Neuroscience Ireland's
Early Career Researchers Network
presents

2022 YOUNG INVESTIGATOR SYMPOSIUM

CONFERENCE PROGRAMME

TRINITY COLLEGE DUBLIN
OCTOBER 26-27, 2022

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Ireland Early Career researchers Network

NSI-ECRN

The 2022 Neuroscience Ireland Young Investigator Symposium will exhibit the most advanced neuroscience research from early-career scientists on the island of Ireland. It will highlight the wealth of scientific talent and the variety and depth of knowledge we as a community have to offer.

This is the future of Neuroscience.

OUR STORY

As the newest branch under Neuroscience Ireland, ECRN is the largest national forum for undergraduate, postgraduate and post-doctoral researchers in neuroscience to discuss research, share technical expertise, foster collaboration, and grow the neuroscience community on the island of Ireland.

Since its founding in 2020, this has been encouraged through:

- Monthly virtual "NeuroConnect" meetings for members to present research and recent publications, and to discuss findings, methods, and future experiments with peers
- Guest seminars from experts on career development, equality in science, thesis and grant writing, and sustainability in the laboratory
- Dedicated communication channels where members can post research, ask technical questions, promote new job opportunities, and share recent advances in the field
- Shared information on relevant scientific conferences, outreach events, grant applications, and available stipends
- Scientific conferences, including the Young Investigator Symposium

Hosted and organised by NSI-ECRN, the 2022 Young Investigator Symposium is a unique two-day event designed by postgraduate and postdoctoral researchers for postgraduate and postdoctoral researchers. Engaging all aspects of neuroscience research in Ireland, this years' symposium will take place in Trinity College Dublin.

OUR COMMUNITY

The 2022 Young Investigator Symposium is organised and hosted by the ECRN Committee. Joining together from all corners of the island, this committee comprises 10 neuroscientists from Dublin City University, National University of Ireland Galway, Maynooth University, Trinity College Dublin, University of Limerick, University College Dublin, University College Cork, Queens University Belfast, and Ulster University. Our larger community continues to expand as our platform grows rapidly:

- 180+ active members (Join ECRN)
- Immediate reach of 860+ twitter followers (@YoungNeuroIRL)
- Extended reach of 10,000+ twitter followers through Neuroscience Ireland & Irish university associates (@NeurosciencecIRL, etc.)
- est. 200+ attendees at biennial nationwide conference (2022 Young Investigator Symposium)

This autumn, we would like to invite you to join the Neuroscience Ireland and ECRN community through attending the Young Investigator Symposium. This symposium offers a unique opportunity for all early-career researchers alike to engage with neighboring Irish researchers, promote scientific engagement, and advance scientific communication.

We hope you will join us as we discover the future of Irish research.

Neuroscience Ireland NSI-ECRN

Early Career researchers Network

THANK YOU TO OUR CONFERENCE ORGANISERS

Oisín Joyce
President

PhD Candidate
Trinity College Dublin

Carmen Elise Pocknell
Vice President

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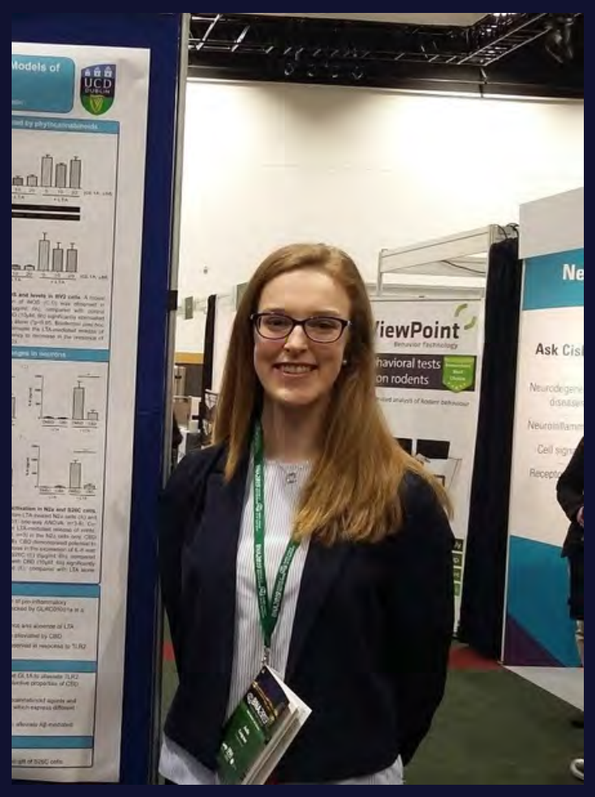
Maynooth University



