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 51: September 2020

Welcome to the Autumn 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

LBC1936 COVID-19 guestionnaire update

You might remember that, in our last edition, we announced the launch of our new LBC1936 COVID-19 guestionnaire, developed by our testing team to assess the impact of the COVID-19 lockdown on our participants. We were delighted by the number of participants who were willing to take part during such a difficult time. By the time the questionnaire was closed, we received a total of 190 responses.



Screen capture of the LBC1936 COVID-19 Questionnaire

The data has been processed and the team are preparing papers for publication. Together the papers explore a range of topics, including: which factors affected coping and behaviour during lockdown; the effect of lockdown on longitudinal trajectories in lifestyle and psychosocial factors, such as sleep, physical activity, and loneliness; associations between garden access during lockdown and health and wellbeing; and a qualitative paper examining the free text section, where participants could tell us anything they'd like about their experiences.

We are excited to use the data in further analyses, including for an exciting collaborative opportunity, which we will describe in the following section.

Sharing results of the LBC1936 COVID-19 questionnaire with Public Health Scotland

In another exciting development, the team was contacted by Public Health Scotland (PHS), and we prepared a special report including a privileged first view of the COVID-19 questionnaire results which Prof Ian Deary presented to one of the working groups. Following the presentation, epidemiologist Markéta Keller, on behalf of PHS, had this to say:

"We all are currently exposed to an unprecedented situation where a fast and sophisticated approach to generate evidence is essential to formulate informed public health decisions. Given the long-term wonderful work conducted by Professor Deary and the Lothian Birth Cohorts team, it comes as no surprise that they responded to the current COVID-19 situation in a pragmatic and wise manner.

The LBC1936 COVID-19 Questionnaire has produced most interesting insights into older people's understanding of, feeling in, and responses to the current situation. It was incredibly kind of Professor Deary and the LBC team to prioritise giving summary results of the questionnaire (linked with previous LBC1936 data) to PHS's Enhanced Surveillance Cell. We were grateful for having been provided with a fast-tracked report, coupled with an offer to present the questionnaire's results, not only in the context of the current situation but also in terms of prospective data analyses.

The presentation, delivered by Professor Deary to PHS's Enhanced Surveillance Cell team, was most fascinating, captured everyone's interest and generated many relevant questions and interesting discussion. We agreed that the presentation has certainly broadened our understanding and perceptions. We are therefore most grateful to Professor Deary and his team, and we have agreed to further collaboration between PHS and the LBCs team with the aim of developing a comprehensive understanding of the aspects and factors that older people are currently experiencing. Such knowledge will ultimately benefit the wider Scottish population.

Many thanks to Professor Deary, the LBCs team and every one of the LBC1936 study participants!"



Staff news

Disconnected Mind team update

The Disconnected Mind team are preparing for a safe return to testing for wave 6 as soon as possible. We are also making some changes: Ian will be retiring at the end of this year (more in the next issue!). Ian will be staying as Professor Emeritus, so the LBCs can still call on all his experience.

We are delighted to congratulate current Disconnected Mind Co-Investigator Dr Simon Cox, who has been promoted and will take over as Principal Investigator. Simon has worked with the study since starting his PhD in 2009. He was LBC1936 Study Co-ordinator before his Medical Research Council (MRC) Post-doc working on topics involving LBC1936 brain imaging data. He is currently Principal Investigator on the MRC funded wave of MRI scanning of the LBC1936.

The team overall will be enhanced; in addition to the previous investigators, Dr Michelle Luciano and Dr Susie Shenkin are now part of the investigator team. Both have a long history of LBCs experience. These changes are also happening at a time when Simon and Michelle are UKRI independent grantholders, as are our team members Judy Okely and David Hill. We're very excited to move into wave 6 with this great new team!

Scientific Highlights

Blood pressure and cognitive function

In a study <u>published</u> in *BMJ open*, Postdoctoral researcher Drew Altschul (who recently won a prestigious British Academy Postdoctoral Fellowship – congrats, Drew!) investigated whether change in cognitive functions were associated with changes in blood pressure, with each having been measured across the many waves of the LBC1936.

He found no longitudinal associations, but, since there are known associations between cognitive dysfunction and high blood pressure, he investigated in more depth by exploring the role of medication. While medication was, unsurprisingly, quite effective at treating hypertension, there was no



evidence that natural or medicationimpacted change in blood pressure and cognitive function are related during the eighth decade.

An LBC1936 participant has their blood pressure taken

Personality and healthy ageing

How does personality change over the life-course? Do personality traits interact to predict health outcomes?

