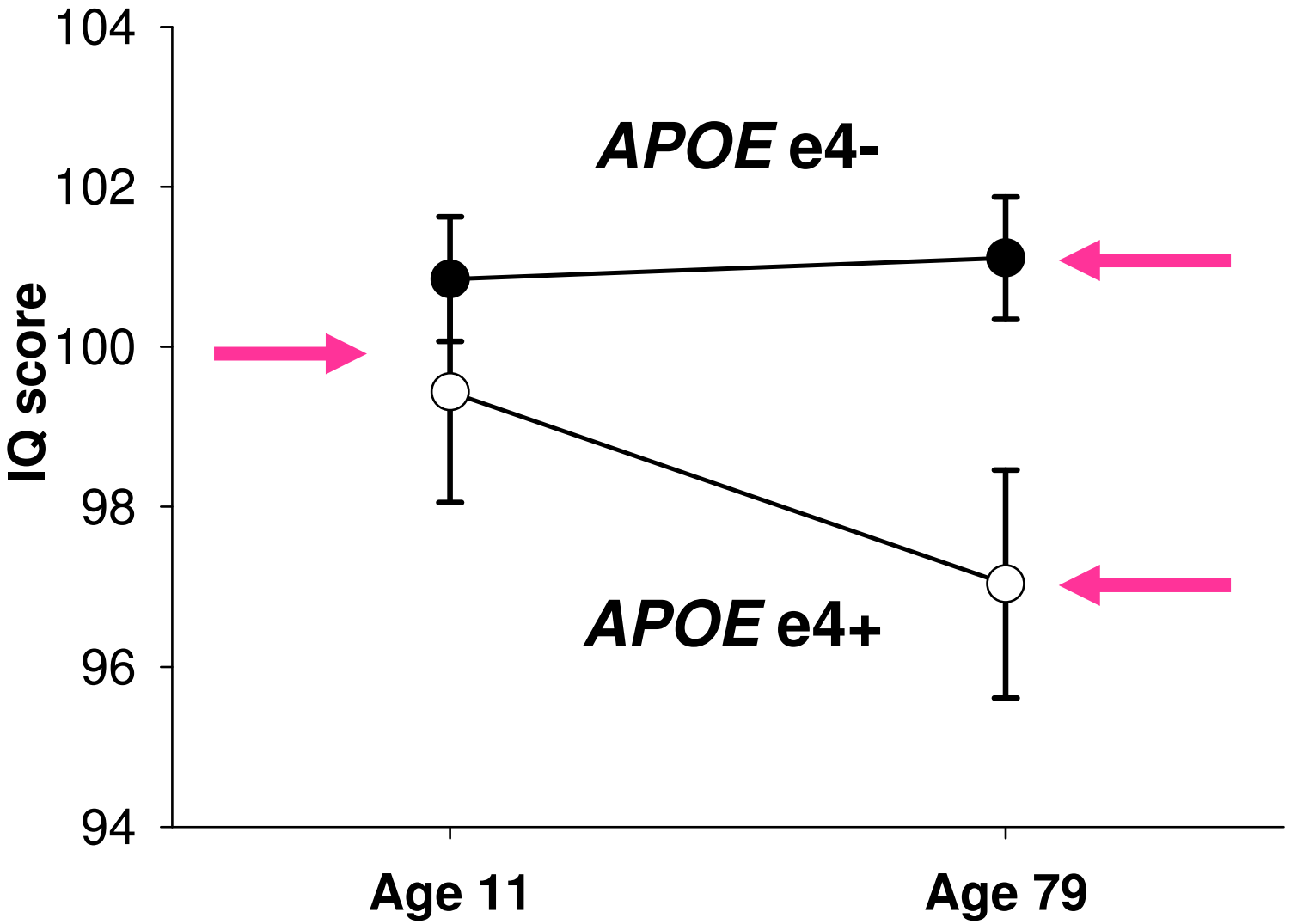


Karama et al. (in press) *Molecular Psychiatry*.

LBC 1936

Genetics

Candidate gene and Genome-wide association studies



Deary et al. (2002) *Nature*, *418*, 932.

