#### The Disconnected Mind Newsletter





The School of Philosophy, Psychology & Language Sciences Department of Psychology Edinburgh Futures Institute

#### Newsletter 71: Autumn 2025

Welcome to the 71st edition of the Disconnected Mind Newsletter. Catch up on the latest updates from the Lothian Birth Cohorts team, including new research publications, recent scientific events, and highlights from our public engagement, knowledge exchange, and impact activities.

# **Updates**Lothian Birth Cohorts settle into new home at EFI

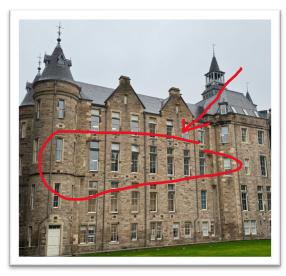


After months of preparation, the Lothian Birth Cohorts team has moved into our new home at the Edinburgh Futures Institute. Since August, we've been enjoying the open office space in this beautifully restored historic building, meeting new colleagues on the ward, and joining EFI-wide welcome events. Professor Simon Cox said: "It's heartening to see the team taking so enthusiastically to our new environment, and I'm very grateful to both PPLS Professional Services teams and EFI staff for helping to make this transition as smooth as possible. It's also been excellent to already welcome collaborators from Psychology and across the University, and industry partners, to meet and work in this flagship hub. We are

looking forward to LBC1936 Wave 8 next year, and to the opportunities beyond, with refreshed optimism."

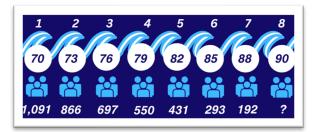
In September, Simon introduced our team and research at the EFI Research Showcase. The event provided a chance to share the LBCs' findings, future plans, and the funding that supports our work. We also heard from Sian Bayne (Centre for Digital Education), Emily Shipp (EFI Associate), and Emily Sullivan (Centre for Technomoral Futures), offering a glimpse into the breadth of research across the Institute. The showcase highlighted opportunities for collaboration with other centres and marked the beginning of a regular series of talks, held on the last Wednesday of each month.

We look forward to meeting more of our EFI colleagues—and to welcoming collaborators and visitors to the ward, as part of EFI's commitment to open, shared working practices.



The LBC team's new home in EFI

### Update on cognitive testing: Preparation for Wave 8



The team has been busy with data entry from Wave 7, carefully preparing these valuable datasets for future research. Once processed, the data will extend the scope of the longitudinal LBC1936 study to over 20 years, providing detailed insights into participants' cognitive abilities, brain health, medical history, and other health-related factors. Meanwhile, preparations are underway for Wave 8 of fieldwork, scheduled to begin in the new year. The testing team is looking forward to welcoming back LBC1936 participants as they reach the milestone of their 90th birthdays—a remarkable stage in this ongoing longitudinal study. We sincerely thank all participants for their continued commitment, which makes this work possible.

#### **Staff News**

#### Dr Ines Mesa-Eguiagaray joins the LBC team



We're delighted to welcome a new member to the team: Dr. Ines Mesa-Eguiagaray, a postdoctoral researcher with expertise in statistical genetics.

At the Usher Institute, Ines contributed to population-based studies that integrated genetic, epigenetic, and lifestyle data to explore molecular and environmental mechanisms underlying breast and colorectal cancer. As part of the LBC group, she will be working with Dr. Sarah Harris on longitudinal proteomic analyses of cognitive and brain changes prior to an Alzheimer's disease diagnosis. Ines said: "I am excited to join and learn from such a collaborative team, and to contribute to identifying proteins that could become diagnostic and treatment targets for Alzheimer's disease, ultimately improving patients' outcomes and quality of life." We're thrilled to have you with us – welcome aboard, Ines!

