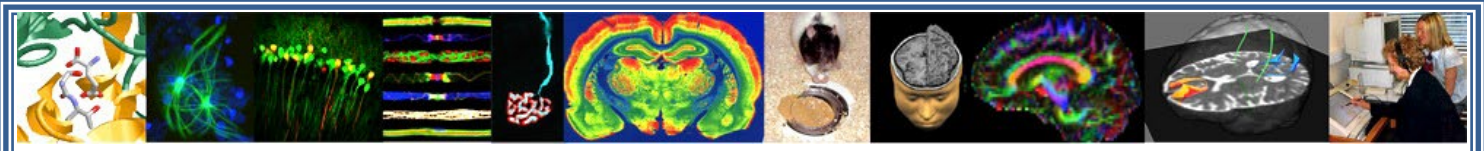
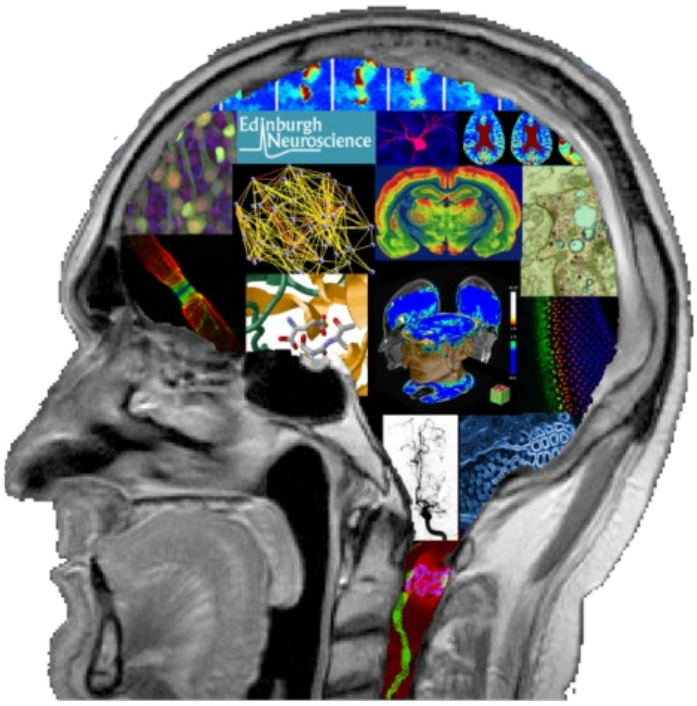


THE UNIVERSITY of EDINBURGH
Edinburgh Neuroscience

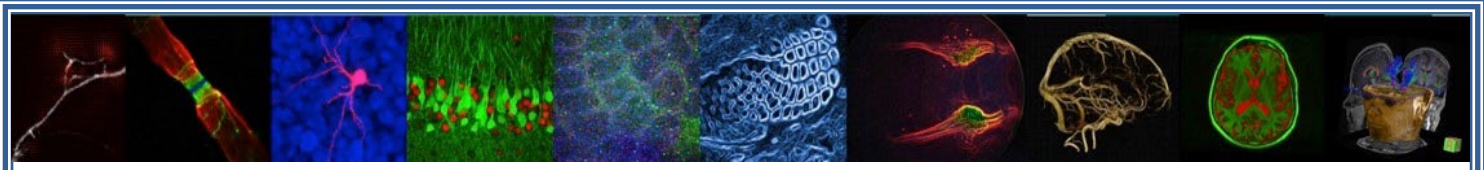
Neuroscience Day 2024



Thursday 18th April
Nucleus Building

#EdNeuroDay

Edinburgh Neuroscience
www.edinburghneuroscience.ed.ac.uk



We are really grateful for the generous support of our Sponsors for Neuroscience Day 2024

clear_Pixel VR

VectorBuilder.com

proteintech

Anne Rowling Regenerative Neurology Clinic

THE UNIVERSITY of EDINBURGH
Row Fogo Centre for Research into Ageing and the Brain

Small Vessel Diseases Research

THE UNIVERSITY of EDINBURGH
Translational Neuroscience PhD Programme

wellcome

SIDB Simons Initiative for the Developing Brain

RWD

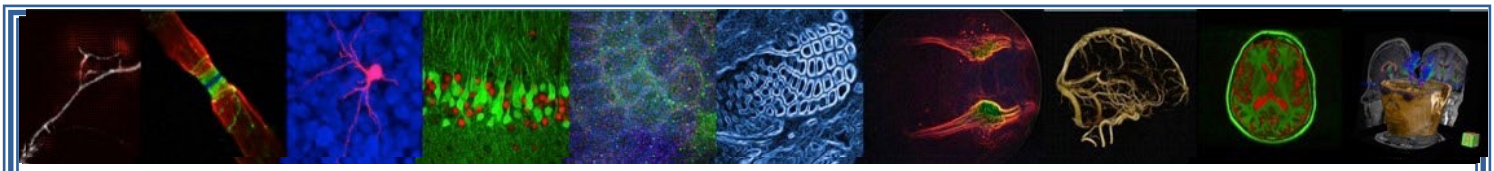
Muir Maxwell Epilepsy Centre
Part of the University of Edinburgh

The Patrick Wild Centre
for Research into Autism, Fragile X Syndrome & Intellectual Disabilities

ThermoFisher SCIENTIFIC

Theirworld
Edinburgh Birth Cohort

PRENCIG
PRETERM NEURODEVELOPMENT COGNITION



Neuroscience Day 2024 Programme

Thursday 18th April 2024, Nucleus Building, King's Buildings Campus, Edinburgh

08.30 Arrival and Registration
Arrival tea/coffee

Session I

Chair: Professor Malcolm Macleod, Edinburgh Neuroscience Co-Director

09.15 Welcome remarks from Edinburgh Neuroscience Co-Directors
Professors Cathy Abbott and Malcolm MacLeod

09.25 Flash talks from new Group Leaders

Unlocking spinal cord regeneration across species
Dr Aida Rodrigo Albors, Centre for Regenerative Medicine
Prefrontal-hypothalamic control of innate drives
Dr Mahesh Karnani, Centre for Discovery Brain Sciences
Unbalanced protein turnover in neurodevelopmental disorders
Dr Susana Ribeiro dos Louros, Centre for Discovery Brain Sciences
The role of astrocyte subtypes in brain (dys)function
Dr Philip Hasel, Centre for Discovery Brain Sciences

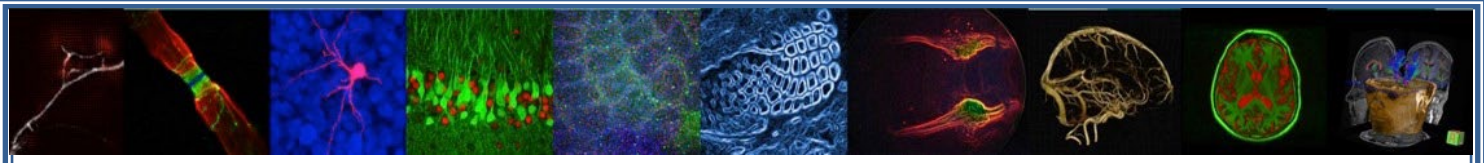
09.45 Memory beyond the hippocampus | the hippocampus beyond memory
Professor Andrew Lawrence, School of Philosophy, Psychology & Language Sciences

10.00 Neurodegenerative Disorders: Mechanisms and Drug Discovery
Dr Kathy Evans, Centre for Genomic and Experimental Medicine