Aoife Cosgrave
Comms and Outreach

PhD Candidate
University College Dublin

Conor Thornberry
Secretary & PRO

PhD Candidate
Maynooth University

Caoimhe Tyndall
Media

PhD Candidate
Trinity College Dublin

Ailís Stevenson
OCM

PhD Candidate
Ulster University

Janeen Laabei
OCM

PhD Candidate
Trinity College Dublin

Kaushik Narasimhan
OCM

PhD Candidate
NUI Galway

WEDNESDAY

October 26, 2022

NeuroREconnect Satellite Event

Tangent Trinity's Ideas Workspace

This online satellite event in partnership with Tangent, Trinity's Idea Workspace will include an introduction to the symposium, short presentations, and a collaborative workshop on innovation, creative thinking, and entrepreneurship tailored to ECRs. It is free to join and open to all researchers and scientists. Please register for this online event on Eventbrite to secure your place.

16:00	Welcome Address
16:10	Dr Rory Boyle (Harvard University)
16:35	Dr Gillian Coughlan (Harvard University)
17:00	Virtual Coffee Break
17:15	Workshop with Tangent *Creative Thinking for Researchers*
18:00	Closing Remarks

REGISTRATION

FREE FOR ALL SCIENTISTS AND RESEARCHERS

Register through Eventbrite here

Dr. Rory Boyle

Postdoctoral Research Fellow,
Harvard Medical School - Massachusetts General Hospital

Rory completed a BSc in Psychology in DCU (2010-2014) and an MSc in Brain Sciences (University of Glasgow, 2015-2016). Following his MSc, he joined the Whelan Lab in Trinity College Dublin as a Research Assistant before starting a PhD in 2018 under the supervision of Prof. Robert Whelan. It was funded by an IRC Enterprise Partnership Scholarship, in partnership with Altoida, Inc. and his thesis focused on the application of machine learning methods to neuroimaging data.

After completing his PhD in 2021, Rory was funded by the Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia to complete a 6-month pilot project investigating the use of functional neuroimaging to measure cognitive reserve. That October, Rory joined the Harvard Medical School/Massachusetts General Hospital as a postdoctoral research fellow. Here, Rory works on the Harvard Aging Brain Study team, under the supervision of Dr. Rachel Buckley. He is currently using multi-modal neuroimaging and longitudinal cognitive trajectories to identify individuals who show cognitive resilience to AD pathology.

Dr. Gillian Coughlan

Postdoctoral Research Fellow,
Harvard Medical School - Massachusetts General Hospital

Dr. Coughlan completed a Bachelor's in Psychology (Hons) (2009-2013) and a Masters in Clinical Psychology at Trinity College Dublin (2013-2014). She became fascinated with cognitive neuroscience during her studies of cognitive ageing at Trinity Institute of Neuroscience (2014-2016). She then worked as a visiting researcher at the Psychology Department of the University of Cambridge (2016) until she started a PhD at Norwich Medical School in UEA (July 2016) under the supervision of Professor Michael Hornberger. Her thesis was focused on spatial navigation as a novel diagnostic marker for preclinical Alzheimer's disease.

She completed a one-year postdoctoral fellowship at the Rotman Research Institute in Canada (2020) and in 2021, she joined Harvard Medical School/ Massachusetts General Hospital as a postdoctoral research fellow under the primary supervision of Dr Rachel Buckley; supported by a fellowship from the Alzheimer's Society of Canada.

Dr. Maeve O'Dwyer

Programme Manager,
Tangent, Trinity's Idea Workspace

Dr Maeve O'Dwyer completed a BA and MPhil in Classics at Christ's College, University of Cambridge, before moving to the University of Edinburgh to undertake a PhD in the History of Art under the supervision of Professor Viccy Coltman & Dr Genevieve Warwick. Her research focused on 18th century interaction with classical sculpture from 1740 to 1830. Since January 2017 Maeve has worked with the Lincoln Academy of Learning and Teaching at the University of Lincoln, firstly as Project Officer, and then as Programme Manager HEA, leading on the successful accreditation and delivery of an internal programme to award Fellowship of the HEA (now AdvanceHE).

She recently joined the Education Team at Tangent in Trinity College Dublin as Human Capital Initiative Programme Manager and is delighted to be getting involved in their fantastic work in innovation, creativity and entrepreneurship. She is now Programme Manager for the PGCert Innovation and Entrepreneurship, the UGCert Innovation and Entrepreneurship, and the TEP Design Thinking elective module, as well as overseeing a wide range of projects.

