

# 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 52: December 2020

Welcome to the Winter 2020 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. A message from our colleagues at Age UK is also included on page 7.

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

### Professor Ian Deary retires

As you will all know, our esteemed director of the LBCs, Professor Ian Deary, retired on 30<sup>th</sup> November 2020 after over 35 years of research at the University of Edinburgh. Ian has led the LBC1921 and LBC1936 projects since their inception, in 1999 and 2004 respectively.



As expected, as news of his retirement spread, we received an outpouring of appreciation for Ian from his very many LBC team members and collaborators, past and present. Ian has had an incredible career, with a scientific legacy that extends far beyond his many discoveries, awards, publications, and successful grants; he also leaves behind a personal legacy of collegiality, support, fun, and inspiration. The success of the LBCs is due, of course, to the strength of the data collected from the LBC participants, and, undeniably, to Ian's extensive experience, knowledge, and infectious passion for discovery. We are grateful to Ian for his leadership, guidance, and friendship, and wish him a long, happy and productive retirement. Thank you, Ian!



Lothian Birth Cohorts Director Dr Simon Cox at the LBCs 2019 reunion event

However, we are pleased to say that we are not saying a proper goodbye to Ian, just yet! He will be staying as a key member of the team as Professor Emeritus, so the LBCs can still count on his invaluable support and guidance.

We are delighted to congratulate Dr Simon Cox, who will take over as Director of the Lothian Birth Cohorts. Simon is Principal Investigator on the current brain scanning part of the study, funded by the Medical Research Council. He has worked with the LBCs since starting his PhD in 2009; some of you may have met him during cognitive testing appointments at the Western General Hospital. In addition, the team welcome two new investigators, Dr Michelle Luciano and Dr Susie Shenkin. Both have a long history of LBCs experience and collaboration, and their respective genetics and clinical expertise will enhance the team's skills. They will join the LBC Investigator Team alongside Simon, and Dr Tom Russ, Dr Mark Bastin and Professor Joanna Wardlaw.



Our new Investigators: Dr Susie Shenkin (left) and Dr Michelle Luciano (right)

The LBCs have attracted world-leading researchers over the years, and Ian has built a team of experts who can lead the project in his stead. We're very excited to move into wave 6 with this great new team!

## Staff news

### Disconnected Mind team welcomes Charley Xin



We have just welcomed a new Post Doc, Dr Charley Xin, who will be working with Disconnected Mind team member Dr W. David Hill on his five year MRC-funded project 'From Genetic Sequence to Phenotypic Consequence: Genetic and environmental links between cognitive ability, socioeconomic position, and health'. David and Charley aim to investigate the contributions of genetic and environmental factors to human cognitive ability and their relationship to health. Charley undertook his MSc in Quantitative Genetics at the University of Edinburgh and his PhD at the MRC Institute of Genetics and Molecular Medicine (IGMM) on the contributions of familial genetics and environment to human complex trait architecture. After his PhD, he joined the Roslin Institute as a research fellow to continue in his research on human complex traits in UK Biobank, studying the impact of partner interaction and indirect genetic effects. Welcome, Charley!

### Welcome to Gergő Baranyi

In September, a new interdisciplinary research project began as a collaboration between human geographers, psychologists, and landscape architects at the University of Edinburgh. The ESRC-funded project, "Lifecourse of Place: how environments throughout life can support healthy ageing" aims to explore how living in different neighbourhoods during childhood, adulthood and old age contributes to ageing. Based on historical residential addresses, the project will link information on green space, neighbourhood deprivation and levels of air pollution in the LBC cohort, and examine how these affect cognitive decline, biological ageing and changes in the brain.



The post-doc researcher working on this project, Dr Gergő Baranyi, recently finished his PhD in Human Geography at the University of Edinburgh. Before moving to Scotland, he studied psychology and public health in Budapest and Berlin, and was involved in various research projects on mental health. In addition to the project, Gergő also works as a consultant for the World Health Organisation. Welcome to the team, Gergő!