PhD Student Data Blitz

Chair: Dr Katy Marshall-Phelps, Centre for Discovery Brain Sciences

10.15 Phosphodiesterase 7 inhibitors: From pre-clinical to clinical development of future drug for addiction disorders
Adana Keshishyan, Centre for Discovery Brain Sciences
Incomes and outcomes: Socioeconomic status, preterm birth and neurodevelopment
Katie Mckinnon, Centre for Reproductive Health
Understanding the consequence of LRRK2 dysregulation in human stem cell derived astrocytes
Áine Heffernan, Centre for Clinical Brain Sciences
Temporal and regional vulnerability of white matter in Alzheimer's disease pathology
Lucy Ryan, Centre for Discovery Brain Sciences
Investigating sleep problems and links to mental ill health in autistic children and adolescents
Reesha Zahir, Centre for Clinical Brain Sciences



Spinal cord processing of touch and pain in a rat model of SYNGAP1 haploinsufficiency
Katarzyna Mazur, Centre for Discovery Brain Sciences
Are microglia important for the brain response to hypoxia in vivo?
Mila Redzic, Centre for Discovery Brain Sciences
Probing the AMPA receptor – con-ikot-ikot toxin interactions through molecular dynamics simulations and residue interaction network analysis.
Natalia Szlachetka, School of Biological Sciences

10.50 Refreshments & Posters

Session II

Emerging Stories

Chair: Professor Cathy Abbott, Edinburgh Neuroscience Co-Director

11:30 The live human brain tissue research team - using our brains better
Dr Paul Brennan (Centre for Clinical Brain Sciences) and Dr Claire Durrant (Centre for Discovery Brain Sciences)
DNA methylation signatures of Major Depressive Disorder and antidepressant use
Dr Xueyi Shen, Centre for Clinical Brain Sciences
Diffusion-weighted MR spectroscopy to measure neuroinflammation in depression
Arish Mudra Rakshasa-Loots, Centre for Clinical Brain Sciences
Machine Learning EEG Biomarkers in SYNGAP1 Rodent Models and Patients
Dr Alfredo Gonzalez Sulser, Centre for Discovery Brain Sciences
Treating childhood dementias with stem cell gene therapy
Professor Brian Biggar, Institute for Regeneration and Repair

13.00 Lunch & Posters

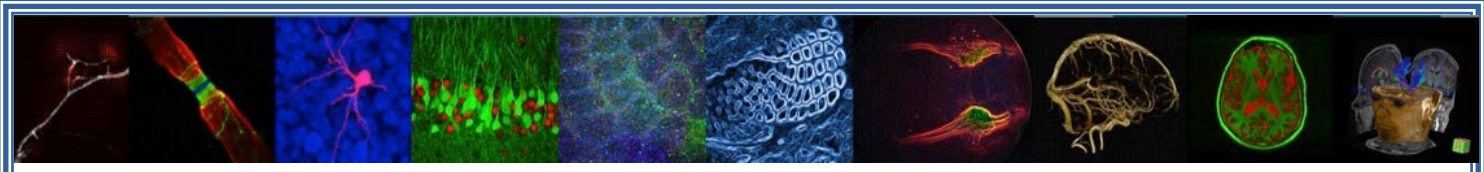
13.30: Lunchtime demo: RWD

Session III

Chair: Prof Anna Williams, Centre for Regenerative Medicine

14.15 Shout-outs
Wellcome Institutional Culture Change Fund
Dr Sara Shinton, Institute for Academic Development
Open Science Framework
Emma Wilson, Centre for Clinical Brain Sciences

14.30 Compensating and recovering from dendritic spine loss in Alzheimer's disease
Dr Patricio Opazo, Centre for Discovery Brain Sciences
Developments in Metabolic Psychiatry
Dr Iain Campbell, Centre for Clinical Brain Sciences
Does brain size affect seizure expression in models of CDKL5 deficiency disorder?
Professor Peter Kind, Centre for Discovery Brain Sciences



15.30 Refreshments & Posters

Session IV

Chair: Professor Joanna Wardlaw, Centre for Clinical Brain Sciences

16.15 The Sir Colin Blakemore Memorial Lecture

Brain – vascular interactions in health and disease: genome to phenome

Professor Stéphanie Debette, University of Bordeaux

17.15 Drinks reception

Edinburgh Neuroscience

Going Green

For this year's Neuroscience Day, we have made a conscious effort to be as sustainable as possible, and have taken the following decisions:

- ✓ Our catering, provided by Blue Sky, is all vegetarian
- ✓ We have printed name tags as stickers to avoid having to use plastic holders
- ✓ This handout is only available digitally, not in print format

If you any further ideas for how we could be even more sustainable next year, please let us know!

Co-Directors' Foreword


We are delighted to welcome you to the 2024 Annual Edinburgh Neuroscience Day. We hope you enjoy an interesting and varied program. This year we are trying out some new formats, including the 'Emerging Stories' session, where researchers will describe work which is very much in progress rather than complete, giving them the opportunity to share with us their thoughts about new phenomena they may be observing, and how they plan to move the work forward. One purpose is to identify opportunities for collaboration – you may have approaches or insights which could contribute to the project – and we will be interested in your feedback on this session.

This is our first EN Day as co-Directors. We wanted to take on the role because we strongly believe that Edinburgh Neuroscience is much more than a collection of scientists doing world class research; and that by nurturing our community we might help all of us to succeed, to be our best selves. Through recognising that success comes in many shapes and forms, and that as individuals we each bring something slightly different to our work, we want to build an environment which is stimulating, supportive, and which challenges us to achieve our full potential. This is as true for well-established researchers (like your co-Directors!) as it is for PhD students and early career researchers.

We want you to be involved in shaping our community, and we want you to hold us to account. To allow this, we published our letter of application – our 'manifesto', on the Open Science Framework. You can read it at https://osf.io/vbzp7. We are reinvigorating the EN Board, to include representatives of early career researchers, research technicians and others, and we are launching 'Edinburgh Neuroscience afternoons', which we hope to have about three times a year at different campus locations. These will feature PhD student flash talks, some research culture or training content – we're planning to focus on narrative CVs in the first one – and a longer, more advanced science talk. The first of these will be on Friday 14th June, and more details will be available soon.

Finally, we are very much looking forward to working with, working for, the Edinburgh Neuroscience community. To get the most out of us, we need to know what you think – what's going well, and what's going not so well, where we are missing opportunities to do useful things, where you think we have got things wrong. Please get in touch – we're always happy to chat over Teams, respond to emails, or meet over a coffee.

Thanks for coming along today, and we hope you enjoy it!

Cathy Abbott and Malcolm Macleod

Neuroscience Day 2024 Speakers

The Sir Colin Blakemore Memorial Lecture

Professor Stéphanie Debette

Professor of Epidemiology/Public Health, University of Bordeaux

Stéphanie Debette, MD PhD, is Professor of Epidemiology/Public Health at the University of Bordeaux and practicing Neurologist at Bordeaux University Hospital. After serving as Director of the Bordeaux Population Health research center (2022-24, Inserm U1219), she is the inaugural director of the Precision and global Vascular Brain Health Institute (VBHI) at the University of Bordeaux, Bordeaux University Hospital, Inserm and Inria. Prof. Debette has been leading large collaborative genomic and epidemiological studies on stroke, cognitive traits, and imaging markers of brain aging, especially cerebral small vessel disease, aiming to decipher the molecular mechanisms underlying brain aging and to improve prevention and treatment of stroke and dementia. Prof. Debette has been leading a European Research Council grant, is principal investigator of a large national investment for the future grant on cerebral small vessel disease (RHU-SHIVA) and has been coordinating or contributes to several European grants. A former Fulbright and Bettencourt-Schueller fellow and adjunct associate professor at Boston University, she was a visiting professor at Kyoto University. She serves in the research steering committee of the CHARGE consortium and chaired the International Stroke Genetics Consortium (ISGC) between 2017 and 2019. She also served as vice-president for external relations at the University of Bordeaux (2018-22). During her term she was involved in establishing and reinforcing strategic partnerships of the university across continent and building new collaborative networks in Europe, in particular the ENLIGHT European University Alliance, of which she chaired the board of directors (2019-22).