LBC 1921

Molecular Psychiatry (2012) 17, 315–324
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www.nature.com/mp

ORIGINAL ARTICLE

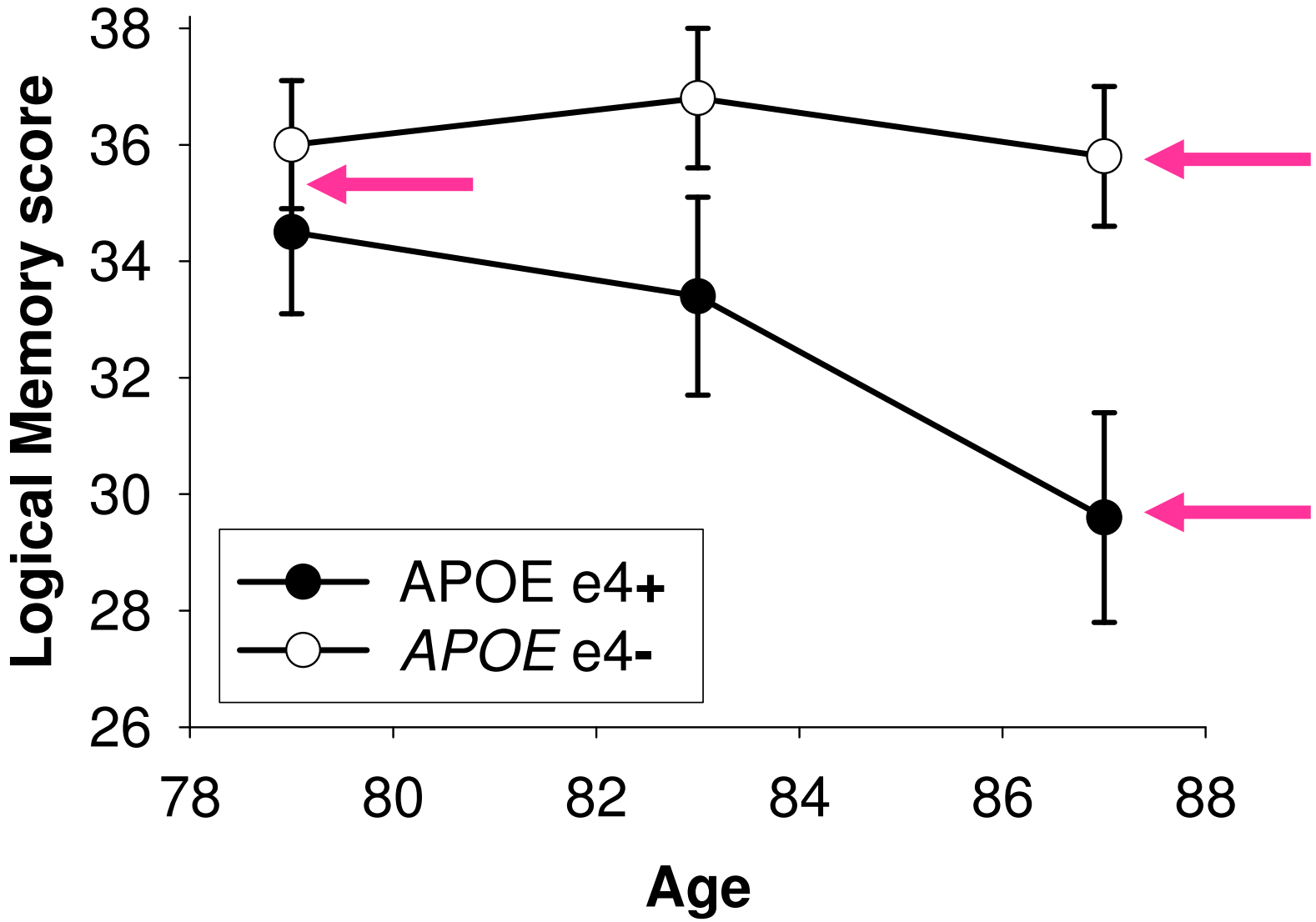
APOE E4 status predicts age-related cognitive decline in the ninth decade: longitudinal follow-up of the Lothian Birth Cohort 1921

