

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.

Professor John Starr

Our dear colleague, John Starr, died suddenly in early December. John was an investigator on the Lothian Birth Cohorts (LBCs) from their inception.

John was Honorary Professor of Health and Ageing at the University of Edinburgh (UoE), founding Director of the Alzheimer Scotland Dementia Research Centre, Co-Director of the Centre for Cognitive Ageing and Cognitive Epidemiology (CCACE), Co-Director of the Scottish Dementia Clinical Research Network, and a practising consultant physician in the medicine of old age for NHS Lothian. This long list of roles is testament to John's energy and breadth of skills in research, clinical practice, and leadership.



John graduated in Medicine from Cambridge and London. He first came to Edinburgh as a research fellow in the Department of Psychiatry in 1989, investigating the relationship between blood pressure and cognition. After a stint away, John returned to Edinburgh as consultant and part-time Senior Lecturer in Geriatric Medicine at the Royal Victoria Hospital. His research excellence was ever to the fore and John was soon promoted to an honorary Chair at the UoE.

Throughout his impressive research career John published over 500 papers, including many highly cited classics, notably on the LBCs. Along with other awards, John's work on the relationship between physical and mental health with Ian Deary and Lawrence Whalley was recognised by the prestigious Tenovus Scotland Margaret MacLellan Award in 2006.

John was a polymath. Largely unbeknownst to his medical and scientific colleagues, John was an expert on ancient languages and the Dead Sea Scrolls. Indeed, he completed a PhD in 2013 in the School of Divinity at the UoE on the "Quantitative Analysis of the Aramaic Qumran Texts".

We remember John with special fondness at the LBCs. As co-investigator, he was an enthusiastic and creative contributor since the studies' inception in 1998. He was the studies' doctor, responsible for the medical side of LBC research. He was an inspiring mentor and supervisor to young scientists, including many of the LBC team. He did much to bring bright young clinical researchers into our research areas, and retain their interest. John was a knowledgeable, inventive, cultured, and witty collaborator and good friend to the LBCs. He fizzed with ideas, many brilliant, some ahead of their time. John wrote the following short piece, not long ago, reflecting his modest and effective scientific approach and his mission to seed it in others:

<https://britishgeriatricsociety.wordpress.com/2018/05/11/my-heart-leaps-up/>

Perhaps in this John authored his own best epitaph: *"for me living isn't about accumulating a list of achievements, or "impacts" as they might be termed, to be read out as a eulogy at my funeral. No, living is about being alive, that sequence of moments strung together from cradle to grave; and moments which inspire me with a sense of wonder, however ephemeral, are when I feel really alive. Research, suddenly seeing things revealed, just like moments when relationships deepen and transform, is able to bring such wonder into our lives."*

We will all miss John terribly. He is irreplaceable, and our lives will be the poorer for his untimely passing.

In sorrow,

Ian Deary

Newsletter 45: March 2019

Welcome to the first Disconnected Mind (DMind) newsletter of 2019. This issue includes news and reports on the team's research activity, events we have been participating in, and some of our recent publications. It also includes the regular contribution from our colleagues at Age UK. Please get in touch for more information about anything in the newsletter, particularly if you have something you would like to be included in a future issue. Contact details can be found on the last page.

OBE for Prof Ian Deary

Congratulations to DMind/LBCs Director Professor Ian Deary, who has been awarded the prestigious Officer of the Order of the British Empire (OBE) in the Queen's New Year Honours list 2019. Professor Deary is receiving the OBE for services to the Social Sciences.

Ian said, *'I am delighted and proud to take this bow for the research team and all our achievements. I include our partners at Age UK in that. From the many heart-warming messages of congratulation, I was especially gladdened by the letter from the Right Honourable Nicola Sturgeon, First Minister of Scotland. She said in her letter to me:*

"Dear Ian... Your work with the Disconnected Mind project has been a great success and has allowed us to take great strides in the understanding of the many factors that contribute to health ageing. I understand the information from the Lothian Birth Cohort Studies 1936 is now used all over the world to help not only with cognitive ageing research but also contributes to a wealth of additional age-related research... Best wishes, Nicola".

