

The Disconnected Mind

Unlocking secrets of healthy mental ageing

The Disconnected Mind aims to understand how changes in the brain's white matter – its connectivity – contribute to age-related cognitive decline in humans.

Newsletter 58: June 2022

Welcome to the Summer 2022 Disconnected Mind newsletter. This issue includes news about the Disconnected Mind/Lothian Birth Cohorts (LBC) team, our latest publications, and recent events.

For further information or to contribute to a future issue, please contact us using the details on page 8.

Lothian Birth Cohorts News

LBC1936 Wave 6 testing update

We begin with another update on our testing progress during Wave 6 of the LBC1936 study. The team has been hard at work, and at the time of publication, they have now seen 199 participants at the Wellcome Trust Clinical Research Facility for their cognitive appointment, and 109 have returned for a brain scan at Edinburgh Imaging Facility, Royal Infirmary of Edinburgh. This means we are now more than half way to our predicted total by the end of Wave 6. This would not be possible, of course, without the dedication of the LBC1936 participants, as well as the hard work of our testers and radiographers. Great work, team!



Team member Dr Janie Corley with LBC1936 participant, Mr Forsyth

In other testing news, one of our cohort members, Mr Forsyth, recently returned to take part in the cognitive and brain scan appointments for a sixth time. Much like many of our cohort members, Mr Forsyth has taken part in every cohort appointment since the study began, but, unlike any other, he is the only participant to have been tested by the same person at every single wave! Dr Janie Corley saw Mr Forsyth for the sixth time this wave, and has been

meeting him since his first appointment back in 2005, at the beginning of the study. We are always delighted to see our cohort members, and it is particularly special to meet the same people over many years and build up personal relationships with them. Janie and the team will be excited to see Mr Forsyth, and all our other cohort members, again in the years to come!

Staff news

Congratulations to Dr Judy Okely

We have some fantastic news to share: at the end of May, Dr Judy Okely left the team to take up a Lecturer position at Napier University. Judy has been a core member of the LBC1936 team since August 2017, running cognitive testing appointments during waves 5 and 6 of the study, while also working on an impressive portfolio of [research](#) often based on LBC data, covering topics such as loneliness, hearing and frailty, and their associations with cognitive ability and decline. She also led an ESRC funded project to explore the effects of musical experience on cognitive health and decline in the LBC1936, resulting in a number of publications and many outreach programmes and public events. Just some of her findings from this project are detailed in this edition, on the next page in the 'Scientific Highlights' section.



Judy represents yet another example of the LBC's ability to develop talented young researchers and help them to get permanent academic positions. We are extremely sad to see Judy go and she will be missed by the entire LBC team and participants alike, but we wish her all the very best in this exciting next step in her academic career.

Scientific Highlights

Experience of playing a musical instrument and lifetime cognitive change in the LBC1936

There is a long-standing interest in the potential effects of musical training on cognitive ability. Studies with children and adults suggest that musical training might confer a cognitive advantage. However, due to a lack of long-term longitudinal studies in this field, it is unknown whether any potential cognitive benefits of musical training are long lasting. Participants in the LBC1936 cohort completed the same test of general cognitive ability at ages 11 and 70 and reported their lifetime experience of playing a musical instrument, retrospectively, at age 82. Using this unique dataset, Dr Judy Okely and team tested whether greater experience of playing a musical instrument was associated with more positive cognitive change over almost 60 years. In a paper now accepted for publication in *Psychological Science*, her results provide support for this hypothesis: after controlling for the effects of childhood environment, years of education, adult social class, and disease history, greater experience of playing a musical instrument was associated with more positive cognitive change between ages 11 and 70. This is one of the first studies to indicate that experience of playing a musical instrument is associated with a long-term cognitive advantage.



