

# 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 62: June 2023

Welcome to the Summer edition of the Disconnected Mind Newsletter! Each issue brings news about the Lothian Birth Cohorts team, our latest research and publications, and scientific and public engagement events.

## LBC reunion 2023

On Saturday the 13<sup>th</sup> of May we celebrated the successful completion of the sixth wave of LBC1936 data collection with a Reunion, bringing together the LBC participants, research team and collaborators in the beautiful space of the National Museum of Scotland! It was an important opportunity to celebrate participants' dedication and commitment to the study, and for them to catch up with friends and staff over coffee and cakes. The team were delighted to tell them how we have been using their data to make important scientific contributions. The study director, Dr Simon Cox, opened the event with a review of the LBCs' past, present, and future contributions to healthy ageing, expressing deep gratitude to the participants and everyone involved in the study. Dr Tom Russ, Lothian Birth Cohorts Health and Medical Lead, then outlined the recently-completed clinical dementia ascertainment which will offer important new data to model both healthy and dementia-related cognitive ageing. Quick fire talks included Highlights from the Team (Ms Danielle Page and Dr Barbora Skarabela) on cognitive testing and Knowledge Exchange and Impact, insights from the LBC brain tissue bank (Professor Tara Spires-Jones and Dr Declan King); exciting new updates about musical experience and cognitive ageing (Dr Judy Okely); and contributions for the LBCs to help understand blood cancer thanks to the valuable longitudinal blood samples (Dr Kristina Kirschner). A reunion would not be complete without a word from the Founding Director, Professor Ian Deary, who delivered a poignant address, reflecting on various changes that have taken place over the years.

The reunion closed with heartfelt thanks to everyone attending the event from the LBCs director, Dr Simon Cox. Simon said: *"These events are a fantastic chance to engage with the participants; to tell them how we have been holding up our end of the bargain, and also to ask them what they think (the LBC brain tissue bank is testament to their good ideas). The team did a super job of putting on such a fantastic day, and I have been delighted to hear the positive feedback from participants. I also took the opportunity to remind them that we are funded for LBC1936 Wave 7, and that we were all looking forward to seeing them in 2024!"*



## Wave 7 of LBC1936 data collection

With the reunion over, the testing team, barely pausing to take a deep breath, is already preparing for Wave 7 of the LBC1936 study! The team has started getting ready for the next phase of data collection, with the first participants anticipated to come back in February 2024. Watch this space!

## Team Updates



The LBC team in front of McEwan Hall (May 2023)

The last three months have been busy with important staff updates, including those who have left the team and welcoming new colleagues and visitors, and drawing attention to the team's many achievements.

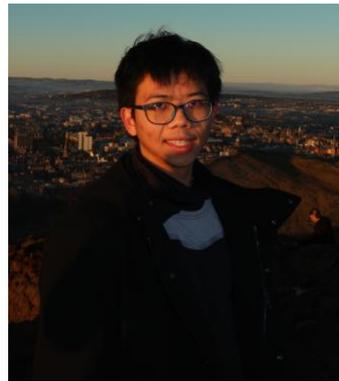
### **Congratulations and welcome to the team, Dr Anna Fürtjes!**



We are delighted to welcome Dr Anna Fürtjes who has recently passed her PhD viva at King's College London! Anna joins the team as Research Associate in Statistical Genetics and will be working on a project aiming to better

understand genetic factors that influence adult cognitive decline and may lead to age-related diseases such as dementia. The project is funded by the NIH and has been set up with our collaborating teams in Colorado and Austin. Anna is also interested in the brain and is hoping to apply genetic analysis methods to further understand brain atrophy and other biological factors involved in ageing. Because the LBC collected a wealth of genetic data and repeated brain scans, it will be instrumental in her work exploring cognitive decline and neurodegeneration. Welcome, Anna!

### **Congratulations, Dr Hon Wah Yeung!**



Dr Hon Wah Yeung completed his PhD in Psychiatry with a thesis on Data Science for Mental Health in December 2022. His thesis focused on applying machine learning and deep learning techniques on neuroimaging data for

depression classification and severity prediction. He joined the Lothian Birth Cohorts as Research Associate to work on a short project on novel graph measures for structural connectome and incremental prediction of cognitive abilities. He has now secured a job with the Royal Observatory and the Department of Astronomy at the University of Edinburgh, which is testament to his broad statistical and computing skills and we are hoping to continue collaborations with him in future. Congratulations, Hon Wah!

