

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 54: June 2021

Welcome to the Summer 2021 Disconnected Mind newsletter. This issue includes news about the Disconnected Mind/Lothian Birth Cohorts (LBC) team, our latest publications, and the events we have participated in recently.

For further information about this newsletter or to contribute to future issues, please contact us using the details on page 8.

Lothian Birth Cohorts News

LBC1936 invited to NHS Research Scotland Restart Advisory Board Meeting

The team have been carefully planning a restart of data collection since the COVID-19 pandemic forced postponement of Wave 6, just over a year ago. Alongside practical and safety concerns, we felt it was vital to consult with LBC1936 participants themselves, to consider their thoughts, feelings, and opinions about attending face-to-face testing. Along with our annual Christmas newsletter in 2020, we asked all prospective participants to complete a brief survey about returning for Wave 6.

At the time of the survey, the vaccination rollout had not yet begun, case numbers and transmission rates were high, and a new COVID-19 variant had just been discovered. Despite the difficult circumstances, the team received an overwhelmingly positive response. We found that respondents were extremely positive about attending Wave 6. Given the measures the LBC team will put in place to mitigate risk, over 85% of respondents said they are likely to attend, and less than 20% said they would not attend unless vaccinated (note, all over 80s in Scotland should now have been offered at least their first vaccination).

Hearing of LBC1936's participant consultation, Dr Alan McNair (Senior Research Manager, Scottish Government Chief Scientist Office) realised its value to inform the work of the NHS Research Scotland's Restart Advisory Board, and contacted the Disconnected Mind team. In April, LBC Study Coordinator, Adele Taylor, presented the survey's



results to the Board, providing a brief overview of the key findings, which were very well received. The LBC team's careful preparations to begin testing with COVID-safe protocols are ongoing, and now that participants and many staff have been vaccinated, we hope that we can begin seeing participants again this summer. Watch this space!

Staff news

An introduction: Dr Joanna Moodie

Dr Joanna Moodie has recently joined the team as the Research Associate on Dr Simon Cox's Henry Dale Fellowship, which is funded by the Wellcome Trust and the Royal Society. Her focus is on identifying, characterising and validating various dimensions of aging and testing how they relate to each other. This will include several features of the brain as well as cognition, proteins and gene expression. Joanna has worked with the Disconnected Mind team in the past when she completed her MSc dissertation in Human Cognitive Neuropsychology at The University of Edinburgh, using LBC1936 data to examine associations between fluctuating asymmetry in the brain and cognitive function, resulting in a [paper](#) published in *Intelligence*. She recently completed her PhD at The University of St Andrews, where she studied neurocognitive overlap between language and music processing. She is delighted to be back with us, and the team is very happy to welcome her. Welcome, Joanna!





Veronique Miron awarded MRC Senior Non-clinical Fellowship

Congratulations Dr Veronique Miron, of the University of Edinburgh's Centre for Reproductive Health, who was recently awarded an MRC senior non-clinical fellowship. Using the LBC1936 post mortem brain tissue is central to one of her work packages. Veronique will be investigating the role of microglia, a type of cell found in the brain and spinal cord, in the loss of myelin integrity. Loss of myelin integrity, also known as demyelination, is a process in which the protective layer of myelin tissue around nerve cells is lost, leaving them vulnerable to damage and interference. Demyelination has been linked to cognitive decline with ageing. Veronique's work will be undertaken within the UK Dementia Research Institute at Edinburgh, and will ask questions that are central the Disconnected Mind project's aims and hypotheses, and we look forward to this promising collaboration.

Scientific Highlights

Apolipoprotein E e4 allele status and later-life depression in LBC1936

The apolipoprotein E e4 allele plays an important role in dementia and cognitive decline in later life, with those who carry this variant of the gene being at increased risk. However, there is growing evidence that the e4 allele also affects the risk of depression in later life. In a [paper](#) published in *Psychological Medicine*, Dr Matthew Iveson and colleagues examined the association between the e4 allele and both depression risk and change in depressive symptoms over time. LBC1936 participants carrying the e4 allele had a similar risk of depression in later-life and experienced similar changes in depressive symptoms over time. Presence of the e4 allele also did not appear to moderate the impact of established risk factors for depression. Although the apolipoprotein E e4 allele plays an important role in dementia, carrying the e4 allele does not appear to increase the risk of depression in later-life.

