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 47: June 2019

Welcome to The Disconnected Mind project's summer newsletter. Read on for more news about what we've been up to over the last few months, and for our regular update on the team's research activity, events we have been participating in, and some of our recent publications. Don't forget to see the contribution from our colleagues at Age UK from page 5 onwards. Please get in touch for more information about anything in the newsletter, or if you would like to contribute to a future issue. Contact details and links to publications are at the end of the newsletter.

Lothian Birth Cohort 1936 participant attends House of Lords Select Committee on Science and Technology

Tom Sommerville and Age UK's Libby Archer in front of the Houses of Parliament

We start this edition with a special article written by one of our Lothian Birth Cohort 1936 (LBC1936) participants, who, earlier this summer, was given a rare opportunity to directly contribute to future policy on ageing. In July, Tom Sommerville was invited to attend a focus group with the House of Lords Select Committee on Science & Technology to help shape the newly launched Inquiry into Ageing: Science, Technology and Healthy Living. On his return, the keen writer jotted down a few words to share his experience with the LBCs team and our Disconnected Mind newsletter readers. Here's what Tom had to say:

Lording It

On Tuesday, July 9, 2019 on a hot, humid day I was, courtesy of Age UK, in the House of Lords as a member of a six-person focus group to discuss the impact of ageing on one's life. We commoners sat with eight peers for one hour and told our stories. We had been given four suggestions for discussion:

- *The impact of ageing on emotional wellbeing and the practicalities of daily life*
- *The importance of social interactions*
- *Access to medicines and products that can help with the impact of ageing*
- *The role of digital services in helping to reduce the impacts of ageing*

But we oldies were a fairly opinionated group who were determined to get over experiences that were not necessarily covered by the four suggestions. I have to say the rapport between the peers and us commoners was excellent and the hour was very informal and often humorous. Five of the group were able-bodied and seemed to be ageing well. Most of the discussion concentrated on the imperative need for social interaction, friends and family and the ways in which digital devices could help. I did shoe-horn the LBC into the talk at one point and got three questions on it. Three of us were computer users and strongly encouraged the others to consider the usefulness of Skype or Face Time and the internet. Computer courses for older people were discussed.

An hour was hardly long enough to do the subject justice and as I walked back over Westminster Bridge I began to think of the things I would have liked to say before we ran of time. I will remember the alfresco lunch overlooking the Thames and the tour of the Palace of Westminster and Portcullis House. My last thoughts were gratitude to Libby Archer of Age UK for looking after me and, well... I wouldn't mind being a lord...for a week or two.

Tom Sommerville

LBC1936 News

LBCs 20 year reunion, coming soon!

Ian Deary and participants at the LBCs reunion 2017

It's that time again. Very soon participants of LBC1921 and LBC1936 will descend on the city centre, to attend the next LBCs reunion. This time we are celebrating 20 years (to the day!) since the very first LBC1921s were tested on 7th September 1999. The reunion also coincides with the end of Wave 5 testing of LBC1936. Ian and the team are looking forward to giving guests a sneak preview of the age 82 cognitive, brain, and health results. More on this in the next edition.

Professor Ian Deary awarded OBE

"It was the Queen!", came the message from Ian, following his visit to the Palace of Holyrood to be awarded the prestigious Officer of the Order or the British Empire (OBE). The LBC team were on tenterhooks, on 2nd July 2019, waiting to hear who would bestow the honour. Ian Deary, Director of the Disconnected Mind project, received the award for services to the Social Sciences. Many congratulations, Ian!