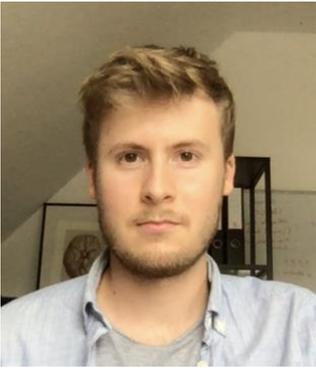
### **Thank you, Beth Jones!**



Beth Jones joined the LBC last July as Research Assistant to support the testing team during a challenging testing wave. Beth embraced her role and quickly became an invaluable part of the team, with her kind and caring

approach. Her role extended beyond data collection and processing, and she was instrumental in providing input and support for many other activities around the office and the study, including helping with school workshops and the reunion! We are sad to see Beth go but the good news is that she is not going far and will continue visiting the LBC as she finishes her MSc degree with the study Director, Dr Simon Cox! Beth said: *"I have really loved my time at LBC, it has been wonderful meeting new people, getting to know the cohort and I have gained so much experience from the opportunity. Though I am sad to leave, I am excited for new opportunities and to continue to work on my MSc dissertation with the LBC."*

## Lukas Duffner visiting from Maastricht



For the last two months, the LBC team has been joined by Lukas Duffner from the School for Mental Health and Neuroscience at Maastricht University in the Netherlands. Lukas has been working on LBC data to understand

associations between lifespan activity and late-life cognitive trajectories and dementia. His overall research examines whether people who engaged in more socio-intellectual activities at age 18, 40, 60 and 70 can better maintain their thinking skills as compared to people who were less active. This LBC-based study is conducted in collaboration with Heriot-Watt University and the [Alzheimer Centrum Limburg](#). Lukas said: *“The Lothian Birth Cohorts contain a wealth of information about experiences throughout the life-course. Examining how people differ with regard to those experiences may be valuable for explaining why some people age better than others. It has been a privilege and an incredible learning experience to spend the last two months with the LBC team, but also to have the opportunity to meet with the participants at the study's reunion! I will take all those impressions with me to Maastricht and hope to visit again soon.”*

## Dr Gail Davies promoted



In May we celebrated Dr Gail Davies' promotion to the post of Senior Research Fellow. Gail joined the LBC team in 2009 as Statistical Geneticist and has contributed to over 70 scientific papers using LBC data. She has participated in many large international

collaborations and contributed to studies published in top scientific journals like Science and Nature. Her work has been, to date, cited in 29 policy documents, including the UK Government, the Centers for Disease Control and Prevention (USA), National Bureau of Economic Research (USA), and National Institute for Health and Care Excellence (USA). You can view Gail's impressive list of publications on [her research profile](#). Congratulations, Gail!

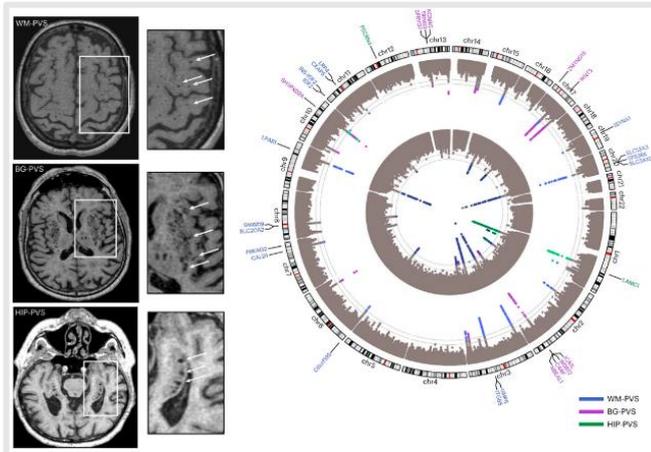
## Eleanor Conole completes her PhD and joins the team as Research Associate



