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.

New funding for larger Lothian Birth Cohorts team as Phase 4 of the Disconnected Mind project begins

LBC1936 began in 2004; even before that, LBC1921 began in 1999. For the past 10 years, The Disconnected Mind project/Lothian Birth Cohorts (LBCs) have been a jewel in the Centre for Cognitive Ageing and Cognitive Epidemiology (CCACE), in The University of Edinburgh's Department of Psychology. CCACE had a 10-year stint. The successful Centre was directed by Professor Ian Deary and funded by the Medical Research Council (MRC), the Biotechnology and Biological Sciences Research Council, and the University of Edinburgh.

Ian said, "*CCACE could only ever last for 10 years. It did, and it was great, with the LBCs at its and my heart. I am delighted that we have now secured new funding for the LBCs from Age UK, University of Edinburgh, MRC, and the USA's National Institutes of Health; these take us through Wave 6 of LBC1936 and on to 2022. It is great that, with this new funding, we have retained CCACE's and LBCs' staff, who are now all dedicated to the LBCs and closely-related work on cognitive ageing and cognitive epidemiology. This is a larger LBCs team than we have ever had before.*"

Now concentrating on the Lothian Birth Cohorts, we in 7 George Square have put up new LBCs signs around the Psychology building. We are increasing our social media presence, to get our latest LBCs news out faster. Follow us on Twitter @EDinUniLBC for our latest publication news and for updates on other LBC goings on. The Lothian Birth Cohorts team will continue to work on all things Disconnected Mind, as well applying their varied expertise to test Disconnected Mind-relevant hypotheses in datasets with appropriately similar data, such as the UK Biobank and Generation Scotland.

Indeed, it was just as we were changing the signs that Age UK confirmed funding for a new Phase 4 of the Disconnected Mind project. That began on 1st April 2019, and lasts three years. The main investigators are Ian Deary, Joanna Wardlaw, Mark Bastin, Tom Russ, Simon Cox, and Stuart Ritchie. Phase 4 will include a 6th wave of testing of LBC 1936 participants, when they are about age 85 years old. The LBCs team are grateful to Age UK for their continued support and are excited to be looking ahead to another 3 years of work on cognitive, brain, and general ageing.

The Lothian Birth Cohorts team in 7 George Square
Back row (from left):David Liewald, Colin Buchanan, Simon Cox, W. David Hill, Paul Redmond, Miles Welstead
Front row (from left): Barbora Skarabela, Danielle Page, Sarah Harris, Ian Deary, Judy Okely, Janie Corley, Adele Taylor. Not in picture, Gail Davies.

Newsletter 46: June 2019

Welcome to the first newsletter of a brand new phase of The Disconnected Mind project. Read on for more news about the start of Phase 4, 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 on page 8. 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 are on the last page.

LBC1936 Study – Wave 5 update

LBC tester, Ms Danielle Page (left), with our 431st and final participant of Wave 5

Just as Phase 3 ended, the 5th wave of LBC1936 testing was also completed. The LBC team are delighted to have seen 431 participants for cognitive and medical assessment at age ~82 years, and that 304 participants returned for their 4th MRI brain scan (first conducted at Wave 2). We'd like to say a big thank you to all of the staff at the Wellcome Trust Clinical Research Facility (WTCRF) and Edinburgh Imaging Facilities (EIF) for their work on and support of the study, which helped the wave run smoothly.

The LBC team are now busy collating, entering, and cross-checking these valuable data. We will keep you up to date with our progress, and will let you know when the data is ready to be released to collaborators. We look forward to filling you in on brand new 5-wave findings, and starting our preparations for Wave 6, due begin in early 2020. Watch this space!

Team news

There have been quite a few changes to the Disconnected Mind/LBC team in last few months, but the next few paragraphs should help to get you up to speed. We've welcomed several new members to the team. As reported earlier in the newsletter, we've adopted some of the CCACE core staff. Dr Gail Davies (Genetic Statistician), Dr Sarah Harris (Geneticist) and Mr David Liewald (Computer Manager) are now fully fledged LBC team members. You can see (almost) all of them in the photograph on page 1.