OJG Schiepers[1,2], SE Harris[2,3], AJ Gow[2], A Pattie[4], CE Brett[4], JM Starr[2,5] and IJ Deary[2]

[1]*School for Mental Health and Neuroscience (MHeNS)/European Graduate School of Neuroscience (EURON), Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, The Netherlands;* [2]*Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, UK;* [3]*Centre for Cognitive Ageing and Cognitive Epidemiology, Medical Genetics Section, University of Edinburgh, Edinburgh, UK;* [4]*Department of Psychology, University of Edinburgh, Edinburgh, UK and* [5]*Geriatric Medicine unit, University of Edinburgh, Royal Victoria Hospital, Edinburgh, UK*

Carriers of the *APOE* E4 allele have an increased risk of developing Alzheimer's disease. However, it is less clear whether *APOE* E4 status may also be involved in non-pathological cognitive ageing. The present study investigated the associations between *APOE* genotypes and cognitive change over 8 years in older community-dwelling individuals. *APOE* genotype was determined in 501 participants of the Lothian Birth Cohort 1921, whose intelligence had been measured in childhood in the Scottish Mental Survey 1932. A polymorphic variant of

Schiepers et al. (2012) *Molecular Psychiatry*, *17*, 315-324.



Schiepers et al. (2012) *Molecular Psychiatry*, *17*, 315-324.

LBC 1921


illumina
4115825154

Molecular Psychiatry (2011) 16, 996–1005
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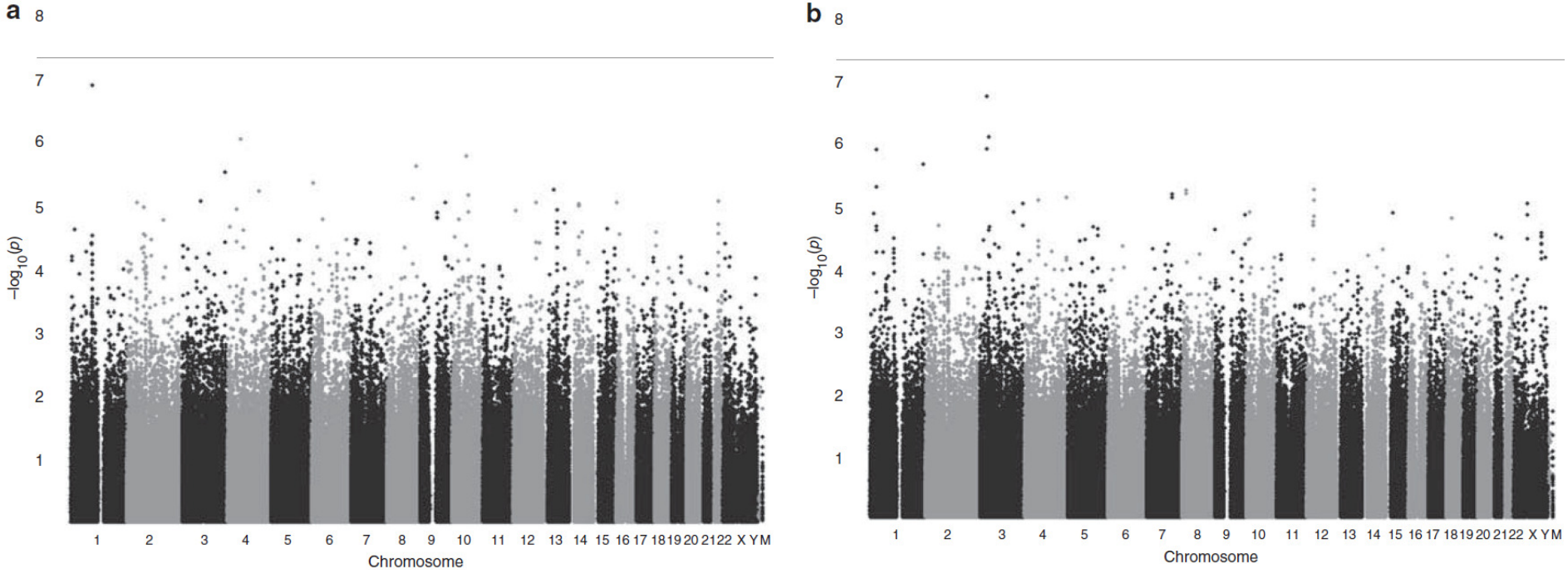
www.nature.com/mp