## Scientific Highlights

### Inflammation and frailty in the LBC1936

Past research has suggested that chronic inflammation in later life is associated with frailty. However, findings have been mixed, potentially due to differing approaches to the measurement of frailty. In a recently published [paper](#) in *Experimental Gerontology*, Disconnected Mind PhD student Miles Welstead explored this by contrasting two different measures of frailty, and examining the longitudinal association between chronic inflammation and frailty progression in the Lothian Birth Cohort 1936 (LBC1936). Frailty was assessed over four waves of the LBC1936 with two widely used measures: the Frailty index and the Fried phenotype. Two blood-based inflammatory biomarkers (Fibrinogen and C-reactive protein) were used to determine inflammation levels for each participant. Analysis showed that over a 12-year follow-up period, higher inflammation in the LBC1936 is associated with worsening frailty over time when measured using the Frailty index but not Fried phenotype. He suggests possible reasons for these disparities, which may reflect the ways in which frailty is conceptualized by different measures, with the Fried phenotype reflecting a biopsychosocial approach, and the Frailty index based in physical approaches.

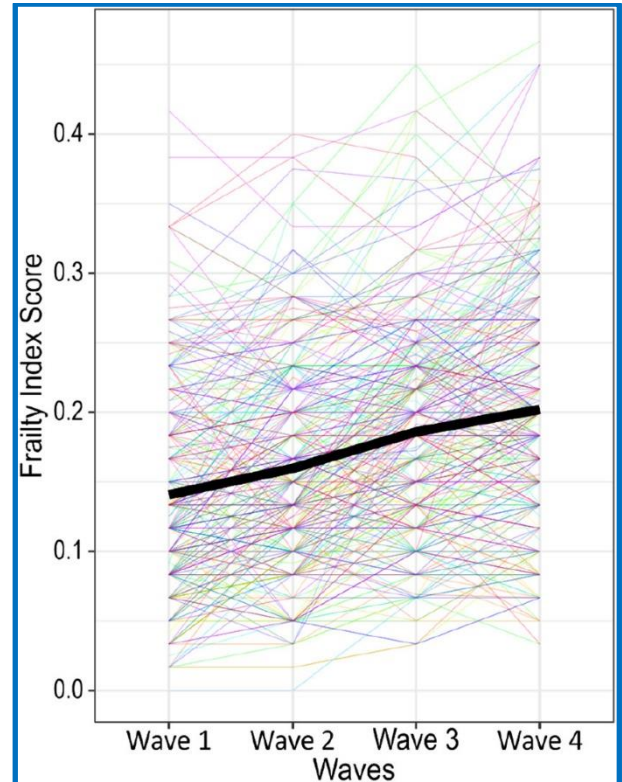
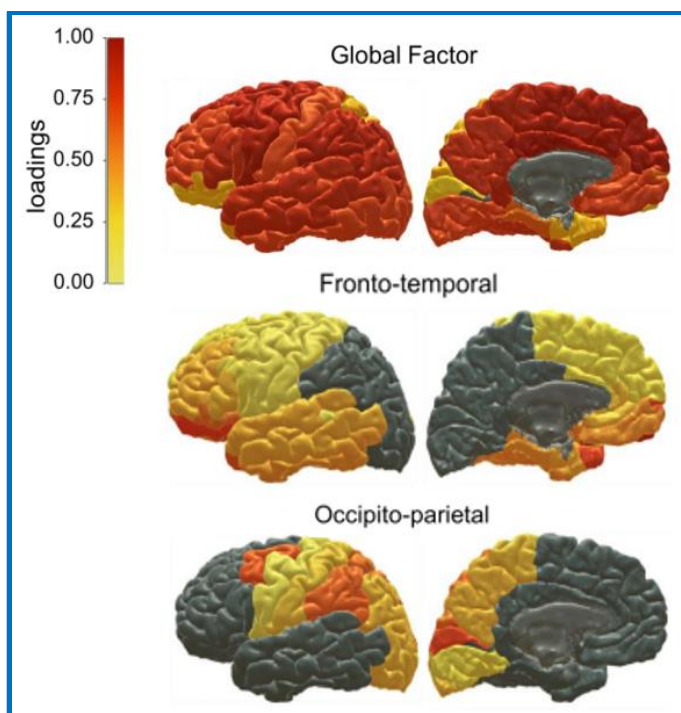


Figure from Welstead et al, 2020: A plot of Frailty Index trajectories and estimated mean over four waves of testing.