Local Speakers (in programme order)

Dr Aida Rodrigo Albors, Centre for Regenerative Medicine

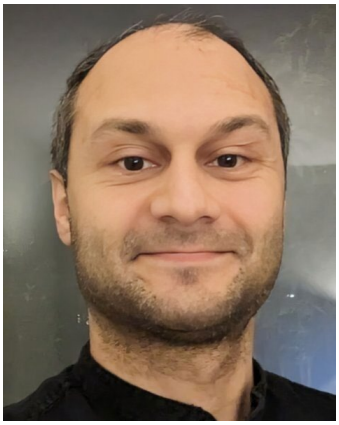
Unlocking spinal cord regeneration across species

Aida studied Biology at the University of Valencia, Spain. She became fascinated by axolotls when she heard that they can regenerate virtually every body part, including the spinal cord. To learn more about their unique regenerative capacity, she moved to Germany to do her PhD with Elly Tanaka at the Max Planck Institute of Molecular Cell Biology and Genetics and the Centre for Regenerative Therapies Dresden. Aida discovered that resident stem cells in the axolotl spinal cord redeploy developmental gene expression programmes to regenerate. To gain a better understanding of

why mouse spinal cord stem cells (or ependymal cells) are not that efficient at repairing the injured spinal cord, Aida joined Kate Storey at the University of Dundee. She uncovered previously unappreciated immature and mature spinal cord stem cells in mice and hints suggesting that mature cells cannot revert to an embryonic-like state that supports regeneration. Since April 2023, Aida is a Chancellor's Fellow at the Centre for Regenerative Medicine. The goal of her lab is to elucidate mechanisms of spinal cord regeneration by working across species with diverse regenerative capabilities: axolotl, mice, and spiny mice – the only known mammal that can recover from spinal cord injury.

On creating and maintaining a positive culture in the lab, Aida said, "I try to create a positive research culture in the lab by putting people first. A happy team that feels supported and valued, willing to take risks or make mistakes and learn from them, is a productive team on track to scientific discoveries!"

"We are benefiting enormously from collaborating with amazing colleagues, and we take every opportunity be helpful/useful to others. We are very excited about our growing axolotl research colony, the only one in the whole UK, and the numerous research opportunities that it will open up not only for our lab but for also for other labs interested in delving into the remarkable biology of the axolotl, in Edinburgh and beyond!"



Dr Mahesh Karnani, Centre for Discovery Brain Sciences

Prefrontal-hypothalamic control of innate drives

Mahesh studies how the cortex and hypothalamus interact to control eating. He uses in vivo calcium imaging and ex vivo synaptic/cellular neurophysiology. He aims to understand the neural mechanisms underlying over-eating as well as eating disorders like anorexia. As a Chancellor's Fellow, he plans to initiate new collaborations within Edinburgh, using open science tools like open-design automated rodent mazes. Before moving to Edinburgh, Mahesh worked as a postdoc at Columbia, the Francis Crick Institute, and ETH Zurich, and started the Drivelab at VU Amsterdam.

In terms of research culture, the Drivelab emphasises public sharing of research works through preprints and modular publications - we all know about bioRxiv by now, but there are so many other diamond-open-access tools to accelerate dissemination and discourse, like ResearchEquals, preLights and Peer Community In Neuroscience. These tools are free to use, and they grow in a use-dependent manner. They find it incredibly satisfying to share knowledge without barriers, while participating in the evolution of dissemination/evaluation systems without barriers.

Dr Susana Ribeiro dos Louros, Centre for Discovery Brain Sciences

Unbalanced protein turnover in neurodevelopmental disorders

Susana holds a BA in Biology from the University of Coimbra, Portugal. During her PhD she investigated the role of stargazin in experience-dependent synapse remodelling and homeostatic plasticity at Harvard Medical School and University of Coimbra. During her first postdoc at the Centre for Neuroscience and Cell Biology, Susana investigated the role of stargazin in neurodevelopmental disorders. In 2015 Susana joined Prof. Emily Osterweil's lab as a postdoctoral fellow where she identified proteostasis dysregulation in Fragile X syndrome and uncovered several molecular mechanisms that contribute to pathology of autism and intellectual disability. In April 2023, Susana was awarded a Chancellor's Fellowship that will support her new established lab looking into the molecular mechanisms governing synapse remodelling, currently focused on how protein degradation dysfunction contributes to neurodevelopmental disorders.

Susana on research culture and citizenship: "Our lab holds a few core values - responsibility, trust, collaboration and openness. We believe in taking ownership of our projects but also in supporting one another, and ensuring that our work is reliable. Our lab is also committed to promoting inclusiveness and maintaining a discrimination-free environment where everyone feels safe, valued and respected. I strive for a lab where everyone is achieving their targets and keep a regular meeting schedule as well as an open-door policy to guide every project and help everyone reach their targets. In our lab, scientific research is target-based, not hourly based. If everyone is producing a constant and evident stream of work, then everyone is doing it right. Our main achievement so far has been in training the future generations of scientists, particularly summer students. Witnessing them become independent in the lab and excited about their experiments is always very rewarding!"

Dr Philip Hasel, Centre for Discovery Brain Sciences

The role of astrocyte subtypes in brain (dys)function

Philip did his PhD at Edinburgh Uni before moving to NYU for his postdoc with Shane Liddelow. He is now a Group Leader and Wellcome Trust Career Development Fellow at the Centre for Discovery Brain Sciences and the Edinburgh UK Dementia Research Institute. Dr Hasel's group is interested in astrocytes that make up brain borders in the mouse and human brain, how they contribute to brain function and what goes awry in disease. They are approaching these questions using a mix of computational approaches (such as scRNA-seq and spatial transcriptomics) and wet lab approaches. If that sounds interesting to you, they're looking for Research Assistants and Postdocs!

Philip on research culture: "My advice if you're a PhD student or Postdoc is to pick a lab not solely based on the papers they publish, but rather whether the group leader strives to create a supportive lab environment and cares for your career progression and mental health."

Professor Andrew Lawrence, School of Philosophy, Psychology & Language Sciences

Memory beyond the hippocampus | the hippocampus beyond memory

Lawrence is a Professor of Cognitive Neuroscience in the Department of Psychology at Edinburgh University. His research focuses on two major aims. Along with his collaborators, he conducts studies to understand the functional architecture of cognitive functions with a special focus on the role of cortico-hippocampal networks in memory, perception and social cognition using structural and functional MRI at 3T and 7T. From a translational perspective, they aim to develop sensitive cognitive markers to detect age-related cognitive impairment and to monitor cognitive decline. Here they focus on digital cognitive markers using remote testing via devices such as tablets and are currently investigating their applicability in a cross-cultural context with colleagues in India.