IMMEDIATE COMMUNICATION

Genome-wide association studies establish that human intelligence is highly heritable and polygenic

G Davies[1], A Tenesa[2,3], A Payton[4], J Yang[5], SE Harris[6,7], D Liewald[1,7], X Ke[8], S Le Hellard[9], A Christoforou[9], M Luciano[1,7], K McGhee[1], L Lopez[1,7], AJ Gow[1,7], J Corley[1], P Redmond[1], HC Fox[10], P Haggarty[11], LJ Whalley[10], G McNeill[10], ME Goddard[12,13], T Espeseth[14], AJ Lundervold[15], I Reinvang[14], A Pickles[16], VM Steen[9,17], W Ollier[4], DJ Porteous[6,7], M Horan[18], JM Starr[7,19], N Pendleton[18], PM Visscher[5,7,20] and IJ Deary[1,7,20]

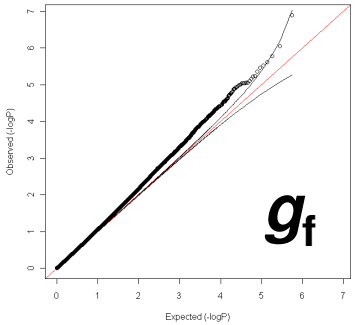


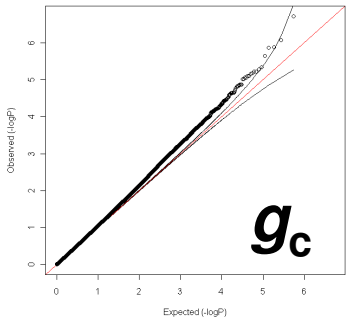
Davies et al. (2011) *Molecular Psychiatry*, *16*, 996-1005.

Cognitive ability in older age is highly polygenic

40% - 51% of variation in cognition between individuals in older age is accounted for by genetic variants in LD with common SNPs

h^2=0.40





h^2=0.51

Davies et al. (2011) *Molecular Psychiatry*,*16*, 996-1005.