### Three major dimensions of human brain cortical ageing in relation to cognitive decline

Different brain regions can be grouped together, based on cross-sectional correlations among their cortical characteristics, and this patterning has been used to make inferences about ageing processes. However, cross-sectional brain data conflates information on ageing with patterns that are present throughout life. In a paper now accepted at *Molecular Psychiatry* and available as a [preprint](#), Dr Simon Cox and co-authors characterised brain cortical ageing across the 8<sup>th</sup> decade of life in the LBC1936 using data from a total of 1376 MRI scans at ages 73, 76 and 79. Simon found a major dimension of atrophy across the cortex that explained 66% of the variance in longitudinal changes in volume; this factor was also associated with declines in general cognitive ability, and specific domains of visuospatial ability, processing speed, and memory. He also discovered distinct dimensions in fronto-temporal and occipito-parietal areas of the cortex which explained an additional 20% of variance of regional volumetric changes. Overall, it seems individual differences in brain cortical atrophy with ageing are manifest across three major dimensions, the first of which is related to declines across multiple cognitive domains. These patterns were not present in cross-sectional data, highlighting the value of longitudinal data and methods for distinguishing lifelong patterns of brain-behaviour associations from patterns that are specific to aging.



Adapted Figure from Cox et al, 2020: Three dimensions of cortical ageing. Warmer colours denote stronger standardised loadings on discovered factors of cortical volumetric change.

### Cerebral small vessel disease genomics and its implications across the lifespan

In a large consortium of over 50,000 older people, including LBC1936, our collaborator Dr Muralidharan Sargurupremraj and colleagues at the University of Bordeaux aimed to identify genetic loci associated with the volume of 'white matter hyperintensities' (WMH) which are like areas of scarring in the brain's white matter. They found 27 genetic loci, and from these results, they computed a genetic risk score for WMH and applied it to brain images of younger people. Younger individuals with greater genetic risk of WMH, based on the score, already had slightly less healthy-looking brain white matter. There was evidence for the genetic loci related to WMH also having some causal influence on stroke and Alzheimer-type dementia. It was suggested that these results might help to group people into risk levels for WMH so that high-risk people could be identified for prevention trials. This paper was accepted in *Nature Communications*.

### Diet, cognitive function, and structural neuroimaging measures of brain aging

Evidence suggests that diet plays a role in healthy cognitive and brain ageing, yet very few studies have examined both cognitive *and* neuroimaging outcomes in the



same sample. This is important if we are to begin to understand whether diets can be 'neuroprotective'. In a paper [published](#) in *Experimental Gerontology*, Dr Janie Corley and co-authors identified two dietary patterns in the LBC1936 using age 79 Food Frequency Questionnaire data, namely, a healthy Mediterranean-style dietary pattern and a processed foods dietary pattern.

Closer adherence to the Mediterranean-style pattern was associated with better global cognitive function, visuospatial ability, memory, and verbal ability. Though there was a trend for poorer cognitive function with closer adherence to the processed pattern, most of the associations were accounted for by a lower childhood IQ. Specific Mediterranean diet features—green leafy vegetables and a low intake of red meat—were consistently associated with better global and domain-specific cognitive functioning. However, there was no evidence of associations between either dietary pattern and structural neuroimaging measures of brain ageing.

## Genetic correlations and genome-wide associations of brain structure

Dr Edith Hofer, our collaborator from the Medical University of Graz, used LBC1936 data as part of a large genome-wide meta-analysis, [published](#) in *Nature Communications*, to identify genes which influence differences in brain cortical measures between people, including cortical thickness, surface area and brain volumes. The proportion of genetic influence and genetic associations of cortical measures across the whole brain cortex was studied in 22,822 individuals from 20 cohorts. Different genes were found for different brain cortical measures and brain regions, and 161 significant associations pointed to some specific biological pathways which may cause differences between people. Many of the significant genes identified were also involved in other interesting processes and changes in the brain, including: anthropometric traits like BMI, development of the hindbrain (the cerebellum and brainstem), vascular and neurodegenerative disease and psychiatric conditions.