Now, that's an endorsement to savour and keep, isn't it?!

Ian will receive his award at Holyrood Palace this July. The team are all looking forward to hearing about the special day.

LBC1936 Study – Wave 5 update

Testing for Wave 5 of the LBC1936 Study is now 95% complete. At last count, 422 participants had attended the Wellcome Trust Clinical Research Facility for cognitive and physical tests at age 82 years. Magnetic Resonance brain imaging is progressing well too, with 265 successful brain

scans thus far. We are still on track to finalise Wave 5 fieldwork in Spring 2019, marking the completion of 5 waves of longitudinal cognitive data collection (from age 70 to 82), and 4 waves of longitudinal MR brain imaging data (from age 73 to 82) in the LBC1936. We are also pleased to report that we completed scanning for our pilot study in January. The pilot study aims to compare 1.5T and 3T brain imaging of LBC1936 participants, to ascertain feasibility of switching to newer MRI scanner technology for future waves of data collection.

20th Birthday for the Lothian Birth Cohorts



Clockwise from left: Professor Ian Deary, Dr Martha Whiteman, and Mrs Alison Pattie on 20th anniversary of the LBC studies

The Lothian Birth Cohorts team got together on January 31st 2019 to mark the exact day when our inimitable LBC team member, Mrs Alison Pattie, completed 20 years of work on the LBC studies. The LBCs began in 1999 with the LBC1921, and in 2004 with the LBC1936. Professor Ian Deary founded both LBCs, and has directed the studies since they began. Mrs Pattie has tested participants at all waves of the LBC1921 and 1936, and was the sole tester for the LBC1921 at ages 90 and 92 years. Ian said, "Alison has been a devoted and highly professional servant to the LBCs. It is not an exaggeration to say she is loved by the participants. Having such continuity of careful and sensitive testing of our participants over all those waves is one of the LBCs' several strengths."

Dr Martha Whiteman, the first LBC Study Co-ordinator, returned to the LBC office to join in with the festivities. A special 20th anniversary LBC reunion event is in planning for later this year. More on that in the next edition.

Scientific highlights

Some of our most recent publications are listed at the end of this newsletter. Here, are a few highlights from the DMind/LBC team and our collaborators, reflecting the broad range of LBCs data available.



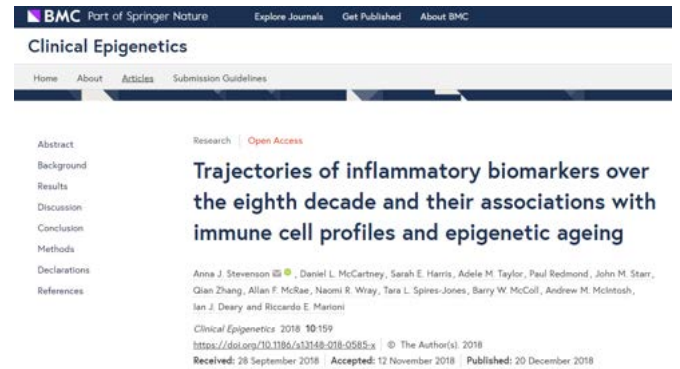
Daytime sleeping and cognitive decline

Recently accepted in *Sleep*, was an investigation led by Dr Simon Cox into the associations between various self-reported sleep measures and declines in cognitive function between 70 and 76 years. Simon tested self-reported quality of sleep, latency (time taken to fall asleep), bedtime and wake time, and duration spent sleeping at night and during the day. He found that individuals who spent longer sleeping during the day showed significantly steeper declines in visuospatial abilities and processing speed between ages 70 and 76, even after accounting for important health measures.