These were the questions asked across four recent collaborative projects, all now published in *Collabra: Psychology*, by researchers in the Integrative Analysis of Longitudinal Studies of Aging and Dementia (IALSA) consortium. The IALSA project brings together researchers from cohort studies around the world to tackle key questions for healthy ageing. The LBC1936 continues to be a major contributor to this work given the high quality longitudinal data after 70 years of age.



Associations between Neuroticism and Odds of Physical Activity, moderated by Conscientiousness, in IALSA studies including LBC1936.

The Disconnected Mind team's contribution to the papers was led by Tom Booth and Ian Deary. In the first project, results suggested small declines in conscientiousness, openness and extraversion across the life course, but also indicated that these estimates were variable across studies. The second set of papers explored the idea of healthy neuroticism. Neuroticism has generally been shown to negatively relate to health. However, it has been suggested that for individuals who also have high conscientiousness, this may not be the case. Results showed limited support for the idea of healthy neuroticism in predicting health behaviours, but no evidence that it was predictive of incidence of chronic conditions or longevity.

The set of papers exploring relationships between neuroticism and <u>longevity</u>, <u>health behaviours</u>, and <u>chronic conditions</u> are now available online.



Aging-sensitive networks within the human structural connectome and cognitive decline

Identifying neurodegenerative processes underlying aging-related cognitive decline may provide critical insights into the precursors of Alzheimer's disease and late-life dementias. In a recently accepted paper in *Biological Psychiatry*, James Madole and coauthors used data from the Lothian Birth Cohort 1936 study (LBC) and UK Biobank (UKB) to examine the aging of structural elements of the brain (different areas of cortical grey matter, and the white matter pathways that connect them) in relation to key domains of late-life cognitive ability. This is the latest output arising from the United States NIH R01 collaboration with The University of Texas at Austin, on which team members Mark Bastin, Ian Deary and Simon Cox are co-investigators.



Maps of each brain network of interest, highlighting networkspecific connectome elements ('edges' and 'nodes')

By using cross-sample LBC and UKB information about how strongly different aspects of the brain age to predict cognitive ability, the team wanted to understand whether those areas of the brain most strongly related to ageing in one sample (UKB) could predict how people differ in their cognitive functioning in another sample (LBC). In UK Biobank, aging of white matter connections and grey matter volumes occurred on broad dimensions of variation in brain architecture. In LBC1936, white-matter integrity was specifically related to processing speed whereas grey-matter integrity was related to both processing speed and visuospatial ability, after controlling for childhood intelligence. Relationships were particularly pronounced within the Central Executive network, a brain network comprised of regions within the prefrontal and parietal cortices. Their finding that the association between brain structure and late-life cognitive function persists after controlling for childhood cognitive ability suggests brain health may be an important indicator of late-life cognitive decline over and above preexisting differences in cognitive ability. A corrected proof is now online.

Changes in 'PSMD' across the lifespan

Advances in brain imaging methods mean that there are an increasing number of ways to exploit water diffusion in the brain's white matter to infer things about its microstructure. However, it's not clear whether they each tell us unique and useful things about normal and pathological brain ageing, and how these measures change across the lifespan is unclear, especially when it comes to 'peak width of skeletonized mean diffusivity' (PSMD). In a paper published in Frontiers in Psychiatry, Gregory Beaudet of the University of Bordeaux used diffusion tensor imaging (DTI) data from 20,000 individuals from 10 cohorts, including LBC1936, to examine PSMD across the lifespan, in comparison to 4 other DTI measures. They found a consistent pattern of change in other DTI measurements, with U-shaped patterns; decreasing in early life and increasing in later life, or the inverse, but PSMD consistently increased across the lifespan. Results show age affects PSMD differently to other DTI measures, and since PSMD increases throughout the lifespan, with even sharper increases over age 60, PSMD might be an early marker of the ageing process.

Adherence to MIND diet is associated with 12year all-cause mortality in older adults

In a paper currently 'in press' at Public Health Nutrition, Dr Janie Corley examined whether diet is associated with risk of mortality in the LBC1936. Using responses to the diet questionnaire at age



70, she calculated scores for three dietary patterns: a Mediterranean-style diet; a traditional (more processed-food) diet, and the MIND diet. The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet was developed to promote healthy cognitive ageing. It is composed of elements from the Mediterranean diet and the DASH (Dietary Approaches to Stop Hypertension) diet and emphasises vegetables, wholegrains, fish, olive oil, and poultry, a low intake of red meat and saturated fat, and specifically includes 'brain healthy foods' such as berries and green leafy vegetables.