## KE & Impact

### Colin Buchanan wins post doc competition: 'Picture that research!'

It's been a busy year for one of our neuroscientists, Dr Colin Buchanan. Colin uses tractography in his research; a 3D modelling technique to represent the brain's white matter connections from your brain scans. These stunning images won Colin a 1st place prize when he submitted a series of his images representing healthy white matter connections to a University Postdoc photography competition 'Picture that research!'. You can see all of the images on Twitter, [@EdinUniLBC](#). Congratulations, Colin!



## Singing and science at the Being Human festival

This year, for the first time, the Lothian Birth Cohorts participated in the national Being Human festival of humanities, which took place in November. Dr Judy Okely, who is leading an ESRC funded project to explore the effects of musical experience on cognitive health and decline in the LBC1936, contributed to a free online 'singing and science' event with Heather Macleod, a professional singer and choir director of the Soundhouse choir.



Over two evenings, Judy shared music psychology findings about the benefits of music, and her own initial findings, which suggest music has benefits for our cognitive health: greater experience playing a musical instrument is associated with slightly healthier lifetime change in general cognitive ability. The online 'choir' also learned a new song together, taught by Heather. This fun and interactive event brought together almost fifty singing enthusiasts, of all ages, from various corners of the UK, and from as far afield as Europe and the US!

We've received many positive comments, with some attendees of the first event returning to join us again at the second. One guest sent us this follow up message: *'I loved singing with you all on Tuesday eve, Heather is a super vocalist and music tutor. I came away feeling so uplifted.'* We hope to continue our collaboration with Heather Macleod for future events and have already started discussing our next festival proposal. We are also exploring collaborations with colleagues at the Alzheimer Scotland Dementia Research Centre to bring online singing to care homes!



## LBC1936 COVID-19 Questionnaire appears in the Times newspaper

You might remember from previous editions the launch of our new project, the online Lothian Birth Cohort 1936 COVID-19 questionnaire. The questionnaire, which had nearly 200 responses from LBC participants, covered over 20 themes, and has formed the basis for four new papers so far. It also attracted the attention of Public Health Scotland, who received a privileged first view of our results, and now, it has also attracted attention in the media.

In November, Mike Wade, senior reporter from *The Times*, published a [story](#) highlighting the important contribution that the LBCs are making to COVID-19 research. Mike has followed the project for many years, and has previously published articles about the LBCs. He was aware that older people have been underrepresented in COVID-19 studies to date, and that their voices have been lacking in news and media coverage too.

Similarly to Public Health Scotland, Mike recognised the value of the LBC1936 COVID-19 survey in addressing this important gap, so he wrote about our research and interviewed two LBC1936 participants about their experience of lockdown, acknowledging the project's vital Age UK funding. He also reflected on some of the initial impressions we had of responses to the survey: *“what they unearthed were stories of loneliness but also of resilience, of individuals sometimes suddenly bereft, but doubly determined to keep family relationships and old friendships burning bright.”* He is already planning a second, longer feature!



Screen capture of the Times article, featuring LBC1936 participant Mrs Sheila McGowan

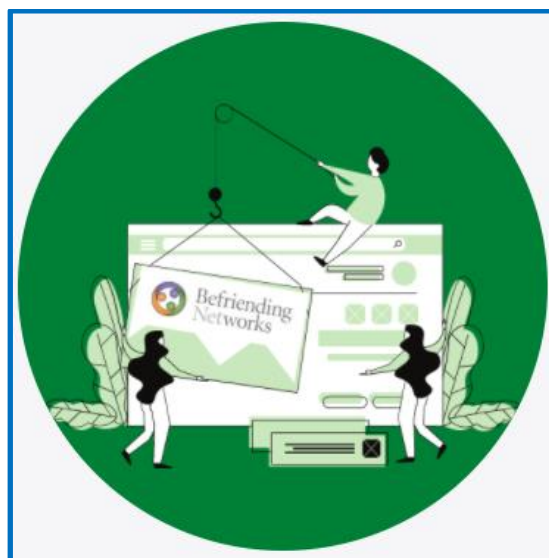
## Ian Deary's 'Ten quite interesting things about human intelligence' at the University of the Third Age

On 9<sup>th</sup> November, Ian gave a talk via Zoom to the University of the Third Age (U3A) in Cockermouth, Cumbria. The title was, 'Ten quite interesting things about human intelligence'. Chairman Ian Hall said it was the largest Zoom attendance they had had at an event to date, with 73 dial-ins, and, with couples watching, the total watching was 80. Ian used the Lothian Birth Cohorts and Scottish Mental Surveys to make several of his points, because they have provided among the best data in the field to address some aspects of human intelligence research. He also took a series of questions from attendees after each of the 'Ten things'. The talk was very well-received and got a lot of very positive feedback from those in attendance.