Eleanor Conole, a Wellcome Trust-funded PhD student in Translational Neuroscience, has recently submitted her thesis, with her viva scheduled for later this June. Her research, conducted across multiple cohorts including the Lothian Birth Cohort 1936 (LBC1936), focused on exploring the impact of chronic inflammation on brain structure and function across the life course. Unlike acute inflammation, which aids in healing, chronic inflammation poses long-term risks to cellular health and has previously been implicated in accelerated cognitive decline. However, accurately measuring this persistent but subtle inflammation at the population level presents challenges due to the daily fluctuations of inflammatory proteins in the blood. Eleanor's PhD research (now published in [Neurology](#) and [Brain Behavior and Immunity](#)) demonstrated that DNA methylation (DNAm) levels of these proteins may offer an augmented means to study the relationship between chronic inflammation and brain ageing, with inflammatory-DNAm signatures (obtained from both blood and saliva) showing stronger associations with cognitive ability and brain structure than traditional inflammatory measures. With her forthcoming role as a Postdoctoral Research Associate in the Lothian Birth Cohorts, Eleanor will further investigate the neurobiology of age-related cognitive change, analysing structural and diffusion MRI data from LBC1936 and UK Biobank. This research, funded by the US National Institutes of Health (NIH), contributes to broader efforts in understanding the human structural connectome and its impact on cognitive ageing. Congratulations on your fantastic achievements, Eleanor!

## Scientific Highlights

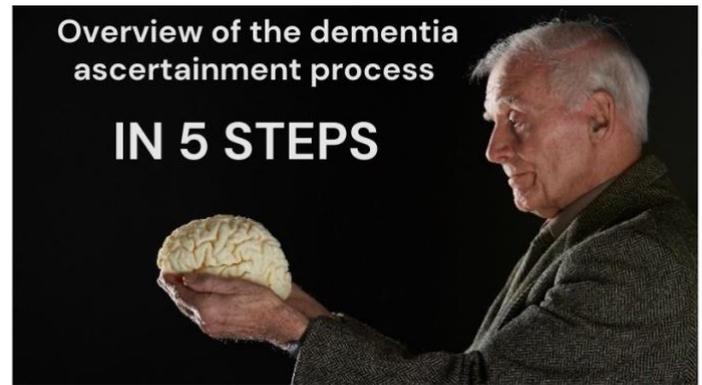
### LBC data used to understand genetic risk loci for perivascular space burden



Perivascular spaces (PVS) burden is an emerging brain imaging marker of cerebral small vessel disease, a leading cause of stroke and dementia. Perivascular spaces are physiological spaces surrounding small vessel walls, and high PVS burden – greater volume or number of such spaces – is thought to reflect impairment of brain fluid and waste clearance. The condition is highly heritable, but its genetic underpinnings were unknown so far. The LBC contributed to the first genomic study, now published in the journal *Nature Medicine*, that investigated the biology underlying PVS. The study, with investigators from 12 countries around the world, was based on DNA samples of more than 40,000 participants of European, Hispanic, East-Asian, African-American ancestry. The researchers identified differential patterns of shared genetic variation with blood pressure and neurological traits according to PVS location, pointing to pathways that were not mediated by established risk factors, involving extra-cellular matrix, blood-brain barrier, membrane transport, and vascular development. The first author of the study, Dr Marie-Gabrielle Duperron of the University of Bordeaux, Inserm, and Bordeaux University Hospital said: “*These findings provide new insight into the biology of PVS across the adult lifespan and its contribution to the pathophysiology of cerebral small vessel disease, a major cause of stroke and dementia worldwide, with potential for genetically informed prioritization of drug targets for prevention trials.*”

[Duperron, M. et al. \(2023\). Genomics of perivascular space burden unravels early mechanisms of cerebral small vessel disease \*Nature Medicine\*.](#)

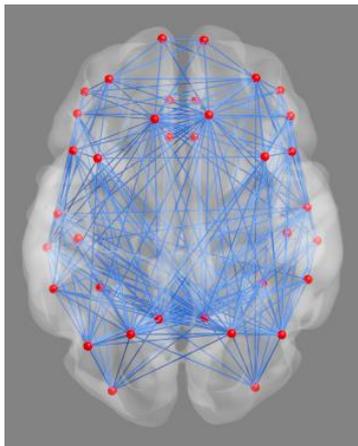
### LBC1936 creates a model for dementia diagnosis using medical data linkage