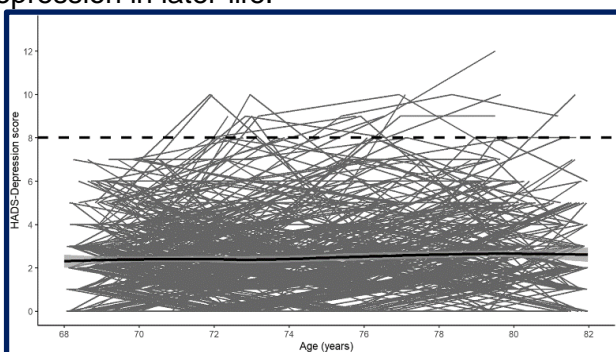


Figure from Iveson et al (2021) showing participants' individual longitudinal trajectories of HADS-depression scores with age. The solid black line is mean trajectory of all participants.

Impact of COVID-19 lockdown on psychosocial factors, health, and lifestyle

In a paper recently accepted for publication in *PLOS ONE*, Adele Taylor, Danielle Page and the LBC team used LBC1936 COVID-19 survey data to examine the impact of the first COVID-19 lockdown on older adults in Scotland. Relatively little is known about the effects of COVID-19 on psychosocial factors, health and lifestyle in older adults, particularly those over the age of 80 years who are considered to be at highest risk of severe illness and death as a result of the virus. We examined the responses from the LBC1936 COVID-19 questionnaire about participants' experience and knowledge of COVID-19; adherence to government guidance; and the impact of lockdown on day-to-day living, social contact, self-reported physical and mental health, loneliness, and lifestyle. We found that very few respondents had contracted the virus themselves (n=4), the majority had good knowledge about COVID-19 (95%), most people found government guidance easy to understand (86%). There were modest declines in self-reported physical and mental health, and almost half of respondents (48%) reported doing less physical activity during lockdown.

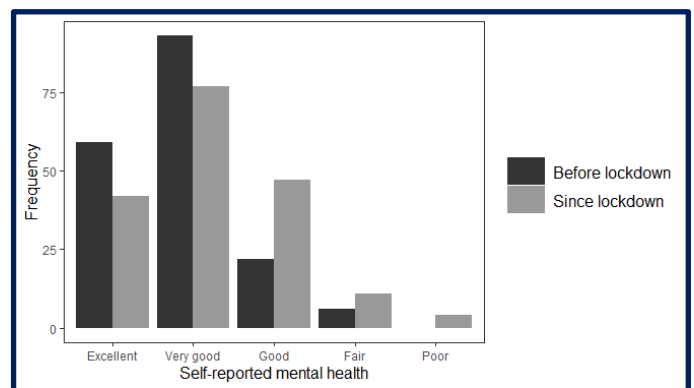
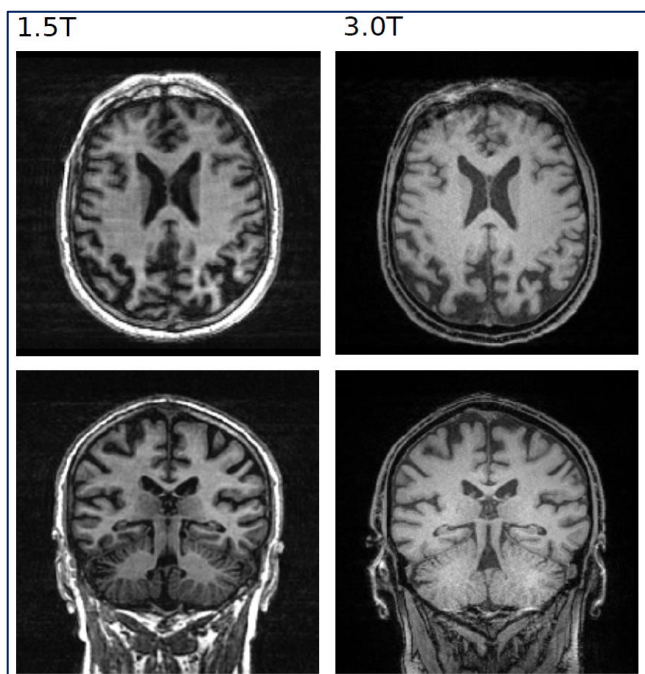