LETTER

nature

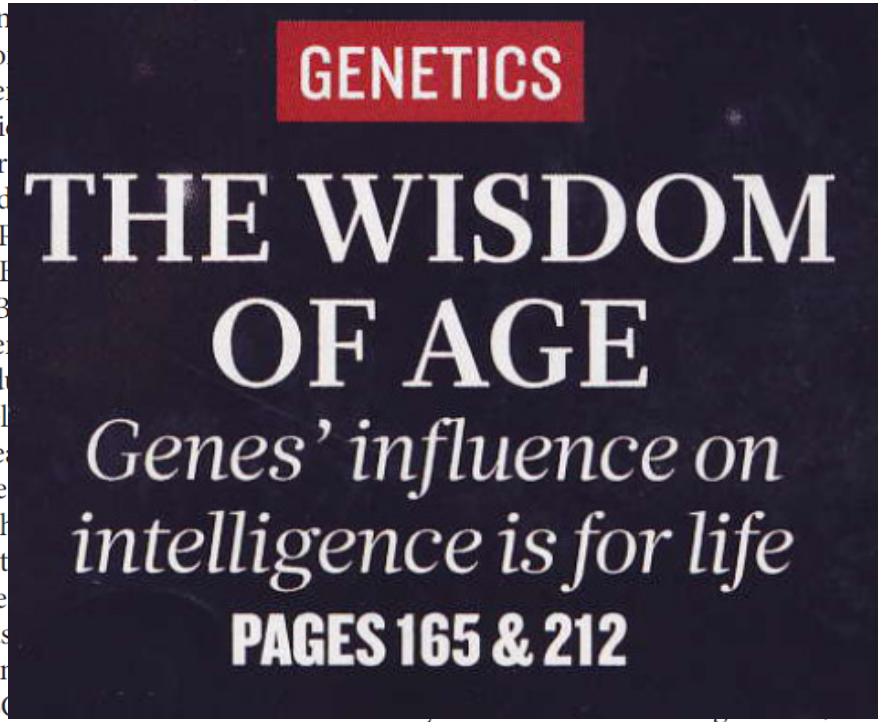
doi:10.1038/nature10781

Genetic contributions to stability and change in intelligence from childhood to old age

Ian J. Deary[1,2]*, Jian Yang[3]*, Gail Davies[1,2], Sarah E. Harris[2,4], Albert Tenesa[4,5], David Liewald[1,2], Michelle Luciano[1,2], Lorna M. Lopez[1,2], Alan J. Gow[1,2], Janie Corley[1], Paul Redmond[1], Helen C. Fox[6], Suzanne J. Rowe[5], Paul Haggarty[7], Geraldine McNeill[6], Michael E. Goddard[8], David J. Porteous[2,4], Lawrence J. Whalley[6], John M. Starr[2,9] & Peter M. Visscher[2,3,10,11]*

Understanding the determinants of healthy mental ageing is a priority for society today[1,2]. So far, we know that intelligence differences show high stability from childhood to old age[3,4] and there are estimates of the genetic contribution to intelligence at different ages[5,6]. However, attempts to discover whether genetic causes contribute to differences in cognitive ageing have been relatively uninformative[7–10]. Here we provide an estimate of the genetic and environmental contributions to stability and change in intelligence across most of the human lifetime. We used genome-wide single nucleotide polymorphism (SNP) data from 1,940 unrelated individuals whose intelligence was measured in childhood (age 11 years) and again in old age (age 65, 70 or 79 years)[11,12]. We use a statistical method that allows genetic (co)variance to be estimated from SNP data on unrelated individuals[13–17]. We estimate that causal genetic variants in linkage disequilibrium with common SNPs account for 0.24 of the variation in cognitive ability change from childhood to old age. Using bivariate analysis, we estimate a genetic correlation between intelligence at age 11 years and in old age of 0.62. These estimates, derived from rarely available data on lifetime cognitive measures, warrant the search for genetic causes of cognitive stability and change.

life course are largely unreplicated[22]. Therefore, an important novel



Deary et al. (2012) *Nature*, *482*, 212-215.