Farewell to Brain Research Imaging Centre

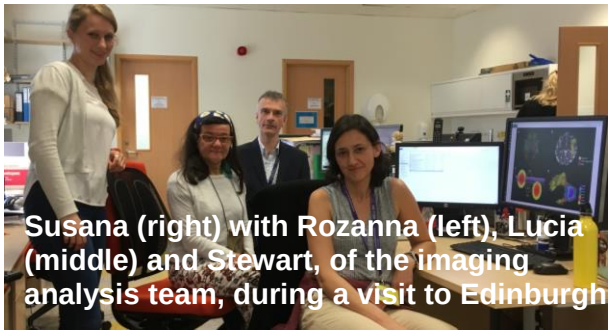
The Brain Research Imaging Centre (BRIC; now Edinburgh Imaging) at the Department of Clinical Neurosciences (DCN) in Edinburgh's Western General Hospital, has been the home of LBCs brain imaging since the studies began. As part of major redevelopment works, the DCN will be moving to the Royal Infirmary of Edinburgh's BioQuarter Campus. In July, to mark the end of BRIC, and to celebrate the enormous success of the facility during its 21-year history, Professor Joanna Wardlaw, Director of Edinburgh Imaging and lead brain imaging Investigator on the Disconnected Mind project, held a farewell tea-party for past and present support staff, radiologists, radiographers, researchers and students, who have been involved with BRIC since it first opened in 1998. Some of the LBC team were among the guests. This marks the end of a 10-year (4 wave) consecutive run of structural brain imaging of LBC1936 participants using the exact same scanner. During Wave 5 of the LBC1936 study, we prepared for the transfer to a new facility and new scanner technology by having 100 participants undergo brain scans on the new 3T scanner, to which we will be moving, as well as their usual 1.5T scan at BRIC. This means that we are able to compare 1.5T and 3T brain imaging of LBC1936 participants.

The last ever LBC1936 participant to be scanned at BRIC

Meet (more of) the team

In the June 2019 Disconnected Mind newsletter we filled you in on some of the latest additions to the LBC team, and shared with you a photo of the current team based in 7 George Square (Department of Psychology, University of Edinburgh). One of our team members based outside of George Square, who did not appear in the photograph, was Dr Susana Muñoz Maniega. Keen for Susana's

important work on the LBCs not to be overlooked, we asked Susan to introduce herself and give our readers an insight into her role. Susana said; "*I have been part of the LBC1936 imaging team since 2007, and I was there for the first wave of MRI. My main job is to measure specific characteristics of the brain's white matter from the images and to investigate how these, and other health parameters, are linked to changes in cognition. I am not based in Edinburgh, but nearly 400 miles away in Hertfordshire! Luckily, I can access the LBC1936 data remotely and securely from home, where I works most of the time, with regular meetings with other team members through Skype. Every 6-8 weeks I travel to Edinburgh for the main LBC1936 imaging meeting, where we discuss progress and plan further analyses, and for a good catch up with the team!*"



Susana (right) with Rozanna (left), Lucia (middle) and Stewart, of the imaging analysis team, during a visit to Edinburgh

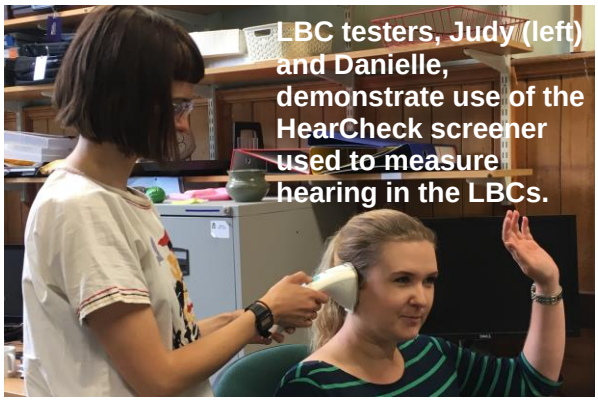
Susana led a recent publication in *Frontiers Neurology*, which described changes in the microstructure of the major brain white matter tracts with distance from the white matter hyperintensities visible in MRI. The study, using LBC1936 data, is the largest of its kind and the findings suggest potentially new channels for the propagation and accumulation of tissue damage from the visible white matter hyperintensities, which need to be explored in the future. Find a link to Susana's paper on page 8.

Scientific highlights

Epigenetic signatures of smoking associate with cognitive function, brain structure, and mental and physical health outcomes in the LBC1936

The relationship between smoking and adverse health is well-established, but less is known about how DNA methylation, a process that influences whether genes are 'switched on or off', may contribute to smoking-related disease and other health outcomes. LBC team member, Dr Janie Corley, recently conducted a study, accepted for publication in *Translational Psychiatry*, in which she and co-authors used DNA methylation data from LBC1936 participants at age 70 to create a methylation score related to lifetime smoking (smoking DNAm). They tested whether smoking DNAm was associated with smoking-related health outcomes. They found that higher smoking-DNAm was associated with poorer cognitive function and measures of brain health including lower brain volume, a thinner cortex, and more white matter lesions. It was also linked to: poorer physical health (e.g. higher inflammation levels, slower walking speed, and higher body mass index); poorer mental health (e.g. lower quality of life); poorer diet; an increased risk of common diseases such as high cholesterol, stroke; and, early death. They also found that smoking DNAm was a more accurate predictor of smoking-related adverse health than self-reported smoking measures such as smoking status and smoking pack years. These results suggest that a DNA methylation score for smoking can be used to improve our prediction of smoking-related health consequences in later life.