Figure from Taylor et al (2021) showing how participants rated their mental health before and after national lockdown in March 2020

We also examined which participant characteristics, measured previously at age 82, were associated with outcomes during lockdown at age 84. Participants with poorer self-rated general health and less professional occupational social class were more likely to adhere to government guidance about staying at home. Overall rates of loneliness were relatively low, but those living alone or with higher anxiety at age 82 were more likely to experience loneliness in lockdown. Less professional occupational social class and lower cognitive ability at age 82 was also associated with decreased physical activity during lockdown. Overall, this study found that characteristics such as lower occupational social class, poorer self-rated general and mental health, and lower cognitive ability level might be related to risk of poorer psychosocial and physical outcomes in adults over the age of 80 during COVID-19 lockdown.

Comparison of brain measures between MRI scanners

In a recently published [paper](#) in *Human Brain Mapping*, team member Dr Colin Buchanan reported the results of our carefully-planned transition from the older 1.5T brain MRI scanner to a newer 3T scanner (Tesla are the units of magnetic field strength). The benefits of this switch include a nearly 2x faster scanning time – this is important for participants as lying still for a long time can become increasingly difficult. At the most recent wave (our last at 1.5T), we scanned 105 participants on both old and new scanners to give us concrete information about any brain image differences to expect (and account for) between scanners. Colin, and LBC researcher Dr Susana Muñoz Maniega, analysed a large set of measures from each scanner and found there were differences in many of the measurements of the brain depending on the scanner used. For example, grey and white matter tissue volumes were measured as 6-11% higher using the 3T scanner compared to the 1.5T scanner. However, they also showed that these differences could be largely eliminated statistically, meaning that tissue volumes and various measures in white matter can be reliably matched between scanners. This is also valuable to other researchers collecting data from multiple MRI scanners, who must account for scanner differences.

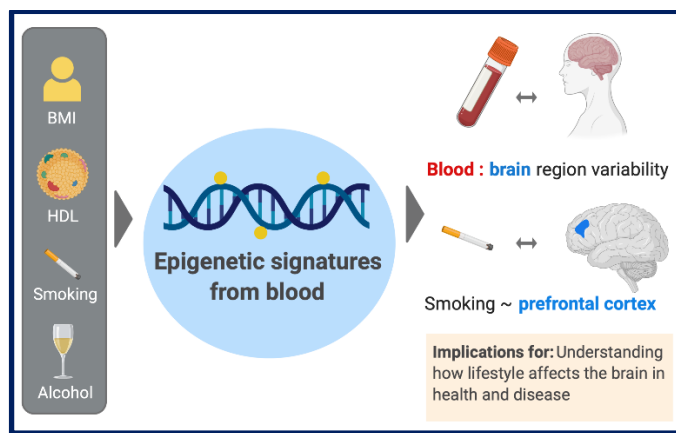


Adapted figure from Buchanan et al (2021) showing brain scans on the 1.5T and 3T scanners

DNA methylation signatures of lifestyle traits in the blood and brain

In a truly collaborative [paper](#) published recently in *Brain Communications*, PhD student Danni Gadd (from the Marioni research lab) worked with data

from the LBC brain tissue bank (collected by Prof Tara Spires-Jones) to report the stability of DNA methylation between blood and brain in 14 members of the LBC1936. DNA methylation describes chemical additions to DNA that help turn genes on and off; different lifestyle traits seem to be related to methylation at different genetic loci, allowing measurement of DNA methylation 'signatures' of lifestyle traits including smoking, alcohol consumption, BMI and cholesterol. In this pilot sample, they found that signatures were highly variable across the five brain regions studied, and the dorsolateral prefrontal cortex emerged as a region with the strongest relationships to smoking. These preliminary findings may help us better understand how lifestyle affects the brain.