Molecular Psychiatry (2012), 1–12
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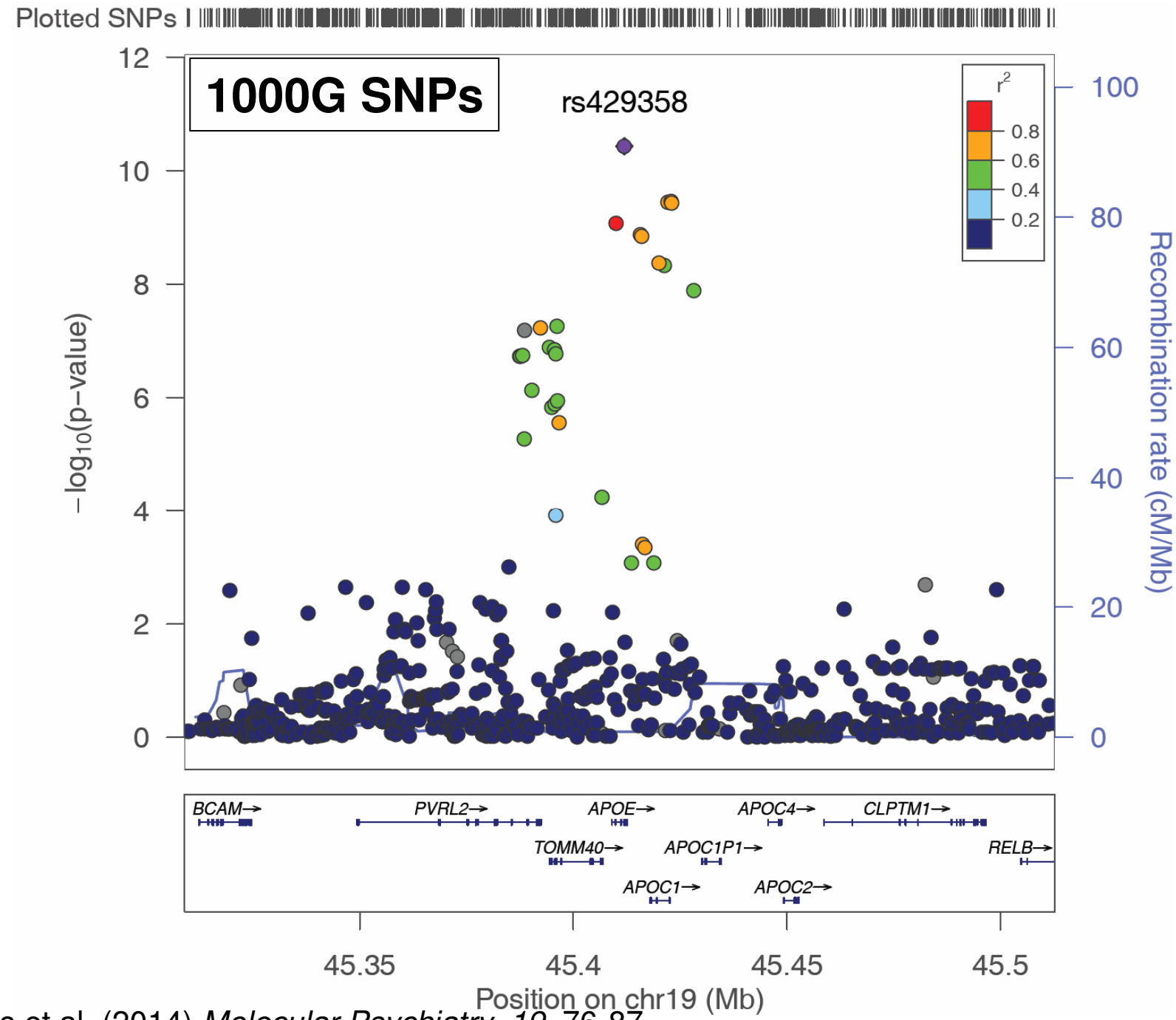
ORIGINAL ARTICLE

A genome-wide association study implicates the *APOE* locus in nonpathological cognitive ageing

G Davies[1], SE Harris[2,3], CA Reynolds[4], A Payton[5], HM Knight[6], DC Liewald[1,3], LM Lopez[1,3], M Luciano[1,3], AJ Gow[1,3], J Corley[1], R Henderson[1], C Murray[1], A Pattie[1], HC Fox[7], P Redmond[1], MW Lutz[8,9], O Chiba-Falek[8,9], C Linnertz[8], S Saith[8], P Haggarty[10], G McNeill[7], X Ke[11], W Ollier[5], M Horan[12], AD Roses[8,9,13], CP Ponting[6], DJ Porteous[2,3], A Tenesa[14,15], A Pickles[16], JM Starr[3,17], LJ Whalley[7], NL Pedersen[18,19], N Pendleton[12], PM Visscher[20,21,22] and IJ Deary[1,3]

Cognitive decline is a feared aspect of growing old. It is a major contributor to lower quality of life and loss of independence in old

Davies et al. (2014) *Molecular Psychiatry*, *19*, 76-87.



Davies et al. (2014) *Molecular Psychiatry*, *19*, 76-87.