Longitudinal associations between hearing loss and general cognitive ability



LBC testers, Judy (left) and Danielle, demonstrate use of the HearCheck screener used to measure hearing in the LBCs.

People with age-related hearing loss are likely to perform less well on tests of cognitive ability. Dr Judy Okely and colleagues used LBC1936 data to test for the potential contribution of childhood cognitive ability to this relationship. Childhood cognitive ability is strongly related to cognitive health in older age, and may be related to hearing loss through its association with risk factors such as smoking and history of chronic disease. Judy and her co-authors found that individuals with a higher cognitive ability at age 11 had a

slightly lower risk of having a hearing impairment at age 76. This association was explained by differences in socio-economic position, smoking status, and disease history. At age 76, hearing loss was associated with poorer cognitive ability level at the same age, but was not related to change in general cognitive ability over the following three years. This former association was partly accounted for by childhood cognitive ability, suggesting that childhood cognitive ability contributes (potentially via demographic, lifestyle, and health differences) to the association between hearing loss and cognitive function in older age. The authors concluded that, overall, these results challenge the view, put forward by some researchers, that hearing impairment can lead to older-age cognitive decline, and point to a potentially causal relationship from early-life cognitive ability to later-life auditory health.

Knowledge Exchange and Impact

Joint Programme into Neurodegenerative Disease Research - Brain Imaging, cognition, dementia and next generation genomics (JPND-BRIDGET)

Ian Deary and members of his team welcomed international attendees to a 2-day, final meeting, in the Psychology Department to report on the progress of a collaborative grant funded by the European Union's Joint Programme into Neurodegenerative Disease Research. This collaborative research project uses magnetic resonance imaging markers of brain ageing to more precisely identify and understand the genetic influences of cognitive decline and dementia. The LBC1936 cohort is one of 9 older aged cohorts participating in this research. LBC researchers presented various findings from the LBC1936 cohort, including how the wiring of their brains related to age.

LBCs staff and collaborators at the final meeting of JPND-BRIDGET

LBCs on BBC Radio Scotland *Brainwaves*

The LBC team were delighted to welcome BBC Radio Scotland's Pennie Latin and Dan Holland to the department in August, to record a special episode of *Brainwaves,* to coincide with the 20th anniversary LBCs reunion in September. Pennie and Dan met with Ian Deary, past and present LBC cognitive testers Alison Pattie and Danielle Page, and artist Fionna Carlisle and to hear about the history of the project, and some of the artistic endeavours that the project has inspired. Pennie and Dan will also interview LBC1936 and LBC1921 participants for the show which is to be aired later in September.

BBC Radio Scotland's Dan Holland and Pennie Latin (outer left and right) with LBCs Danielle Page (2nd left) and artist Fionna Carlisle and her portrait of Ian Deary for recording of an LBC edition of

3D brain visualisation with the Scottish Cabinet Secretary for Health and Sport

On a recent visit to Edinburgh, the Cabinet Secretary for Health and Sport, Jeane Freeman MSP, was hosted by Prof Andrew McIntosh at the Royal Edinburgh Hospital and had the opportunity to learn about some research funded by the MRC in Scotland.

During the visit, Lothian Birth Cohorts researcher Dr Colin Buchanan guided the Cabinet Secretary through a demonstration of 3D brain visualisation using state-of-the-art augmented reality (AR) smart glasses. The AR display showed brain ageing based on findings from LBC1921 and LBC1936 data. The Cabinet Secretary was impressed with the potential of AR and she asked Colin about the next steps for the project. Colin mentioned plans to develop a multipurpose tool for researchers to explore complex imaging data. Colin said that AR could also be used to illustrate brain health, such as highlighting brain regions most affected by lifestyle

factors, such as smoking. The Cabinet Secretary was enthusiastic about using AR to convince people to make lifestyle changes and she said, “If someone was considering whether to quit or not, this could be the tipping point.” The AR project is being led by Dr Simon Cox and developed by Dave Liewald of the LBCs. Funding for the development phase was awarded by the MRC Engagement in Science Activities Seed Fund. A public demonstration of the AR display will be available at the upcoming LBC1936 cohort event in September.