White matter hyperintensities and ventricular enlargement in the LBC1936

White matter hyperintensities (WMH) are signs of damaged brain tissue caused by diseased small vessels. They are commonly observed in the brain as people age, and more of them appear as we grow older. The lateral ventricles, C-shaped cavities inside the brain filled with cerebrospinal fluid, also tend to become larger with age. WMH tend to appear around the ventricles, but we don't know whether they contribute to the enlargement of the lateral ventricles, or if the ventricles grow because of increased generalised brain tissue loss, considered to be brain atrophy. In a [paper](#) published in *Neuroimage: Clinical*, PhD student Angela

Jochems used data and brain scans from LBC1936 participants at ages 73, 76 and 79 to investigate the longitudinal relationship between the ventricle enlargement and WMH changes, as well as the influence of other risk factors, such as blood pressure, smoking, history of stroke or cardiovascular disease and diabetes. She found that lateral ventricles increase steadily by 3% per year on average, while the WMH change was more varied, showing little change in some participants while increasing in others. The analysis suggested that the contribution of WMH to the changes in the lateral ventricles was small; however, they both were related to blood pressure.

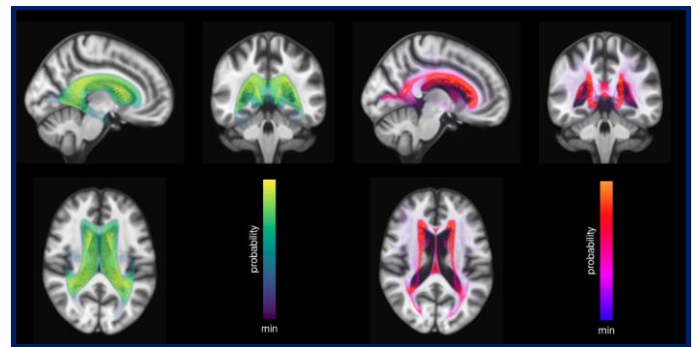


Figure showing common areas of lateral ventricles enlargement (yellow/green) and WMH growth (orange/red)

Mediterranean-type diet and brain structural change from 73 to 79 years in the Lothian Birth Cohort 1936

LBC1936 Co-Investigator Dr Michelle Luciano and team have previously shown in LBC1936 that greater adherence to a Mediterranean type data at age 70 years was associated with slightly less subsequent total brain volume atrophy over a 3-year period. In a follow-up [study](#) published in *Journal of Nutrition, Health and Aging*, they used LBC1936 data from three brain imaging waves, at mean ages 73, 76 and 79, to test whether this association was present over a six year period. No significant association was found, suggesting that dietary effects may not be long lasting or that they get less important with increasing age, perhaps due to the increased influence of age-related disease on brain health. It could also be because any possible effects are smaller than we could reliably detect. Because dietary information was collected several years before the first brain imaging scan, another possibility is that people's diet had changed. They conclude that future work should focus on more frequent collections of dietary data.

Original Research | [Open Access](#) | [Published: 17 March 2022](#)

Mediterranean-Type Diet and Brain Structural Change from 73 to 79 Years in the Lothian Birth Cohort 1936

[Michelle Luciano](#) [✉](#), [J. Corley](#), [M. C. Valdés Hernández](#), [L. C. A. Craig](#), [G. McNeill](#), [M. E. Bastin](#), [I. J. Deary](#), [S. R. Cox](#) & [J. M. Wardlaw](#)

The journal of nutrition, health & aging 26, 368–372 (2022) | [Cite this article](#)

Circulating Metabolome and White Matter Hyperintensities in Females and Males

White matter hyperintensities (WMH) identified on magnetic resonance images (MRI) of the brain are a major risk factor for stroke, dementia and death. Circulating metabolites, including lipids, sugars and amino acids, are small molecules produced during chemical reactions within cells (metabolism) that then enter the blood stream. They can be measured by 'mass spectrometry' and 'nuclear magnetic resonance spectroscopy'. In a [paper](#) published in *Circulation* by our collaborator Dr Eeva Sliz and team at the University of Toronto, Canada, LBC1936 contributed data to the first large-scale study (N=9290 individuals) investigating the association between levels of circulating metabolites and WMH. We discovered that 30 circulating metabolites, including multiple lipid measures and nonlipid metabolites, were found to associate with WMH in a general population of middle-aged and older adults. Some metabolites showed associations with WMH only in males or only in females.