#### Wishing a happy retirement to David Liewald

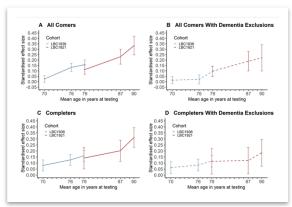


We'd like to extend our heartfelt thanks and warmest wishes to David Liewald — Dave, as he's the known to team - who has retired after more

than two decades of dedicated service to the Lothian Birth Cohorts. Since joining the team in 2004, Dave has been an invaluable member of the core support group, providing expert computational support across a wide range of projects. His contributions have included everything from setting up and maintaining our computer systems, to developing software that supports genetic studies, brain imaging datasets, and even our popular Augmented Reality Glasses that illustrate brain ageing for the public. Dave's technical expertise, dedication, and good humour have been a cornerstone of our work. He has supported the team with generosity and skill, and his presence will be deeply missed. We wish Dave a retirement filled with fun, relaxation, and adventure — and we thank him for everything he's brought to the LBC team. Thank you, Dave!

#### Scientific Highlights

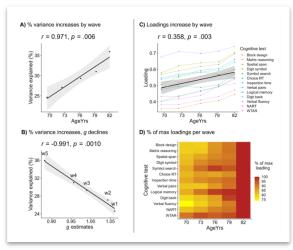
## Tracking the impact of *APOE* e4 on thinking skills over time



This study used long-term data from the Lothian Birth Cohorts of 1921 and 1936 to explore how a genetic variant—APOE e4 affects cognitive ability across the lifespan. APOE e4 is known to increase the risk of agerelated cognitive decline and dementia, but its influence at different ages has been less clear. Researchers analysed scores from the Moray House Test, taken by participants at ages 11, 70, 76, 79, 87, and 90. They found that APOE e4 had little to no effect on thinking skills in childhood to early older age. However, its impact grew steadily with age, becoming more pronounced by age 90. The effect remained even after accounting for health conditions like stroke or diabetes. But when participants who later developed dementia were excluded, the influence of APOE e4 was weaker and often not statistically significant. These findings suggest that APOE e4 may make the brain more vulnerable to cognitive decline later in life, especially in the context of dementia. The LBC data provided a rare opportunity to track this genetic influence over nearly eight decades, helping researchers understand how genetic risk unfolds over time.

Deary, I. J., et al. (2025). Effect sizes of *APOE* e4 on the same general cognitive ability test taken by the same people from age 11 to age 90: The Lothian Birth Cohorts 1921 and 1936. *Molecular Psychiatry*.

#### Cognitive dedifferentiation in later life: Longitudinal findings from the Lothian Birth Cohort 1936

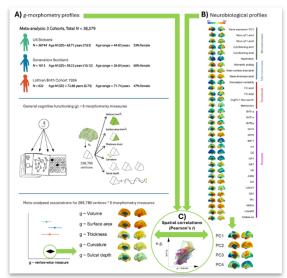


We know that cognitive test scores tend to be positively correlated in that people who perform well on one test usually perform well on others. But does this interrelation between cognitive abilities change as we age? In a recent study led by Dr Joanna Moodie, data from the Lothian Birth Cohort 1936 were analysed across five waves of testing, from age 70 to 82. The team examined how correlations among different cognitive domains changed over time. The results showed that as people got older, their fluid cognitive abilities (such as memory, processing speed, and visuospatial skills) became more strongly interrelated, a process known as cognitive dedifferentiation. In other words, performance on one type of cognitive test increasingly predicted performance on others. This pattern closely overall cognitive decline, individual participants also showed reduced variability across tests with advancing age. A hierarchical model revealed that while fluid abilities converged, the crystallised domain became less central to the overall structure of general cognitive functioning ("g") over time. These findings suggest that g's composition changes with age, highlighting an important consideration for researchers cognitive function longitudinally. longitudinal research will be important in incremental clarifying the validity,

determinants, mechanisms, and implications of cognitive differentiation and dedifferentiation across the lifespan.

Moodie, J. E., et al. (2025a). Cognitive dedifferentiation in later life: Longitudinal findings from the Lothian Birth Cohort 1936. *The Journals of Gerontology: Series B*.