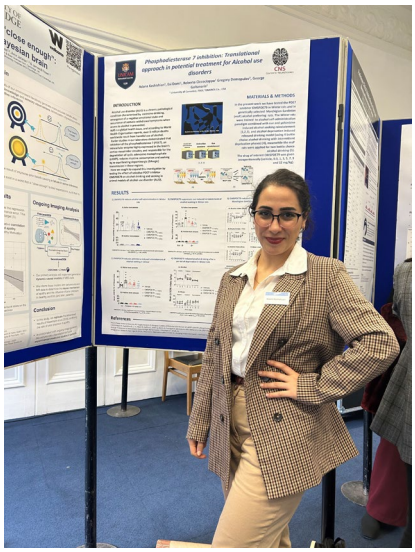
Previously, Lawrence was a Professor in the Cardiff University Brain Research Imaging Centre and Dean of Research for Cardiff University College of Biomedical and Life Sciences, where he led several large-scale institutional awards. He has an interest in open science, having been involved in the UK reproducibility network programme on Open and Responsible Researcher Reward and Recognition (OR4) and also in ECR development, having been involved in the UKRI Future Leaders Fellows Development Network.

Dr Kathy Evans, Centre for Genomic and Experimental Medicine

Neurodegenerative Disorders: Mechanisms and Drug Discovery

Following research in the fields of genetics and genomics, more recently the focus of Kathy's group research has moved to cell biology. They are interested in neurodegenerative disorders, specifically in understanding mechanisms, including the impact of stress and of DNA damage, and on drug discovery. Much of Kathy's work is centred around the sortilin gene family. This comprises five multifunctional neuronal receptors and trafficking molecules that have been implicated in both neurodegenerative and psychiatric conditions. The group comprises two postdocs (Amina McDiarmid and Melissa Eccles), two PhD students (Elly Stamp and Kevin Carr) and a part-time Research Assistant (Susan Anderson).

PhD Student Data Blitz



Adana Keshishyan, Centre for Discovery Brain Sciences

Phosphodiesterase 7 inhibitors: From pre-clinical to clinical development of future drug for addiction disorders

Substance use disorders or simply SUD-s are modern public health issue as the prevalence of it spreads with devastating addiction derived neuropsychological disturbances, yet the effective approach to fighting against SUD still remains unknown.
In the present work we have tested the PDE7 inhibitor OMSPDE79 in 48 Wistar rats of the AUD-like behavior animal model, and in 30 Wistar rats of the CUD-like behavior animal model. In the AUD-like behavior, we have tested the OMSPDE79 in the Wistar rats that have had a long history of 4 bottle choice alcohol drinking and subsequent alcohol deprivation effect (ADE). In the CUD-like behavior, we have tested the OMSPDE79 in relapse of the rats that have undergone repetitive cocaine self-administration sessions and have been deprived of the substance after gaining cocaine reward baseline.

Results: The tested PDE7 enzyme inhibitor OMSPDE79 has reduced the ADE to the baseline alcohol drinking level, and was able to remit relapse-driven cocaine seeking behavior after cue and stress induced relapse.

Katie Mckinnon, Centre for Reproductive Health

Incomes and outcomes: Socioeconomic status, preterm birth and neurodevelopment

Preterm birth and social deprivation are both associated with differences in brain development and increased chances of difficulties across the lifespan. My PhD explores the relationship between these two exposures within the Theirworld Edinburgh Birth Cohort, which follows a group of preterm- and term-born infants through childhood and into adulthood. We found that both preterm birth and socioeconomic status (SES) are associated with differences in regional brain volumes and white matter microstructure on neonatal brain MRI at around their due date, although preterm birth is associated with more widely spread differences. There are different ways of measuring SES, and we found family-level measures were more associated with brain development in the neonatal period than neighbourhood-level measures. We then explored whether inflammation was the mechanism through which preterm birth and SES have their effects, using epigenetic scores. We found a range of differences in the proteome of preterm infants, suggesting immune dysregulation, but minimal associations with SES, suggesting inflammation is unlikely to be the primary axis through which SES is embedded in development in the neonatal period. There is an opportunity for interventions to reduce social disparity in the perinatal period, which could promote healthier brain development after preterm birth.

Áine Heffernan, Centre for Clinical Brain Sciences

Understanding the consequence of LRRK2 dysregulation in human stem cell derived astrocytes

Mutations in *leucine-rich repeat kinase 2* (*LRRK2*), which result in increased kinase activity, are a common genetic cause of Parkinson's disease (PD). Impairment of astrocytic homeostatic functions including inflammatory dysregulation are observed in PD, but the role of LRRK2 in this context is unclear.

To investigate this, a suite of human stem cell derived isogenic *LRRK2* mutant astrocytes were generated via CRISPR/Cas9 genome editing; *LRKK2*$^{R1441C/R1441C}$ and LRRK2$^{G2019S/G2019S}$ pathogenic mutations, as well as loss-of-function *LRRK2 knockout (KO)* and *LRRK2*$^{D2017A/D2017A}$ kinase dead mutants.

Unbiased proteomic analysis highlighted dysregulation of the innate immune response across *LRRK2* mutants. This was validated by mRNA expression and immunofluorescence, which showed decreased levels of interferon signalling genes including MX1. Moreover, when challenged with interferon gamma, the *LRRK2* mutant astrocytes exhibit an impaired inflammatory response. Interestingly, a similar phenotype was noted when cells were subject to a LRKK2 kinase inhibitor (GNE-0877).

Overall, the results show that astrocytes with *LRRK2* mutations exhibit an alerted inflammatory profile. Future work aims to mechanistically understand the involvement of LRRK2 in modulating these pathways and whether the phenotype observed in the *LRRK2* mutants can be rescued.

Lucy Ryan, Centre for Discovery Brain Sciences

Temporal and regional vulnerability of white matter in Alzheimer's disease pathology

White matter health is critical for healthy cognitive function. White matter abnormalities are detected in individuals up to 20 years before the onset of Alzheimer's disease (AD) symptoms and are predictive of cognitive decline. Importantly, the associated neuropathological changes in white matter are unclear. Here, we aimed to understand the cellular changes underpinning white matter damage in the context of AD pathology. Oligodendrocyte lineage cells were characterized in the white matter in the AppNL-G-F mouse, a second-generation model of amyloidopathy in AD. No pathology was observed when amyloid plaques begin accumulating in the CNS at 3 months of age. However, at 6 months of age, when cognitive impairment has been documented, there was a decrease in mature oligodendrocytes in the lateral white matter, which was further decreased by 9 months of age. Medial white matter was unaffected, indicating regional impacts on oligodendrocytes. The oligodendrocyte loss at 9 months of age was associated with axonal loss in lateral white matter. Overall, we uncover marked regional and temporal vulnerability of the white matter in the context of AD pathology.

Reesha Zahir, Centre for Clinical Brain Sciences

Investigating sleep problems and links to mental ill health in autistic children and adolescents

Characterising trajectories of sleep and mental health across childhood and adolescence for autistic and non-autistic participants in a longitudinal birth cohort:
Autistic people experience high rates of sleep and mental health problems, which are thought to change across life stages. Current findings about these changes are limited by small sample sizes, and lack of sufficient longitudinal evaluation.

We aimed to characterise trajectories of sleep and mental health problems in autistic and non-autistic people from early childhood to late adolescence.