## Alan Gow at the Befriending Networks Annual Conference

During Befriending Week in early November, Disconnected Mind collaborator and former team member Dr Alan Gow was one of the keynote speakers at Befriending Networks Annual Conference, hosted remotely this year. He spoke about 'Social connections and healthy ageing', exploring the associations between social contact and support and cognitive ageing within the LBC and other studies, and highlighted the Global Council on Brain Health report, from the American Association of Retired Persons and Age UK, on social connectedness and brain health as a key resources on the topic.



## Federica Conte presents at the 2020 conference of the Italian Psychological Association

In September, Federica Conte, a visiting PhD student from Italy, was invited to present her work on lifetime cognitive change in a talk at the 2020 conference of the Experimental Psychology chapter of the Italian Psychological Association. Federica has been studying cognitive trajectories from age 11 to age 82 of the LBC1936 cohort, to test whether cognitive change in an earlier period of life can predict rates of cognitive decline in older age. Her results showed that cognitive change between 11 and 70 years is indeed a significant predictor of decline between 70 and 82 years. Individuals who achieved the largest gains in general cognitive ability from childhood to age 70, also tended to show slower decline in older age.

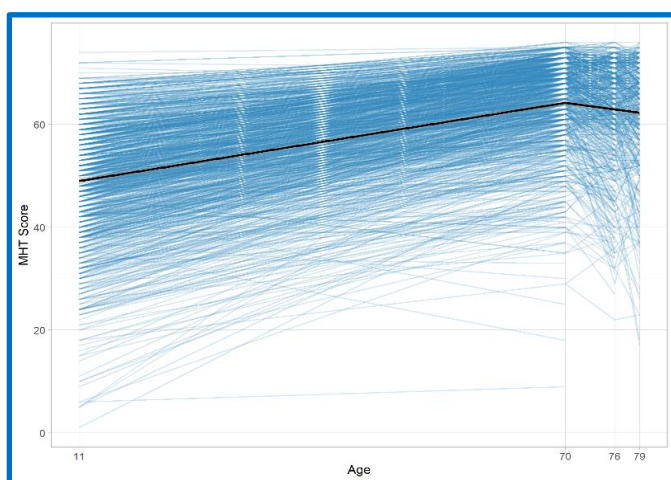


Figure showing trajectories of MHT scores with age

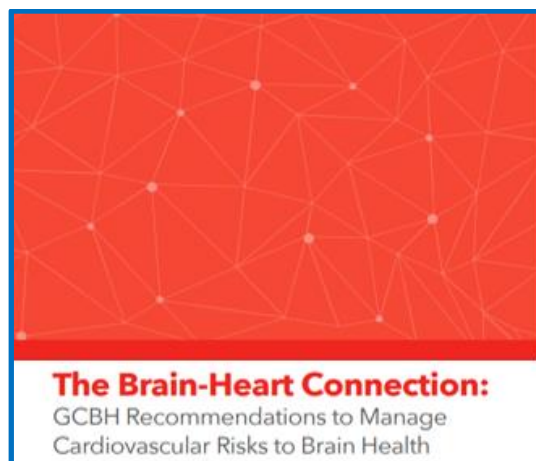
This furthers our understanding of cognitive ageing processes and supports the timely identification of people at greater risk of age-related cognitive decline. Her results sparked a lot of interest and discussion from those in attendance from the scientific community, and, in fact, there was so much interest that Federica was invited to speak again in November, at a special seminar held at the University of Padova. The talk was extremely well-received and sparked a lot of interest in Federica's LBC findings!