We said goodbye to Alison Pattie, who retired in March this year. Alison worked continuously with Ian on the LBC studies since they began in 1999. She was a real asset to the studies, loved by the LBC team and participants alike. We will all miss having her around.

LBC researcher, Alison Pattie (left), testing her last LBC1936 participant after 20 years of work on the study

In the last newsletter we told you about the untimely death of Disconnected Mind Principal Investigator (PI), John Starr. John and Ian started the Lothian Birth Cohorts together in 1998. This is to let you know that John's protégé in the Alzheimer Scotland Dementia Research Centre (ASDRC)—which is just downstairs from us in the Department of Psychology—is Dr Tom Russ. Tom has joined the Disconnected Mind project as a PI and our research 'medic'. He is a consultant psychiatrist specialising in older age, and he is an Honorary Senior Lecturer at UoE.

Also from the ASDRC, we are joined by Dr Sahan Mendes. Sahan is a Clinical Research Fellow and honorary Speciality Registrar in General Adult Psychiatry funded by Alzheimer Scotland and is currently undertaking a PhD in Clinical Brain Sciences at the University of Edinburgh. He will be responsible for ascertaining any new cases of dementia in LBC1936.

New to the Phase 4 is a fully-funded Disconnected Mind PhD post. Mr Miles Welstead (pictured left), successfully applied for the position and joined the team on day 1 of Phase 4, on 1st April. Miles has a background in academic research, specifically in the field of dementia. He is excited to develop ideas throughout his PhD but is initially interested in exploring the changes in frailty across the 5 waves of LBC1936, looking at how these trajectories differ from person to person. He hopes to use the wealth of information in the LBC1936 to investigate why certain groups of people may have more rapid declines in frailty than others.

Dr Barbora Skarabela joined us one month later as the LBCs' Knowledge Exchange and Impact Officer. At the end of Barbora's first week, LBCs Director, Ian Deary, set her the challenge of summarising her first impressions of the project. Here is what Barbora said, "*I am excited to be joining the Disconnected Mind team as a new Knowledge Exchange and Impact Officer. I'll be spending two and a half days in the LBC corridor in F4 while for the rest of the week I continue working as a child language researcher in the Wee Science developmental lab two floors down.*

In the first week in my new post I quickly learned that my initial priority is to keep the website updated with the team's publications and the Twitter account, with over a thousand followers, active and growing. This appeared straightforward until I realised that the team -- with their collaborators from across many disciplines and physical locations -- produce over a hundred publications a year. There are several of us on the team keeping track of the articles as they progress through various stages, from acceptance to their online availability, for funding bodies, PURE, or the public. The topics, just in the last few weeks, have ranged from health literacy, the effect of mineral deposits in perivascular spaces on cognitive ageing, risk loci of susceptibility to colorectal cancer, cardiovascular health and mental health related to sedentary behaviour. The breadth and depth of these findings is astonishing.

I was delighted to have the opportunity to meet a few of the LBC 1936 participants in person at the Western General Hospital. I joined them for a long morning of cognitive, medical and physical tests, and witnessed one of the 40-minute MRI sessions. I was humbled by the participants' commitment to the project and inspired by their attitude. I hope to meet many of them in September during their re-union. In the meantime, I'll enjoy learning -- and sharing with others – what Professor Ian Deary's team discovered with their help about the secrets to healthy cognitive ageing!"

You can contact Barbora for information on Knowledge Exchange, public engagement and events at lbc.ke@ed.ac.uk.

Visit from Professor Benjamin Aribisala

In May, we had the pleasure of hosting Professor Benjamin Aribisala, Dean of the Faculty of Science at Lagos State University (LASU). Benjamin is well known to the Disconnected Mind project, having worked closely with Joanna Wardlaw (LBC Brain Imaging lead) and Ian Deary during his post as Post-Doctoral Research Associated on the LBC1936 between 2011 and 2013.

