

# 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 53: March 2021

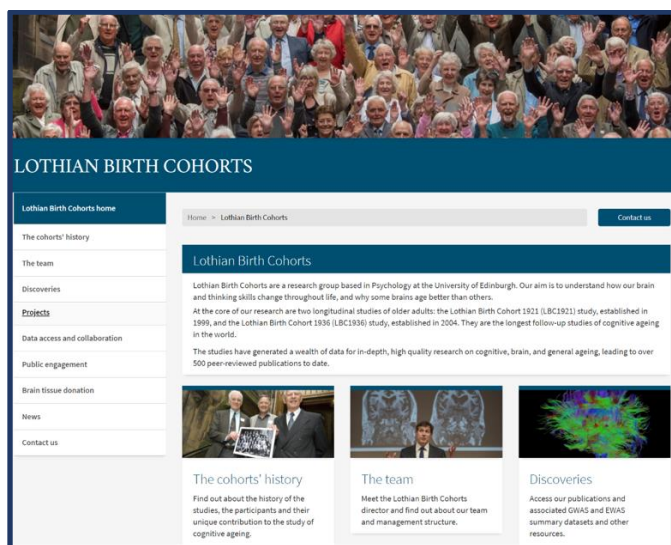
Welcome to the Spring 2021 Disconnected Mind newsletter. This issue includes news about the Disconnected Mind/Lothian Birth Cohorts (LBC) team, our latest publications, and the events we have participated in recently.

For further information about this newsletter or to contribute to future issues, please contact us using the details on page 7.

## Lothian Birth Cohorts News

### New LBC website goes live!

We are excited to announce the launch of our brand new [website](#). The LBC website covers a great deal of information for all kinds of audiences, including researchers, participants and their families, and the public. We have designed it to improve readers' experience when navigating all of this information, and have included pages explaining the unique history of the study and its participants, highlighting the wealth of data and research outputs we have produced thus far, and reflecting our commitment to sharing our research with a wide of range of audiences. Please enjoy browsing, and let us know what you think!



Screenshot of the new LBC website

### Simon Cox is awarded Sir Henry Dale Fellowship

Many congratulations to Study Director Dr Simon Cox, who has recently been awarded a prestigious Sir Henry Dale Fellowship from Wellcome and the Royal Society. It will provide nearly £1M over 5 years, including an additional post-doctoral researcher, to support his research project '*Factors of biological ageing – does it all go together when it goes?*'



Simon said, "*The focus of the project is to use some of the largest and most informative datasets in the field – including the Lothian Birth Cohorts – to understand the nature of the ageing process by integrating information across multiple aspects of ageing, from cognitive, to brain, to physical to multi-omics. The ideas and methods follow directly from my recently-published discoveries of dimensions of cortical ageing, and promising pilot data. Identifying the degree to which different facets of ageing change in concert may help us identify different dimensions along which people decline (or stay stable) – this may then offer novel potential for these to be differentially linked to groups of risk factors. I am absolutely delighted to have been awarded this prestigious and generous fellowship. My directorship of the LBCs is built into this, and it represents a stable platform from which to build further capacity, and to apply cutting-edge approaches to improve our understanding of the hows and whys of the ageing process.*"

The first paper related to this fellowship was recently [published](#) in *Molecular Psychiatry*, and a new post-doctoral researcher will join the team in May. We look forward to providing further updates on Simon's research on this project in the coming years, and once again congratulate him on this wonderful news that builds on his previous grant successes.

## Scientific Highlights

You may remember from previous editions of our Disconnected Mind newsletter that we conducted an LBC1936 COVID-19 survey during the national COVID-19 lockdown in May 2020. An important advantage of the LBC1936 survey was that it included a series of questionnaires that had been administered to LBC1936 participants in years prior to the pandemic, meaning we could compare responses to the same questionnaires administered before and during lockdown. We are excited to present the results of the first two papers published using this exciting new data!

