

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 49: March 2020

Welcome to the Spring 2020 Disconnected Mind newsletter. This issue includes news about recent events the Disconnected Mind/Lothian Birth Cohorts (LBC) team have participated in, details of our latest publications, and the regular contribution from our colleagues at Age UK. For information about this newsletter, or to contribute to a future issue, please get in touch. Contact details are on the last page.

We're now well into the new year. As this newsletter will reveal, our team has been busy and already published their first articles of the new decade. Just as a reminder of the years past, in the last decade the Disconnected Mind team published over 480 articles based on the LBC data, with a further 320 articles on related topics. In 2019 alone, they published over 100 articles, with more than 60 on the LBC. Most publications are open access and you can find them all on our [website](#). You can find our publications on page 8.

Lothian Birth Cohorts News

New funding for research on musical experience, environment, and brain imaging.

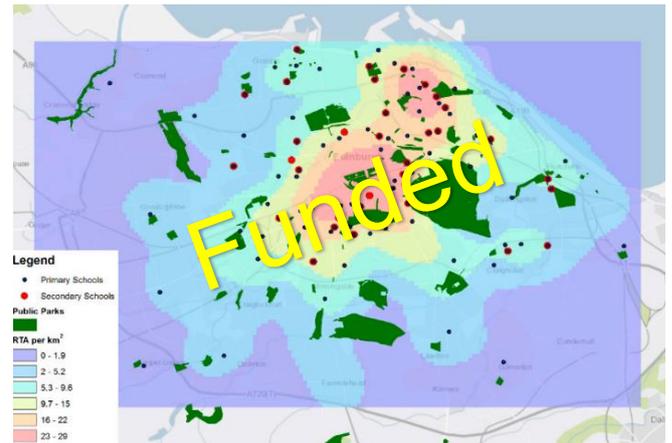
We are delighted to tell you about three new grants awarded for research on the LBC.

(1) Following her successful application for an **ESRC** New Investigator grant, Dr Judy Okely together with Professor Ian Deary and Dr Katie Overy (Reid School of Music) began a [new project](#) with the LBC looking at the relationship between lifetime musical experience and healthy ageing. Judy said, "Making music is a demanding task which involves the combination of different mental processes including attention, emotion, memory, physical coordination and skill. Research with older people has shown that learning to play a musical



instrument is related to better performance on some cognitive tests in older age. But we don't know if musical experience is related to changes in cognitive function, brain structure or psychological wellbeing with ageing. The LBC data we've collected gives us a unique opportunity to test these potential associations."

You can listen to Judy discuss her new project on [Forward Thinking](#), a podcast from the University of Edinburgh's (UoE) School of Philosophy, Psychology and Language Sciences (PPLS).



(2) **ESRC** funding was also secured for an LBC collaboration with the UoE's School of Geosciences. Professor Jamie Pearce will head the project which will conduct new investigations into whether lifetime exposure to green space, air pollution, and area-level deprivation relate to healthy cognitive, brain, and biological ageing.

(3) Dr Simon Cox was successful at securing funding from the UoE's **Institutional Strategic Support Fund (ISSF3)**, and matched funding from the **PPLS Neuroimaging Fund**, which will support a new 5th wave of brain imaging in LBC1936 participants, at mean age of 85 years. This will coincide with a new wave of cognitive and physical testing in LBC1936. The team are looking forward to welcoming our participants back for a 6th visit, starting in the spring time. More on this next time!



Knowledge exchange and Impact

Professor John Starr Winter Lecture

Alzheimer Scotland's showcase 'winter lecture' has been renamed the 'Professor John Starr Winter Lecture' in John's memory. The first lecture under its new name was given by our own Ian Deary on 2nd December, close to a year after we lost John. The lecture was titled: 'Twenty years of mostly-healthy, mostly-cognitive ageing in the Lothian Birth Cohorts'. John's wife Claire and his sister attended the lecture, with about 200 others, at Glasgow's Old Fruitmarket Hall. Henry Simmons, Alzheimer Scotland's Chief Executive, described Ian's lecture as a "tour de force" and "the perfect way to mark... a great man".