We conducted multilevel growth curve modelling on data from the Avon Longitudinal Study of Parents and Children (ALSPAC, total n ~ 14,000). We explored trajectories of average frequency of night-time waking (from parent-report questionnaires) and internalising difficulties (from the Strength and Difficulties Questionnaire; SDQ – used as a proxy for mental ill health) in autistic and non-autistic participants.

Results: Night-time waking trajectories for both groups steadily decreased over time, eventually stabilising from 8 years onward. Overall, autistic participants had a higher trajectory of night-time waking frequency, which decreased at a slower rate compared to non-autistic participants. Autistic participants had a higher trajectory of internalising difficulties compared to non-autistic participants. However, there were no structured changes in trajectories for either group.

Conclusion: These results align with findings from the current literature that autistic people experience increased sleep and mental health problems compared to the general population, that persist over time. Further analyses will assess whether there might exist a critical time window for intervention on sleep in this group.

Katarzyna Mazur, Centre for Discovery Brain Sciences

Spinal cord processing of touch and pain in a rat model of SYNGAP1 haploinsufficiency

Investigation of spinal cord processing of touch and pain in a rat model of SYNGAP1 haploinsufficiency
Katarzyna Mazur, Ying Sze, Sarfaraz Nawaz, Sally M Till, Peter C Kind, Carole Torsney

De novo mutations in SYNGAP1 are one of the most common genetic causes of neurodevelopmental disorders linked to intellectual disability, epilepsy, and autism spectrum disorder (ASD) (Satterstrom et al., 2020). SYNGAP1 haploinsufficiency has also been associated with somatosensory processing alterations in humans and in mice (Michaelson et al., 2018). Many ASD-associated genes are key components of activity-dependent processes, suggesting potential

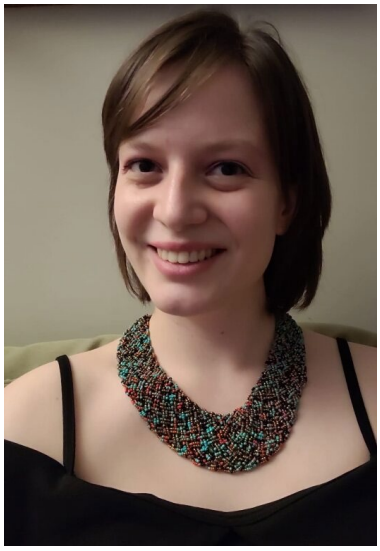
involvement in postnatal maturation of spinal somatosensory circuits (Ebert and Greenberg, 2013; Beggs et al., 2002).
Aim: investigate touch and pain behavioural phenotypes and underlying spinal somatosensory processing in a rat model of SYNGAP1 haploinsufficiency (Mastro et al., 2020).
Adult Syngap heterozygous knockout (Syngap+/-) and wild-type rats underwent somatosensory behavioural testing. Syngap+/- rats showed reduced tactile reactivity, but unaltered response to noxious stimuli. SynGAP protein expression in the spinal dorsal horn was reduced by 50% in Syngap+/- rats compared to wild-type. Spinal cord immunostaining for markers of tactile and nociceptive inputs showed unaltered termination patterns. Glabrous skin structure and tactile corpuscle innervation density did not differ between genotypes. Spinal reflex networks displayed an increased response threshold in dorsal root-ventral root potential recordings. These electrophysiological studies indicate a spinal functional deficit contributes to the tactile hypo-reactivity phenotype observed in Syngap+/- rats.

Mila Redzic, Centre for Discovery Brain Sciences

Are microglia important for the brain response to hypoxia in vivo?

Hypoxia associated with neurovascular dysfunction is a putative mechanism contributing to many neurological conditions. Microglia, the primary immune cells of the brain, respond to hypoxia-associated triggers and are implicated in supporting brain microvasculature. Previously, we showed signalling via the microglial immunoreceptor triggering receptor expressed on myeloid cells 2 (TREM2) supports microvascular integrity in an experimental model of vascular cognitive impairment (VCI). However, if TREM2 is specifically involved in hypoxia-induced microglial reactivity and microvascular status is unclear.

We examined this relationship *in vivo* by exposing mice to 8-9% O_2. RNA sequencing conducted on microglia from *Trem2*$^{+/+}$ and *Trem2*$^{-/-}$ mice following four days of hypoxia detected significant transcriptional changes in response to hypoxia, including upregulation of genes involved in cell cycle, glycolysis, and cell migration. Interestingly, these changes were *Trem2*-independent. Brain tissue analyses demonstrated hypoxia-induced angiogenesis, cell proliferation, and microbleeds associated with plasma protein fibrinogen leakage, which were not impacted by TREM2 deficiency. Therefore, TREM2 does not control microglial and wider brain responses to hypoxia and its resilience-promoting signalling in VCI is likely in response to a different, hypoxia-unrelated trigger. Future work will employ microglia depletion strategies to assess whether other TREM2-independent microglial responses are important for supporting the brain during hypoxia.



Natalia Szlachetka, School of Biological Sciences

Probing the AMPA receptor – con-ikot-ikot toxin interactions through molecular dynamics simulations]and residue interaction network analysis.

Con-ikot-ikot (CII) is a toxin found in the venom of a marine cone snail, Conus striatus. It binds specifically to AMPA receptors (AMPARs), a subtype of glutamate receptors which play an important role in synaptic plasticity – the molecular mechanism behind the processes of memory and learning. Con-ikot-ikot is small compared to antibodies and other available tools for targeting AMPARs, and binds at a unique site within the receptor's extracellular domains, between the amino-terminal and ligand-binding domains.

Conotoxins and other toxins derived from animal venoms are widely used as research tools and therapeutics, therefore we are interested in studying CII and understanding the details of its interactions with AMPARs.

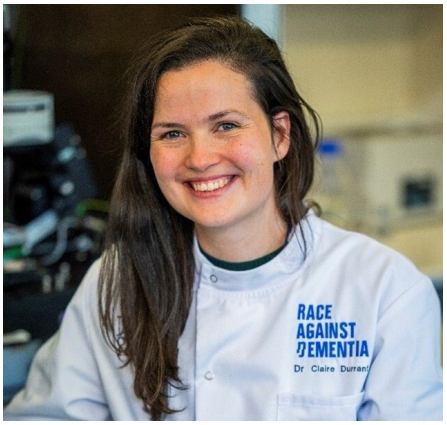
kaWe used molecular dynamics (MD) simulations and developed a residue interaction network (RIN) analysis approach to unravel the network of interactions between con-ikot-ikot and AMPAR and identify key residues responsible for the binding between the two proteins. Our analyses recapitulate previously described interactions between con-ikot-ikot and the ligand-binding domain layer of AMPAR, as well as uncover novel and unique interactions with the amino-terminal domain layer. We plan to use our findings as the basis for designing small con-ikot-ikot inspired peptides, amenable to chemical synthesis, that could become scientific tools and therapeutic agents.

Dr Paul Brennan, Centre for Clinical Brain Sciences

The live human brain tissue research team - using our brains better

Paul is Reader, Honorary Consultant Neurosurgeon and Clinical Director at the University of Edinburgh and NHS Lothian. His research spans the laboratory and the clinic, combining molecular, epidemiology and clinical investigation to guide rationale innovation to improve patient care.

Critical to accelerating the discovery of new therapies for brain tumours, and their translation into the clinic, is to investigate diagnosis, treatment and outcomes at a population level, mapping this to molecular interrogation of resected tumour tissue, and liquid biopsies from patients. With this data we are better understanding tumour diagnosis, treatment efficacy and patient outcome, feeding the data back into discovery science and clinical trial design.