### Associations between home garden use and physical and mental wellbeing during COVID-19 lockdown

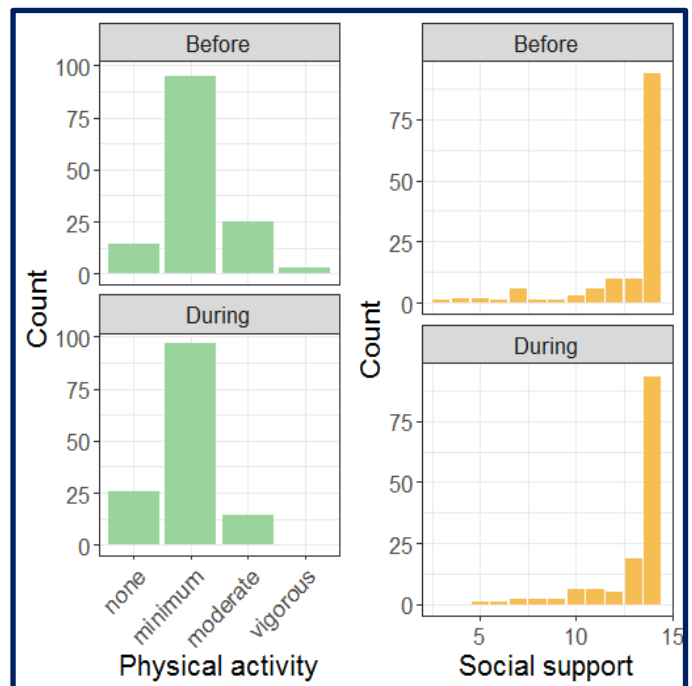
In a recently [published](#) paper in *Journal of Environmental Psychology*, Dr Janie Corley and the LBC team examined whether home garden usage was associated with self-reported mental and physical wellbeing in the LBC1936 during the COVID-19 lockdown, using data collected in our LBC1936 COVID-19 survey, launched in May 2020. At the time, national guidelines for the over 70s were to remain at home and socially isolate, during the initial COVID-19 lockdown in the UK.



Janie found that spending more time in the garden during lockdown than before lockdown was associated with better self-rated physical health, emotional and mental health, and sleep quality, but specifically 'doing' garden activities or using the garden for relaxation purposes were not significantly associated with wellbeing. She concluded that spending time outdoors in a home garden could be a potential health resource during the COVID-19 pandemic for older people.

### Change in Physical Activity, Sleep Quality, and Psychosocial Variables during COVID-19 Lockdown

In this study, [published](#) in *International Journal of Environmental Research and Public Health*, we used the LBC1936 COVID-19 Questionnaire data to test whether LBC1936 participants experienced changes in physical activity, sleep quality, loneliness, self-reported memory problems, neighbourhood cohesion, and psychological wellbeing during the first national lockdown. Compared to assessments taken two years earlier, we found that levels of physical activity were slightly decreased, and that social support was slightly increased during lockdown. We also tested whether participant characteristics predicted whether participants would experience more positive or negative changes during lockdown. We found that personality traits (intellect, emotional stability, and extraversion) and a higher general cognitive ability were associated with more positive changes in some outcome variables during lockdown. History of cardiovascular disease, more symptoms of anxiety, and living alone were associated with more negative changes. In combination with findings from other studies, this information could be used to identify individuals who may particularly benefit from support during the pandemic.



Comparison of outcome variables physical activity and social support before and during lockdown.

## Dietary patterns and trajectories of global- and domain-specific cognitive decline

Healthy dietary patterns may protect against age-related cognitive decline but the results of studies have been mixed and few have had extensive longitudinal follow-up with comprehensive cognitive testing. In a recent paper by Dr Janie Corley and Professor Ian Deary, [published](#) in *British Journal of Nutrition*, they used LBC1936 data to examine associations of two dietary patterns—a healthy Mediterranean-style pattern and a traditional (processed-food) pattern—measured at age 70, with general- and domain-specific cognitive decline over 12 years (age 70-82) across 5-waves of testing.



Those with more Mediterranean-style diets had better verbal (word-knowledge) ability cross-sectionally at age 70, and the converse was true of those with more processed diets. Neither dietary pattern was associated with cognitive change from age 70 to age 82, with the exception of a slightly steeper decline in verbal ability over time in those with a more Mediterranean-style diet at age 70. Overall, dietary patterns were not associated with general cognitive ageing, or with decline in visuospatial-, processing speed- or memory abilities over 12 years of follow-up.