Polygenic predictors of cognitive ageing

Variation in the degree to which the genes of an individual are similar to those of a specific trait, or condition (e.g. Alzheimer's disease) is thought to carry meaningful information for cognitive ageing, even among groups without the condition. Dr Stuart Ritchie has had a paper accepted in *Molecular Psychiatry*, which analysed associations between 14 polygenic scores and 9-year cognitive change in the LBC1936. He found that several polygenic scores were associated with cognitive ability at age 70-baseline, but that only *APOE* e4 (a well-known and well-replicated risk allele for dementia) was significantly associated with steeper cognitive decline from age 70-79 years.



Trajectories of inflammatory biomarkers

Wellcome Trust Translational Neuroscience PhD student, Anna Stevenson, led a study published in *Clinical Epigenetics*, using the unique longitudinal data from LBC1936 to see how inflammatory, immunological, and methylation measures change over the 8th decade from age 70 to 79 years. There is a complex interplay between these three biomarkers of ageing and, by understanding their associations at a single time point and over time, we will be better placed to define their impact on cognitive decline and dementia. Anna will continue to use LBCs' data throughout her PhD project, which focuses on inflammation, DNA methylation (chemical additions to the DNA that turn genes on and off), and cognitive decline.



Identification of 55,000 Replicated DNA Methylation QTL

Dr Riccardo Marioni, Dr Sarah Harris, and Professor Ian Deary were co-authors on a large scale study investigating how genetics influences chemical changes that help to turn genes on and off, published in *Scientific Reports*. This project, led by Dr Allan McRae, was an international collaboration with our colleagues at the University of Queensland, Brisbane. The study is important as it will enable future projects to better determine whether genetic differences are causally involved in health and ageing. For example, does a genetic difference influence how much protein is produced and does this affect health outcomes.



Sedentary behaviour and depressive symptoms

Research shows that too much sitting (sedentary behaviour) is a risk factor for ill health even among people who are physically active at other points in the day. Sedentary behaviour is particularly common in older age, with very few older adults reaching the recommended levels of activity. Understanding why older people spend time sitting down will be key to promoting a more active lifestyle in this population.

A series of papers have recently been published, based on the collection of objective sedentary behaviour data from the LBC1936 at age 79, as part of a collaboration with Glasgow Caledonian University. 300 LBC1936 participants wore activity monitors for a week in Wave 4. In the latest study, published in *BMC Geriatrics*, and led by Dr Judy Okely, we investigated the link between symptoms of depression, anxiety and positive psychological wellbeing and levels of sedentary behaviour in three separate groups of older people, including LBC1936 participants. Looking across all three groups, we found that people who reported more symptoms of depression also spent more time being sedentary.

Co-author, Dr Catharine Gale said, *“In this study, because sedentary behaviour was only measured once, we cannot be certain of the direction of the relationship between depression and time spent sitting. Our findings could have arisen because being depressed makes people more sedentary. Alternatively, being more sedentary might have a lowering effect on mood. Further studies, in which depression and sedentary behaviour are measured repeatedly, are needed to understand the nature of the relationship.”*

Knowledge exchange, policy and impact

In the last few months, we have continued in our efforts to communicate our findings to scientific audiences, to translate our findings to inform the public about healthy cognitive ageing and to influence policy makers, practitioners and service providers. A few highlights come next.

MSPs ♥ LBCs @ MRC



LBCs Director, Ian Deary (left) shows crystal etching of an LBC1936 participant’s brain white matter connections to Lewis MacDonald MSP.

On 6th February, from 6-8pm, the LBCs were on show in the Members’ Room of the Scottish Parliament. This was part of the Medical Research Council’s Science Showcase in Scotland. “It was an important event for me to be at, with LBC materials,” said Professor Ian Deary, Director of the Lothian Birth Cohorts, “because ageing and its effect on cognitive skills is such a large issue. And because Scotland—via the Lothian Birth Cohorts—is so well set up to address it.”