Ian Deary gives the Alzheimer Scotland Professor John Starr Winter Lecture

"Really," said Ian, "it was at the same time the saddest and one of the easiest lectures I have given. Easy, because John and I did so much---including over 400 journal articles---together. It was a tribute to my pal and closest collaborator over the last 20-odd years." Ian's emphasis was on the contributions made by the Lothian Birth Cohorts to understanding people's differences in cognitive and brain ageing. And, on top of that, the contributions to biological and social aspects of ageing more generally, and to the new areas of LBC research, such as epigenetics, stem cells, post-mortem brain tissue examination, musical experience, lifetime environments etc. Ian said, "I tried to illustrate how John and I had built an unusually valuable resource and produced useful results with our talented team of researchers. Recalling John's puckish presenting style, in the middle of my lecture I went through 12 examples of LBC results, each introduced by the phrase: 'The *n*th clue to thinking well we found in LBC....'--yes, they were each styled to scan like the 12 days of Christmas".

BBC Horizon visits the Lothian Birth Cohorts



Disconnected Mind/LBC Director Ian Deary (left) with Dr Michael Mosely

Professor Ian Deary, Dr Simon Cox, and two enthusiastic LBC1936 participants spent a whirlwind few days in February sharing what they know about cognitive ageing with Dr Michael Mosely and Bobby Seagull (of University Challenge fame), for an episode of the BBC's Horizon all about intelligence. The Horizon team heard what the LBC studies have taught us so far about maintaining your cognitive skills in older age (from Ian); what brain imaging can tell us about cognitive function (from Simon); and what older people think is important for cognitive health (from the participants). Watch this space for more news on where and when you can see the show, and see page 8 for more photos from our filming fun.

Dr Alixe Kilgour talks sarcopenia at British Geriatrics Society Autumn Meeting 2019

Along with her roles as a Clinical Lecturer and Honorary Registrar in Geriatric Medicine, Dr Alixe Kilgour is a long-term research collaborator of the LBC. Alixe's research focusses on sarcopenia, the age-related loss of muscle mass and function, and she was recently invited to give a platform presentation at the National British Geriatrics Society (BGS) meeting. Alixe presented results of a recent study based on new guidelines from the European Working Group on Sarcopenia in Older People (EWGSOP2). When applied to LBC1936 study data, Alixe found that the number of people found to have sarcopenia varied considerably depending on which tests were used. Alixe and her co-investigators recommend more equivalent cut-offs are used in future guidelines.



Alixe Kilgour presents at National British Geriatrics Society (BGS) meeting

Cardiovascular risks to brain health: Global Council on Brain Health report

BETTER HEART BETTER BRAIN

A heart-healthy lifestyle reduces the risk of cognitive decline

Take steps to improve your brain health



Stay active & exercise

Strive for at least 150 minutes of weekly, moderate aerobic activity.



Don't smoke

If you smoke, quit. If you don't smoke, don't start.



Check your blood pressure & cholesterol

Work with your doctor to manage blood pressure and cholesterol levels.



Manage blood sugar levels

Diabetes increases the risk of stroke, cognitive decline, and dementia.



Sleep well

Aim for 7 to 8 hours of sleep in a 24-hour period.

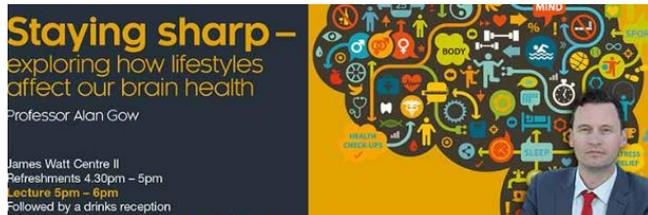


Eat healthy

Limit salt intake. Avoid excessive alcohol consumption.

Disconnected Mind/LBC investigator, Professor Joanna Wardlaw, was part of the expert investigator group on a newly published report from the Global Council on Brain Health (GCBH), 'The Brain-Heart Connection: GCBH Recommendations to Manage Cardiovascular Risks to Brain Health'. Based on published peer-reviewed observational studies and randomized controlled trials, the report summarises the current evidence on the relationship between heart and brain health, and has recommendations for healthy older adults and healthcare providers on how individuals can help maintain their brain health as they age. Simon Cox's [study](#) published in the *European Heart Journal* last year is featured amongst the key references mentioned in the report. You can read the full report [here](#).