Graphic showing findings from Gadd et al (2021)

Small vessel disease and cognitive test scores

Cerebral small vessel disease affects the small vessels that carry blood deep into the brain. With age and other risk factors such as high blood pressure, diabetes and smoking, these vessels can become dysfunctional, causing a range of physical and cognitive symptoms. Previously, slowed processing speed and poor executive function were thought to be the main cognitive symptoms of small vessel disease, but the extent of changes in other cognitive domains was largely unknown. In a [paper](#) recently published in *Neurobiology of Ageing*, PhD student Olivia Hamilton and colleagues tested associations between markers of small vessel disease seen on MRI scans and cognitive test scores in the LBC1936. Using data from Wave 2, the results of the study suggested that whereas small vessel disease might have a specific impact on processing speed, a greater brain burden of small vessel disease also associates with poorer verbal memory and visuospatial ability. These findings suggest that in clinical practice and research, all major domains of cognitive ability should be tested to capture the full extent of the cognitive impact of small vessel disease.

Assessing individual-level change in dementia research

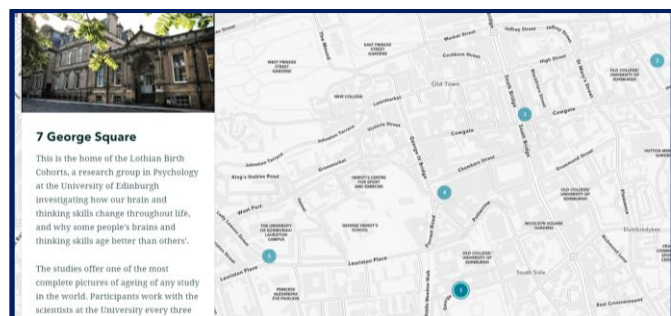
A major challenge in dementia research is determining when an individual has undergone meaningful change in symptoms and other relevant outcomes such as cognitive test performance. The challenge lies in differentiating genuine improvement or deterioration from change in scores due to random and systematic error. In this [paper](#) published in *Alzheimer's Research & Therapy*, Dr Aja Murray and colleagues review the challenges and the methodological approaches to estimating change across two points in time. They focused on the advantages of taking an Item Response Theory (IRT) approach, which emphasizes the fact that the tests we use are differentially reliable for people of differing levels of the symptom being studied, and provide an empirical example of the benefits of this approach using data from the LBC1936. Overall, they concluded that the way we estimate change over time matters for whether we classify an individual as having undergone meaningful change or not, and IRT methods provide a useful tool for estimation of reliable individual level change.



KE & Impact

'Secrets of healthy cognitive ageing': LBC walking tour at Edinburgh Science Festival

Edinburgh Science Festival is back, with a wide range of online and outdoor experiences to connect the public with science. The LBC1936 team have joined the programme with a walking tour around 7 George Square and the local neighbourhood, uncovering five key locations for the Lothian Birth Cohorts. Join us on our [self-led walk](#), which links to videos, podcasts, and images about the LBC studies, our history, people and findings, and to learn about the secrets of healthy cognitive ageing.



LBC walking tour map at Edinburgh Science Festival 2021

Sarah Harris presents LBC1936 findings at Genomics of Brain Disorders Conference

LBC geneticist Dr Sarah Harris presented a poster at the online Wellcome Genome Campus, Genomics of Brain Disorders Conference, in April. She presented early results from her study looking at 90 potential protein biomarkers of late-life cognitive function and cognitive decline in the LBC1936. Four proteins increased and six decreased in level between ages 73 and 79. Of the four proteins that increased between age 73 and 79, protein levels were associated with cognitive ability levels at a given time point, but not with the trajectory of cognitive decline across older age.

LBC1936 team shortlisted for CAHSS Recognition Award

Congratulations to the LBC1936 team, who were on a shortlist of 7 from 173 nominations for a College of Arts, Humanities and Social Sciences (CAHSS) 'Adaptation to Change' award. Their nomination recognised their exceptional hard work in spotting the contribution that could be made from implementing, and then publishing findings from, the LBC1936 COVID-19 Questionnaire. The nomination recognised how they '*acted quickly and decisively to identify and realise contributions to scientific understanding in unprecedented times*'. Even though they did not win, being recognised at college level for their hard work was a great achievement. Congratulations Adele, Danielle, Janie, Paul, Judy, Miles and Barbara!