Dr Donncha Mullin was the lead author on an important LBC study that presents a new approach for identifying dementia in research cohorts. For dementia diagnosis, researchers typically rely on participants’ self-reports or substitute assessments, such as low scores in cognitive tests. Such assessments can be misleading. This is why Dr Mullin and colleagues reviewed electronic health records of over 800 LBC1936 participants, with the aim to identify those with any record of cognitive dysfunction. In addition, when there were any concerns about a participant’s thinking or memory, the team’s clinicians performed in-person clinical assessments. Based on the obtained data, a diagnostic team of clinical dementia experts then reviewed and agreed on a diagnosis. As a result, they were able to map the incidence and prevalence of all-cause dementia and dementia subtypes in LBC1936 for the first time. The study found that dementia was more common in older ages, especially in women, and Alzheimer’s disease was the most common type. Importantly, the study showed that self-reported dementia diagnoses were positive in only 17.8% of clinically identified dementia diagnoses, highlighting the importance of a robust clinical dementia outcome instead of less reliable self-reported diagnoses. Dr Mullin said: “*We hope the study can serve as a guide for other studies of dementia diagnosis. The information can help researchers understand more about what causes dementia as people get older. What is particularly exciting is the prospect of combing the results of this study with all the additional information available in the LBC1936, which could provide vital data for further analyses and insights into predictors of dementia over a person’s lifetime.*”

[Mullin, D.S. et al. \(2023\). Identifying dementia using medical data linkage in a longitudinal cohort study: Lothian Birth Cohort 1936. \*BMC Psychiatry\*.](#)

## Putting network neuroscience to the test: Less is more



Network neuroscience is a recent approach that offers insights into how the human brain is connected and organised. It builds on abstract concepts from formal mathematics, such as graph theory. Graph theory originated in geometry and was first

popularly used in Euler's Königsberg bridge problem in the eighteenth century, a puzzle involving crossing each of seven bridges exactly once in the Prussian city of Königsberg. In neuroscience, similar concepts are used to represent physical and functional connections within the brain as a network, which is referred to as the *connectome*. Conceptualising the brain as a network offers insights into the neural foundations and complexity of interactions across distributed brain regions. For example, *global efficiency* is one such graph theory metric that measures overall information integration and communication efficiency within a network. Dozens of graph-theory metrics have now been introduced to measure different aspects of connectivity. One important question is how useful these metrics are in capturing unique information about the brain's organisation. In a new paper published in the journal *NeuroImage*, James Madole of the University of Texas together with his LBC collaborators examined a range of these metrics. Using structural connectomes from over 8000 people derived from neuroimaging data in UK Biobank, the study found that the derived metrics are good for reducing a high-dimensional system of neural connections to a valuable summary of brain organization. Dr Colin Buchanan said: "This research is important as it demonstrates, at a practical level, the surprising similarity of many commonly-used global network metrics in a large sample. It highlights the importance for connectome researchers to circumspect and make transparent which metrics genuinely provide unique insights into brain connectivity."

[Madole, J.W. et al. \(2023\). Strong intercorrelations among global graph-theoretic indices of structural connectivity in the human brain. \*NeuroImage\*.](#)

## Musical instrument experience and cognitive ageing: Differential preservation or preserved differentiation?



In her previous work, published in *Psychological Science*, Dr Judy Okely, now at Napier University, has shown that musical instrument training is associated with higher cognitive performance in older age. Is this association a reflection of a reduced rate of cognitive decline in older age (differential preservation) or the persistence of cognitive advantages associated with childhood musical training (preserved differentiation)? This is what Judy assessed in her most recent study, now accepted in *Psychology and Ageing*. Judy and her LBC colleagues examined the nature of this cognitive advantage in a sample of 420 LBC1936 participants. While the study showed that older adults who reported greater lifetime experience playing a musical instrument tended to perform at a slightly higher level on tests of processing speed and visuospatial ability, the rates of decline across each cognitive domain between ages 70 and 82 were similar between participants with varying levels of experience playing a musical instrument. This suggests that earlier musical training affords cognitive advantages some of which are maintained during older age, pointing to a case of preserved differentiation and highlighting the importance of childhood activity and stimulation for healthier later life. Dr Okely said: "This study was made possible by the invaluable contributions of LBC1936 participants, who completed detailed and repeated assessments of cognitive ability. This allowed us to examine the relationship between early life musical experience and cognitive performance in later years over time and spanning multiple domains of cognitive ability."

Okely, J. et al. (accepted). Cognitive Ageing and Experience of Playing a Musical Instrument. *Psychology and Ageing*.