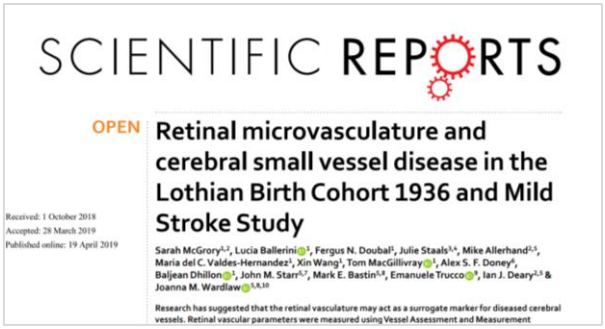
Benjamin Aribisala (right) with Ian Deary, on his visit to the LBCs

Benjamin has returned to UoE on a 3-week long research visit, which was made possible by funding from the UoE's International Development Research (IDR) Hub. He previously worked with Joanna and LBC researchers investigating cross-sectional associations between sleep patterns, brain structure and cognitive ability in older age. On his visit to Edinburgh this year he aims to develop this research to examine the effect of sleep on longitudinal measures of brain and cognitive ageing. He is particularly interested in the association between sleep and perivascular spaces (which provide pathways for clearing metabolic waste products in the brain), and their potential link with the development of dementia in older age.

We asked Benjamin how he manages to combine hands-on research with his high-level duties at LASU. He said, "*My ability to combine hands-on research with high-level duties in LASU is largely based on the grace of God. Of course, I have passion for research works and for serving my University, but I must say that it has not been easy combining the two passions. As the Dean of the Faculty of Science in LASU, a faculty with close to 4000 students and 120 academic staff, I am busy with meetings almost every day. I also need to think of my research work, also I have to mentor colleagues, teach and supervise BSc, MSc and PhD students. I don't believe in failure and I believe that anything that is worth doing at all is worth doing well. In view of these, I have to ensure that I combine hard work with pro-activeness, excellent organization and team spirit. I set goals and plan my programmes carefully at all times.*

Another thing that helps me greatly is the excellent teams that I work with. The LBC1936 team under the able leadership of my two mentors and collaborators, Professor Joanna Wardlaw and Professor Ian Deary, is blessed with fantastic members who are ready to offer support at all times. They have a good understanding that I have a full time job in Nigeria. Similarly, I am blessed with excellent team members in LASU. I have nine Heads of Department (HODs) who work with me to manage the affairs of the Departments of Botany, Biochemistry, Chemistry, Computer Science, Fisheries, Physics, Microbiology, Mathematics and Zoology. I want to use this opportunity to thank my HODs in LASU and LBC1936 team in Edinburgh for their support to make it possible for me to combine my research with administrative responsibilities."

Scientific highlights


SCIENTIFIC REPORTS

OPEN

Retinal microvasculature and cerebral small vessel disease in the Lothian Birth Cohort 1936 and Mild Stroke Study

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Sarah McGrory[1,2], Lucia Ballerini[3], Fergus N. Doubal[2], Julie Staals[3,4], Mike Allerhand[2,5], Maria del C. Valdes-Hernandez[3], Xin Wang[3], Tom MacGillivray[3], Alex S. F. Doney[6], Baljean Dhillon[3], John M. Starr[6,7], Mark E. Bastin[3,8], Emanuele Trucco[9], Ian J. Deary[2,5] & Joanna M. Wardlaw[3,8,10]

Research has suggested that the retinal vasculature may act as a surrogate marker for diseased cerebral vessels. Retinal vascular parameters were measured using Vessel Assessment and Measurement

Retinal microvasculature and cerebral small vessel disease in the Lothian Birth Cohort 1936 and Mild Stroke Study