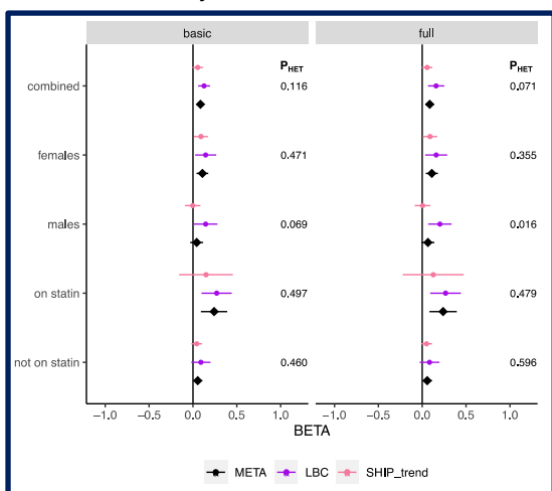


Figure showing cohort-specific significant associations between WMH and 31 metabolic measures

Cognitive change age 11-70 predicts cognitive change during older age

Age-related cognitive decline is a significant threat to the quality of life in older age. Researchers have made significant advances in identifying protective and risk factors for cognitive decline, but most studies focus on a limited age range, and cognitive change mechanisms are not yet completely understood. In a paper accepted by *Psychological Science*, PhD student Federica Conte examined how cognitive change from 11 to 70 years is associated with cognitive change within older age (70 to 82 years) in the LBC1936. Using latent growth curve models, she estimated rates of change from age 70 to 82 in general cognitive ability (g) and in three cognitive domains: visuospatial, memory and processing speed. Greater 11-70 cognitive gain predicted slower decline in g over 12 subsequent years, even after controlling for cognitive ability at

age 11 and age 70, and domain-specific change beyond g. Overall, these findings show that earlier change is associated with later change in cognitive ability. Some factors related to individual differences in cognitive change might thus operate over much of the adult life course, and certainly before older age.

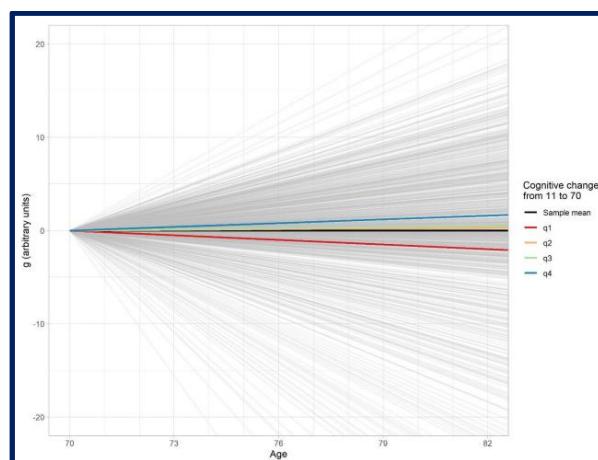


Figure showing estimates of standardised change in general cognitive ability (g) from age 70-82 by age 11-70 change

Genetic variants associated with longitudinal changes in brain structure across the lifespan

Human brain structure changes throughout the lifespan. Altered brain growth or rates of decline are implicated in a vast range of psychiatric, developmental and neurodegenerative diseases. In a [paper](#) published in *Nature Neuroscience*, collaborator Dr Rachel Brouwer of Utrecht University, The Netherlands, LBC1936 contributed to a study to help identify common genetic variants that affect rate of brain growth or atrophy in what is, to our knowledge, the first genome-wide association meta-analysis of changes in brain structure across the lifespan. Longitudinal magnetic resonance imaging (MRI) data from 15,640 individuals, including LBC1936, were used to compute rates of change for 15 brain structures. The most robustly identified genes, called *GPR139*, *DACH1* and *APOE*, were associated with metabolic processes. Identifying these variants involved in structural brain changes may help to determine biological pathways underlying optimal and dysfunctional brain development and aging.