THURSDAY

October 27, 2022

Trinity Biomedical Sciences Institute (TBSI)

Neuroscience Ireland Members:

1. Register for the in-person event free of charge with your NSI membership number through EventBrite

Register through Eventbrite here

Non-Neuroscience Ireland Members:

1. Activate your Neuroscience Ireland membership through Keynote
    - Students: €35
    - Non-Students: €70

Activate NSI membership here

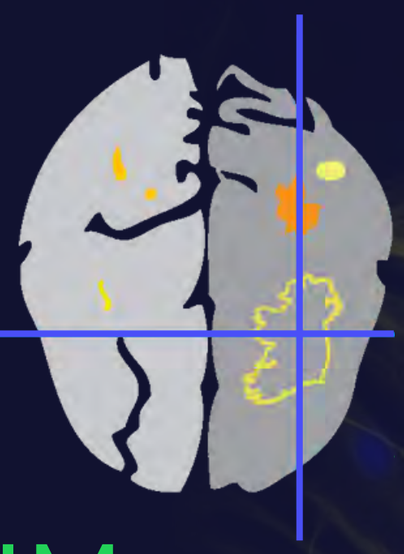
2. Receive Neuroscience Ireland membership number
3. Register for the in person event with your NSI membership number through EventBrite

REGISTRATION

FREE FOR ALL NEUROSCIENCE IRELAND MEMBERS

Neuroscience Ireland strongly encourage PI's/managers to support their students/lab members by providing them with the financial support to gain NSI membership and thus attend the in-person segment of this symposium.

Neuroscience Ireland's
Early Career Researchers Network



YOUNG INVESTIGATOR SYMPOSIUM GREEN GUIDE

How to attend this conference sustainably:

Packing List:

- Re-fillable water bottle
- Re-fillable coffee/tea mug
- Smart phone/tablet to access digital abstract booklet
- Notebook and pen
- Poster (if presenting)

Pick up one of our **recycled tote bags** at registration to pack everything in and carry comfortably throughout the conference!

Travelling from afar? Use public transport if possible

Driving? Tweet us @YoungNeuroIrl to organise a carpool

CONFERENCE SCHEDULE

Young Investigator Symposium
October 27, 2022
Trinity Biomedical Sciences Institute (TBSI)

8:30	Registration	TBSI Foyer L0
9:30	Welcome address	Tercentenary Hall L2.15
9:40	Speaker: Dr David Loane, TCD	Tercentenary Hall L2.15
10:05	Speaker: Dr Olga Baron, UCD	Tercentenary Hall L2.15
10:30	Coffee break (provided)	Knowledge Exchange L2
11:00	ECR presentations	Tercentenary Hall L2.15
12:00	Poster session 1	Bullnose & Knowledge Exchange L2
13:00	Lunch (provided)	Knowledge Exchange L2
14:00	Poster session 2	Bullnose & Knowledge Exchange L2
15:00	Meet the sponsors Book launch Coffee break (provided)	Knowledge Exchange L2
15:30	Workshop: *PPI in Research*	Tercentenary Hall L2.15
	Case Study: *Commercialisation of Research*	TBSI Lecture Basement B2.36
16:30	ECR prize winner presentation	Tercentenary Hall L2.15
17:00	ECR presentations	Tercentenary Hall L2.15
18:00	Closing address & prize giving	Tercentenary Hall L2.15
18:30	Networking & social reception	Doyles Pub

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SPEAKERS

Dr. Olga Baron

Lecturer & Assistant Professor of Neuropharmacology,
University College Dublin

My research integrates the use of Drosophila and mouse genetics to understand mechanisms important for healthy ageing and function of the nervous system. The primary focus lies in the study of maladaptive mechanisms that may lead to dysfunction of the sensorimotor circuit. This work is highly relevant for shaping our understanding of human genetic predisposition in developing chronic pain in highly prevalent age-related diseases, for instance musculoskeletal conditions.

Olga is a newly appointed Assistant Professor in Neuropharmacology at University College Dublin since July, 2022. She completed her studies in general Biology at University of Rostock and PhD studies at the Hannover Medical School in Germany, specializing in Systems Neuroscience and Developmental Neurobiology. In 2013 Olga joined the laboratory of Dr Manolis Fanto at King's College London in the UK, where she used in-vitro cell cultures, fruit flies and mice to understand how nerve cells cope with metabolic stress challenges in genetic models for neurodegeneration. In November 2018, she started developing her independent research program under mentorship of Professor Stephen McMahon at Wolfson Center for Age related Diseases, KCL, UK. As NC3Rs David Sainsbury fellow and as recipient of Versus Arthritis ECR Pain award, she established paradigms for the use of the fruit fly Drosophila melanogaster for functional analysis of nociceptive sensory neurons in response to muscular wasting.