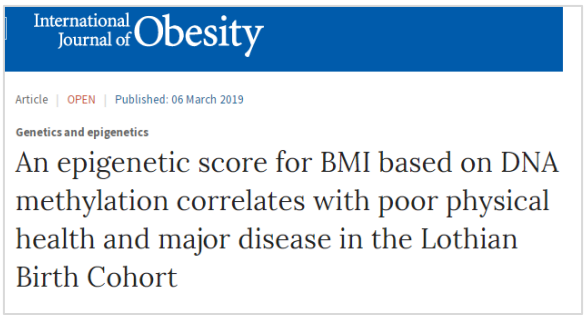
Retinal imaging was conducted in the LBC1936 study at Wave 2, when participants were about age 73, and a second round of imaging has newly been completed at age ~82 (Wave 5). There is increasing interest in the potential of non-invasive imaging of blood vessels of the retina as a method of providing information about the health of the brain. In a study recently published in *Scientific Reports*, LBC collaborator Dr Sarah McGrory and colleagues used retinal and brain imaging data from LBC1936 participants and patients with recent minor ischaemic stroke, from the Mild Stroke Study to look at associations between retinal vascular features and brain imaging markers of small vessel disease. They found that lower arteriolar fractal dimension (a measure of retinal vascular complexity) was associated with brain imaging markers of small vessel disease, providing some support for the use of retinal imaging in the study of cerebral small vessel disease.

Associations between dietary inflammatory index scores and inflammatory biomarkers in older age

In addition to administering cognitive tests to LBC1936 participants, Dr Janie Corley is also an expert in diet and healthy ageing research.

Janie's recent paper, accepted for publication in the *Journal of Nutrition, Health, & Aging,* is the first study to validate The Dietary Inflammatory Index (DII®), a measure which estimates the overall inflammatory potential of a person's diet in a sample of exclusively older adults, and the first study to validate this measure in a UK population. Chronic, low-level inflammation is a risk factor for many age-related diseases, and is influenced by diet. Using responses from a food frequency questionnaire, Janie and colleagues calculated the Dietary Inflammatory Index (DII) score for each LBC1936 participant at age 70. This summary score estimates how inflammatory a diet is based on a number of commonly eaten foods, drinks, other food components, vitamins, and minerals. Whether or not the DII score is associated with levels of inflammation in the body, measured in the blood, was examined in the LBC1936. They found that higher DII scores (indicating a more inflammatory diet) were associated with higher levels of commonly used blood biomarkers of inflammation, namely C-reactive protein (measured at age 70 years) and Interleukin-6 (measured at age 73 years). The results suggest that those who ate a more pro-inflammatory diet had significantly higher levels of inflammation, and support previous studies which have found that healthy diets rich in fruits, vegetables and fibre, such as the Mediterranean diet, are the most beneficial.

Epigenetic score for BMI based on DNA methylation correlates with poor physical health and major disease


International Journal of Obesity

Article | OPEN | Published: 06 March 2019

Genetics and epigenetics

An epigenetic score for BMI based on DNA methylation correlates with poor physical health and major disease in the Lothian Birth Cohort

The relationship between a high body mass index (BMI) and adverse health is well established, but little is known about how DNA methylation, a process that influences whether genes are 'switched on or off', may contribute to obesity-related poor health and disease. Olivia Hamilton, a Wellcome Trust Translational Neuroscience PhD student who works with LBC data, recently conducted a study in which she and her co-authors used DNA methylation data from age 70 of the LBC1936 to create a methylation score related to participants' body mass index (BMIm). They tested whether BMIm was associated with obesity-related health outcomes, and found that BMIm was associated with many factors relating to poorer physical function (e.g. poorer lung function and slower walking speed), increased levels of biomarkers for metabolic syndrome, poorer health-related quality of life, doing less physical exercise and social deprivation. They also tested associations between these outcomes and regular BMI score and found that they were associated independently of BMIm, suggesting that BMIm can be used alongside phenotypic BMI to improve our prediction of obesity-related adverse health and disease.