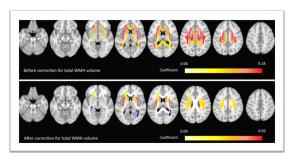
# Brain maps of general cognitive functioning: neuroimaging and neurobiological signatures



How general cognitive functioning ("g") relates to measures of brain structure varies across the cortex, and so do many biological features of the brain, such as gene expression, cytoarchitecture, neurotransmitter receptor densities, and metabolism. In a recent study, Dr Joanna Moodie and colleagues examined these relationships across nearly 40,000 participants from three cohorts, the Lothian Birth Cohort 1936, Generation Scotland, and UK Biobank, analysing vertex-wise measures from over 300,000 regions across the cortical surface. The regional patterns of gbrain associations were highly consistent across the three cohorts. To understand what biological properties might underlie these the team calculated patterns, spatial correlations between the g-brain maps and 33 cortical describing different maps neurobiological properties. These 33 maps covaried along four major biological dimensions of cortical organisation, which together explained most of the variation across measures (66.1%). By examining the spatial relationships between the *g*-brain maps and these dimensions, the study points to key neurobiological features that underpin cognition-brain associations.

Moodie, J. E., et al. (2025b). Brain maps of general cognitive functioning: Neuroimaging and neurobiological signatures. *Translational Psychiatry*.

### Mapping White Matter Changes Linked to Vascular Risk



This international study, coordinated by the Meta VCI Map Consortium, explored how common vascular risk factors—like hypertension, smoking, and diabetes—relate to changes in the brain's white matter. These known as white changes, hyperintensities (WMHs), are often seen in older adults and can be linked to cognitive decline. Researchers pooled MRI and health data from over 15,000 participants across 16 population-based studies, including the Lothian Birth Cohorts. LBC data contributed valuable insights from community-dwelling older adults, helping to strengthen the study's findings across a wide age range. The team examined WMH volume in 50 brain regions and its association with six vascular risk factors. They found that hypertension, smoking, diabetes, and a history of vascular disease were linked to higher overall WMH volume. Importantly, hypertension showed a distinct regional pattern, affecting ten specific white matter areas. Other risk factors were

associated with more general increases in WMH, without clear regional signatures. These findings suggest that hypertension may lead to targeted white matter changes, while other risk factors contribute to broader effects. The study highlights the value of large-scale collaboration and shared data—like that from LBC—in understanding how vascular health shapes the ageing brain.

Biesbroek, J. M., et al. (2025). Signature white matter hyperintensity locations associated with vascular risk factors derived from 15 653 individuals. *Stroke*.

# Knowledge Exchange, Public Engagement & Impact

### LBC Data Helps Inform NHS Clinical Guidance



Data from Lothian
Birth Cohort
participants has long
been used to
advance scientific
understanding of
ageing. In addition, it
is being used to

inform clinical guidelines and healthcare practice — demonstrating the value of longitudinal research beyond academia. A recent example comes from NHS Lothian, where Dr Sara Jenks, Consultant in Chemical Pathology and Metabolic Medicine and Clinical Lead for Biochemistry, drew on LBC data to support revisions to internal guidance on hyponatraemia. In discussions around updating sodium (Na) reference ranges for older adults, the LBC dataset provided robust evidence from over 1,000 individuals aged 70 and above who were generally well and not acutely unwell. This offered a rare opportunity to evaluate sodium levels in a healthy ageing population. Analysis of their blood samples suggested that the existing lower limit of 135 mmol/L may not be appropriate for this age group. Findings supported a revised lower

threshold of 132–133 mmol/L, leading to the development of age-adjusted sodium reference ranges. These updated ranges allow for more clinically relevant interpretation of sodium levels in older adults and reflect how cohort data can directly inform healthcare decisions. Ongoing work with Dr Jenks and the NHS Lothian working group will seek other LBC biomarkers to inform clinical cutoffs.