Dr. David J. Loane

Assistant Professor of Neuroscience
School of Biochemistry and Immunology
Trinity Biomedical Sciences Institute &
Trinity College Institute of Neuroscience

David Loane is Assistant Professor of Neuroscience in the School of Biochemistry and Immunology, Trinity College Dublin, Ireland, and Adjunct Associate Professor at the Shock, Trauma, and Anesthesiology Research (STAR) Center at the University of Maryland School of Medicine (UMSOM), Baltimore, MD, USA. Dr. Loane conducted his graduate studies in the Department of Pharmacology and MRC Center for Synaptic Plasticity, University of Bristol, England. He then pursued postdoctoral training in CNS injury and neuroinflammation at Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland and the Department of Neuroscience, Georgetown University, Washington DC, USA. He was a Faculty member in the Department of Anesthesiology and STAR Center, UMSOM from 2009-2018, and he returned to Dublin in 2019 to establish a preclinical neurotrauma and neuroimmunology research group in Trinity College Dublin. Dr. Loane leads a multi-disciplinary research team dedicated to studying brain/systemic inflammation and chronic injury responses following TBI. The mission of his group is to elucidate the pathophysiological mechanisms underlying post-traumatic neuroinflammation, neurodegeneration and loss of neurologic function, and to develop novel treatment strategies for neuroprotection and post-traumatic repair that will translate to the clinic for human head injury.

Dr Mark O'Sullivan

Lead Investigator,
INFANT Research Centre
University College Cork

Dr. Mark O'Sullivan is a Lead Investigator in the INFANT Research Centre in University College Cork. He completed a Bachelor's degree in electronic engineering, followed by a Masters degree in audio technology. Mark began his PhD research in the INFANT Research Centre and School of Engineering in 2016 investigating novel technologies for neonatal EEG recording and interpretation. In the final years of his PhD, Mark began exploring research commercialisation and entrepreneurship, completing the UCC Gateway and IGNITE accelerator and business incubation programmes, winning awards several awards including Enterprise Ireland Student Entrepreneur of the Year.

Dr. O'Sullivan is the Principal Investigator on the NeuroBell project, which received commercialisation funding from Enterprise Ireland. The NeuroBell team have developed a novel medical device for early detection and monitoring of seizures in newborns. The team are due to spin-out of the University in 2023.

Edel Murphy

National Programme Manager,
Trinity PPI Ignite Office

Joining the PPI Workshop Edel Murphy is the national Programme Manager for the PPI Ignite Network. Edel has worked in the area of public and patient involvement (PPI) in research for a number of years, working with researchers across all disciplines and with the public to build PPI capacity among both constituencies, delivering education and training and providing support to help researchers understand how to plan for and embed the public and patient voice across their research.

In her current role, Edel is driving the development and growth of an energetic, collaborative and innovative Network, bringing together a diverse range of stakeholders nationally and internationally to build a shared voice for PPI in research in Ireland.

Kevin Quaid

Member of the Irish Dementia Working Group,
Vice-chair of the European Working Group of People with dementia
Co-founder of Lewy Body Ireland

I am Kevin Quaid, 59 years old, and married to Helena. I was first diagnosed with Parkinson, just over 6 years ago, and then later on, I was diagnosed with Lewy body dementia. I am Chair of the Irish dementia working group, Vice-chair of the European working group, and co-founder of Lewy body Ireland.

I am very involved in PPI and I am the author of two books about Lewy body dementia. When I wrote my first book called 'Lewy Body Dementia Survival and Me' I became one of the first people in the world to write a book about Lewy body dementia from the patients point of view, I recently published my second book called 'I am KEVIN not Lewy!', and I am currently writing my third book. Recently,

I received The Presidential award from Longford International College in Ireland for outstanding achievements in bringing awareness of Lewy Body Dementia, to people not just in Ireland but around the world.

Michael Foley

National Programme Manager,
Trinity PPI Ignite Office

Michael Foley is the Programme Manager for the Trinity PPI Ignite Office. Within the national PPI Ignite Network, the Trinity office is leading out on the process of considering how to improve the quality of PPI across the country. It also has a focus on the development of a culture of capturing the impact of PPI-influenced research. As well as this, the office has a Trinity-focused programme to celebrate and support PPI activity across the institution.

Michael has been facilitating public processes for over twenty years as part of his work in the National Disability Authority, Age & Opportunity and now Trinity College Dublin. He has developed PPI Ignite engagement activities for the dementia, intellectual disability, neurodiverse and vision impaired communities. He has worked with Health Research Charities Ireland to co-produce Making a Start, a toolkit for research charities to begin a PPI relationship. He has also developed the Campus Engage How-To Guide on Engaged Research Online Workshop to facilitate engaged research and innovation through digital platforms. He was the lead facilitator on the IPPOSI Citizens' Jury on Access to Health Information and a trainer on the Campus Engage train-the-trainer course Engaged Research and Innovation for Societal Impact.