Among the several MSPs who showed much interest in the LBCs, were representatives from different parties. The Minister for Further Education, Higher Education and Science, Richard Lochhead, was keen to hear about protective and risk factors for cognitive ageing, and how the LBCs were unusually valuable in finding those. Health and Sport Convener, Lewis Macdonald was similarly enthralled. Another Member of the Health and Sport Committee—Brian Whittle—spent a long time discussing the LBCs’ importance with Ian. “I think it was Brian’s history as a top international athlete that added to his interest in how the ageing of the mind is related to the ageing of the body,” Ian said, “and he was already keen on the idea of life-long contributions to health ageing.” Ian hopes to follow-up on these meetings with more in-depth discussions about contributions to policies.

Storytelling with Parkside Primary School



Participants of LBC1936 and Parkside Primary school pupils sharing their memories and experiences of being 11 years old

On the 30th of January, the P7s at Parkside Primary School in Edinburgh welcomed a group of LBC1936 participants for a creative afternoon of art and storytelling. P7s are all around 11 years old – the same age the LBCs were when they took the Moray House Test in 1947. LBC team members, Dr Judy Okely and Ms Danielle Page, along with Dr Kate McAllister and Ms Denise Munro (Centre for Cognitive Ageing and Cognitive Epidemiology), organised and coordinated the event. It began with an afternoon of energetic ice-breaking activities and some enchanting stories from Claire McNicol, the professional storyteller who facilitated the event.

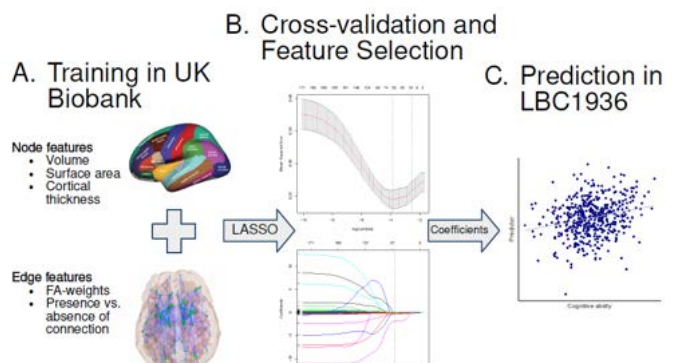
Then the class and LBCs broke off into smaller groups to share, and compare, experiences and memories of school at age 11. The P7s were interested to hear about life at school 70 years ago, particularly about rationing of sweets, getting ‘the belt’ and life without any smart phones! The P7s also spotted some things that haven’t changed that much over 70 years, including a love for sweets and playing football at break time.

After a short tea break, Claire told the story of the Goodbye Cloak – a beautiful cloak covered with colours and symbols that represents a

person’s life. The P7s and LBCs then designed their own cloaks reflecting the lives they have lived so far. The afternoon was rounded off with a lovely rendition of the song, *Lean on Me*, from the P7s. Deputy Head teacher at the school Christine MacLeod said, “*The class really enjoyed talking to our visitors and hearing their stories.*”