Dr Claire Durrant, Centre for Discovery Brain Sciences

The live human brain tissue research team - using our brains better

Dr Claire Durrant received a first-class degree in Natural sciences from the University of Cambridge then undertook her PhD in the lab of Professor Michael Coleman at The Babraham Institute (University of Cambridge 2013-2016). Having developed a novel mouse slice culture model of Alzheimer's disease during her PhD, she went on to undertake a postdoc using this model to dissect the role of inflammation, angiogenesis, Aβ and tau pathology in Alzheimer's disease. In 2019, Claire moved to Edinburgh having received a competitive 5 year Race Against Dementia Fellowship where she began to closely collaborate with Prof Tara Spires-Jones, Dr Paul Brennan and Dr Sam Booker. Over the last 4 years, Claire's group has focused on understanding causes and consequences of synapse loss in Alzheimer's disease, with a focus on the physiological and pathological roles of Aβ and tau. Her latest work has been to develop a live human brain slice culture model of Alzheimer's disease, working alongside neurosurgeons in Edinburgh to utilise ethically obtained waste tissue from neurosurgery procedures for academic research. Her group has expanded to include 2 postdocs, a research assistant, and several primary supervised and co-supervised PhD students. Claire's group pride themselves on creating a highly collaborative working environment, ensuring valuable human brain tissue is used to maximal effect to explore key questions relating to Alzheimer's disease and related disorders.

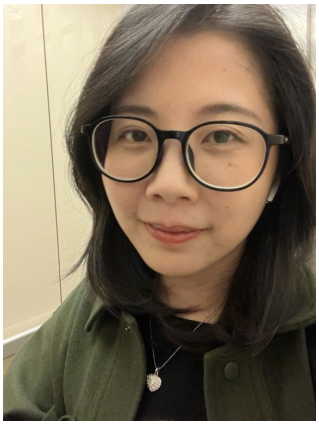
On lab culture Claire says, "The nature of working with live human brain tissue from surgeries is that we have to work effectively as a team. We have weekly briefing meetings planning how tissue will be used in upcoming cases, assign everyone roles for the day (from collecting tissue from surgery, coordinating with research nurses, processing tissue in the lab etc) and create a priority list of experiments for best- and worst-case scenarios. Each piece of tissue is unique, so we have to be able to assess and act quickly when we get it on the day. We try and treat human case days like a formula one pitstop- everyone working together to get the best outcome from such a valuable resource. Whilst

everyone in the group has distinct projects, working together as a team is essential for the success of our work.

Further on research culture and citizenship, Claire says, “We are extremely passionate about generating robust, repeatable data, so are constantly refining our techniques and interrogating the best ways to perform experiments. Ensuring we take into account as many variables as possible, such as sex, age, genotypes and brain region from our human samples can provide rich data sources to further probe disease mechanisms. For too long, female subjects have been excluded from research, so we always ensure that whether our experiments are in mice or human tissue we are always taking into account sex as part of our statistical models. “

Which of your collective achievements give you greatest satisfaction?

“One of my proudest moments in science was securing an additional £1,000,000 donation from The James Dyson foundation to set up our human brain slice lab. This enabled me to expand my fabulous team, bring in state of the art equipment, and enable us to work closely with the amazing research nurse teams to assist with identifying and consenting patients. This turned our work using human brain tissue from a nice side project into the main focus of our group. It has been so rewarding to start seeing the outputs from this coming out, having papers under review, PhD students joining the group and exciting new discoveries that would not have been possible without the donation.”



Dr Xueyi Shen, Centre for Clinical Brain Sciences

DNA methylation signatures of Major Depressive Disorder and antidepressant use

Depression is a disabling and highly prevalent condition, the underlying mechanism of which has been unclear. DNA methylation (DNAm) has emerged as a significant biomarker that captures both genetic predisposition and dynamic environmental factors in relation to disease risk. Xueyi Shen will present a series of recent studies that leverage large-scale international collaborations within the Psychiatric Genomics Consortium and utilize newly available electronic health records. These studies collectively outline the DNAm signatures of depression, the genetic risk of depression, and antidepressant use.

Dr Shen’s research reflection: Our lab is enthusiastic about having front-line experience in public engagement. There is a specialised, in-house team of public engagement officers to help researchers to publicise research outcomes effectively and accurately. We involve the public and patients from the initial development of research questions to the end point of publicising findings. This is especially relevant in our study of mental health disorders and use of electronic health records. This experience reshaped my own research, gave me valuable opportunity to clarify our research process, and generated many inspiring conversations within the team.

Arish Mudra Rakshasa-Loots, Centre for Clinical Brain Sciences

Diffusion-weighted MR spectroscopy to measure neuroinflammation in depression

Arish's primary goal is to help improve mental health outcomes for people living with HIV. He is currently completing his PhD in Translational Neuroscience at Edinburgh, where his work has been funded by the Wellcome Trust and South African MRC Unit on Genomics of Brain Disorders, among others. His current research, which he has been carrying out in Brighton (UK) and Cape Town (South Africa), explores peripheral and central nervous system inflammation as a potential mediator for the increased risk for depression in people with HIV. He also hold a Thomas J. Watson Fellowship, through which he worked with grassroots HIV movements around the world, and a BA in Liberal Arts from Earlham College (USA), where he studied Biochemistry, Neuroscience, and Ancient & Classical Studies. Arish aspires to train the next generation of conscientious scientists in neuroscience and global health.

On his approach to doing research, Arish says, "I am deeply passionate about integrating social justice and equity in research. On one hand, we must ensure that our research is inclusive (whatever that may mean for each individual study), for example by working on cell lines from diverse ancestries, testing mixed-sex animal models, or adequately resourcing clinical studies to minimise socioeconomic barriers to participation. On the other hand, we need to welcome and support researchers from marginalised backgrounds to thrive in neuroscience, while working to dismantle the systemic barriers that continue to disenfranchise certain groups of researchers. I regularly support other early career researchers, particularly those from the Global South like myself, to find their footing in academia. My most prized 'achievements' are little notes I have received from folks that I have taught or mentored over the years and who have gone on to secure opportunities for developing their research careers, which I keep in a folder on my computer to scroll through on days when existing as a multiply-minoritised individual in academia feels particularly onerous."

Dr Alfredo Gonzalez Sulser, Centre for Discovery Brain Sciences

Machine Learning EEG Biomarkers in SYNGAP1 Rodent Models and Patients

Alfredo is a researcher in the Centre for Discovery Brain Sciences focused on rodent models of epilepsy and neurodevelopmental disorders. He studied Biology at the University of Pennsylvania and then undertook his PhD in Neuroscience at Georgetown University in Washington DC. Alfredo has been focused on epilepsy for a long time but, as the rest of his field, he is focusing more and more on epilepsy rodent models with genetic aetiologies similar to those seen in patients. This has led to overlapping interests and multiple collaborations with the Simons Initiative for the Developing Brain (SIDB). Neurodevelopmental disorders studied by the SIDB result in severe autism and intellectual disability often are comorbid with epilepsy. Alfredo's lab specializes in EEG recordings in rodents, where in collaboration with engineers and informaticians they

have developed advance analyses for automated seizure detection, sleep scoring and biomarker identification in those models.

On research culture, Alfredo's take is "I am passionate about reproducible science and I make all data and code freely available. I run the lab with an emphasis on attaining good work-life balance with individualized plans and aims for all trainees, while encouraging everyone to undertake career-development coursework. On the side I write Wikipedia biographies for underrepresented or minority scientists."