## Genome wide analysis estimates more than 10,000 genes modulate cognitive ability

Copy number variants (CNVs) are a type of variation in DNA, where a stretch of DNA is duplicated in some people. When examining a region of the DNA, you might see that some people have more copies of a gene than others. Genomic CNVs can be totally benign, but they are also thought to sometimes be associated with neuropsychiatric disorders including mental illnesses. Researchers have examined their contribution to neuropsychiatric disorders, but little is known about how they might affect important traits such as cognitive ability. In a study of 24,092 individuals including the LBC1936, [published](#) in *Molecular Psychiatry*, our collaborator Dr Guillaume Huguet of the Université de Montréal used statistical

models of the genes included in CNVs to predict their effect size on measures of cognitive ability. Overall, they found that around 10,000 genes had an influence on cognitive ability. These effects on cognitive ability could be related to genomes' effects on biological pathways related to intelligence.

## Genetic variation, brain, and intelligence differences

There are robust findings in intelligence research showing that individual differences, as assessed by cognitive test scores, are stable across the lifespan and predict multiple life outcomes such as in educational achievements and health outcomes. In recent years, researchers have turned more and more to studying the underlying genetics and brain structures which form the foundations of intelligence. In a commentary recently [published](#) in *Molecular Psychiatry*, LBC team members Professor Ian Deary, Dr Simon Cox & Dr David Hill aimed to summarise the last decade of research on the underlying origins of intelligence, including new contributions from studies of molecular genetics, brain imaging, and studies combining both.



This paper represents a cornerstone commentary in our mission as the Disconnected Mind project, which is to apply our understanding of genes and brain to understand why cognitive differences occur in ageing. Many key studies from the LBC are part of the evidence base for the genetic and cerebral bases of cognitive differences. After covering some of the controversies and consensuses in intelligence research, the team summarise studies of heritability, genome-wide association studies (GWAS), and pleiotropic associations: where variation at one region of a genome is associated with multiple observable characteristics across individuals. They also cover a range of new findings about the associations between intelligence and whole brain volume, grey matter, and white matter, as well as summarising associations with specific brain regions, and how these relate to current theories about the architecture of intelligence in the brain. Finally, they identify some points which might contribute to an integrated 'systems biology' account of intelligence differences, but conclude that there are still large explanatory gaps to be addressed in future work, many of which the LBCs can contribute to substantially, before we can fully account for individual differences in intelligence.

## Mild Cognitive Impairment in the LBC1936

Disconnected Mind PhD student Miles Welstead has had two papers published on the topic of Mild Cognitive Impairment (MCI) in LBC1936. MCI is a useful diagnosis which captures the borderland between healthy cognitive ability and dementia, but there are debates as to how to best conceptualise it, which has led to varying estimates of how prevalent MCI is in older individuals. In a paper [published](#) in *Alzheimer Disease & Associated Disorders*, Miles derived MCI categories to examine prevalence in the LBC1936, finding that there was a proportional increase from age 76 (wave 3) to 82 (wave 5), from 15% to 18% prevalence, in line with most previous research.

Studies of MCI prevalence are usually cross-sectional, so they can't account for factors which might predict change over time. In a second paper, [published](#) in *Journal of Alzheimer's Disease*, Miles examined factors which predicted change in MCI status in the LBC1936 over time, including progression from healthy cognition to MCI, stable MCI status, or reversion from MCI to healthy cognition. From age 76 (wave 3) to age 82 (wave 5), 74% of participants remained healthy, 12% transitioned to having an MCI, 7% had an MCI which remained stable, and 7% reverted from MCI to healthy cognition. The likelihood of change was associated with age, cardiovascular disease and depressive symptoms, but not with other factors including age 11 cognitive function, years of education or whether they were a carrier of the APOE  $\epsilon$ 4 gene, which is associated with developing Alzheimer's disease.