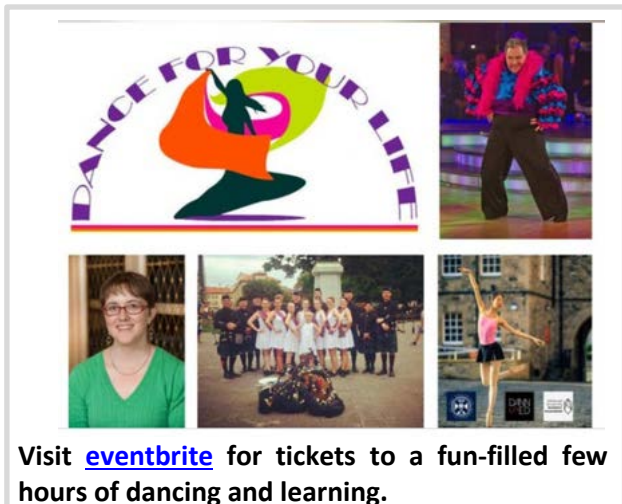
Talking brains, in Texas

As part of a 5-year USA National Institutes of Health-funded grant, studying the brain structural connectome and its relation to cognitive ageing, Dr Simon Cox and Dr Colin Buchanan visited the project’s Principal Investigator, Dr Elliot Tucker-Drob, at The University of Texas at Austin, in January. Simon said, “*Elliot was an excellent host, and we had meetings with collaborators on the Texas-side of the project, and made good progress on our current analyses. At the end of the week, we drove to The University of Texas at Dallas where we presented some of our work on brain and cognitive ageing (which uses both LBC1936 and UK Biobank data in concert) at the Dallas Aging and Cognition Conference. The conference was well-attended, and the work drew some interesting and appreciative comments and lively discussion.*” Colin presented a poster at the conference, based on structural brain network analysis in participants of The LBC1936 and UK Biobank. The team developed subnetwork-specific measures of “brain-age” and predicted cognitive abilities from these indices. They found that subnetworks vary in the degree to which brain-age predicts cognitive performance, indicating that aging of some subnetworks may be more relevant to cognitive aging than others (e.g. Salience network).



Part of Colin’s poster, describing the development of subnetwork-specific measure of “brain-age”, from training the model in ~3500 Biobank participants, to brain-age prediction in LBC1936 participants.

Dance for Your Life



Visit [eventbrite](#) for tickets to a fun-filled few hours of dancing and learning.

Tickets are now available for a public engagement event on 22nd March, organised by Disconnected Mind collaborator, Professor Tara Spires-Jones. *Dance For Your Life* promises 2 hours of music, dance, and learning. In addition to Tara imparting her knowledge on the subject of dementia and exercise, there will be a workshop with Strictly Come Dancing Celebrity Russell Grant, and performances by University of Edinburgh Dancers Ed and the Dunbar Highland Dancers. The WISE foundation, Alzheimer's Research UK, and Alzheimer's Scotland are supporting the event, and ticket revenue will be donated to these charities to support dementia research. Find out more and purchase your tickets on [eventbrite](#).

News from Age UK

As you might have seen, our winter campaign this year has focused on how our Age UK Advice Line is there for older people when they need us, making sure that everyone has someone to turn to. With this theme, we were excited to work on a very special pre-Christmas show in partnership with Channel 4 called 'Celebrity Call Centre', where celebs tackle dilemmas large and small, from troublesome affairs of the heart to struggling with the prospect of loneliness at



Christmas. Taking calls from the great British public were Strictly Come Dancing finalist Debbie McGee, Countdown's Nick Hewer, Goggleboxers Steph and Dom Parker, Coronation St legend Amanda Barrie, Ackley Bridge star Sunetra Sarker, comedian James Acaster, and Radio 1 DJ Gemma Cairney.

Our campaign to save TV licences for over 75s has also been doing really well. This is important because for over a million of our oldest citizens, the TV is their constant companion and window on the world. We've now got over 68,000 signatures on our petition and have had front page stories in the Mail on Sunday and the Mirror.



Age UK's Public Affairs and Policy teams have succeeded in improving the Mental Capacity (Amendment) Bill. We fought for a Deprivation of Liberty definition to be included in the bill to make it clear when an older person's liberty is being deprived – this will make it easier for practitioners and families to treat older people with dignity and respect even when their mental capacity is impaired. Other important topics we're working on include challenging the Government's '[Age Gap Tax](#)' - the way it is proposing to effectively penalise mixed-age couples; and arguing why the UK needs the Government to finally publish their [Green Paper on Social Care](#).