## Knowledge Exchange

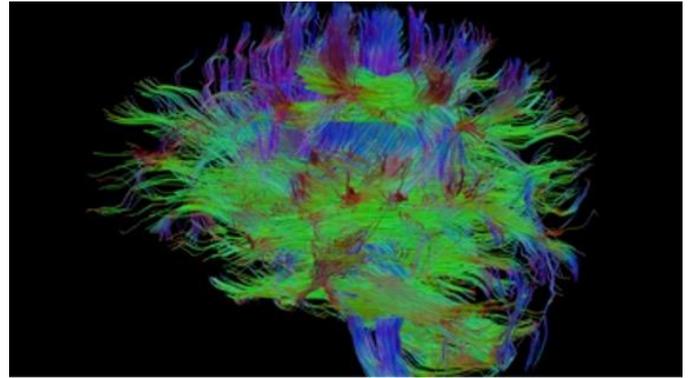
### Psychology Taster Sessions with Danielle Page



Attempting to put Brian the brain back together!

For a third year, Danielle Page was invited to join the University of Edinburgh's Widening Participation team to deliver a Psychology workshop for primary school children, as part of a scheme addressing educational inequalities and patterns of under-representation in Higher Education. In a series of workshops, children from target primary schools learn what university is like, with fun 'real university lectures', that raise aspirations and show them university is for everyone. In April and May this year, over 100 children from Liberton and Craigroyston primary schools learned about the LBC studies, and – having tried just one tricky cognitive test themselves - marvelled at our participants' ability to get through 4.5 hours of tests at the clinic! Children heard how we can see inside brains with an MRI machine, and had a go at reconstructing a brain with one of our '*Brian the brain*' models. They also discussed their own ideas about how they could keep their brains sharp as they get older, after watching our Staying Sharp [video](#). The children were incredibly engaged and had some brilliant questions about why thinking skills change over time, how MRI machines work, and what an average day working with the LBC studies looks like for Danielle. We can't wait to welcome back more children next year! Beth Jones who joined Danielle in the April sessions said: *"The two P7 workshops ran really well and it was lovely to see how engaged the pupils were with Psychology. It was particularly great to hear their reflections at the end of the day; they explained how they learned about MRIs, how to make hypotheses and how to lead a healthy brain lifestyle. Many said how keen they were to go to University. It was really rewarding to see the P7s inspired and I hope they will keep up the great work!"*

## Discover Neuroscience with Lothian Birth Cohorts



The LBC team engages with a wide range of audiences, and it is particularly exciting when we can share our work with young people as it is their generation who will benefit from the LBC expertise and findings the most. This is why we were delighted to hear from Rohit Gopakalje, an S4 high-school student, who approached us with an invitation for a workshop for the members of the Boroughmuir High School's Medics Club. With Rohit's help and input on the workshop content, we joined a group of 20 pupils and their teachers in March to share the LBCs' history and research aims and findings, and the role neuroscience plays in the process. The students heard from Dr Barbora Skarabela and two of the team's neuroscientists, Drs Colin Buchanan and Jo Moodie, who not only reviewed some of the key concepts in neuroscience and their own research interests and projects but also explained their diverse journeys from high school to becoming neuroscientists. Inspired, the students were keen to ask questions while they explored features of healthy and unhealthy ageing brains with 3D printed brain models and MRI scans; they tried on our popular Augmented Reality Glasses with important messages about some of the risk factors associated with brain function and cognitive decline, and admired a model of crystal etching of the connectome. The students were focused and engaged and the teachers, equally engaged and supportive, had to encourage the students to end the session and continue in a lively discussion on the impact of smoking on the brain and dementia in another meeting! One of the teachers emailed us to say: *"Thank you all so much for coming in, the students really enjoyed it. My 4<sup>th</sup> years were telling the rest of the class about the workshop today, which is always a positive sign. We look forward to another visit in the new academic year!"*

## Keeping the brain sharp at the International Women's Club Edinburgh



The International Women's Club Edinburgh, founded in 2000, is open to women of international background and experience, or who have an interest in international issues. In March, Dr Barbora Skarabela was invited to join the members at the Royal Scots Club to present a talk on how to keep our brains sharp in older age, based on the LBC studies. The talk, presented to the audience of over 80 women, opened with the history of the studies and a photo of a class of Scottish 11-year-olds born in 1936 when suddenly one of the Club members stood up and announced she was one of the children in the school photograph! She and the rest of the audience were intrigued by the study's history and participants. They were impressed by the participants' long-term commitment to research and the important findings that the study has generated. The audience was engaged and asked many questions about the findings, participants and the team as well as evidence used to understand what factors may contribute to keeping our mind and brain healthy in later life. The President of the Club said: *"Barbora gave a most engaging presentation on the Lothian Birth Cohorts on a topic close to our hearts, with tips on enjoying life and stimulating the brain's white matter into older age, including meeting together, making friends, playing cards, and as we are all aware, healthy diet and exercise. Everyone said how much they enjoyed the meeting, and we should invite Barbora again."* Barbora enjoyed meeting the members and giving the talk, and would be delighted to join the Club again!