Professor Brian Biggar, Institute for Regeneration and Repair

Treating childhood dementias with stem cell gene therapy

Brian Bigger graduated from Bath University with a degree in Applied Biology and later a PhD in gene therapy from Imperial College London. Brian set up the Stem Cell & Neurotherapies group at the University of Manchester in 2006 to understand pathology and develop treatments for neurological lysosomal storage disorders, essentially childhood dementias. His group was the first to separate lysosomal storage from neuro-inflammation and show the role of both processes in the pathology of neurological lysosomal diseases. His lab developed several gene and cell therapy treatments for lysosomal diseases including three clinical trials.

Brian moved to the University of Edinburgh in 2023 to take up a Chair in Advanced Therapeutics at the Institute for Regeneration and Repair and retains an Honorary Chair in Cell and Gene Therapy at the University of Manchester. The Bigger lab continues to develop innovative gene and cell therapies for neurological diseases, including lysosomal diseases and bring these treatments to patients.

The lab's focus is much more translational than most basic science labs due to the nature of cell and gene therapies, and has a history of bringing treatments from basic science right through to clinical trials and even company formation and licencing. They have a close interaction with patient groups at family meetings and this really helps to create enthusiasm for the research in the lab.

Brian says, "Of course having some of those clinical trials of gene therapies actually work in patients is an incredible feeling and it really feels like we give something back to the community."

Dr Patricio Opazo, Centre for Discovery Brain Sciences

Compensating and recovering from dendritic spine loss in Alzheimer's disease

Patricio's research has been driven by a desire to understand how memories are stored in the brain at the synaptic level and how synaptic dysfunction contributes to memory loss in Alzheimer's disease. As a Group leader, Patricio aims to find ways of boosting the intrinsic synaptic repair mechanisms of the brain, with the

ultimate goal of delaying or even preventing the onset of cognitive decline.

Originally from Chile, Patricio obtained his PhD at the University of California, Los Angeles (UCLA) in the lab of Dr Thomas O'Dell investigating the molecular mechanisms underlying Long-term potentiation (LTP) of synaptic transmission – an electrophysiological correlate of memory.

For his first postdoc, Patricio joined the lab of Dr Daniel Choquet in Bordeaux to investigate the molecular mechanism underlying the synaptic trapping of AMPA receptors - the main mediators of synaptic transmission – during LTP using a single-particle tracking approach. For my second postdoc, He joined the lab of Dr Tobias Bonhoeffer at the Max-Planck Institute in Munich, to assess the causal relationship between synaptogenesis and memory, using a combination of two-photon microscopy and behaviour.

Patricio started my own independent group first in the Queensland Brain Institute (QBI) at The University of Queensland in Brisbane, Australia in 2016 and then in the UK Dementia Research Institute at the University of Edinburgh in 2021, where he is leveraging his long-standing expertise in synaptic plasticity to investigate the synaptic compensatory and repair mechanisms counteracting synaptic loss at the early stages of Alzheimer's disease.

On research culture, Patricio says, "We are committed to implement a research programme that i) explore meaningful biological questions, ii) use state-of-the art technology, iii) undertake high-risk high-pay projects, iv) establish meaningful collaborations and more importantly, v) empower and motivate team members by creating an environment that values independence of thought, creative thinking and a "feedback" culture in a relaxed, flexible and friendly work environment."

Dr Iain Campbell, Centre for Clinical Brain Sciences

Developments in Metabolic Psychiatry

Dr. Iain Campbell is the Baszucki Research Fellow in Metabolic Psychiatry at the University of Edinburgh. His primary research interests focus on the role of metabolic dysfunction in the brain and central nervous system and how these relate to symptoms of serious mental illness. He has a PhD in Global Health from the University of Edinburgh and is a principal investigator on a pilot trial of a ketogenic diet for bipolar disorder, and a co-investigator on the UKRI MRC Metabolic Psychiatry Hub at The Division of Psychiatry within the Centre for Clinical Brain Sciences. He is a co-investigator leading workstreams on Wellcome Trust funded projects Helios-BD and Ambient-BD. Dr. Campbell has lived experience of Bipolar Disorder Type 2 which has informed his research

Reflecting on his research, Iain says: "As a researcher who has lived with a mental health condition I have observed that many of the clean concpetual lines drawn between mental and physical health dissolve in the lived experience of patients experiencing concomitant physical and mental health symptoms. The divides between neuroscience and psychiatry, Kraeplin and Freud, physical and mental health, represent a deep stratum which runs through research and care of mental health conditions. As a result of this, many of the primary treatments for serious mental illness have significant negative consequences for physical health. I am committed to involving lived experience in research because I

believe that this will naturally begin to bridge this divide between separated disciplines in the interest improved treatments for patients."

Professor Peter Kind, Centre for Discovery Brain Sciences

Does brain size affect seizure expression in models of CDKL5 deficiency disorder?

Peter Kind is Director of the Simons Initiative for the Developing Brain and Co-Director of the Patrick Wild Centre for Research into Autism, Fragile X Syndrome and Intellectual Disability. He is also Site Manager and Senior Advisor to the SFARI Autism Rat Consortium.

Professor Kind received his PhD from Oxford University in 1993, after which he completed his postdoctoral training with Professor Colin Blakemore (Oxford University) and Professor Susan Hockfield (Yale University). He moved to Edinburgh in 2023 where he is currently the Professor of Developmental Neuroscience at the University of Edinburgh.

His laboratory uses electrophysiological, imaging and behavioural techniques to examine the pathophysiology associated with rodent models of single gene causes of neurodevelopmental disorders (NDDs) such as autism spectrum disorders and intellectual disabilities. His group investigates whether there is convergence of developmental trajectories for different genetic forms of ASDs/IDs and whether there are critical periods during which therapeutic strategies are more effective.

POSTERS

Please follow this QR code to read the abstracts for the posters or click this link here.

POSTER NUMBER	NAME	AFFILIATION	POSTER TITLE
1	Samuel Gibbon	Centre for Clinical Brain Science	Optic disc pallor in neurodegenerative diseases
2	Dorota Stefancova	UK Dementia Research Institute, Center for Clinical Brain Sciences	Exploring the consequences of genetically ablating brain pericytes in a novel animal model
3	Arish Mudra Rakshasa-Loots	Biomedical Sciences	Inflammation as a possible contributor to depression in young people living with HIV
4	Miracle Ozzoude	College of Medicine and Veterinary Medicine	Endotyping neurodegeneration through the eye using multi-modal retinal imaging.
5	Eleanor Stamp	Genomics and Experimental Medicine	Understanding the Role of SORCS2 in DNA Double-Strand Break Formation: Implications for Age-Related Cognitive Decline and Neurodegeneration
6	Tamsin Baxter	Institute of Genetics and Cancer (Centre for Genomic and Experimental Medicine)	Repurposed Drug Screening for eEF1A2-Related Neurodevelopmental Disorders
7	Natalia Szlachetka	Centre for Doctoral Training in Biomedical AI	Probing the AMPA receptor – con-ikot-ikot toxin interactions through molecular dynamics simulations and residue interaction network analysis
8	Karl Baldacchino	Precision Medicine	Why Don't Spinal Cord OPCs Remyelinate Well in MS and How Do We Fix This?
9	Animesh Talukder and Ioanna Kougianou	Centre for Clinical Brain Sciences-Psychiatry	Sensitivity of the Clinical High-Risk and Familial High-Risk Approaches to Capture Risk of Future Psychosis – A Systematic Review
10	Sasha Pokrovskaya	The Royal (Dick) School of Veterinary Studies	Microglial heterogeneity in chronic neurodegeneration in CNS prion disease
11	Inés Jiménez Pulido	EastBIO PhD student	Neuron specific modulations of vertebrate myelination and their effects on neuronal function
12	Grant Marshall	Institute of Genetics & Cancer	Developing Allele-Specific ASO Therapies for EEF1A2 Related NDD