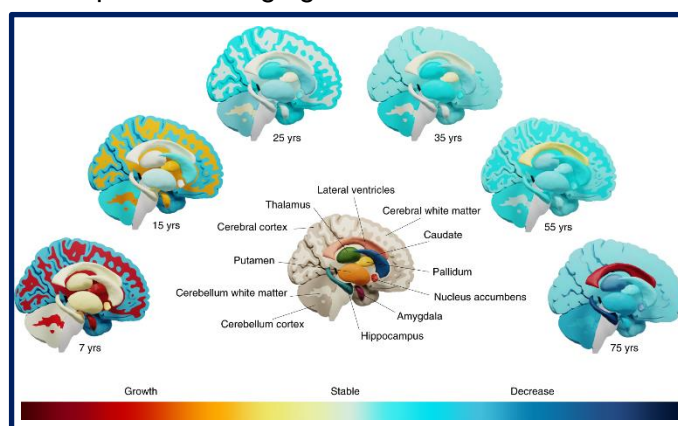


Figure showing visualisation of the growth and decline of brain structures across the lifespan

Meta-GWAS Reveals Novel Genetic Variants Associated with Urinary Excretion of Uromodulin

Uromodulin is the most abundant protein excreted in urine. It plays a major role in kidney physiology and disease. In a [paper](#) published in *Journal of the American Society of Nephrology* by PhD student Christina Joseph, working with our close collaborator Prof Caroline Hayward, LBC1936 contributed to a genome-wide association study of two measures of uromodulin: levels of uromodulin (uUMOD) and uromodulin indexed to creatinine (uUCR). Two genome-wide significant signals were identified for uUMOD, including a new signal in a region of the genome coding for 'KRT40', a protein expressed in the kidney. Two genome-wide significant signals for uUCR were identified, including one in the new 'WDR72' region previously associated with kidney function and kidney stones. Thus, LBC1936 contributed to a study that identified novel genetic signals associated with uromodulin (uUMOD) levels and uromodulin indexed to creatinine (uUCR) in urine.

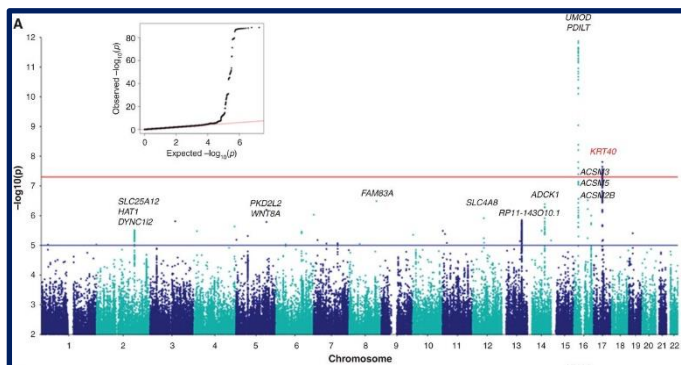
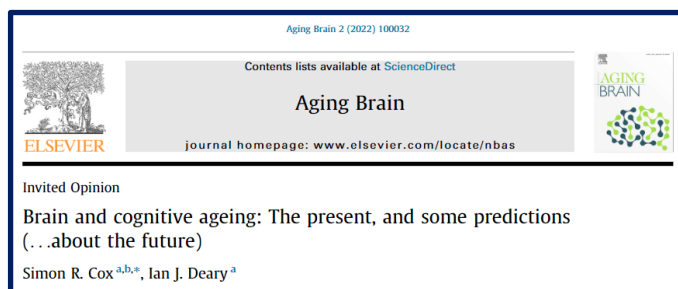


Figure showing genetic loci associated with uromodulin levels (uUMOD)

Dr Simon Cox & Prof Ian Deary publish 'Brain Ageing' Opinion Piece

Former and Current Directors of the Lothian Birth Cohorts, Professor Ian Deary and Dr Simon Cox, were recently asked to write an Invited Opinion article for journal *Aging Brain*. In their article, "Brain and cognitive ageing: The present, and some predictions (about the future)", they discuss lessons for cognitive and brain ageing research that have come from neuroimaging research, what neuroimaging still has to teach us, and views on some possible ways forward in this multidisciplinary field. Simon said, *'It was great fun to discuss how we might address the many remaining gaps in our knowledge, but we went about the task of addressing the future with heavy caveats, in the spirit of the well-known Danish parliamentary howler "It is hard to make predictions, especially about the future".'* They also included commentary on important emerging methods in neuropsychology, the necessity to bridge the explanatory gap from micro-to-macro, and some general principles for

doing better with the data and information we have now.