Professor Alan Gow Inaugural Lecture



Staying sharp –
exploring how lifestyles affect our brain health
Professor Alan Gow

James Watt Centre II
Refreshments 4.30pm – 5pm
Lecture 5pm – 6pm
Followed by a drinks reception

The LBC studies have proved to be a fertile training ground for young scientists. Among the many of researchers who've gone on to become senior scientists and professors is Alan Gow. Professor Gow, now at Heriot Watt University, has been involved with the LBCs since his student days, supervised by Ian Deary during his PhD, followed by a post as LBC Study Co-ordinator and post-doc research positions. While Alan heads his own Ageing Lab, he continues to collaborate with the LBC, and in February gave his Inaugural Lecture which referenced his PhD and Postdoc with the LBC, connecting where Alan started with his current work on [Staying Sharp](#) in older age.

Augmented Reality Brains shown at Science Communication Showcase



Towards the end of 2019, the LBC's Dr Colin Buchanan, and PhD students Eleanor Conole and Emily Wheeler were invited to a science communication showcase for the new intake of MSc Biomedicine students at UoE. Students got to experience a diverse array of inspirational science communication activities and technology, including a demonstration from the LBC team of 3D brain visualisation using augmented reality (AR) smart glasses. The demonstration based on LBC findings showed how brain health can be affected by factors such as smoking, high blood pressure and diabetes. It also showed a brain ageing from the 8th to 10th decade.



Colin had another chance to show off the 3D brain display in January, during a visit from the Chief Medical Officer for Scotland, Dr Catherine Calderwood. LBC collaborator Prof Andrew McIntosh hosted an event at the Royal Edinburgh Hospital to highlight research funded by the Medical Research Council (MRC). Colin talked Dr Calderwood and UoE Principal, Professor Peter Mathieson, through the results of LBC1921 and LBC1936 brain imaging research shown in the AR display. Dr Calderwood was impressed with the AR technology and said it was remarkable but scary to see the potential impact of lifestyle on brain health. The AR project is being led by Dr Simon Cox and is funded by the MRC Engagement in Science Activities Seed Fund.

New Funding for LBC at MRC Festival



Medical
Research
Council

We are delighted to report that the MRC Festival Open Award application by Dr Barbora Skarabela and Dr Simon Cox was successful and we have secured full funding to support our workshop for high school students during the MRC Festival in June 2020. Congratulations Barbora and Simon!

Scientific highlights

Playing Analog Games is Associated with Reduced Declines in Cognitive Function



LBC researcher, Dr Drew Altschul's recent publication on analog game playing and reduced cognitive decline has been gaining a lot of traction in the media, with coverage by more than 120 news outlets globally, and currently sitting at an [Altmetric score of 1145](#), placing it in Altmetric's top 5% of all research outputs. Digital brain training and intellectual engagement have been extensively studied, but only mixed and controversial evidence suggests that they protect against cognitive decline. Some work suggests that playing analog games, such as card games, is associated with better cognitive function but, to date, studies have not presented extensive longitudinal follow-up. This study used cognitive data from LBC1936 at ages 11, 70, 73, 76, and 79, and controlled for sociodemographic, health, and early-life confounders. Playing more analog games was associated with higher cognitive function at age 70, even after controlling for age 11 cognitive function and other variables. Playing more analog games was also associated with less general cognitive decline from age 70 to age 79, and in particular, less decline in memory ability. Increased games playing between 70 and 76 was associated with less decline in cognitive speed. Overall, playing more analog games appears to predict less lifetime decline in cognitive function.

Neurology-related protein biomarkers are associated with cognitive ability and brain volume in older age

LBC group geneticist, Dr Sarah Harris, and colleagues have recently had a paper accepted for publication in *Nature Communications*. This study based on LBC1921, LBC1936 and INTERVAL data, investigated associations between plasma levels of 90 neurology-related proteins and general fluid cognitive ability. Later life cognitive ability is highly heritable and polygenic. As proximal products of transcribed and expressed genetic code, measurement of the levels of these proteins might help to identify biological pathways in later-life cognitive function. Sarah and her co-authors found a number of blood proteins associated with cognitive ability, some of which are mediated by brain volume. These proteins are potentially useful biomarkers of cognitive ability in later life. Read Sarah's paper [here](#).