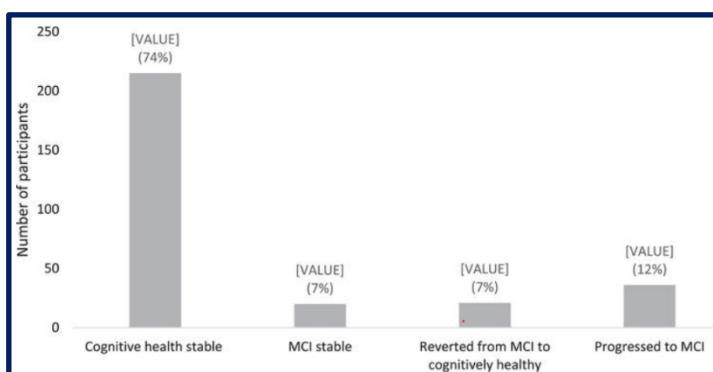


Figure from Miles' 'Predictors of MCI' paper: MCI transition rates in LBC1936 over 6 year follow up

There are opportunities to explore many other factors associated with cognitive change using this new LBC1936 MCI variable. Plans are currently in place to use MCI coding to identify common and low-frequency variants associated with MCI using available genome-wide association (GWAS) data. We will be contributing LBC1936 summary GWAS results to a larger consortium effort led by members of the NeuroCHARGE cognitive working group.

## Air pollution and cognition across the lifespan

Recently [published](#) in *Journal of Alzheimer's Disease*, LBC1936 Co-investigator Dr Tom Russ and team authored a paper which is the first to examine exposure to air pollution across the life course in relation to cognitive decline; this has not been possible up to now due to a lack of data on air pollution before the 1990s. Tom and colleagues used estimated pollution levels and lifetime residential history data to model exposure to air pollution levels at multiple time points between 1935-1990. Higher air pollution levels in 1935, when LBC1936 participants would have been in utero, were associated with worse change in cognitive abilities from age 11 to age 70, but not with cognitive trajectories from age 70 to 79.