Jeane Freeman MSP views LBCs brain ageing with AR technology. Photos by Graham Clark.

Date for your diary: Ageing, Dementia and Music, BBC Music Day

On Thursday 26th September, LBCs Director, Ian Deary, and members of his research team will join the Scottish Chamber Orchestra on BBC Music Day 2019 to share knowledge about healthy ageing and the musical brain. The free event is aimed at healthcare professionals, arts practitioners working in the field of dementia, researchers and the general public. Tickets can be booked here.

News from Age UK

For June’s newsletter, I (Susan) bemoaned the wet, soggy spring. After the hottest July on record and now record-breaking rain…as a non-native, I’m beginning to understand your obsession with the weather!

So, catching up on Age UK’s latest work. Previously, I mentioned the campaign to keep the TV licence for over-75s free. We turned in a petition to the Government asking them to honour their previous pledge, with just under 635,000 signatures! This is a remarkable number considering that the people most directly affected - the over-75s - are mostly offline. You can read more about why this issue matters and what we hope to achieve here.

We have a load of publications to tell you about, so I’ll jump right in!

Brain health and supplements

Age UK is a founding collaborator of the Global Council on Brain Health (GCBH) who have released a new report quashing the link between taking dietary supplements and improvements in brain health.

The GCBH concludes that there's 'no convincing evidence' that nutritional supplements specifically designed for brain health actually benefit thinking skills, memory, or improve symptoms of dementia or Alzheimer's disease. 'The best way to get nutrients for brain health is from a healthy diet', say the experts. The full report 'The real deal on Brain Health Supplements' is available to read here.

We have linked to this report from our Staying Sharp web pages, which discuss the actions everyone can take to help maintain and improve their brain health - largely based on (and written by) members of the DMind team.

Decent Accessible Homes for Older People

The All Party Parliamentary Group on Ageing and Older People published the results of its inquiry into decent accessible housing for older people – supported by Age UK. This is a comprehensive overview across different tenures and types of housing with specific recommendations to tackle the poor housing conditions face by millions of older people.

Home Truths

Staying on the topic of homes, Age UK has published a myth-buster factsheet on the need for accessible new homes. It counters the arguments of home-builders who have opposed the universal implementation of the lifetime homes accessibility standard for all new homes. Here's a fact:

Pensions Freedoms are letting down many ordinary older people - possible solutions

'Fixing the Freedoms' – written by Dominic Lindley, an independent consumer consultant – was commissioned by Age UK to investigate the development of retirement income products, customer support and industry thinking since the pension freedoms came into effect in 2015.

Volunteering with veterans

As D-Day commemorations took place in June, we took the opportunity to look at our network's voluntary services which support veterans, their families, and their carers.

Keith's story: writing with dementia

Ending on a very worth-while read: Keith shares his journey with dementia from diagnosis at age 55 to finding solace in writing and publishing three books! An honest account of the difficulties and support he's needed. Read about Keith's experience of living with a diagnosis of dementia.

Publications

In press

Corley, J., Cox, S., Harris, S.E., Valdes Hernandez, M., Munoz-Maniega, S., et al., (2019). Epigenetic signatures of smoking associate with cognitive function, brain structure, and mental and physical health outcomes in the Lothian Birth Cohort 1936. *Translational Psychiatry*.

E-published ahead of print

Lu, A.T., Seeboth, A., Tsai, P.-C., Sun, D., Quach, A., et al., (2019). DNA methylation-based estimator of telomere length. *Aging*.
PMID: 31422385

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.
PMID: 31338413

Okely, J.A., Akeroyd, M.A., Allerhand, M., Starr, J.M., Deary, I.J., (2019). Longitudinal associations between hearing loss and general cognitive ability: The Lothian Birth Cohort 1936. *Psychol Aging*.
PMID: 31393145

Valdés Hernández, M. del C., Ballerini, L., Glatz, A., Muñoz Maniega, S., Gow, A.J., et al., (2019). 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*.
PMID: 31250262

Published 2019

Bateson, M., Aviv, A., Bendix, L., Benetos, A., Ben-Shlomo, Y., et al., (2019). Smoking does not accelerate leucocyte telomere attrition: a meta-analysis of 18 longitudinal cohorts. *R. Soc. open sci.* 6, 190420.
PMID: 31312500