#### Exploring Ageing Across Species: Austėja Čiulkinytė's Research on Brain and Vascular Changes



Mouse models are a cornerstone of biomedical research, but how closely do they mirror human biology—especially in the context of ageing? Austėja Čiulkinytė, a final-year PhD student in Translational Neuroscience, is investigating this question by comparing agerelated molecular changes in the brains and brain vasculature of mice and humans. Her preliminary findings suggest that while overall brain ageing shows notable similarities between the two species, the ageing of the brain's blood vessels may follow more divergent paths. This distinction is crucial for understanding which aspects of mouse-based research can reliably inform human health interventions—and which may require more nuanced interpretation. Earlier in October, Austėja presented her work at the 2nd Barcelona Blood-Brain Barrier Conference, a highly specialised meeting that brought together leading experts in brain vascular research. Her talk sparked thoughtful discussion and drew insightful questions from attendees. Although the research is still

ongoing, we look forward to sharing further developments as the project progresses.

### Second Year of Healthy Brains at Boroughmuir High School



Boroughmuir High School Students at Simon's talk on neuroscience at EFI

The second year of the S5 Healthy Brains programme at Boroughmuir High School is well underway. We've now completed the first phase, where students heard from an inspiring line-up researchers and clinicians connected to the Lothian Birth Cohorts and beyond. The talks spanned a wide range of themes—from cognitive ageing and long-term testing to genetics, mental health, and clinical care. Ian Deary set the scene with the history and key findings of cognitive ageing research, followed by Sabela Mendez, who described the cognitive tests participants have completed over the past 20 years. Sarah Harris highlighted how genes and proteins influence brain health, while Matthew Iveson examined mental health across the lifecourse. Catriona Nieven then offered a clinical perspective, sharing her experiences as a doctor on a geriatric ward. The programme also included a visit to the Edinburgh Futures Institute, where Simon Cox, LBC study director, gave an inspiring talk on neuroscience. Building on these insights, the students will now turn their attention to creating science communication materials based on what they've learned. These will include activities designed for younger pupils, with a small group preparing to join our team in local primary schools next spring. We're

delighted to be working with a group of S6 volunteers and our PhD volunteers, who will support this next phase and collaborate with the S5 class. We're looking forward to seeing what the students create—and how they bring brain health research to life for new audiences.

#### Doors Open Day at Edinburgh Futures Institute



The LBC team at Doors Open Day at EFI (Photo credit: Chris Scott)

On Saturday 27 September, the Lothian Birth Cohorts team took part in Doors Open Day at the Edinburgh Futures Institute (EFI), hosting a lively and engaging stall on brain and cognitive ageing. The event attracted around 1,500 visitors from a wide range of backgroundsincluding families with children of different ages, local residents, guests from across Scotland, and international visitors—all keen to learn more about the study and its findings. Throughout the day, Professor Simon Cox, Dr Gail Davies, and Dr Barbora Skarabela shared insights and answered questions, supported by PhD students Rita Dargham and Austeja Čiulkinytė, who were outstanding communicating complex science with clarity and warmth. Volunteers from Boroughmuir High School—Eve, Mia, and Nicky—also played a key role, continuing their involvement through our Healthy Brains programme. Visitors explored 3D-printed brains, tested Augmented Reality glasses, and engaged in conversations about ageing and brain health. Several attendees had personal connections to the study, including offsprings and relatives of the LBC participants as well as one of the participants! The event was also a valuable opportunity to connect with our EFI colleagues. Special thanks to Dr Sandra Mackenzie, the EFI Public Engagement Officer, for her outstanding organisation, hospitality, and steady supply of coffee, tea, and biscuits. We're already looking forward to future collaborations and events.