13	Meg Watt	Roslin Institute	Age-related neurodegeneration and dementia: comparison of neuropathological changes and genetic predisposition in diverse species
14	Lian Hollander Cohen	Centre for Clinical Brain Sciences	Incorporating oligodendrocyte precursor cells in the regulation of neuronal circuit formation and function
15	Eleonora Scalia	Multiple Sclerosis Society funded PhD student	Does remyelination by oligodendrocytes that survive demyelination provide neuroprotection?
16	Alexander Edwards	The Institute of Quantitative Biology, Biochemistry and Biotechnology; EASTBIO PhD student	Activation of AMPA-type glutamate neuroreceptors in health and disease
17	Emma Dumble	Centre for Clinical Brain Sciences, EastBIO PhD student	Investigating how the remodelling of axonal pre-synapses is governed by oligodendrocyte precursor cells in the Zebrafish visual system.
18	Denis Yuan	Centre for Clinical Brain Sciences	Live imaging of exocytosis in oligodendrocyte precursor cells as a putative mechanism to regulate neural circuit development.
19	Patrícia Bispo	Centre for Clinical Brain Sciences; Chancellor's Fellow Studentship	Investigating mechanisms of oligodendrocyte recruitment in plasticity and demyelinating conditions
20	Lucy Wheatley	Centre for Clinical Brain Sciences	Investigating the roles of oligodendrocyte-encoded δ-protocadherins in neural circuit development.
21	Julia van de Korput	MS Society Edinburgh Centre for MS Research, Translational Neuroscience PhD Program, Institute for Regeneration and Repair	Investigating the prevention and rescue of demyelination in the central nervous system
22	Donia Arafa	Centre for Discovery Brain Sciences	Resilience of individual myelin sheaths following damage
23	Cavan Bennett-Ness	Institute of Genetics and Cancer	Investigating the impact of EEF1A2 missense mutations on protein synthesis in neurodevelopmental disorders
24	Danilo Negro	UK Dementia Research Institute (Wellcome Trust PhD programme in Translational Neuroscience)	Investigating the role of tau in mechanisms of synaptic resilience
25	Austeja Ciulkinyte	Wellcome Trust Translational Neuroscience PhD programme	Proteome-guided identification of mechanisms and biomarkers in age-related cerebrovascular dysfunction
26	Anuj Vadher	University of Stirling, PhD in Psychology	Assessment of Landmark Usage in Fmr1-/y, Syngap1+/-, and Grin2b+/- Rats on a Variation of the Watermaze Experiment
27	Simo Lenci	Centre for Discovery Brain Sciences, PhD student in Precision Medicine	Characterising Preneoplastic Glioma Functional Networks in a Zebrafish Model
28	Kellie Horan	Centre for Regenerative Medicine, Institute for Regeneration and Repair	Investigating mitochondrial and metabolic alterations in neurons in a

			mouse model of grey matter demyelination
29	Maira Pyrgioti and Phoebe Lyster-Binns	Centre for Discovery Brain Sciences	Developing in vivo reporters of endogenous neurodevelopmental disorder-linked proteins in zebrafish
30	Bastien Rioux	Centre for Clinical Brain Sciences	Rare variant genetic risk scores to assess type I interferons in brain health
31	Soraya Meftah	UK Dementia Research Institute, Centre for Discovery Brain Science	Using live human brain slice cultures to model aspects of Alzheimer's disease
32	Ulku Gunar	Centre for Clinical Brain Sciences, Grant Lab (Research Technician)	Mouse model of preclinical Alzheimer's Disease shows early changes to the synaptome and its architecture
33	Steven Hill	UK Dementia Research Institute, Centre for Discovery Brain Science	Identifying astrocyte endfoot functions using proteomics
34	Lucy Ryan	Dementia Research Institute	Temporal and regional vulnerability of white matter in Alzheimer's disease pathology
35	Amy Ferguson	Division of Psychiatry	Mental Health and the Body Clock
36	Lucy Pritchard	Simons Initiative for the Developing Brain PhD student	Investigating the role of sleep in the relationship between anti-epileptic drugs and absence seizures in a rat model of SYNGAP1.
37	Rebecca Graham	Centre for Clinical Brain Sciences	Computational Approaches and Machine Learning to Advance Therapeutic Discovery in ALS
38	Daniel Lewis-Fallows	Centre for Discovery Brain Sciences; Simons Initiative for the Developing Brain	Using a two-reward cheeseboard maze to create long-term memories in mice
39	Kelly Panichnantakul	Centre for Clinical Brain Sciences, PhD student	Characterisation of synaptic networks in a preclinical model of multiple sclerosis
40	Raven Hickson	Centre for Discovery Brain Sciences	The Habitat: A More Species-Appropriate Experimental Housing Paradigm for Rats
41	Lydia Lorenzo Cisneros	Centre for Regenerative Medicine (Martin Lee PhD Scholarship)	A toolkit to investigate the role of ependymal maturation in spinal cord regeneration
42	Iain Porter	Centre for Discovery Brain Sciences	IMPACT Imaging Facility Equipment and Services
43	Harry Bradford-Dunk	Centre of Discovery Brain Sciences; Precision Medicine Doctoral Training Programme	Investigating the dysregulation of cardiovascular activity in genetic forms of autism
44	Britt van de Gevel	Simons Initiative for the Developing Brain, Centre for Discovery Brain Sciences	Defining the roles of somatostatin interneurons on hippocampal circuit function in a rat model of 16p11.2-microdeletion.
45	Ying Sze	Simons Initiative for the Developing Brain, Centre for Discovery Brain Sciences	Characterisation of tactile and pain behaviour in GRIN2B haploinsufficiency and CDKL5 deficiency disorder rat models
46	Han Tan	Centre for Discovery Brain Sciences	Investigating the mechanism underlying dysfunctional synaptic vesicle recycling in a mouse model of Huntington's Disease.
47	Julia Meng	Centre for Discovery Brain Sciences	In developing neural circuits, does neuronal activity influence action potential conduction?

48	Jingjing Zhao	School of Psychology, Shaanxi Normal University	How “dyslexia genes” influence brain structural connectivity?
49	Noelia Perez Ramos	UK Dementia Research Institute, Centre for Discovery Brain Science	Astrocyte characterization throughout age and pathology progression in the APP/PS1 amyloidopathy mouse model and aged-matched controls.
50	Irenie Shiangoli	Simons Initiative for the Developing Brain	Investigating reward and fear learning circuit deficits in a rat model of SYNGAP1 haploinsufficiency
51	Sarah Catherine Gillard	Centre for Clinical Brain Sciences	Anisomycin-mediated Protein Synthesis Inhibition Affects the Mouse Brain Synaptome
52	Jack Barrington	UK Dementia Research Institute	Brain macrophage diversity underpins temporally evolving human perihaematomal inflammation
53	Katarzyna Mazur	Centre for Discovery Brain Sciences	Spinal cord processing of touch and pain in a rat model of SYNGAP1 haploinsufficiency