Dr Corley found that individuals whose diets more closely conformed to the MIND diet had a significantly lower odds of mortality over 12 years of follow-up; those in the top compared with the bottom third of MIND diet scores had a 37% lower risk of death. This suggests the MIND diet is associated with increased survival among older people.

A Celebration of Scottish Health Research

Lothian Birth Cohort members are some of the most intensely studied individuals in the world. They contribute to research with a range of health and lifestyle data. But what are their thoughts on the use of data in research? Would they be willing to change an aspect of their lifestyle or take a new drug?



A 'Thank you' cake from the event, thanking members of all the cohorts invited

In a paper by former Disconnected Mind Knowledge Exchange Officer, Dr Iona Beange, now available online in Wellcome Open Research, Iona took the opportunity to answer these questions. She used data collected during a public engagement event. "A Celebration Scottish Health Research: of Participatory Research in Cohort Studies of Mental and Physical Health", held in Edinburgh on 10th June, 2018. The aim of the event - attended by around 250 cohort members from a number of Scottish cohort studies, with almost half of the audience composed of Lothian Birth Cohort members - was to share the key results from the studies but also to measure the public's attitudes towards future research. Participants were invited to express their views via an interactive voting pad.

The results, live and accessible immediately during the event, showed an overwhelming support in the audience for access to health records for researchers and doctors, but not when they serve commercial interests. This is a great example of successful knowledge exchange event that benefits both researchers and the public.



Cohort members vote on their interactive voting pads

Knowledge exchange and Impact

Alan Gow at Cabaret of dangerous ideas

August would usually be a time for the festivals to arrive in Edinburgh, and Disconnected Mind collaborator and former team member, Dr Alan Gow, has been a regular presenter at the Cabaret of Dangerous Ideas, discussing the lifestyle factors that might promote brain health with lots of references to LBC research! Although the Fringe isn't happening this year, the Cabaret of Dangerous Ideas put on a series of online shows throughout July, and Alan appeared in a triple bill with "This Will Make You Sharper!". The show was recorded in The Stand Comedy Club, Edinburgh, and beamed live into people's homes. If you missed it, you can now catch up <u>online</u>.



Alan filming in The Stand Comedy Club

Joanna Wardlaw presents at Alzheimer's Association International Conference

Disconnected Mind Principal Investigator, Professor Joanna Wardlaw, was invited to present at the 2020 Alzheimer's Association International Conference (AAIC) in July. As part of an online virtual symposium, Joanna presented her talk 'Neuroimaging of White Matter Hyperintensities'. which is a key area of investigation for the Disconnected Mind project. In her talk, Joanna aimed to describe how to identify and gauge severity of white matter lesions in brain imaging, their clinical implications, and discuss current thinking on the mechanisms of, and risk factors for, white matter lesions. At its peak, the symposium was viewed online by nearly 700 people.



Judy Okely's music research in Global Council on Brain Health report

Dr Judy Okely is leading an ESRC funded project on the potential association between lifetime musical experience and healthy ageing. Using LBC1936 data, Judy and her colleagues Prof Ian Deary, Dr Katie



Music on Our Minds: The Rich Potential of Music to Promote Brain Health and Mental Well-Being

Overy, and Dr Michelle Luciano plan to examine whether experience playing a musical instrument is associated with better cognitive, brain, or psychological health in older age or with less decline in these capacities over time.

Results so far have shown that around 40% of participants played an instrument in the past, though only a small proportion (9%) of them currently play a musical instrument at age 82. The first longitudinal analysis of the data suggests that greater experience playing a musical instrument is associated with slightly healthier lifetime change in general cognitive ability (between ages 11 and 70). These preliminary findings were featured in a new report from the Global Council on Brain Health on the potential for music to promote healthy brain ageing. The full report is available <u>online</u>.



LBC data presented at OHBM2020

This year, two PhD students working with Disconnected Mind project data, Eleanor Conole and Emily Wheater, attended the 2020 Organisation for Human Brain mapping conference, where they both presented posters on work conducted with data from the LBC1936. Sadly, being a virtual conference, they enjoyed it from their living rooms rather than the more exciting city of Montreal!

Emily used LBC MRI scans and hospital birth records to explore the impact of birth weight on brain structure at 73 years old. She found that birthweight contributes to larger brain volumes and greater regional cortical surface area in later life, but does not modify the trajectory of age-related change, such as brain tissue atrophy, nor ageing-related WM damage. This gives the clearest details yet about brain size benefits of birthweight that are present 73 years later.