With an MSc in Applied Social Research, Michael has a specific interest in research translation and impact. He was the Research Module Coordinator on the MA in Mediation and Conflict Intervention in Maynooth University for a number of years. He has also worked as a copywriter and editor, with a particular focus on developing accessible material, Plain English and easy-read.

Dr Roisin McMackin

NSI Early Career Investigator Award Winner 2022
Assistant Professor in Physiology,
Trinity College Dublin

Congratulations to Dr Roisin McMackin, winner of the NSI Early Career Investigator Award 2022.

Dr McMackin recently received her PhD in Clinical Medicine from Trinity College Dublin for investigation of electrophysiological biomarkers of Amyotrophic lateral sclerosis (ALS). Dr McMackin's research includes the use of electroencephalography (EEG) and transcranial magnetic stimulation (TMS) to investigate the change in neural networks in ALS, to progress understanding the mechanism of ALS and to enhance categorisation of different clinical presentations of ALS. This innovative approach also has broader utility in measuring changes in other neurodegenerative diseases and in the development of new therapeutic drugs, particularly those with multimodal activity. Dr McMackin has already published four research and two review papers as first author in high-profile journals including Neurobiology of Aging and Cerebral Cortex

She is currently a UK Motor Neuron Disease (MND) Association Postdoctoral Non-Clinical Research Fellow, and is already an internationally-recognised expert in Threshold-Tracking TMS. Even at this early career stage Dr McMackin is known as an outstanding researcher that actively supports more junior peers and the upcoming generation of female scientists. As described by one nominee, 'she is an embodiment of the saying 'a rising tide lifts all boats with it". Just this week, at the age of 28, she has announced that she is now taking on a new role as Assistant Professor in Physiology at TCD.

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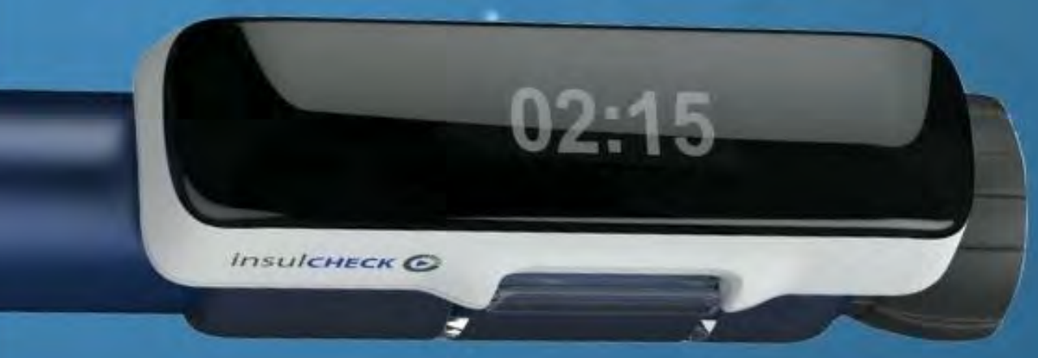

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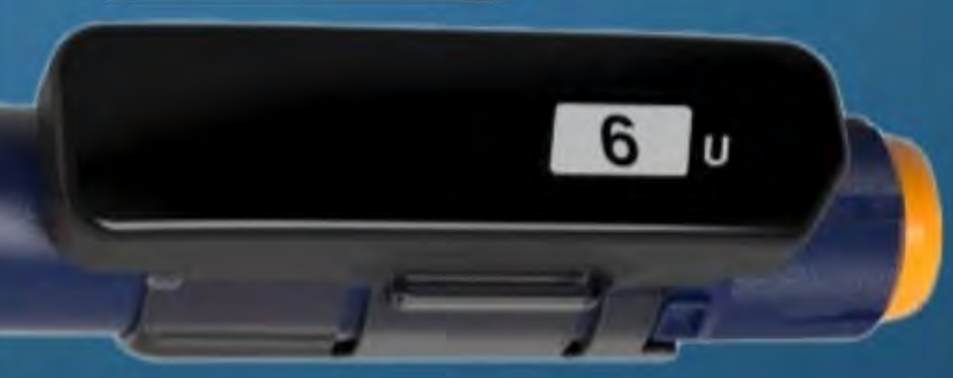

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SCAN FOR MORE INFO

ORAL PRESENTATIONS

Session 1: 11:00-12:00

Session 2: 17:00-18:00

TBSI Tercentenary Hall (Level 2)

Oral Presentation Session 1
October 27, 2022, 11:00-12:00
TBSI Tercentenary Hall (Level 2)