Knowledge Exchange, policy, and impact

The Disconnected Mind have had a busy season of national and international travel. In this quarter, we shared our research findings with scientists and the general public from Scotland to Italy, and even as far at Vietnam. But before we get stuck in to telling you about the latest findings from the Lothian Birth Cohorts data, first some news about a recent publication led by Dr Simon Cox, PI on the Disconnected Mind project. Simon has developed his expertise in individual differences and brain imaging analysis over

several years on the LBC studies. He recently applied this expertise to a study investigating the effects of multiple vascular risk factors on brain structure in healthy participants from the UK Biobank cohort. Simon's study was the largest of its kind, to date, and he was invited to discuss his findings with the New Zealand Listener, a well-circulated publication viewed by about 6% of the NZ population.

HEALTH

The heart of the matter

New research into the brain has found that cardiovascular ill health is linked to cognitive decline and dementia.

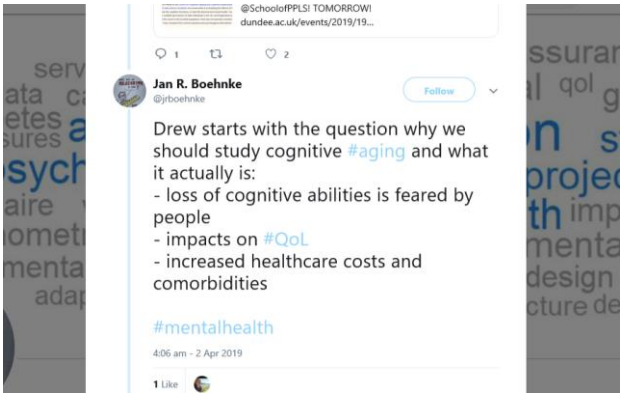
Maintaining healthy blood pressure, body weight and blood sugar should be just some of the things we do to stave off dementia.

Dr W. David Hill's presentation at the World Conference on Personality

In April, Dr W. David Hill was invited to present at the World Conference on Personality in Hanoi, Vietnam, as part of a symposium on Genes and Personality. This symposium was set up to highlight the recent success of applying molecular genetic methods to questions regarding individual differences in intelligence and personality. As a part of this symposium, Dr Hill described his work using large international data sets, along with the data from the LBCs, to show which genes were involved with intelligence, as well as the biological systems that they are a part of. In addition, Dr Hill's work showing that rare genetic effects are linked to differences in intelligence and personality was presented, along with his new study showing how neuroticism, the propensity to experience psychological distress, is composed of multiple genetically distinct traits, some of which are genetically linked to better health, higher intelligence, and a longer life. You can read David's latest paper on neuroticism, available here.

Dr Drew Altschul gives a seminar at University of Dundee

Disconnected Mind collaborator, Dr Drew Altschul was invited to deliver a seminar at the University of Dundee School of Nursing and Health Sciences, entitled: 'Latent growth curve models: a framework for analysing longitudinal mental and physical health data.' The talk focused on the methods used in and results of several studies of the LBC1936, in particular, how trajectories of cognitive function can be measured, what key physical, mental, and behavioural factors are associated with cognitive decline, and how to apply longitudinal models to real health data. The seminar was live-tweeted; the whole thread with links to some of Drew's LBC papers is available here.



Snapshot of the live-tweets from Drew Altschul's seminar

LBCs at the Scottish Dementia Research Consortium (SDRC) 'Cohort Corner'

The annual SDRC conference, which was held on the 15th of April, showcases dementia research taking place in Scotland. The LBC studies team were invited to the event which was attended by experts working in all areas of dementia research as well as practitioners working in dementia care and members of the public. The LBCs were one of several studies in 'cohort corner' which provided a showcase of observational studies taking place in Scotland. Dr Judy Okely (pictured below), who represented the LBCs at the event said *"It was a really exciting conference, which spanned all areas*

of dementia research from fundamental science to delivery of dementia care. The LBC table attracted many interested conference delegates, and I had a great time introducing the LBC studies to researchers, some of whom expressed interest in using our data in future studies."