Figure from Emily's research, displaying birth weight associations with cortical surface area.

Using structural and diffusion MRI data from 521 LBC participants when they were 73 years old, Eleanor Conole presented research showing that a DNA methylation (DNAm) proxy for C-reactive protein (a marker of low-level chronic inflammation) is more strongly associated with brain health outcomes such as grey and white matter volume and cognitive ability, than blood serum levels of Creactive protein. DNAm levels may provide more stable accounts of cumulative inflammatory burden than traditional serum approaches, and this work indicates that chronic inflammation may have wider cognitive consequences than previously thought.



Figure from Eleanor's research, displaying cortical thickness associations with inflammation.

LBC in Cambridge Handbook of Cognitive Aging

Our collaborator and former team member, Dr Alan Gow, has joined an international group of experts in a new volume on cognitive ageing, "The Cambridge Handbook of Cognitive Aging: A Life Course Perspective", now <u>available to purchase</u>.

In over 700 pages and more than 30 chapters, the handbook offers a comprehensive review of the latest research on the topic, from models and mechanism of cognitive ageing to the role of cognitive, social and biological factors in the process. Alan's chapter, 'Association between activity participation and cognitive aging', building on his work with the Lothian Birth Cohorts, contributes to this perspective with an overview of studies examining the modifiable factors that may protect the brain and cognitive abilities, such as participation in mental, physical and social activities across the lifespan. While the cognitive benefits for some of these activities are not uncontroversial, the chapter sends a clear message that there is no harm in staying active and engaging in new activities.



Alan receives his first copy of the book, 'The Cambridge Handbook of Cognitive Aging'.

New Statesman article including LBC1936 research: Why people need parks

One of the few positive consequences of the pandemic is that politicians and policy-makers alike have come to understand the 'importance of public parks and gardens for people's wellbeing', writes journalist Julia Thrift in a recent <u>article</u> in the New Statesman.



In her article, Julia noted the increase in scientific investigation, since the early 2000s, of the effects of green space on short term outcomes such as stress reduction, but also drew on exploration of longerterm effects: such as those reported by our collaborators, Dr Mark Cherrie, Dr Niamh Short, and Professor Catharine Ward Thompson, based on LBC1936 data. In their original study, published in 2019 in International Journal of Environmental Research Public Health, and they linked geographical information about where LBC1936 participants had lived throughout their lives, with cognitive data collected at ages 70-76. They found evidence that access to green space during childhood and adolescence had a beneficial effect on cognitive ageing in older age.

Julia argued that these LBC1936 results, along with many other findings about the effects of green space, it is clear that investing in making green space accessible to all is necessary for a 'more equitable and resilient society'.

LBC feature in Swedish daily Svenska Dagbladet

We often say that the Lothian Birth Cohorts are world-renowned, and in July, we saw evidence of this once more! Professor Ian Deary received an email from journalist Maria Sundén Jelmini, of the Swedish daily 'Svenska Dagbladet', to let him know she would be including the story of the discovery of the Lothian Birth Cohort records, when they were discovered in a basement in Moray House in the 1990s, as part of a series of articles she was writing about intelligence. The articles have not yet been published, but watch this space!



Age UK News

Greetings from the Research Team at Age UK. It's been another busy few months for us, still working from home to help slow the spread of the virus, and doing our best to work with our colleagues across Age UK to advocate for older people.



We're continuing to campaign for the free TV licence to be retained for all over 75s, despite the current impasse between the BBC and the government. At the moment the BBC has only committed to offering free TV licences to people aged 75 and over and who receive Pension Credit, and we know that about two fifths of those who are eligible for Pension Credit aren't receiving it. If you're not sure whether you might be eligible for Pension Credit either <u>visit our</u> <u>website</u> or give our Information and Advice line a call on 0800 678 1602.



We're also campaigning to protect older workers who are worried about going back to work as lockdown eases – we know that there are 319,000 older workers who have been told to shield themselves because of health conditions they have. We're working with lots of health charities to try to convince the Chancellor to extend the 'furlough' scheme for these older workers so that they don't feel forced to choose between their job and their health. Alongside all this, we're continuing our longstanding campaign for improvements to social care so that the 1.5 million older people with an unmet need for care can get the support they need. We've seen how the coronavirus epidemic has affected older people who live in care homes so severely, and know that this is just more evidence that the system isn't up to doing the best for older people.