KE & Impact

Dr Janie Corley discusses LBC at Brain Health Scotland workshop

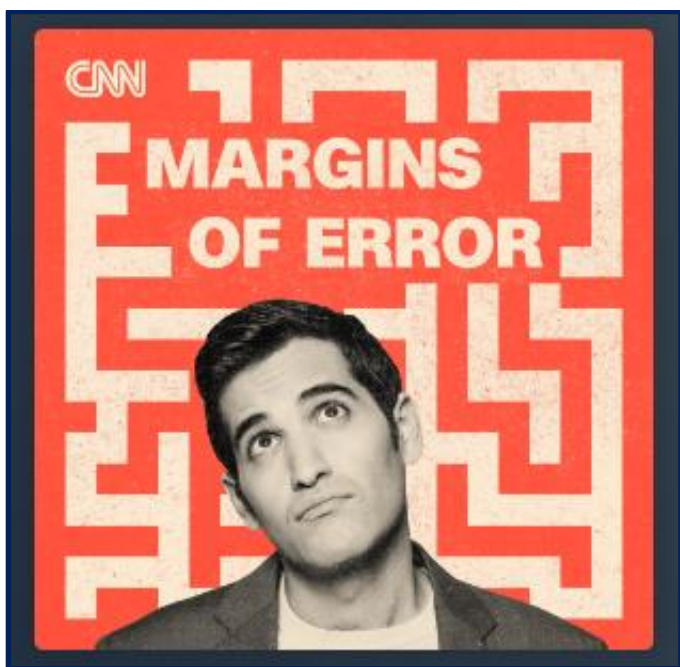
In March, team member Co-Investigator Dr Janie Corley presented some LBC findings at the Brain Health Scotland workshop. Janie's presentation, all about identifying factors which promote brain health, included findings from previous LBC research on the risk and protective factors for cognitive ageing, as well as some new results (in a paper currently under review) from a study of 12-year cognitive change over five waves of assessments. The key message with regard to predictors was much like the conclusion of Janie's [paper](#) 'Marginal Gains Not Magical Bullet'; brain health is affected in small but significant ways based on a great number of small changes one can make to their lifestyle. The day also included talks from researchers at the Global Council on Brain Health, Brain Health Scotland, and the Universities of Strathclyde, Stirling, and Heriot-Watt.



Janie presents at the Brain Health Scotland workshop

Dr Michelle Luciano discusses LBC1936, genetics and near-sightedness on CNN podcast

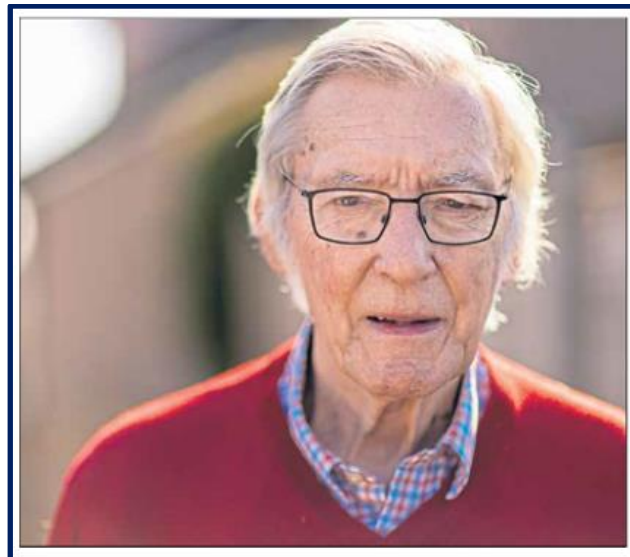
In the podcast 'Margins of Error' on CNN audio, presenter Harry Enten aims to break down data, translating the numbers into saying something about who humans are and what they believe. In a new [episode](#), 'Harry Makes a Spectacle of Himself', he discussed the topic of sight, and in particular, whether there might be any truth in the stereotype that those who wear glasses are more intelligent than those who do not. LBC team member Dr Michelle Luciano appeared on the podcast to discuss findings from a genome-wide association study including LBC data, in a paper she co-wrote in 2018 with team members including first author Dr Gail Davies, which revealed a small but significant correlation between near-sightedness, or 'myopia', and cognitive ability at a genetic level.