Screenshot from virtual CAHSS Recognition Award ceremony

Alan Gow appears on BBC's 'Just One Thing'

In our March edition, we told you that our collaborator Dr Alan Gow had recorded a podcast for a BBC series. 'Just One Thing', hosted by Dr Michael Mosley on BBC Radio 4, focuses each week on everyday things people might consider to benefit their health and wellbeing. Alan discussed key LBC findings in an episode focussed on learning new things and the best ways to keep your brain active, which was broadcast in April. If you missed it, you can now listen to the podcast [online](#).

Unlock & Revive: events for the dementia community

During the COVID-19 pandemic, we have seen many events move online, but this has introduced new challenges, including how to deliver activities to those living with dementia. The LBC team have joined 'Unlock & Revive', a multi-disciplinary public engagement project, bringing together researchers, cultural providers and health care professionals seeking to explore what makes online events beneficial and effective for the dementia community. The project involved 27 online events from providers including the National Library of Scotland, Royal Botanic Garden and Historic Environment Scotland. The LBC team contributed by leading a series of online singing sessions, delivered in a collaboration between choir instructor and singer, Heather Macleod, and LBC researcher Dr Judy Okely, who is leading an ESRC funded project on Lifetime musical experience and healthy ageing in the LBC1936. Findings from the programme will inform training and future events, and social and cognitive benefits of events will be highlighted to the health and social care sector.



Simon Cox delivers Plenary Address at Society of Biological Psychiatry 2021 Annual Meeting

Study director Simon Cox was invited to deliver a plenary address at this global meeting, attended by more than 1,000 delegates, in which he centred on the contributions of the LBC studies to our understanding the nature and determinants of brain and cognitive ageing. Simon said, "it was an honour to deliver a plenary at this fantastic international meeting. I had fun bringing the story and findings of the LBC study to the conference, and the content was a perfect fit for the theme of 'Variability Across the Lifespan'". Simon presented some of the study's core findings, and just a few examples of the cutting-edge contributions LBC data will continue to make to understanding how and why some age more than others in their brain health and cognitive skills.



LBCs at the Longitudinal Studies virtual conference

Dr Judy Okely presented some of the team's recently published research from the LBC1936 COVID-19 Questionnaire at the Longitudinal Studies virtual conference. Compared with two years earlier, LBC1936 participants experienced slightly higher levels of social support and were less physically active during the first national lockdown.



Dr Judy Okely presents at the Longitudinal Studies conference

Judy said, "this was a really interesting context to present our findings, as many other longitudinal studies represented at the conference had also adapted in response to the pandemic. There were many interesting talks that highlighted the role of longitudinal studies in tackling the challenges presented by COVID-19". Visitors to Judy's 'virtual poster' were particularly interested to hear whether LBC1936 participants had experienced any changes in sleep quality or social support.



Genetic variation, brain, and intelligence differences: an update

In a previous edition, we summarised a [commentary](#) published in *Molecular Psychiatry* written by team members Professor Ian Deary, Dr Simon Cox and Dr David Hill, which aimed to review the last decade of research on the underlying origins of intelligence, including new contributions from studies of molecular genetics, brain imaging, and studies combining both. The paper is key in our mission at the Disconnected Mind project: to apply understanding of genes and brain to understand why cognitive differences happen with age. The paper, which drew heavily on LBC findings, has garnered significant attention in the scientific community, and in only 3 months it has been accessed over 10 thousand times, ranking 7th most accessed of all the articles of a similar age in the journal. Congrats, Ian, Simon and David!

Article metrics Last updated: Wed, 26 May 2021 8:49:19 Z		
Genetic variation, brain, and intelligence differences		
Access & Citations		
10k Article Accesses	1 Web of Science	3 CrossRef

Susana Muñoz Maniega presents LBC1936 brain imaging findings at ISMRM & SMRT exhibition

In May, LBC researcher Dr Susana Muñoz Maniega presented her research in the 'Brain in Healthy Elderly & Dementia' session at the International Society for Magnetic Resonance in Medicine and Society for MR Radiographers & Technologists annual meeting and exhibition. Her video presentation 'Automatic tract segmentation in the older brain', presented newly-derived data on brain white matter connections. Susana showed that, compared our existing methods in LBC, this new approach showed promise, though further work would be needed to further 'train' the method.