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



Some new publications

Accepted/In press

Ballerini, L.*et al.* (2020) 'Quantitative Measurements of Enlarged Perivascular Spaces in the Brain are Associated with Retinal Microvascular Parameters in Older Community-Dwelling Subjects.', *Cerebral Circulation—Cognition and Behavior*.

Corley, J. (2020) 'Adherence to the MIND diet is associated with 12-year all-cause mortality in older adults', *Public Health Nutrition*.

Hofer, E. *et al.* (2020) 'Genetic correlations and genome-wide associations of cortical structure in general population samples of 22 824 adults', *Nature Communications*.

Knol, M. J. *et al.* (2020) 'Association of common genetic variants with brain microbleeds: a genome-wide association study', *Neurology*.

Partida, G. C. *et al.* (2020) 'Genome-wide association study identifies 48 common genetic variants associated with handedness', *bioRxiv*, p. 831321. doi: <u>10.1101/831321</u>.

Welstead, M. *et al.* (2020) 'Inflammation as a Risk Factor for the Development of Frailty in the Lothian Birth Cohort 1936', *Experimental Gerontology*.

Some new publications (continued)

Epub before print

Madole, J. W. *et al.* (2020) 'Aging-Sensitive Networks Within the Human Structural Connectome Are Implicated in Late-Life Cognitive Declines', *Biological Psychiatry*, p. S0006322320316796. doi: 10.1016/j.biopsych.2020.06.010.

Published

Altschul, D., Starr, J. and Deary, I. (2020) 'Blood pressure and cognitive function across the eighth decade: a prospective study of the Lothian Birth Cohort of 1936', *BMJ Open*, 10(7), p. e033990. doi: 10.1136/bmjopen-2019-033990.

Armstrong, N. J. *et al.* (2020) 'Common Genetic Variation Indicates Separate Causes for Periventricular and Deep White Matter Hyperintensities', *Stroke*, 51(7), pp. 2111–2121. doi: 10.1161/STROKEAHA.119.027544.

Colicino, E. *et al.* (2020) 'Blood DNA methylation sites predict death risk in a longitudinal study of 12,300 individuals', *Aging.*

Graham, E. K. *et al.* (2020) 'Is Healthy Neuroticism Associated with Health Behaviors? A Coordinated Integrative Data Analysis', *Collabra: Psychology*, 6(1), p. 32. doi: <u>10.1525/collabra.266</u>.

Hillary, Robert F. *et al.* (2020) 'Multi-method genome and epigenome wide studies of inflammatory protein levels in healthy older adults', *Genome Medicine*.

Ma, J. *et al.* (2020) 'Whole blood DNA methylation signatures of diet are associated with cardiovascular disease risk factors and all-cause mortality', *Circulation: Genomic and Precision Medicine*. Lippincott Williams and Wilkins Ltd.

Okely, J. A. and Deary, I. J. (2020) 'Associations Between Declining Physical and Cognitive Functions in the Lothian Birth Cohort 1936', *The Journals of Gerontology: Series A.* doi: 10.1093/gerona/glaa023.

Shin, J. *et al.* (2020) 'Global and Regional Development of the Human Cerebral Cortex: Molecular Architecture and Occupational Aptitudes', *Cerebral Cortex*, 30(7), pp. 4121–4139. doi: 10.1093/cercor/bhaa035.

Stevenson, A. J. *et al.* (2020) 'Characterisation of an inflammation-related epigenetic score and its association with cognitive ability', *Clinical Epigenetics*, 12(1), p. 113. doi: <u>10.1186/s13148-020-00903-8</u>.

Toombs, J. *et al.* (2020) 'Generation of twenty four induced pluripotent stem cell lines from twenty four members of the Lothian 4 Birth Cohort 1936', *Stem cell research*. Elsevier.

Trejo Banos, D. *et al.* (2020) 'Bayesian reassessment of the epigenetic architecture of complex traits', *Nature Communications*, 11(1), p. 2865. doi: <u>10.1038/s41467-020-16520-1</u>.

Turiano, N. A. *et al.* (2020) 'Is Healthy Neuroticism Associated with Longevity? A Coordinated Integrative Data Analysis', *Collabra: Psychology*, 6(1), p. 33. doi: <u>10.1525/collabra.268</u>.

Weston, S. J. *et al.* (2020) 'Is Healthy Neuroticism Associated with Chronic Conditions? A Coordinated Integrative Data Analysis', *Collabra: Psychology*, 6(1), p. 42. doi: <u>10.1525/collabra.267</u>.

Contact

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