#	Presenter	Institution	Career Stage	Abstract Title
1	Conor Thornberry	MU	PhD	Neural Correlates of Human Spatial Navigation
2	Cameron Keighron	NUIG	PhD	Lund human mesencephalic (LUHMES) cells as a new Neurodegenerative Disease model
3	Judith Evers	UCD	PostDoc	Conventional open-loop DBS and closed-loop DBS result in similar behavioural improvement in Parkinsonian rats
4	Sakshi Hans	UL	PhD	Polar lipids modify Alzheimer's disease pathology by reducing astrocyte pro-inflammatory signalling through platelet-activating factor receptor (PAFR) modulation
5	Qing Qi	TCD	PhD	Sex differences in the associations of lifestyle activities, risk factors and cognition of middle-aged individuals at risk for late-life AD
6	Mary Glass	Ulysses	RA	Behavioural and molecular effects of acute ketamine on depression-like alterations in the interferon-alpha model of neuroinflammation
7	Jonathon McLaughlin	UU	PhD	Investigating childhood adversities and DNA methylation patterns in young adults with depression
8	Aoife Warren	NUIG	PhD	The Role of Omega-3 and Omega-6 Essential Fatty Acids in Bipolar Disorder Diagnosis and Prediction
9	Michael Connaughton	TCD	PhD	Longitudinal neuroimaging analysis of the limbic lobe network in ADHD
10	Julia Paterson	TCD	PhD	A multimodal approach to understanding the neural mechanisms of stimulant medication in ADHD
11	Rachel Humphrey	NUIG	PhD	Sensory and affected pain responding in a preclinical rat model of Autism is altered in sex-dependent manner and associated alterations in gene expression in the anterior cingulate cortex

1. Neural Correlates of Human Spatial Navigation

Conor Thornberry, University of Maynooth

Navigating our environment and recalling important locations is a vital cognitive task we perform every day. Navigation, along with the required learning and memory, has been examined in animals using the Morris water maze (Morris, 1981). In this task animals are required to find a platform, hidden somewhere in a large circular pool of water (below surface level). As animals cannot see the goal directly, they must use various cues in the environment to locate it and escape. With the advancements in virtual reality technologies, navigation can now be examined in humans using a virtual version of the task. For this project, we used our open-source virtual water maze software NavWell (Commins et al., 2020) to record real-time navigation learning and recall in humans. We also simultaneously recorded neural activity using Electroencephalography (EEG) from 32 electrode sites. Here, we examine 25 adult participants (mean age = 22.5 years). All participants showed good learning across 12 trials of the task. Furthermore, we examine frequency-band power changes in theta (4 - 8Hz) and alpha (8 - 12Hz) that correlate with learning. Results are discussed in terms of the interaction between the two bands and their possible role in place learning and recall.

2. Lund human mesencephalic (LUHMES) cells as a new Neurodegenerative Disease model

Cameron Keighron, University of Galway

Neurodegeneration (ND) is hallmarked by the progressive loss of dopaminergic neurons and/or significant protein aggregates in the brain. ND diseases are considered to be a leading cause of death worldwide. There is an unmet need to develop new robust ND models both in vitro and in vivo. Sh-Sh5Y cells have become a hallmark of Parkinson's Disease research despite controversy over their presence of dopaminergic markers and lack of electrical activity, proving nearly impossible to assess electrophysiological functional change/improvements. Lund human mesencephalic (LUHMES) cells, has emerged as a potential new in vitro method of ND disease modelling including the possibility of evaluating the functionality of neurons pre and post interventions aimed at ameliorating dysfunction associated with ND. The study evaluates the metabolic parameters of 6-hydroxydopamine induced ND. Our results show that LUHMES cells positive for both neuronal marker TUJ1 and dopaminergic marker TH while Sh-Sh5Y cells are TUJ1 positive and TH negative. Furthermore, treatment with 6-hydroxydopamine significantly impairs metabolic activity, ATP production and ROS production in LUMHES cells while in Sh-Sh5Y cells higher treatment concentrations are required. These results elucidate the potential of LUMHES cells as an alternative cell for ND modelling.

3. Conventional open-loop DBS and closed-loop DBS result in similar behavioural improvement in Parkinsonian rats

Judith Evers, University College Dublin

Aims: Closed-loop deep brain stimulation (DBS) automatically adjusts stimulation delivered and potentially improves efficacy and reduces side effects in Parkinson's disease (PD) treatment. PD animal models provide an effective platform for testing different closed-loop algorithms before patient trials. Here we compared two closed-loop DBS to open-loop DBS in parkinsonian rats. Methods: A multi-electrode array for stimulation and recording was implanted into the left subthalamic nucleus and 15ug 6-OHDA(n=7), or vehicle(n=3), were injected into the left medial forebrain bundle in 7 rats. Open-loop, on-off and proportional closed-loop DBS based on recorded STN beta-power and control algorithms were applied using W2100 system(Multichannel systems). Behaviour was assessed during cylinder and stepping tests. Successful model creation was confirmed via apomorphine-induced rotation test and TH-immunocytochemistry. Electrode location was histologically confirmed. Data were analysed using linear mixed models(R Studio). Results: Contralateral paw use in parkinsonian rats was reduced to 20% in cylinder and 25% in stepping tests. Open-loop, on-off and proportional closed-loop DBS, but not random on-off nor low amplitude stimulation improved motor function significantly. Conclusions: Wireless closed-loop DBS is feasible in rats. Closed-loop DBS was as effective as open-loop DBS in reducing motor symptoms of PD. In the future, more complex closed-loop algorithms can be studied.