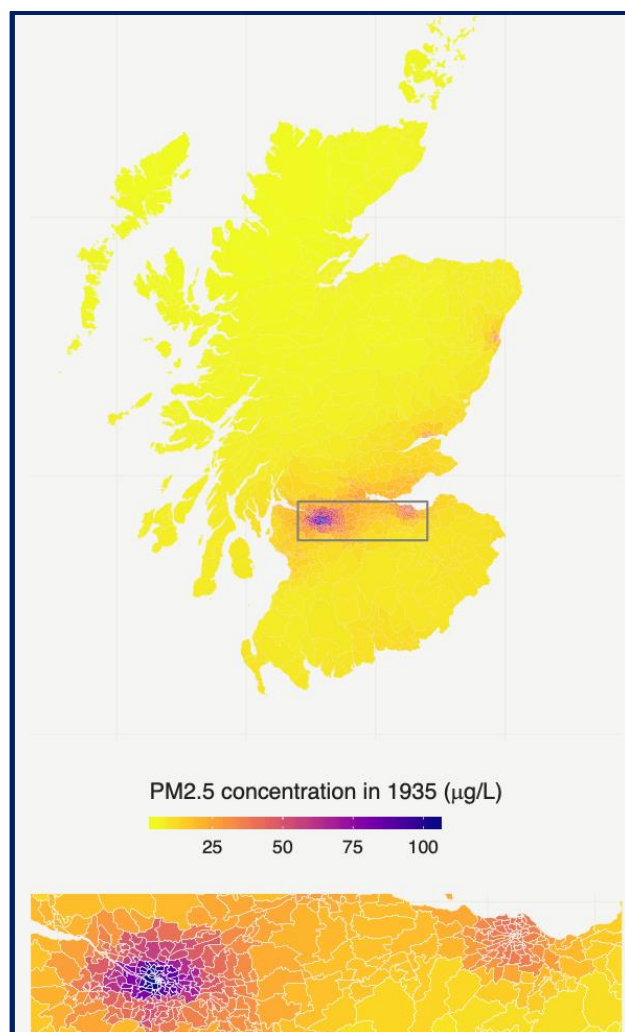


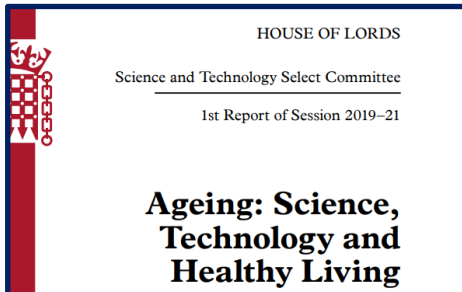
Image from paper: Modelled air pollution levels in Scotland in 1935 when the LBC1936 would have been in utero

Tom said: "For the first time we have shown the effect that exposure to air pollution very early in life could have on the brain many decades later. This is the first step towards understanding the harmful effects of air pollution on the brain and could help reduce the risk of dementia for future generations." The exciting findings received a lot of media attention from local and national [newspapers](#).

## KE & Impact

### House of Lords' report: how science and technology can enable healthier living in old age

In January, the House of Lords released a [report](#) on their inquiry 'Ageing: Science, Technology and Healthy Living', which aimed to explore themes of improving health in older age, and understand the role of science and technology in meeting this goal.



LBC research was featured prominently in the report. It drew on the evidence given by expert witnesses, including Disconnected Mind Co-Investigator Dr Stuart Ritchie, and long-term collaborator Dr Riccardo Marioni. Both drew on important LBC findings throughout. It also features the work of team member Dr Janie Corley, citing her [paper](#) in *Psychological Medicine*, which shows that “there is no silver bullet for protecting cognitive function in old age, but a number of protective factors can give marginal gains”. Drawing on this paper, the report notes a number of factors which affect cognitive function, including smoking, loneliness, social isolation, and physical activity.

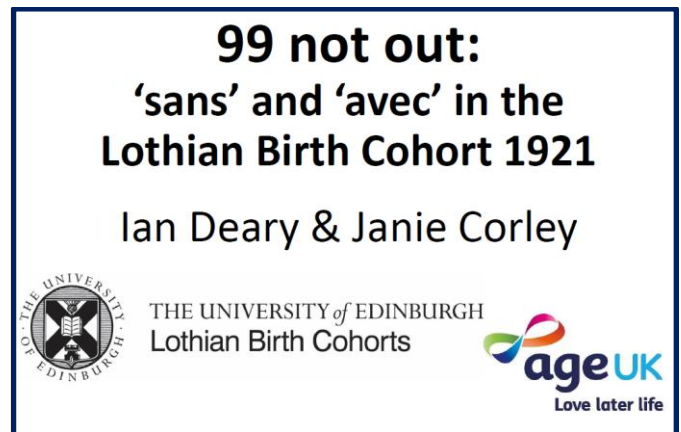
Links have been identified between lifestyle factors and cognitive and mental health. A report on the findings of the Lothian Birth Cohort studies<sup>361</sup> noted: “An individual’s cognitive trajectory is the result of a combination of shared influences with the rest of the body.”<sup>362</sup> Analysis of data from this study found that there is no “silver bullet” for protecting cognitive function in old age, but a number of protective factors can give “marginal gains”.<sup>363</sup> For example, there is clear evidence that cognitive function is harmed by smoking, loneliness and social isolation, and is aided by maintaining physical activity into older age.<sup>364</sup>

Screenshot from the House of Lords report, citing the LBCs

In addition, the report recognizes the immense value and need for funding of longitudinal studies such as the LBCs, and their importance as the fundamental source of information for our understanding of lifestyle factors and how they influence health across the lifespan. Unfortunately, the report concluded that the Government is not currently on track to meet their objective: to ensure that older people have, on average, an extra five years of healthy and independent life. However, we look forward to continuing to contribute to research into healthy ageing, along with Age UK, and influencing policy and public health advice in the hope of achieving this aim.

## Getting to age 99 and beyond

The seven ages of man(kind); that was the theme of the British Neuroscience Association's 2020 Festive Symposium, held on 14th December 2020. Professor Ian Deary gave the last online talk of the day, co-authored by Janie Corley, on the final, 7th age of man. In Shakespeare's play 'As You Like It', he wrote that this is the age at which we are in, "second childishness and mere oblivion, sans teeth, sans eyes, sans taste, sans everything".