Finally, a bit of 'serious' fun from a collaboration with Dr Alan Gow—a previous Study Co-ordinator of the Lothian Birth Cohorts and Disconnected Mind—from Heriot-Watt University. Our new quiz challenges readers: *Do you think you know how your thinking skills might change as they get older?* [Give your brain a workout](#) and see how your answers compare to other people's from across the UK. The quiz is based on a survey of over 3,000 people age 40 – 90+ across the UK which Alan conducted under Intervention Factory funding from Velux Fonden.

Publications

In press

Cherrie, M. P. C., Shortt, N., Ward-Thompson, C., Deary, I. J., & Pearce, J. R. (in press). The association between activity space exposure to park in childhood and adolescence and cognitive ageing in later life. *International Journal of Environmental Research and Public Health*.

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Chauhan, G., Adams, H. H., Satizabal, C. L., Bis, J. C., Teumer, A., Sargurupremraj, M., ... & DeBette, S. (2019). Genetic and lifestyle risk factors for MRI-defined brain infarcts in a population-based setting. *Neurology*. [PMID: 30651383](#)

Cox, S. R., Ritchie, S. J., Allerhand, M., Hagenaars, S. P., Radakovic, R., Breen, D. P., ... & Deary, I. J. (2019). Sleep and cognitive ageing in the 8th decade of life. *Sleep*. [PMID: 30668819](#)

Erzurumluoglu, A. M., Liu, M., Jackson, V. E., Barnes, D. R., Datta, G., Melbourne, C. A., ... & Howson, J. M. M. (2019). Meta-analysis of up to 622,409 individuals identifies 40 novel smoking behaviour associated genetic loci. *Molecular Psychiatry*. [PMID: 30617275](#)

Marini, S., Crawford, K., Morotti, A., Lee, M. J., Pezzini, A., Moomaw, C. J., ... & Anderson, C. D. (2019). Association of Apolipoprotein E with Intracerebral Hemorrhage Risk by Race/Ethnicity: A Meta-analysis. *JAMA Neurology*. [PMID: 30726504](#)

Prendergast, J. G. D., Pugh, C., Harris, S. E., Hume, D. A., Deary, I. J., & Beveridge, A. (2019). Linked mutations at adjacent nucleotides have shaped human population differentiation and protein evolution. *Genome Biology and Evolution*. [PMID: 30689878](#)

Ritchie, S. J., Hill, W. D., Marioni, R. E., Davies, G., Hagenaars, S. P., Harris, S. E., ... & Deary, I. J. (2019). Polygenic predictors of age-related decline in cognitive ability. *Molecular Psychiatry*. [PMID: 30760887](#)

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Kilpeläinen, T.O., Bentley, A.R., Noordam, R., Ju Sung, Y., Schwander, K., Winkler, T., ... & Loos, R.J. (2019). Multi-ancestry study of blood lipid levels identifies four loci interacting with physical activity. *Nature Communications*, *10*(1), 376. [PMID: 30670697](#)

ja, A. T., Liu, C., Fetterman, J. L., Graff, M., Have, C. T., Gu, C., ... & North, E. K. (2019). Associations of Mitochondrial and Nuclear Mitochondrial Variants and Genes with Seven Metabolic Traits. *The American Journal of Human Genetics*, *104*(1), 112-138. [PMID: 30595373](#)

Lund, J. B., Li, S., Baumbach, J., Svane, A. M., Hjelmborg, J., Christiansen, L., ... & Tan, Q. (2019). DNA methylome profiling of all-cause mortality in comparison with age-associated methylation patterns. *Clinical epigenetics*, *11*(1), 23. [PMID: 30736859](#)

Marioni, R. E., Suderman, M., Chen, B. H., Horvath, S., Bandinelli, S., Morris, T., ... Hägg, S. (2019). Tracking the Epigenetic Clock Across the Human Life Course: A Meta-analysis of Longitudinal Cohort Data. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *74*(1), 57–61. [PMID: 29718110](#)