4. Polar lipids modify Alzheimer's disease pathology by reducing astrocyte pro-inflammatory signalling through platelet-activating factor receptor (PAFR) modulation

Sakshi Hans, University of Limerick

The platelet-activating factor (PAF) molecule is a pro-inflammatory phospholipid mediator that functions by binding its receptor PAFR. PAF is a key player in the mechanism of chronic inflammation. The pathology of disorders such as cardiovascular disease, cancer, rheumatoid arthritis, and neurodegenerative diseases has been linked to chronic inflammation. The amyloid-beta hypothesis of Alzheimer's disease (AD) suggests that neuroinflammation due to amyloid-beta in the brain is a driving cause behind this disorder. Studies have shown that polar lipids (PL) have significant anti-inflammatory and antithrombotic effect, and thus could protect against the detrimental effects of pro-inflammatory processes. This has important implications for chronic disease, including AD. We set out to test the hypothesis that marine and dairy-derived PL can downregulate neuroinflammation using an in vitro model and various bioassays. Preliminary results show that PAFR expression is significantly upregulated after treatment with Aβ and LPS, both on gene and protein level. Protein levels of PAFR are significantly decreased after treatment with PL following treatment with Aβ, and oxidative stress levels are significantly downregulated after incubation with PLs. Further research underway aim to analyse expression of downstream cytokines to fully understand the role of PL in inflammation.

5. Sex differences in the associations of lifestyle activities, risk factors and cognition of middle-aged individuals at risk for late-life AD

Qing Qi, Trinity College Dublin

It is now acknowledged that Alzheimer's Disease (AD) processes are present decades before the onset of clinical symptoms, but it remains unknown whether lifestyle factors can protect against these early AD processes in mid-life and whether the protective effect varies by sex. To address this gap, we collected 491 participants (40–59 years) data from cognitive tests, clinical assessments, and lifetime of experiences questionnaires. We assessed the impact of lifestyle activities, risk factors for AD, sex, and their interactions on cognition. We replicated the previous finding which more frequent engagement in physically, socially and intellectually stimulating activities was associated with better verbal, spatial and relational memory. We also found sex differences in the associations of lifestyle activities, risk factors and cognition. Critically, females with greater occupational complexity and managerial experience performed better in verbal, spatial and relational memory. Males didn't show the same effect. For APOE Ɛ4 carriers, males with greater occupational complexity and managerial experience performed worse, whereas females were prone to perform better, in verbal, spatial and relational memory. These findings suggest that the effect of modifiable lifestyle activities on cognitive attenuation due to AD risk differs between mid-life females and males.

6. Behavioural and molecular effects of acute ketamine on depression-like alterations in the interferon-alpha model of neuroinflammation

Mary Glass, Ulysses Neuroscience Ltd

Interferon-alpha (IFN-), an innate cytokine, is used clinically to treat various cancers and hepatitis. Up to 70% of patients report depression-like symptoms, which can be reversed with SSRIs. This phenomenon has been back-translated into rodents, creating a neuroinflammatory model of depression. In addition to inflammation, alterations in synaptic plasticity have been more generally linked to the pathophysiology and treatment of major depressive disorder. We investigate the behavioural and molecular effects of ketamine, a fast-acting antidepressant with known effects on synaptic plasticity, in the IFN- model of neuroinflammation. Wistar rats were treated (3x/week for 3-4 weeks) with IFN-α (170,000IU/kg, SC) to induce a depression-like behavioural phenotype. Depression-like behaviour was assessed with the forced swim test (FST) 24-hours post-administration of ketamine (single dose; 5mg/kg, SC). Using Multiplex Infrared Western Blotting (IFWB), relative levels of synaptic proteins (Pre-synaptic: Synaptophysin, SV2a; Post-synaptic: PSD-95) were analysed in the mPFC as markers of synaptic function. IFN- -treated rats displayed significantly higher immobility than saline-treated rats, which was reversed by ketamine. All synaptic markers were significantly decreased in the IFN- model, and SV2a and PSD-95 were rescued by ketamine. These results suggest that depression-like behaviour and alterations in synaptic plasticity in the IFN- model are sensitive to ketamine.