Booth, T., Dykiert, D., Corley, J., Gow, A., Morris, Z., et al., (2019). Reaction time variability and brain white matter integrity. *Neuropsychology* 33, 642-657.
PMID: 31246073

Chundru, V.K., Marioni, R.E., Prendergast, J.G.D., Vallerga, C.L., Lin, T., et al., (2019). Examining the Impact of Imputation Errors on Fine-Mapping Using DNA Methylation QTL as a Model Trait. *Genetics* genetics.301861.2018.
PMID: 31040117

de Vries, P.S., Brown, M.R., Bentley, A.R., Sung, Y.J., Winkler, T.W., et al., (2019). Multiancestry Genome-Wide Association Study of Lipid Levels Incorporating Gene-Alcohol Interactions. *American Journal of Epidemiology* 188, 1033–1054.
PMID: 30698716

Deary, I.J., Ritchie, S.J., Muñoz Maniega, S., Cox, S.R., Valdés Hernández, M.C., et al., (2019). Brain Peak Width of Skeletonized Mean Diffusivity (PSMD) and Cognitive Function in Later Life. *Front Psychiatry* 10, 524.
PMID: 31402877

Fawns-Ritchie, C., Davies, G., Hagenaars, S.P., Deary, I.J., (2019). Genetic Contributions to Health Literacy. *Twin Res Hum Genet* 22, 131–139.
PMID: 31250787

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. *Nature Communications*.
PMID: 31320639

Imboden, M., Wielscher, M., Rezwan, F.I., Amaral, A.F.S., Schaffner, E., et al., (2019). Epigenome-wide association study of lung function level and its change. *Eur Respir J* 1900457.
PMID: 31073081

Lam, M., Hill, W.D., Trampush, J.W., Yu, J., Knowles, E., et al., (2019). Pleiotropic Meta-Analysis of Cognition, Education, and Schizophrenia Differentiates Roles of Early Neurodevelopmental and Adult Synaptic Pathways. *Am. J. Hum. Genet.* 105, 334–350. PMID: 31374203

MacPherson, S.E., Allerhand, M., Cox, S.R., Deary, I.J., (2019). Individual differences in cognitive processes underlying Trail Making Test-B performance in old age: The Lothian Birth Cohort 1936. *Intelligence* 75, 23–32. PMID: 31293282

Muñoz Maniega, S., Meijboom, R., Chappell, F.M., Valdés Hernández, M.D.C., Starr, J.M., et al., (2019). Spatial Gradient of Microstructural Changes in Normal-Appearing White Matter in Tracts Affected by White Matter Hyperintensities in Older Age. *Front Neurol* 10, 784. PMID: 31404147

Palmer, V.J., Gray, C.M., Fitzsimons, C.F., Mutrie, N., Wyke, S., et al., (2019). What Do Older People Do When Sitting and Why? Implications for Decreasing Sedentary Behavior. *The Gerontologist*. PMID: 29771308

Parker, N., Vidal-Pineiro, D., French, L., Shin, J., Adams, H.H.H., et al., (2019). Corticosteroids and Regional Variations in Thickness of the Human Cerebral Cortex across the Lifespan. *Cerebral Cortex* bhz108. PMID: 31240317

Robertson, N.A., Hillary, R.F., McCartney, D.L., Terradas-Terradas, M., Higham, J., et al., (2019). Age-related clonal haemopoiesis is associated with increased epigenetic age. *Curr. Biol.* 29, R786–R787. PMID: 31430471

Zhang, Q., Vallerga, C.L., Walker, R.M., Lin, T., Henders, A.K., et al., (2019). Improved precision of epigenetic clock estimates across tissues and its implication for biological ageing. *Genome Med* 11, 54. PMID: 31443728

Contact

Please get in touch with any items for inclusion in future newsletters:

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For the latest Disconnected Mind news:

twitter.com/EdinUniLBC

You can stay up to date on the most recent Disconnected Mind research by checking the regularly-update list of publications at:
www.lothianbirthcohort.ed.ac.uk

Those requiring a PDF version of any publications listed should get in touch with LBC Data Manager, Paul Redmond:
lbc1936@ed.ac.uk

Do also keep Paul updated with your 'in press' or recently published papers. They'll be added to the website to ensure everyone can see these as soon as possible, and may be profiled in a future newsletter.

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age UK Love later life

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MRC Medical Research Council

NIH National Institutes of Health