### Dr Janie Corley's Expert Commentary in RHS Call for Gardens in New Housing



Our team's expertise was recently highlighted when Dr Janie Corley was

invited to provide an expert comment for Environmental Health News, the magazine of the Chartered Institute of Environmental Health. The request followed the Royal Horticultural Society's (RHS) landmark State of Gardening report, which for the first time used Al mapping to assess cultivated green space across the UK. The study revealed both the scale and disparity of access to gardens: while 41% of London's land is categorised as garden, the figure drops to 19% in Leeds, 25% in Edinburgh, and 27% in Cardiff. To maximise the benefits of cultivated green space, the RHS is calling on government to guarantee "Space to Grow" in all new housing developments, ensuring every household has access to a garden. Commenting on the findings, Dr Corley said: "The RHS report highlights just how valuable gardens are – not only for the environment but also for our health. Our research shows that people who spend more time in their gardens, and who garden frequently, tend to have better cognitive, physical and emotional health in later life. Gardens also help buffer the effects of heat, flooding and pollution, supporting both environmental and public health. Yet, access is not equal: many people, particularly in urban areas, lack any garden space. As we build new homes, gardens – private, shared, or community - should be treated as essential infrastructure, not a luxury." This recognition

underscores the relevance of the LBC research in shaping national debates on environmental and public health.

## Standing Up for Science: VoYS workshop



On 10 October, Dr Barbora Skarabela joined a panel of academics at the Standing Up for Science: Voice of Young Science workshop held at the University of Edinburgh. Organised by Sense about Science—an independent charity that promotes the public interest in sound science and evidence - the workshop was part of the Voice of Young Science (VoYS) programme, a European network of early career researchers working to strengthen public conversations about science and evidence. Speaking to around 40 early career researchers, the panel shared practical insights into science communication. Barbora contributed by drawing on her experience with the Lothian Birth Cohorts team, highlighting prior media engagement and school outreach as well as public-facing events like Doors Open Day. The panel explored both the challenges and opportunities of communicating complex, evidence-based ideas to broader audiences. The discussion was open and reflective, with attendees considering the value of public engagement, how it's recognised within institutions, and how to balance it alongside other responsibilities. Participant feedback shared by programme lead Katherine Brown highlighted the workshop's impact, with many expressing interest in further training and opportunities to connect their research with wider audiences. Reflecting on the event, Barbora said: "I was delighted to contribute as a panellist at the Sense about Science workshop. The charity's commitment to

promoting evidence-based science and public debate is vital, and it was inspiring to see early career researchers not only valuing public engagement but actively seeking to integrate it into their future careers."

#### **Publications**

Bernabeu, E., et al. (2025). Blood-based epigenome-wide association study and prediction of alcohol consumption. *Clinical Epigenetics*, 17(1), 14. https://doi.org/10.1186/s13148-025-01818-y

Biesbroek, J. M., et al. (2025). Signature white matter hyperintensity locations associated with vascular risk factors derived from 15 653 individuals.

Stroke.

https://doi.org/10.1161/STROKEAHA.125.051 159

Chamberlain, J. D., et al. (2025). Development and validation of an epigenetic signature of allostatic load. *Bioscience Reports*. https://doi.org/10.1042/BSR20241663

Chybowska, A. D., et al. (2025). A blood- and brain-based EWAS of smoking. *Nature Communications*.

https://doi.org/10.1101/2024.05.21.24307663

Conole, E. L. S., et al. (2025). Epigenetic clocks and DNA methylation biomarkers of brain health and disease. *Nature Reviews Neurology*. https://doi.org/10.1038/s41582-025-01105-7

Corley, J., et al. (2025). Dietary exposures and risk of anxiety and depression symptoms in the Lothian Birth Cohort 1936: A cohort-level GLAD Project analysis. *Wellcome Open Research*. https://doi.org/10.12688/wellcomeopenres.2 4950.1

Davyson, E., et al. (2025). Insights from a methylome-wide association study of antidepressant exposure. *Nature Communications*, 16(1), 1908. https://doi.org/10.1038/s41467-024-55356-x

Deary, I. J., et al. (2025). Effect sizes of *APOE* e4 on the same general cognitive ability test taken

by the same people from age 11 to age 90: The Lothian Birth Cohorts 1921 and 1936.