Ian described the Lothian Birth Cohort 1921 (LBC1921) and some of their remarkable results, especially those at age 90 and after. He explained how thinking skills at age 11 were still correlated with thinking skills at 90--and whether people had survived to that age--but not with life satisfaction. He looked at what LBC1921 had found out about eyes and teeth in older age, and related those to intelligence. Finally, Ian looked at whether eyes, teeth, thinking, and feeling at age 79 were related to surviving to 99, which will be updated when the LBC1921 are 100: this year in 2021! The talk ended with some great questions from the 250 people in attendance.

### Alan Gow speaks at Glenrothes Probus

In December, LBC collaborator Dr Alan Gow gave an online talk for Glenrothes Probus on “Keeping sharp: what promotes brain health as we age?”, covering a range of lifestyle factors investigated in the LBC and other studies, with Janie Corley's excellent 'marginal gains' [paper](#) providing the perfect jumping off point for the discussion. LBC researchers have done many Probus talks over the years and the discussion was just as good online!



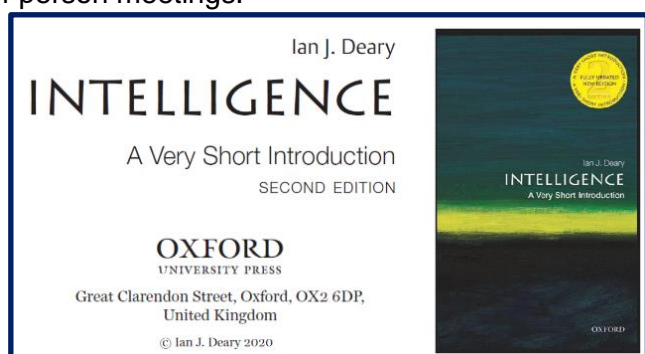
## Susie Shenkin speaks at the Edinburgh & Lothians Prostate Support Group

LBC investigator Dr Susie Shenkin was invited to speak at Maggie's ELPSG (Edinburgh & Lothians Prostate Support Group) on the topic of 'Healthy (and not so healthy) ageing: can we stop our brains (and bodies) from ageing?' Using LBC data, she spoke about the differences between individuals as they age, in their physical appearance, their cognitive function, and their physical abilities. She also discussed the differences between normal ageing and dementia, and used LBC data to show the differences between individuals of the same age in their cognitive ability, appearance of their brain scans, and physical function, and how early life is important in shaping later life health. They also discussed measures that people can take to stop their brains from ageing, basing this on the 'LBC Practical [Guide](#) to Ageing Well'. People were particularly interested in the role of exercise, as the previous speaker from Prostate Scotland had been promoting their new exercise [videos](#) for people with prostate cancer.



## A short introduction to intelligence for retired staff

The University of Edinburgh and Heriot Watt University Retired Staff Association had their first ever online talk on January 12th 2021, given by Professor Ian Deary. Ian's talk entitled, 'Ten quite interesting things about human intelligence', took the audience through the chapters of his newly-revised book: *Intelligence: A Very Short Introduction* (Oxford University Press). He used examples from the LBCs and the Scottish Mental Surveys. Example topics included ageing, survival, sex differences, genetics, and brain imaging. Ian especially enjoyed the good question session. There was a good attendance, with over 40 callers, comparable to the in-person meetings.



## Alan Gow in BBC's 'Just One Thing' podcast

In February, Dr Alan Gow was invited to speak with Michael Mosely for a recording of a new BBC podcast named '*Just One Thing*'. The podcast will look at different kinds of lifestyle and behaviour related to health outcomes, and aims to encourage people to change 'just one thing' in a manageable way to influence their health. During the episode, Alan spoke about activities and learning new things, and drew on Janie Corley's 'marginal gains' [paper](#) in order to highlight that to influence your cognitive health and 'age well', it is more about making small changes across many dozens of things, not 'just one thing'! The episode is due for release in the Spring; watch this space!