Federica (2<sup>nd</sup> row, centre) and attendees of the 2020 conference of the Experimental Psychology chapter of the Italian Psychological Association

## The Disconnected Mind in Policy

As well as drawing attention via our public events and media coverage, the Disconnected Mind team continue to contribute to policies and interventions for improving the health and quality of life of older people across the world, using LBC data. Over the past seven years, LBC findings have appeared in more than 60 policy documents, and guidelines from six Governments and organisations such as the NHS and World Health Organisation (WHO). Insights from LBC research reached hundreds of thousands of households: in the United States, the American Association for Retired Persons (AARP), an Age UK partner and organisation of over 38 million members, launched a version of the Staying Sharp campaign in 2015, rooted in LBC findings, with a programme aimed at influencing changes in behaviour to reduce people's risks of cognitive decline. AARP estimate that its Staying Sharp programme alone reaches over 500,000 people.



Another route for our research to enable older adults to take action to protect themselves against cognitive decline is with the AARP's initiative, Global Council of Brain Health (GCBH). The Council published three reports this year, and all three of them featured LBC researchers and collaborators: February brought the report on [Cardiovascular risks and Brain Health](#) (pictured above), with recommendations by Disconnected Mind Investigator Professor Joanna Wardlaw, as the only UK consultant on the team of experts, and featured a recent study of [cardiovascular risk factors and brain health](#) by Dr Simon Cox. The report was released with a featured AARP news story which has accumulated 21,966 page views and 368 downloads. In June, the [Music and Brain Health](#) report, featuring on-going LBC research by Dr Judy Okely, was released, garnering 135,916 page views and 926 downloads, to date. Even during a challenging year like 2020, the Disconnected Mind continues to contribute to healthier cognitive and brain around the world.

## Age UK News

Greetings from all of us at Age UK, our thoughts and best wishes go to you and yours at such a challenging time. Here are some recent updates.

The local network of 130 Age UKs continues to be very busy responding to the crisis, particularly when large numbers of older people were advised to 'shield' over summer, avoiding leaving their homes or having contact with others. But, good news: we were able to offer a range of practical support which maintained safety for older people, including food parcels, shopping services and befriending.



At national level, our Information and Advice services were in very high demand and we created a 'coronavirus hub' on our website to provide clear advice specifically for older people: [www.ageuk.org.uk/information-advice/coronavirus/](http://www.ageuk.org.uk/information-advice/coronavirus/)

Our very own Dr Elizabeth Webb, Senior Research Manager, has been writing a series of blogs and longer pieces demystifying much of the background science which surrounds coronavirus guidelines and research, and explaining what it means for the daily lives of older people in the UK. Her most recent article, about vaccines, is [here](#). She explains the current situation regarding coronavirus vaccines, how the current front-runner (produced by Pfizer and BioNTech) works, and what we know about how well it works for older people.

Very sadly, for many older people, shielding meant an increase in anxiety and loneliness. We found that demands for our telephone friendship services increased. To meet demand and improve wellbeing for older people, we joined forces with The Silverline to provide more access to telephone support during the social distancing measures that have had to be in place. Two types of service are available, in the first an older person is matched with a volunteer who calls them once a week to find out how they are and have a chat. In the second, a 24-hour helpline is available for anyone needing to talk at any hour of the day or night. You can find out more [here](#).



Unfortunately, the lockdown did take its toll on our local shops and over 100 have had to close. This and cancelled events has greatly reduced Age UK's income. However, to raise funds, we ran a very successful emergency fundraising appeal at national level, with the proceeds going to local Age UK services.

With such large losses in income and the uncertainties of the future, like many other organisations, Age UK has been forced to make staff redundancies. We have said sad goodbyes to many colleagues, including people in the Research team. Dr Susan Davidson and Su Ray have left Age UK, having spent many years between them being fascinated with the Disconnected Mind Project and enjoying the great privilege of working with the LBC1936 and the team at Edinburgh University.

Finally, and most importantly, our work continues to ensure that older people in the greatest need are supported. The pandemic has intensified feelings of loneliness in many older people and this Christmas might be one of the most difficult times for many. So a lot of work from our fundraisers has gone into launching our Christmas appeal: 'Now more than ever, no one should have no one'. [This webpage](#) focuses on our campaign and the types of help we have been able to offer.