Lothian Birth Cohorts feature in the Sunday Post

In March, the LBC1936 were featured in an article in the Sunday Post. Journalist Tracey Bryce spoke to LBC1936 study director Dr Simon Cox, and LBC1936 participant Mr Hamish Coghill, about the study and its key findings. After detailing the fascinating history of the LBC1921 and LBC1936 studies, Simon explained why the LBCs are such a unique group, and the main aims of the study: finding out why some people experience more cognitive decline with age than others. He also touched on key factors which might help us keep our brains sharper with age, including lower BMI, not smoking, and more physical activity. Our LBC1936 participant, Hamish, spoke of how he was delighted to be involved in such an important project; *"People are living much longer now so if I can do something that helps people have a better life, I'm happy about*

that." Hamish also described the sorts of tests he takes part in during his visits with the Cohort, as a Cohort member, and how he tries to keep his cognitive skills active as he is getting older, including doing a lot of walking, reading, and being part of the local History Society. Hamish said, *"I'm a great believer in that we've got to keep going. We're only as old as we feel"*.



LBC1936 participant Mr Hamish Coghill from Sunday Post article

Dr Simon Cox contributes to BBC Future article

'The bigger the better' is often what we hear in relation to brains. A recent BBC Future [article](#) explores this traditional account in light of a recent claim that our distant ancestors had brains bigger than ours. Journalist Chris Baraniuk reviews evidence and hypotheses to account for the loss of brain volume in our ancestors about 3,000 years ago, from the brain-body ratio to the complexity of social systems, population size, and invention of writing and intelligence. In clarifying the relationship between brain size and our cognitive capacity, Simon drew on the team's prior work on brain, intelligence and sex differences, pointing out that brain volume alone does not reveal much about intelligence. Instead, more detailed measures of brain structure are likely to provide better insights into the nature of cognitive ability differences.



Beautiful Brain conference

After the last couple of years, we have been excited to get back to engaging with in-person public events. The 'Beautiful Brain' conference was organised by Salvesen Mindroom Centre, a Scottish charity supporting and empowering children and young people with learning difficulties. The event took place at the Edinburgh International Conference Centre and brought together world-renowned brain health experts from the University of Edinburgh who shared what we know about how brains develop, and what makes a healthy brain. The LBC team contributed with a hands-on interactive pre-conference exhibition, including our pair of 3D-printed ageing brains, laser-etched crystal brains, and very popular Augmented Reality headsets illustrating brain ageing based on the LBC brain imaging data. Artist Penny Kay also presented the 'Strategy of the Genes', an art piece created in collaboration with the Lothian Birth Cohorts in 2017.

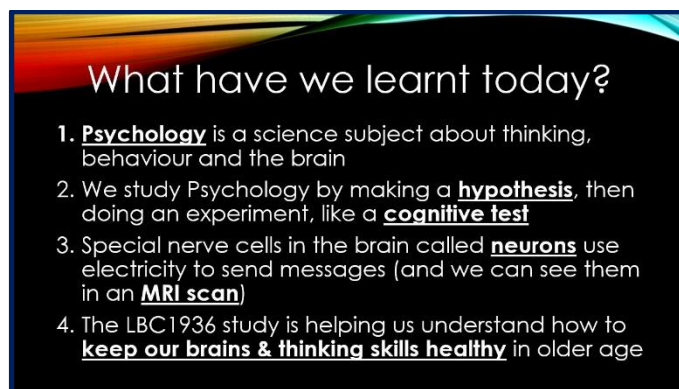
The event was very well attended with over 400 guests, and our exhibition received a lot of attention and questions. The team spoke to many guests, explaining all about the study, its history and participants, the protective and risk factors that influence cognitive ageing, and covered topics such as neuroplasticity and brain structural measures that can help us understand neurodiversity in development. The AR glasses triggered queries about AR technology and specific findings (e.g., smoking), reminding the team how effective this method is for engaging the public with our research! The keen interest of the attendees and the organisers in our research made the event an excellent and rewarding return to live engagement!