Alan Gow and Michael Mosely record the BBC podcast 'Just One Thing' via Zoom call

## Janie Corley's paper in International Press

In our December edition, we summarised Dr Janie Corley's recent [paper](#) in *Experimental Gerontology*, which examined associations between Food Frequency Questionnaire data, cognitive ability, and brain structure. Janie found that "eating more green leafy vegetables and cutting down on red meat might be two key food elements that contribute to the cognitive benefits of the Mediterranean-style diet. In the LBC1936, the positive relationship between a Mediterranean diet and thinking skills is not accounted for by having a healthier brain structure, as one might expect." The study is one of the first to test cognitive and neuroimaging outcomes in the same sample, and has drawn a huge amount of interest from national and international media, with global coverage, and particularly high profile titles in Russia and India.



Screenshot of coverage of Janie's paper in an Italian newspaper

## Contact

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

### Email

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

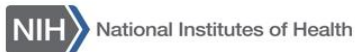
### Website

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)



## Some new publications

### Epub before print

Corley, J. and Deary, I. (2020) 'Dietary patterns and trajectories of global and domain-specific cognitive decline in the Lothian Birth Cohort 1936', *British Journal of Nutrition*. doi: [10.1017/S0007114520005139](https://doi.org/10.1017/S0007114520005139).

Cuellar-Partida, G. *et al.* (2021) '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).

Huguet, G. *et al.* (2021) 'Genome wide analysis of gene dosage in 24,092 individuals estimates that 10,000 genes modulate cognitive ability', *Molecular Psychiatry*. doi: [10.1038/s41380-020-00985-z](https://doi.org/10.1038/s41380-020-00985-z).

Stevenson, A. J. *et al.* (2021) 'Creating and validating a DNA methylation-based proxy for interleukin-6', *The Journals of Gerontology: Series A*, p. glab046. doi: [10.1093/gerona/glab046](https://doi.org/10.1093/gerona/glab046).

### Published

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).

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Cuellar-Partida, G. *et al.* (2021) '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).

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Muralidharan Sargurupremraj *et al.* (2020) 'Cerebral small vessel disease genomics and its implications across the lifespan', *Nature Communications*, 11(1), p. 6285. doi: [10.1038/s41467-020-19111-2](https://doi.org/10.1038/s41467-020-19111-2).

Murray, A. L. *et al.* (2021) 'Assessing individual-level change in dementia research', *A review of methodologies*, 13(26). doi: [10.1186/s13195-021-00768-w](https://doi.org/10.1186/s13195-021-00768-w).

Okely, J. A. *et al.* (2020) 'Change in Physical Activity, Sleep Quality, and Psychosocial Variables during COVID-19 Lockdown: Evidence from the Lothian Birth Cohort 1936', *International Journal of Environmental Research and Public Health*, 18(1), p. 210. doi: [10.3390/ijerph18010210](https://doi.org/10.3390/ijerph18010210).

Praveen Surendran *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).

Russ, T. C. *et al.* (2021) 'Life Course Air Pollution Exposure and Cognitive Decline: Modelled Historical Air Pollution Data and the Lothian Birth Cohort 1936', *Journal of Alzheimer's Disease*, pp. 1–12. doi: [10.3233/JAD-200910](https://doi.org/10.3233/JAD-200910).

Welstead, M., Luciano, M., Muniz-Terrera, G., Saunders, S., *et al.* (2021) 'Predictors of Mild Cognitive Impairment Stability, Progression, or Reversion in the Lothian Birth Cohort 1936', *Journal of Alzheimer's Disease*, pp. 1–8. doi: [10.3233/JAD-201282](https://doi.org/10.3233/JAD-201282).

Welstead, M., Luciano, M., Muniz-Terrera, G., Taylor, A. M., *et al.* (2021) 'Prevalence of Mild Cognitive Impairment in the Lothian Birth Cohort 1936', *Alzheimer Disease & Associated Disorders*, Publish Ahead of Print. doi: [10.1097/WAD.0000000000000433](https://doi.org/10.1097/WAD.0000000000000433).