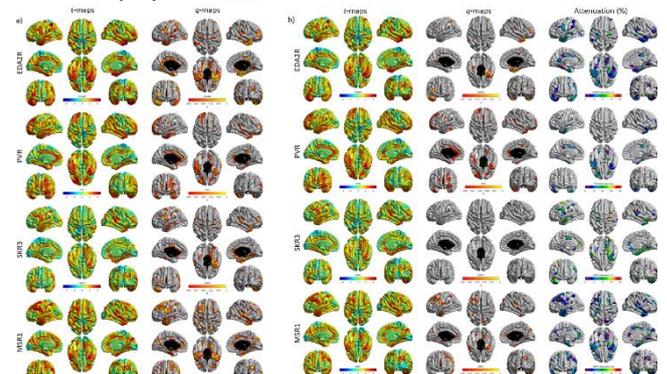


Figure from Harris et al. (2020) showing regional distribution of protein-cortical associations for each protein-cognitive ability association found to be mediated by brain grey matter volume.

LBC in new Knowledge Exchange paper

A new paper from former LBC Knowledge Exchange Officer, Dr Iona Beange, investigates public attitudes to research. It presents results obtained live during a reunion-style event attended by LBC participants, members of other cohorts and their guests. Overall, participants were very positive about health data research: 98% of voters would encourage their children and grandchildren to take part in a research cohort. Similarly, voters were positive about accessing NHS data such as neonatal 'Guthrie Spots' (97% said yes) and routinely collected health care records (95% said yes). The paper, [now online](#), awaiting peer review, demonstrates that public engagement events can provide valuable insights for future research use.

Associations Between Declining Physical and Cognitive Functions in the LBC1936

Accepted for publication in *The Journals of Gerontology: Series A*, and available to [view online](#), is a new paper from Dr Judy Okely and Professor Ian Deary on the association between physical and cognitive function. Describing the study, Judy said, “The ageing process is characterised by a gradual decline in some cognitive abilities and physical strength and function. However, the relationship between declining physical and cognitive functions with ageing is not clear. We firstly tested whether people who experience more cognitive decline also experience more physical decline. Using four waves of data from the LBC1936, collected between ages 70 and 79, we found that a steeper 9-year decline in walking speed and grip strength was related to a steeper 9-year decline in certain cognitive abilities (verbal memory, processing speed, and visuospatial ability). We next tested whether earlier decline in one domain (cognitive or physical function) could be used to predict upcoming declines in the other. Our most consistent finding was that steeper 3-year decline in processing speed predicted subsequent steeper 3-year decline in grip strength. Our findings provide further evidence of an association between cognitive and physical declines with ageing and point to the potential order in which those changes occur. In particular, individuals who experience a steeper decline in processing speed may have a higher future risk of declining upper body strength.”

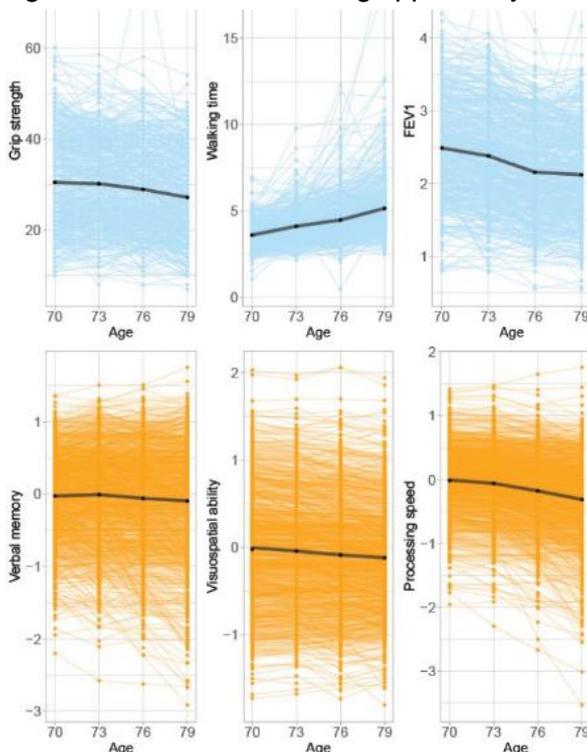


Figure (above) shows 4-wave decline in physical and cognitive function in LBC1936

In Other News...