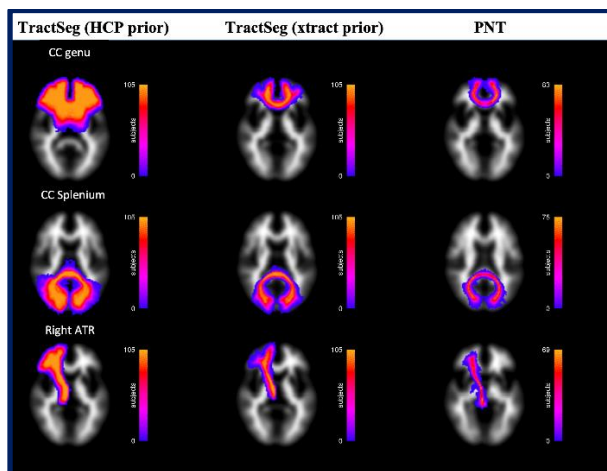


Image of maps of brain white matter tracts in the front and back of the corpus callosum, and anterior thalamic radiation, using two TractSeg options (a new approach) and our existing method Probabilistic Neighbourhood Tractography (PNT)

Ian Deary featured in British Neuroscience Association Bulletin

Professor Ian Deary was featured in the Spring Bulletin of the British Neuroscience Association, a publication circulated to over 2,000 BNA members. The article, with the fitting title 'Never too old', dedicates three pages to Ian and his contribution to the field of cognitive ageing. It describes his unorthodox journey to medical training and later academic career in the Department of Psychology at the University of Edinburgh, and the discovery of data that would change his life and form the foundation of cognitive epidemiology with the longest study of cognitive ageing in the world. In his interview, Ian doesn't fail to acknowledge the dedication of the participants and commitment of his team, the fantastic collaborators and expertise available on our doorsteps at the University of Edinburgh. The piece is a wonderful celebration of Ian's academic achievements, and also his contribution to experimental pop music, as he continues writing scientific papers and, in his words, much more challenging song lyrics.

Never too old

Supposedly now retired, **Ian Deary** is still making key contributions to the field of cognitive ageing – and to experimental pop music.

Some 35 years after securing his first lectureship position, **Ian Deary** formally retired in 2020. As befits someone who has long been a leader in the field of cognitive ageing, Ian is certainly not going gently into that good night, continuing to be actively involved in research.

His early days provided little clues to his future in academia. "Growing up I never knew anybody who went to university," he recalls. However, excelling in the Scottish qualifying exam, he found himself at a state grammar school, Hamilton Academy, and discovered an aptitude for and interest in the sciences and maths, which he planned to study for his highers (Scottish post-16 exams). "That turned out not to be possible due

"I WANTED TO TEST THIS IDEA THAT ONE OF THE THINGS THAT WAS CONTRIBUTING TO WHY SOME PEOPLE WERE SMARTER THAN OTHERS WAS THAT THEY HAD A BRAIN THAT WORKED THAT LITTLE BIT FASTER."

lives'. And it did."

"We discovered that Scotland had twice tested the nation's cognitive ability," Ian says. "On Monday June 1st, 1932, Scotland tested 87,498 children born in 1921 on exactly the same mental test, Murray House Test no. 12." Remarkably, the organisers managed to reach about 95% of eligible children. "Scotland at that moment was the only country

Alan Gow at CABHI Summit 2021

Collaborator Alan Gow was invited to join a panel at the Centre for Aging and Brain Health Innovation (CABHI) Summit 2021, held online in March, where he drew on key LBC findings about social support. There were more than 800 attendees from 10 countries. Alan was involved in the panel "We Are Social Animals: Why Your Brain Needs Connection", where he discussed the potential benefits of social relationships, contacts and networks for brain health across the life course, and specifically with respect to ageing.