Molecular Psychiatry.

https://doi.org/10.1038/s41380-025-03274-9

de Kort, F. A. S., et al. (2025). Cerebral white matter hyperintensity volumes: Normative age-and sex-specific values from 15 population-based cohorts comprising 14,876 individuals. *Neurobiology of Aging*, 146, 38–47. https://doi.org/10.1016/j.neurobiolaging.2024.11.006

Foote, I. F., et al. (2025). Uncovering the multivariate genetic architecture of frailty with genomic structural equation modeling. *Nature Genetics*. <a href="https://doi.org/10.1038/s41588-025-02269-0">https://doi.org/10.1038/s41588-025-02269-0</a>

Fürtjes, A. E., et al. (2025). Measurement characteristics and genome-wide correlates of lifetime brain atrophy estimated from a single MRI. *Nature Communications*. https://doi.org/10.1038/s41467-025-61978-6

Hill, W. D., & Deary, I. J. (2025). Shared genetic etiology between childhood cognitive function and longevity. *Genomic Psychiatry*, 1(5), 36–37. https://doi.org/10.61373/gp025l.0098

Jutila, O.-E. I., et al. (2025). Life-course exposure to air pollution and the risk of dementia in the Lothian Birth Cohort 1936. *Environmental Epidemiology*, 9(1), e355. https://doi.org/10.1097/EE9.000000000000355

Malkowski, O. S., et al. (2025). Correlates and determinants of physical activity among older adults of lower versus higher socio-economic status: A systematic review and meta-analysis. International Journal of Behavioral Nutrition and Physical Activity. https://doi.org/10.1186/s12966-025-01775-y

Moodie, J. E., et al. (2025a). Cognitive dedifferentiation in later life: Longitudinal findings from the Lothian Birth Cohort 1936. *The Journals of Gerontology: Series B.* https://doi.org/10.1093/geronb/gbaf189

Moodie, J. E., et al. (2025b). Brain maps of general cognitive functioning: Neuroimaging and neurobiological signatures. *Translational Psychiatry*. <a href="https://doi.org/10.1038/s41398-025-03617-8">https://doi.org/10.1038/s41398-025-03617-8</a>

Nagarajan, P., et al. (2025). A large-scale genome-wide study of gene-sleep duration interactions for blood pressure in 811,405 individuals from diverse populations.

Molecular Psychiatry. https://doi.org/10.1038/s41380-025-02954-w

Park, W., et al. (2025). Al-based deformable hippocampal mesh reflects hippocampal morphological characteristics in relation to cognition in healthy older adults. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2025.12 1145

Perez-Correa, J.-F., et al. (2025). Weighted 2D-kernel density estimations provide a new probabilistic measure for epigenetic age. *Genome Biology*. https://doi.org/10.1186/s13059-025-03562-1

Shen, X., et al. (2025). A methylome-wide association study of major depression with ut-of-sample case-control classification and trans-ancestry comparison. *Epidemiology*. https://doi.org/10.1101/2023.10.27.23297630

Smikle, R., et al. (2025). Parental report of language, attention and executive functions at two years: Correlational structure of measures and applications to prematurity. *Wellcome Open Research*, 10, 317. https://doi.org/10.12688/wellcomeopenres.2 4065.1

Smith, H. M., et al. (2025). DNA methylation-based predictors of metabolic traits in Scottish and Singaporean cohorts. *The American Journal of Human Genetics*, *112*(1), 106–115. https://doi.org/10.1016/j.ajhg.2024.11.012

Xia, C., et al. (2025). Deciphering the influence of socioeconomic status on brain structure: Insights from Mendelian randomization.

Molecular Psychiatry. https://doi.org/10.1038/s41380-025-03047-4

Yeung, H. W., et al. (2025). Relative strength variability measures for brain structural connectomes and their relationship with cognitive functioning. *Human Brain Mapping*, 46(11), e70314.

https://doi.org/10.1002/hbm.70314

#### Contact

You can contact the LBC team by email and keep up with our latest news on our website. Email lbc1936@ed.ac.uk to reach the LBC1936 cognitive testing team, or lbc.ke@ed.ac.uk for knowledge exchange, public engagement, media inquiries, and policy.

https://lothian-birth-cohorts.ed.ac.uk/

If you no longer wish to receive our newsletter, please email us to <a href="mailto:lbc.ke@ed.ac.uk">lbc.ke@ed.ac.uk</a> to let us know.