Prof Ian Deary was named on the Web of Science Group's Highly Cited Researchers 2019 list, together with LBC collaborators Profs Joanna Wardlaw, John Starr, and Andrew McIntosh. This recognises 'the world's most influential researchers'. Congratulations!

Highly Cited Researchers 2019 — Executive Summary

Celebrating the world's most influential researchers

Experts from the Institute for Scientific Information provide exclusive insight into the list of Highly Cited Researchers 2019, including:

- the methodology;
- country and institutional breakdowns;
- using citation analysis to predict Nobel Laureates; and
- much more.



This winter, Dr Adele Goman from the [Johns Hopkins Cochlear Center for Hearing and Public Health](#) joined the LBC as a visiting scholar. Adele has expertise in hearing loss. Here's what she told us about her research with the LBC: “Hearing loss is very common as we get older, affecting nearly two thirds of adults over the age of seventy. I am investigating the impact of hearing loss on the health and wellbeing of older adults with a particular focus on mental and social wellbeing. It has been a wonderful experience working with the LBC team to further explore the impact of hearing loss in older adults.”



Federica Conte, a visiting PhD student from the University of Milano-Bicocca [@unimib](#), has joined our team to study the relationship between early cognitive change and late cognitive and brain change in LBC1936. Welcome aboard, Federica!



PhD student Federica Conte joins LBC team

Age UK News

Greetings from Age UK! Is that a hint of Spring in the air? Over the winter months and holidays, Age UK sought to shine a light on some of the more difficult issues that can be overlooked, like mental health and domestic abuse. Fortunately, these are being more openly addressed these days, but we want to ensure that the older population are part of the conversation. We have also just published some of our own research on wellbeing, so let's start with that...



Making the most of it - experiences of wellbeing in later life

Why do some people have high wellbeing while others have low wellbeing, despite facing similar circumstances? What are some people able to do for themselves to help their wellbeing, and what support do others need? Our research report aimed to find out.

Read the report [here](#). The web page has a short video of one of our participants talking about wellbeing as well.

Mental health

The [NHS Improving Access to Psychological Therapies programme](#) was developed to provide talking therapies for those with anxiety disorders and depression.

But while the programme was created with all ages in mind, there are fewer over-65s using the service than any other group despite boasting some of the most encouraging results. Age UK commissioned some research to find out why. The research showed there were three main reasons why older people weren't accessing the help available to them:

- Older people don't want to talk about their mental health
- Low mood seen as a natural part of ageing
- Mental health considered less important than physical health

Read more, and watch some videos of people talking about [mental health in later life](#).

No age limit: older people and domestic abuse



People of any age can be affected by domestic abuse, but older people can be particularly vulnerable to certain forms of domestic abuse, including abuse by a carer and financial abuse, and face significant barriers in leaving abusive situations.

We do not want vital resources diverted from younger to older victims, but rather want more recognition that these problems exist at all ages (official domestic abuse data collection stops at age 74, for example). We're calling on the Government to make sure the voices of older people are heard, their rights are protected, and their needs included in future legislation addressing domestic abuse. Read more [here](#).

Growing old and being green



Finally, let's end on a cheerier note! While the media seems to love to pit younger and older generations against each other, and portray those in later life as greedy guzzlers of resources, there are plenty of older people who do not fit this negative stereotype. Read and watch one 82-year-old's suggestions for [combatting climate change](#).

Some new publications

Accepted

Shin, J., Ma, S., Hofer, E., Patel, Y., Vosberg, D., et al., (2020). Global and regional development of the human cerebral cortex: molecular architecture and occupational aptitudes. *Cerebral Cortex*.

Sibbett, R., Altschul, D.M., Marioni, R., Deary, I., Starr, J.M., et al., (2020). DNA methylation-based measures of accelerated biological ageing and the risk of dementia in the oldest-old: A study of the Lothian Birth Cohort 1921. *BMC Psychiatry*.

Altschul, D.M., Iveson, M.H., Deary, I.J., (2019). Generational differences in loneliness and its psychological and sociodemographic predictors: an exploratory and confirmatory machine learning study. *Psychological Medicine*.