Okely, J. A., Čukić, I., Shaw, R. J., Chastin, S. F., Dall, P. M., Deary, I. J., ... & Gale, C. R. (2019). Positive and negative well-being and objectively measured sedentary behaviour in older adults: evidence from three cohorts. *BMC geriatrics*, *19*(1), 28. [PMID: 30700261](#)

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Aichele, S., Ghisletta, P., Corley, J., Patti, A., Taylor, A. M., Starr, J. M., & Deary, I. J. (2018). Fluid Intelligence Predicts Change in Depressive Symptoms in Later Life: The Lothian Birth Cohort 1936. *Psychological Science*, *29*, 1984–1995. [PMID: 30359210](#)

Franceschini, N., Giambartolomei, C., de Vries, P. S., Finan, C., Bis, J. C., Huntley, R. P., ... & O'Donnell, C. J. (2018). GWAS and colocalization analyses implicate carotid intima-media thickness and carotid plaque loci in cardiovascular outcomes. *Nature communications*, 9(1), 5141. [PMID: 30510157](#)

McRae, A. F., Marioni, R. E., Shah, S., Yang, J., Powell, J. E., Harris, S. E., ... & Montgomery, G. W. (2018). Identification of 55,000 replicated DNA methylation QTL. *Scientific Reports*, 8(1), 17605. [PMID: 30514905](#)

Stevenson, A. J., McCartney, D. L., Harris, S. E., Taylor, A. M., Redmond, P., Starr, J. M., ... & Marioni, R. E. (2018). Trajectories of inflammatory biomarkers over the eighth decade and their associations with immune cell profiles and epigenetic ageing. *Clinical Epigenetics*, 10(1), 159. [PMID: 30572949](#)

Contact

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

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March 2019

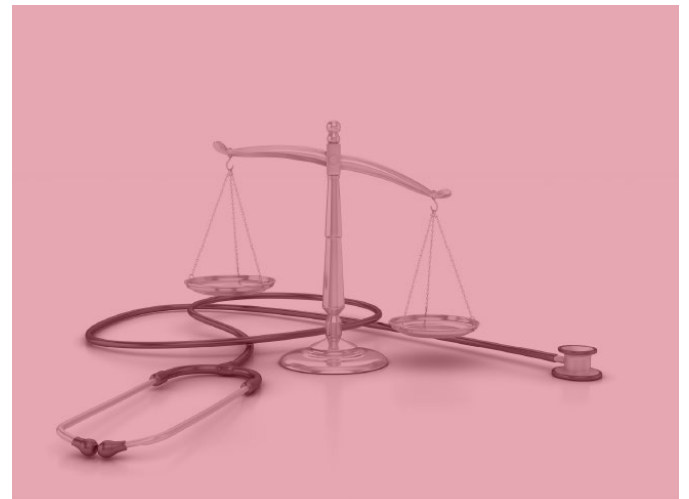
You can stay up to date on the most recent Disconnected Mind research by checking the regularly-update list of publications at: www.lothianbirthcohort.ed.ac.uk

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.

One more thing...

In September last year (Newsletter 43) we told you about Dr W. David Hill's invited presentation at the FEAM (Federation of European Academies of Medicine) and ALLEA (All European Academies) symposium on 'Health inequalities – an interdisciplinary discussion of socioeconomic status, health and causality' at the Royal Dutch Academy of Sciences. This symposium was set up to review the evidence that socioeconomic position may be causally related to inequalities in health. As a part of this symposium, Dr Hill was invited to contribute to a report describing what is currently known about the causal relationship between socioeconomic position and health. This [symposium report](#) is available now available.



Health Inequalities

AN INTERDISCIPLINARY EXPLORATION OF
SOCIOECONOMIC POSITION, HEALTH AND
CAUSALITY

SYMPOSIUM REPORT
November 2018



THE UNIVERSITY
of EDINBURGH