Judy Okely manning the LBC display at the SDRC Cohort Corner

Ian Deary's keynote at the Bologna Festival della Scienza Medica

It was hard to get Ian to tell us about his talk at the Bologna Festival of Medical Science on May 11th 2019. "*Well*," said Ian, "*it was very memorable… The theme of the whole conference was 'Intelligence and Health', which was perfect for our team's work. As I was speaking, a time trial in the Giro d'Italia was starting off, about 100 yards away. My keynote talk was in the Archiginnasio complex, once the main building of the University of Bologna, which is the oldest University in the world. I was speaking in the highly-ornate Stabat Mater congress room, where Einstein gave lectures on relativity in 1921. On the night after my talk I had the honour of a half hour's walk in Bologna's old town with Sir John Gurdon, who was also speaking at the meeting. It was the first time I have been translated simultaneously with my talk."* And your talk, Ian? *"Oh yes, I had a full room, with something above 200 people: researchers, doctors, medical students, and the public. They seemed very interested in our research on why childhood intelligence relates to later health and survival. After my 40 minute talk, there were 30 minutes of very good questions*."

The audience gathers for Ian's talk in the Stabat Mater room

The Italian press were also keen on the LBC team's research. There were substantial stories in *La Republicca* ("L'intelligenza fa ammalare di meno. Ecco perché") and *Corriere Della Sera* ("Essere intelligenti aiuta (anche) a non ammalarsi"), and other Italian newspapers.

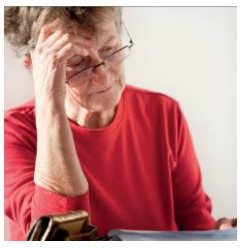
News from Age UK

Since 'spring' has been mostly too cold and wet to get outside and enjoy, we've been head down at Age UK, producing some great reports and resources to benefit older people. We're still campaigning on TV licences for the over-75s and the mixed-age couple Pension Credit penalty, as mentioned last time.

Guinness World Record-holders!

Well, one of us is! Our research team member Phil Rossall has been a passionate supporter of the DMind work, even obtaining a fellowship at Edinburgh to be part of Ian's team. He has unfortunately developed Motor Neurone Disease, but still manages to put in a few hours of work each week on this project and others. On 10 February this year, he and a former member of our staff, Marcus Green, achieved fastest half marathon pushing a wheelchair (male) in 1 hr 29 min 38 sec, at the Worthing Half Marathon, with Marcus pushing Phil around the course. Their friend Nick Di Paolo (on the right) ran with them, carrying Phil's very heavy back-up respirator.

Financial hardship



We're always keen at Age UK to enable older people to talk openly about the things that are important to them, and our new report Struggling On contains stories showing the financial hardships that too many face. As well as shining a light on how people are coping, the report makes a number of recommendations about ways to improve the situation, which in turn challenges Age UK to shape our services effectively.

Older Men at the Margins

We are delighted to announce the launch of a new resource, resulting from a comprehensive study by the University of Bristol's Paul Willis, with Age UK support.

The study looked at older men's experiences of seeking social engagement and combating loneliness in later life. The men included were carers, living with hearing loss, gay, or living alone in rural areas.

Our webpage includes a report briefing, a handbook for practitioners, tips for older men, videos of older men speaking about their experiences, and a podcast about the project. Click here to take a look.

How to have difficult conversations

Age UK recently conducted research to find out more about how older people, their families, and the professionals working with them feel when someone is showing signs they're struggling to cope. As a result of this research, Age UK has developed a series of webpages designed to help anyone who is worried about someone open up a conversation with them.

"Lots of us don't feel as confident when we're trying to talk about sensitive or uncomfortable topics, especially if it's with someone like a parent, aunt or uncle who once took care of us," says Age UK's Su Ray, who was involved in the research. "We're not telling people what to say, but we hope we can give them some things to think about so they feel more prepared to talk openly. And a big part of that talk is going to be listening – and understanding what the other person has to say, even if we don't like it."

Publications

IN PRESS.

Corley, J., Shivappa, N., Herbert, J. R., Starr, J. M., & Deary, I. J. (in press). Associations between dietary inflammatory biomarkers among older adults in the Lothian Birth Cohort 1936 study. *Journal of Nutrition, Health, & Aging*.