Team member Barbora Skarabela at the Beautiful brain conference.
Photo credit: Jess Shurte Photography

Danielle Page teaches P7 pupils about the LBC1936, the brain, and cognitive ageing

For some years, team member Danielle Page has collaborated with the University of Edinburgh's Widening Participation (WP) team, delivering a Psychology workshop based on the Lothian Birth Cohorts as part of their Primary School project. The WP team aim to address educational inequalities and patterns of under-representation in Higher Education through a range of projects working with young people aged 11 to 18. In this project, during P6-P7, primary school children from target schools are led through a series of workshops to normalise the higher education experience, culminating in them attending a 'real university lecture' with an academic.



Slide from Danielle's P7 workshop

In March and May this year, Danielle delivered workshops to more than 60 children from Canal View Primary School and Pirniehall Primary School. The classes were keen and engaged, and learned about Danielle's work with the Lothian Birth Cohorts, and how the study of thinking skills and memory relates to the brain and what we can do to maintain good brain health until old age. The children were introduced to terms like 'hypothesis' and 'neurons', and learned how to study the brain with the MRI machine. The children were quizzed about the identity of some puzzling MRI images that made regular fruit and veg look very exotic, and learned about things we can do to protect our brain from Professor Ian Deary's narration of the 'Staying Sharp' [video](#). At the end, the class reviewed what they learned in a short interactive quiz, and the children had some great questions about the brain in childhood and older age. Danielle kept her audience on their toes, with her passion for the Lothian Birth Cohorts, their attention glued to the screen, fully engaged and interactive. The session was packed with fun stories and interesting photos and videos, facts and questions, and the children were left inspired and keen to learn more. It was joy to watch. Excellent job, Danielle!

Lothian Birth Cohorts join Prescribe Culture at the University of Edinburgh

“Cultural prescribing” has become an important movement helping to improve people’s health and wellbeing. Last Spring, the Lothian Birth Cohorts participated in piloting one of the social prescribing programmes at the University of Edinburgh, with a series of singing sessions for people living with dementia and its evaluation. [Prescribe Culture](#) at the University of Edinburgh Museums offers a range of other heritage-based programmes designed to support those who may be experiencing difficulties with sense of loneliness and isolation, anxiety, depressive symptoms, and lack of connection. One of these is Take 30 Virtual Together ([T30TV](#)).



Take 30 Virtual Together takes participants on virtual tours around heritage collections, venues, and sites across the globe, and gets people lost in stories of characters, events, discoveries, and places on various themes. Team member Dr Barbora Skarabela was invited to share the story of the Lothian Birth Cohorts, with its unique history and findings. The session was organised by Ruthanne Baxter, the Prescribe Culture lead, and brought together participants of various ages, walks of life, and corners of the world, including Scotland, England, Spain, the USA, Canada, and China. One participant said: *“The lovely old photos were super and also the use of the example of the ‘real’ exam paper page; what really brings anything like that alive for me is the use of individual stories, like those two ladies from [the Who gets to be 100 podcast](#).”*

The story of Lothian Birth Cohorts was met with a lot of interest and triggered many memories of school days and tests, and led to a lively discussion about education, intelligence, mental health, cognitive ageing, and what individuals do to keep sharp and well. LBC team member Barbora said *“It was a great session. I really enjoyed meeting everyone. The group was so lovely and diverse. I was really pleased that every single member felt free to contribute and join the discussion!”*. Barbora is delighted to join the session again for **Farmers Take 30 Together Pilot Programme** in the autumn.

Contact

You can contact the LBC team by email, and keep up with our latest news on our website and Twitter.



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THE ROYAL
SOCIETY



New publications

Accepted/in press

Conte, F., Okely, J., Hamilton, O., Corley, J., Page, D., et al., (2022). Cognitive change before old age (11 to 70) predicts cognitive change during old age (70 to 82). *Psychological Science*.

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Lothian Birth Cohorts

Published

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