We are Social Animals:
Why Your Brain Needs Connection

SHUSMITA RASHID
Senior Manager,
Knowledge Mobilization, CABHI
+ Associate Director,
Scientific and Academic Affairs,
Roeman Research Institute

RENEE LEVENTHAL
Seniors Advisory
Panel Member, CABHI

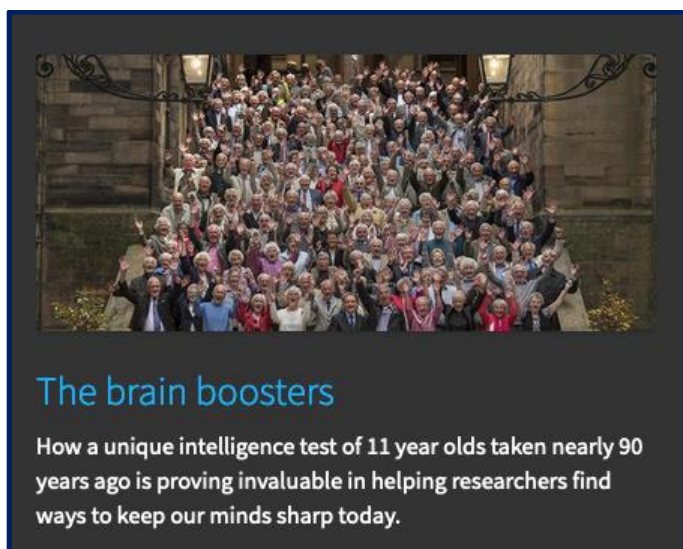
PAUL YOUNG
Acting Administrator,
Princes County Hospital

DR. ERIC S. KIM
Assistant Professor,
University of British Columbia

ALAN GOW
Professor in Psychology,
Heriot-Watt University

University of Edinburgh Impact article features LBCs

The Lothian Birth Cohorts have been prominently featured on the University of Edinburgh webpages in an [article](#), 'The Brain Boosters', highlighting the study's invaluable contribution to the field of cognitive ageing, and in finding ways to keep our minds sharp into old age. The article contributes to Edinburgh Impact, an online magazine about how the University community is making its mark upon the world through its research, innovation, ideas and actions.



Simon Cox delivers talk to U3A Cockermouth on brain and cognitive ageing

Simon had a lively afternoon with 60+ members of the Cockermouth University of the 3rd Age (U3A), in May. He discussed "Brain and Cognitive Ageing in The Lothian Birth Cohort 1936: From Ages 11 to 70 and Beyond". The talk covered lots of ground, and was punctuated with many taxing and insightful questions from the group, meaning it went well over the allotted hour mark. Simon said, *"I've had the pleasure of talking to the Cockermouth Café Scientifique in the past, many of whom are also U3A members, and this talk didn't disappoint! They are a fantastic bunch, and it was as fun and engaging as I'd expected. I had a warm welcome, and the topics that came up in response to the talk were wide-ranging and often technical which made for a really stimulating discussion."*



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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Website

Stay up to date with the most recent Disconnected Mind events and publications at:

www.ed.ac.uk/lothian-birth-cohorts

Twitter: [@EdinUniLBC](https://twitter.com/EdinUniLBC)



THE UNIVERSITY of EDINBURGH



Some new publications

Accepted/In press

Taylor, A. M., Page, D., Okely, J. A., Corley, J., Welstead, M., Skarabela, B., Redmond, P., Russ, T. C., & Cox, S. R. (2021). Impact of COVID-19 lockdown on psychosocial factors, health, and lifestyle in Scottish octogenarians: The Lothian Birth Cohort 1936 Study. *PLoS ONE*.

Epub before print

Buchanan, C. R., Muñoz Maniega, S., Valdés Hernández, M. C., Ballerini, L., Barclay, G., Taylor, A. M., Russ, T. C., Tucker-Drob, E. M., Wardlaw, J. M., Deary, I. J., Bastin, M. E., & Cox, S. R. (2021). Comparison of structural MRI brain measures between 1.5 and 3 T: Data from the Lothian Birth Cohort 1936. *Human Brain Mapping*, hbm.25473. <https://doi.org/10.1002/hbm.25473>

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Altschul, D., Iveson, M., & Deary, I. J. (2021). Generational differences in loneliness and its psychological and sociodemographic predictors: An exploratory and confirmatory machine learning study. *Psychological Medicine*, 1–10. <https://doi.org/10.1017/S0033291719003933>

Deary, I. J., Hill, W. D., & Gale, C. R. (2021). Intelligence, health and death. *Nature Human Behaviour*, 5(4), 416–430. <https://doi.org/10.1038/s41562-021-01078-9>

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