## Lothian Birth Cohorts featured in guided tours around Edinburgh



In partnership with Edinburgh Neuroscience, our team organises walking tours that feature information and findings about the Lothian Birth Cohorts. The tours are led by Dr Thomas Bak, a researcher in Human Cognitive Neuroscience at the University of Edinburgh and a licensed tour guide. Thomas offered two sold-out 'Discover Neuroscience'-Guided Walking Tours at the *Edinburgh Science Festival* in April, taking visitors from Summerhall to the National Museum of Scotland, highlighting LBC research on cognitive and brain ageing. In May, Thomas created and led a special walk to mark *Mental Health Awareness Week* and *Dementia Action Week*. In a tour 'From the Enlightenment to the neuroscience of emotions', Thomas brought together topics from local philosophy, literature, neuroscience and medicine, and invited the participants on a journey to discover empathy as a window into the mental life of others and what someone else might be feeling and thinking. Thomas is now working with a group of undergraduate and postgraduate students who aspire to train as tour guides and follow in his footsteps, sharing local research and history on tours around Edinburgh. Thank you, Thomas, we are delighted that locals as well as visitors from other parts of the world can now find out about the Lothian Birth Cohorts and local neuroscience in such engaging way!

## Publications

### Published:

Aribisala, B. S., et al. (2023). 'Sleep Quality, Perivascular Spaces and Brain Health Markers in Ageing - A Longitudinal Study in the Lothian Birth Cohort 1936'. *Sleep Medicine*. <https://doi.org/10.1016/j.sleep.2023.03.016>.

Baranyi, G., et al. (2023). 'Neighbourhood Deprivation across Eight Decades and Late-Life Cognitive Function in the Lothian Birth Cohort 1936: A Life-Course Study'. *Age and Ageing*. <https://doi.org/10.1093/ageing/afad056>.

Chundru, V. K., et al. (2023). 'Rare Genetic Variants Underlie Outlying Levels of DNA Methylation and Gene-Expression'. *Human Molecular Genetics*. <https://doi.org/10.1093/hmg/ddad028>.

Duperron, M., et al. (2023). 'Genomics of Perivascular Space Burden Unravels Early Mechanisms of Cerebral Small Vessel Disease'. *Nature Medicine*. <https://doi.org/10.1038/s41591-023-02268-w>.

Hahn, J., et al. (2023). 'DNA Methylation Analysis Is Used to Identify Novel Genetic Loci Associated with Circulating Fibrinogen Levels in Blood'. *Journal of Thrombosis and Haemostasis*. <https://doi.org/10.1016/j.jth.2023.01.015>.

Mathieson, I., et al. (2023). 'Genome-Wide Analysis Identifies Genetic Effects on Reproductive Success and Ongoing Natural Selection at the FADS Locus'. *Nature Human Behaviour*. <https://doi.org/10.1038/s41562-023-01528-6>.

Mullin, D. S., et al. (2023). 'Identifying Dementia Using Medical Data Linkage in a Longitudinal Cohort Study: Lothian Birth Cohort 1936'. *BMC Psychiatry*. <https://doi.org/10.1186/s12888-023-04797-7>.

Saunders, T. et al. (2023). 'Neurogranin in Alzheimer's Disease and Ageing: A Human Post-Mortem Study'. *Neurobiology of Disease*. <https://doi.org/10.1016/j.nbd.2023.105991>.

### Accepted /In Press:

Okely, J., et al. 'Cognitive Ageing and Experience of Playing a Musical Instrument'. *Psychology and Aging*.

## Contact

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



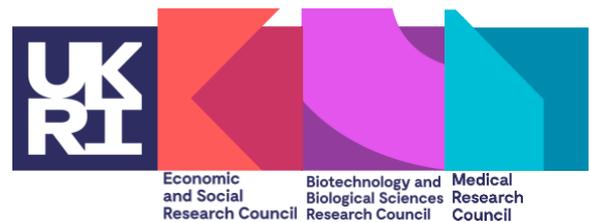
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