McGrory, S., Ballerinia, L., Okely, J. A. Ritchie, S. J., Doubal, F. N., Doney, A. S. F., … & Deary, I. J. (in press). Retinal microvascular features and cognitive change in the Lothian Birth Cohort 1936. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring.*

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2019

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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 eighth decade of life. *Sleep, 42,* zsz019. PMID: 30668819

McGrory, S., Ballerini, L., Doubal, F. N., Staals, J., Allerhand, M., Valdes-Hernandez, M. D. C., ... & Wardlaw, J. M. (2019). Retinal microvasculature and cerebral small vessel disease in the Lothian Birth Cohort 1936 and Mild Stroke Study. *Scientific Reports, 9*, 6320. PMID: 31004095

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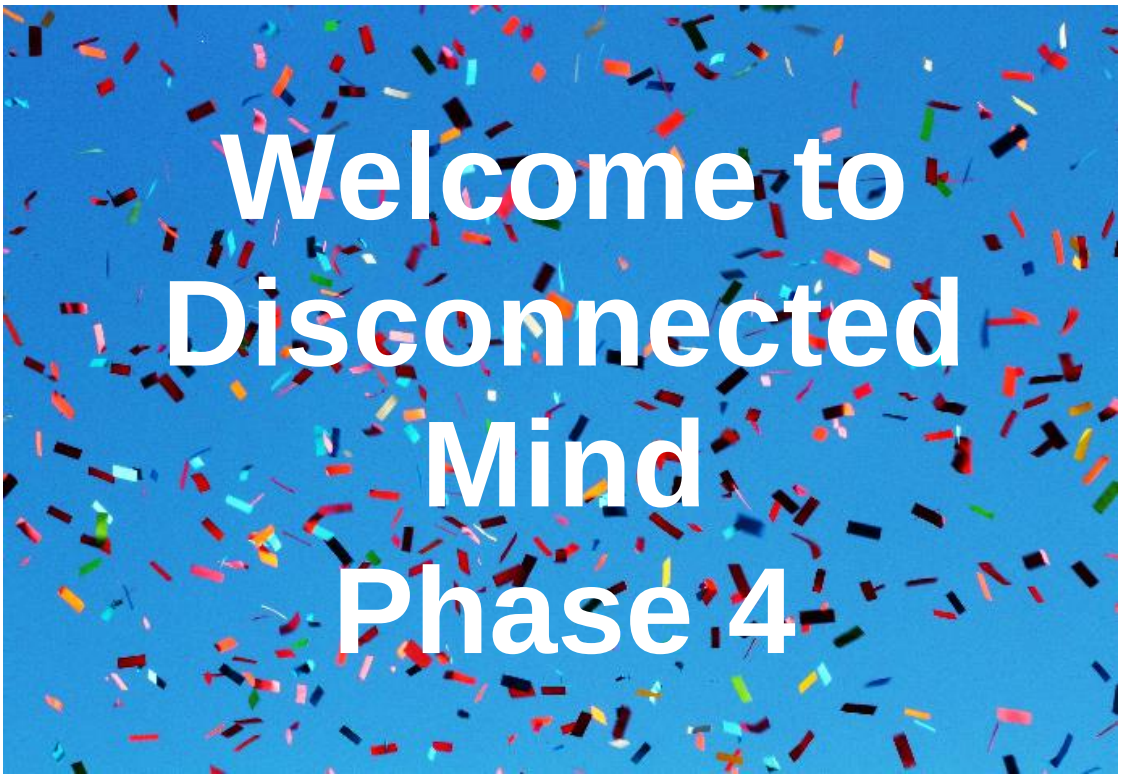
Contact

Please get in touch with any items for inclusion in future newsletters: lbc.ke@ed.ac.uk

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.



LBC 1921 Lothian Birth Cohorts LBC 1936 THE UNIVERSITY of EDINBURGH

age UK Love later life MRC Medical Research Council NIH National Institutes of Health