E-published ahead of print

Alonso, N., Larraz-Prieto, B., Berg, K., Lambert, Z., Redmond, P., et al., (2019). Loss-of-function mutations in the *ALPL* gene presenting with adult onset osteoporosis and low serum concentrations of total alkaline phosphatase. *J Bone Miner Res* jbmr.3928. <https://doi.org/10.1002/jbmr.3928>

Hillary, R.F., Stevenson, A.J., Cox, S.R., McCartney, D.L., Harris, S.E., et al., (2019). An epigenetic predictor of death captures multi-modal measures of brain health. *Molecular Psychiatry*. <https://doi.org/10.1101/703504>

Jia, T., Chu, C., Liu, Y., Dongen, J. van, Armstrong, N.J., et al., (2019). Epigenome-wide meta-analysis of blood DNA methylation and its association with subcortical volumes: findings from the ENIGMA Epigenetics Working Group. *Molecular Psychiatry*. <https://doi.org/10.1101/460444>

McLachlan, K.J.J., Cole, J.H., Harris, S.E., Marioni, R.E., Deary, I.J., et al., (2020). Attitudes to ageing, biomarkers of ageing and mortality: the Lothian Birth Cohort 1936. *J Epidemiol Community Health* jech-2019-213462. <https://doi.org/10.1136/jech-2019-213462>

Okely, J.A., Deary, I.J., (2020). Associations Between Declining Physical and Cognitive Functions in the Lothian Birth Cohort 1936. *J Gerontol A Biol Sci Med Sci*. <https://doi.org/10.1093/gerona/glaa023>

Published

Ballerini, L., Booth, T., Valdés Hernández, M.D.C., Wiseman, S., Lovreglio, R., et al., (2020). Computational quantification of brain perivascular space morphologies: Associations with vascular risk factors and white matter hyperintensities. A study in the Lothian Birth Cohort 1936. *Neuroimage Clin* 25, 102120. <https://doi.org/10.1016/j.nicl.2019.102120>

Gale, C., Ritchie, S.J., Starr, J.M., Deary, I.J., (2020). Physical frailty and decline in general and specific cognitive abilities: the Lothian Birth Cohort 1936. *J Epidemiol Community Health*. <https://doi.org/10.1136/jech-2019-213280>

Harris, S.E., Cox, S.R., Bell, S., Marioni, R.E., Prins, B.P., et al., (2020). Neurology-related protein biomarkers are associated with general fluid cognitive ability and brain volume in older age. *Nature Communications*. <https://doi.org/10.1101/692459>

Moodie, J.E., Ritchie, S.J., Cox, S.R., Harris, M.A., Muñoz Maniega, S., et al., (2020). Fluctuating asymmetry in brain structure and general intelligence in 73-year-olds. *Intelligence* 78, 101407. <https://doi.org/10.1016/j.intell.2019.101407>

Wragg, D., Liu, Q., Lin, Z., Riggio, V., Pugh, C.A., et al., (2020). Using regulatory variants to detect gene–gene interactions identifies networks of genes linked to cell immortalisation. *Nat Commun* 11, 343. <https://doi.org/10.1038/s41467-019-13762-6>

Hillary, R.F., McCartney, D.L., Harris, S.E., Stevenson, A.J., Seeboth, A., et al., (2019). Genome and epigenome wide studies of neurological protein biomarkers in the Lothian Birth Cohort 1936. *Nat Commun* 10, 3160. <https://doi.org/10.1038/s41467-019-11177-x>

McGrory, S., Ballerini, L., Okely, J.A., Ritchie, S.J., Doubal, F.N., et al., (2019). Retinal microvascular features and cognitive change in the Lothian-Birth Cohort 1936. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 11, 500–509. <https://doi.org/10.1016/j.dadm.2019.04.012>

Veluchamy, A., Ballerini, L., Vitart, V., Schraut, K.E., Kirin, M., et al., (2019). Novel Genetic Locus Influencing Retinal Venular Tortuosity Is Also Associated With Risk of Coronary Artery Disease. *Arterioscler. Thromb. Vasc. Biol*. ATVBaha119312552. <https://doi.org/10.1161/ATVBaha.119.312552>

More from the BBC Horizon visit to LBC group



Images (from top): Dr Michael Mosely interviews LBC1936 participants; filming with Prof Deary; Dr Simon Cox and Bobby Seagull talk brain imaging.

Contact

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

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Website

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

www.lothianbirthcohort.ed.ac.uk



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