Polygenic risk of schizophrenia and cognitive ability and change: LBC1921 and LBC1936

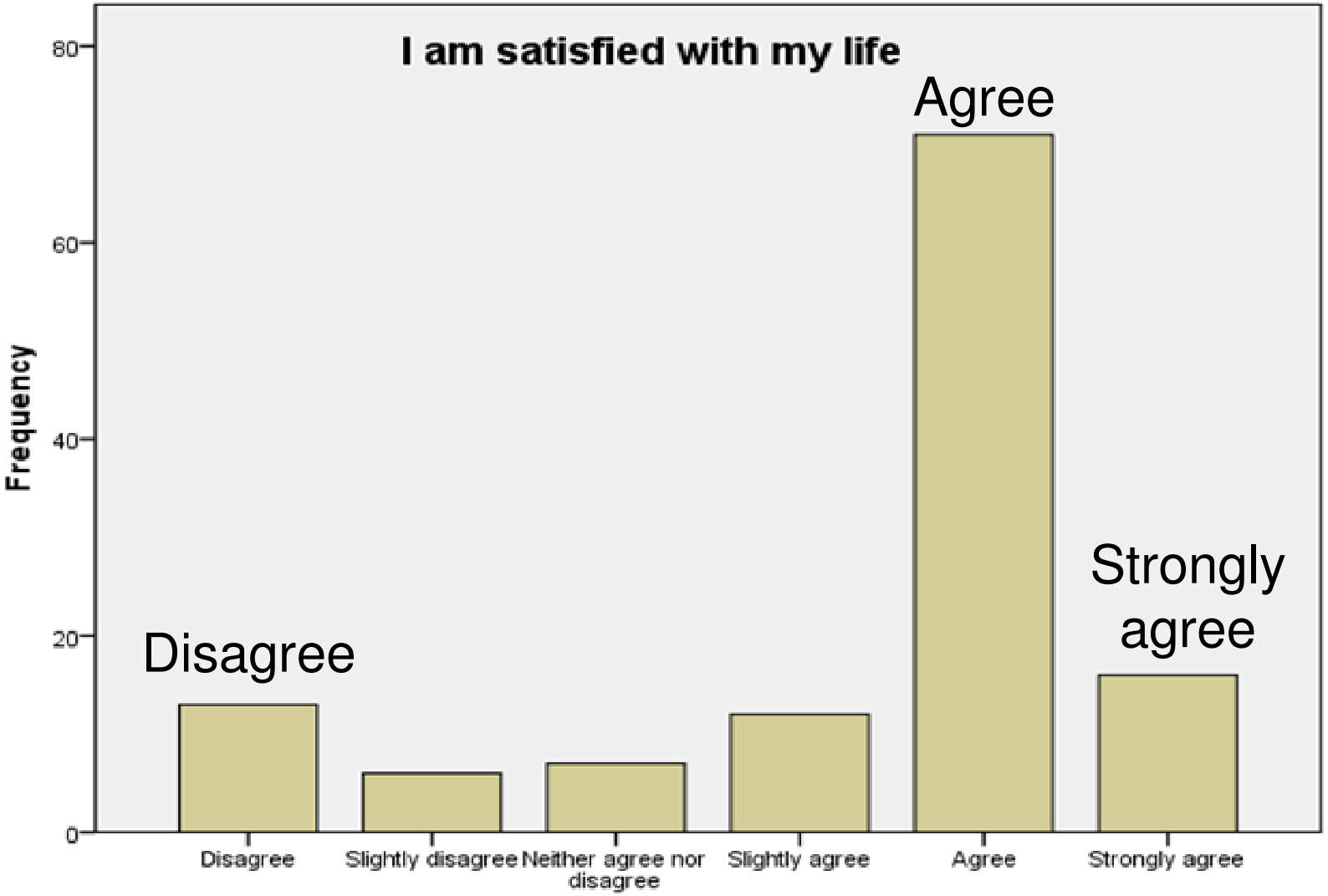
SNP p threshold	General cognition in old age	Change in Moray House Test from 11 to old age	Change in general cognition from age 11 to old age
p = .1	**-.08***		**-.07***
p = .05	**-.08***		**.07***
p = .01	**-.09***	**-.06***	**-.09***

McIntosh et al. (2013) *Biological Psychiatry*, *73*, 938-943.

LBC LBC 1921 1936

Cognition isn’t everything…

Life Satisfaction in Lothian Birth Cohort 1921 at age 90



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