Visit the Age UK website: <https://www.ageuk.org.uk/>

## Contact

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

## Email

For newsletter queries: [lbc.ke@ed.ac.uk](mailto:lbc.ke@ed.ac.uk)

For publication queries: [lbc1936@ed.ac.uk](mailto:lbc1936@ed.ac.uk)

## Website

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

[www.lothianbirthcohort.ed.ac.uk](http://www.lothianbirthcohort.ed.ac.uk)

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

## Merry Christmas

Merry Christmas from all at the Disconnected Mind. We hope you have a very happy Christmas, and wish you and your loved ones all the best for 2021.



THE UNIVERSITY of EDINBURGH  
Lothian Birth Cohorts



THE UNIVERSITY of EDINBURGH



National Institutes of Health





## Some new publications

### Accepted/In press

Huguet, G. *et al.* (2020) 'Genome wide analysis of gene dosage in 24,092 individuals estimates that 10.000 genes modulate cognitive ability', *Molecular Psychiatry*. Available at: <https://www.biorxiv.org/content/10.1101/2020.04.03.024554v3>.

Sargurupremraj, M. *et al.* (2020) 'Cerebral small vessel disease genomics and its implications across the lifespan', *Nature Communications*.

### Epub before print

Corley, J. (2020) 'Adherence to the MIND diet is associated with 12-year all-cause mortality in older adults', *Public Health Nutrition*, pp. 1–10. doi: [10.1017/S1368980020002979](https://doi.org/10.1017/S1368980020002979).

Corley, J. *et al.* (2020) 'Dietary patterns, cognitive function, and structural neuroimaging measures of brain aging', *Experimental gerontology*. doi: [10.1016/j.exger.2020.111117](https://doi.org/10.1016/j.exger.2020.111117).

Cuellar-Partida, G. *et al.* (2020) 'Genome-wide association study identifies 48 common genetic variants associated with handedness', *Nature Human Behaviour*. doi: [10.1038/s41562-020-00956-y](https://doi.org/10.1038/s41562-020-00956-y).

Knol, M. J. *et al.* (2020) 'Association of common genetic variants with brain microbleeds: a genome-wide association study', *Neurology*. doi: [10.1212/WNL.0000000000010852](https://doi.org/10.1212/WNL.0000000000010852).

Surendran, P. *et al.* (2020) 'Discovery of rare variants associated with blood pressure regulation through meta-analysis of 1.3 million individuals', *Nature Genetics*. doi: [10.1038/s41588-020-00713-x](https://doi.org/10.1038/s41588-020-00713-x).

### Published

Cadar, D. *et al.* (2020) 'The long arm of childhood intelligence on terminal decline: Evidence from the Lothian Birth Cohort 1921.', *Psychology and Aging*, 35(6), pp. 806–817. doi: [10.1037/paq0000477](https://doi.org/10.1037/paq0000477).

Erzurumluoglu, A. M. *et al.* (2020) 'Meta-analysis of up to 622,409 individuals identifies 40 novel smoking behaviour associated genetic loci', *Molecular Psychiatry*. doi: [10.1038/s41380-018-0313-0](https://doi.org/10.1038/s41380-018-0313-0).

Hofer, E. *et al.* (2020) 'Genetic correlations and genome-wide associations of cortical structure in general population samples of 22,824 adults', *Nature Communications*, 11(1), p. 4796. doi: [10.1038/s41467-020-18367-y](https://doi.org/10.1038/s41467-020-18367-y).

Lund, J. B. *et al.* (2020) 'Weighted gene co-regulation network analysis (WGCNA) of promoter DNA methylation on all-cause mortality in old-aged birth cohorts finds modules of high-risk associated biomarkers', *The Journals of Gerontology: Series A*, p. glaa066. doi: [10.1093/gerona/glaa066](https://doi.org/10.1093/gerona/glaa066).

Valdés Hernández, M. del C. *et al.* (2020) 'Perivascular spaces in the centrum semiovale at the beginning of the 8th decade of life: effect on cognition and associations with mineral deposition', *Brain Imaging and Behavior*. doi: [10.1007/s11682-019-00128-1](https://doi.org/10.1007/s11682-019-00128-1).

Welstead, M. *et al.* (2020) 'Inflammation as a risk factor for the development of frailty in the Lothian Birth Cohort 1936', *Experimental Gerontology*, 139, p. 111055. doi: [10.1016/j.exger.2020.111055](https://doi.org/10.1016/j.exger.2020.111055).