7. Investigating childhood adversities and DNA methylation patterns in young adults with depression

Jonathon McLaughlin, Ulster University

Mental health problems are one of the main causes of the global disease burden, with psychiatric and behavioural problems reported to be a primary driver of disability in the 20-29 age group. Individuals who suffer from depression are at a high risk of developing co-occurring negative behaviours such as non-suicidal self-harm or attempted suicide, with biological and environmental factors known to play a role. The aim of this project is to identify environmental and demographic risk factors in a student population for the development of depression alone and with co-occurring self-harm or suicide attempt. These risk factors will be investigated further with validation through investigation of whole methylome patterns and differential methylation in candidate genes linked with HPA axis regulation associated with depression. Methylation analysis was performed using data from Illumina's 850k EPIC array to identify epigenetic modifications linked with negative mental health outcomes. Functional enrichment analysis was performed to identify pathways in which key epigenetic modifications are involved. Differentially methylated regions within HPA axis-linked genes were identified in individuals with depression. Immune response and receptor activity display differential levels of methylation between cases and controls. In addition, specific demographic characteristics, and childhood adversity lead to elevated risk for depression.

8. The Role of Omega-3 and Omega-6 Essential Fatty Acids in Bipolar Disorder Diagnosis and Prediction

Aoife Warren, University of Galway

Bipolar disorder is a complex psychiatric condition characterised by (hypo)manic and depressive episodes. Blood levels of omega-3 and omega-6 essential fatty acids have been demonstrated to be altered in bipolar disorder compared to healthy controls. This paper aimed to examine if baseline omega-3 and omega-6 essential fatty acid levels were altered in bipolar disorder dependent on the type and frequency of mood episodes experienced. Eighty patients (n=40 in control and placebo groups) with bipolar disorder were recruited for this 12-month randomized, double-blind, placebo-controlled trial. Blood samples were drawn at screening, 6- and 12-months for essential fatty acid analysis. Psychometric measures were recorded at screening, randomisation, 3-, 6-, 9-, 12-months and 3-month follow-up. Eicosopentanoeic acid ($p = .034$) and linoleic acid levels ($p = .021$) were significantly different between patients experiencing equal numbers of (hypo)manic and depressive episodes and those experiencing more (hypo)manic than depressive episodes. There was a significant difference in docosapentanoeic acid dependent on the number of previous episodes experienced ($p = .004$). Variation existed in essential fatty acid levels dependent on the type and frequency of episodes experienced, indicating potential for prediction of illness course from these levels. Furthermore, reduced levels of docosapentaenoic acid suggested reduced mood stability.

9. Longitudinal neuroimaging analysis of the limbic lobe network in ADHD

Michael Connaughton, Trinity College Dublin

Emotion dysregulation is a highly prevalent and impactful symptom in children with Attention Deficit Hyperactivity Disorder (ADHD). The limbic lobe plays a key role in emotion regulation but has not been widely studied in ADHD. We investigated 1) the structure/organisation of key grey and white matter structures of the limbic lobe, 2) the developmental trajectories of these key limbic lobe structures in children with ADHD. Structural and diffusion MRI data were collected (protocol:https://doi.org/10.1186/s12888- 016-0770-4) at ages 10, 11.5 and 13. Between-group longitudinal grey-matter volumetric analysis of the key limbic lobe structures were performed using Freesurfer (n=167). White matter organisation of all major limbic lobe tracts were examined using constrained spherical deconvolution based-tractography (n=80) using ExploreDTI. Linear mixed modelling found children with ADHD displayed reduced volume in the amygdala, hippocampus, orbitofrontal cortex and cingulate gyrus across all three scans. We found no between-group difference in the developmental trajectory of limbic lobe grey matter. We found no between-group difference in white matter fractional anisotropy. This study suggests that ADHD is characterised by a delay in the maturation of limbic lobe grey matter structures during the transition from childhood to adolescence. These results provide support for the theory of maturation delay in ADHD.

10. A multimodal approach to understanding the neural mechanisms of stimulant medication in ADHD

Julia Paterson, Trinity College Dublin

Methylphenidate, a stimulant medication, is used as the first-option pharmacological treatment for attention deficit hyperactivity disorder (ADHD) and while often can be extremely effective, it does not work for every individual. This project, a double blind, placebo controlled study, will investigate the specific brain processes that are affected by methylphenidate by recording brain activity and behaviour in adolescents with ADHD. Additionally, as previous research on ADHD has overwhelmingly focussed on cisgender men, this study will recruit adolescents who are 'Assigned Female At Birth'. Brain activity will be recorded using two separate approaches: electroencephalography (EEG) and functional magnetic resonance imaging (fMRI), while participants complete a Stop Signal Task, a standard measure of response inhibition. Data will then be analysed using neurally informed Drift-Diffusion Models to better understand how methylphenidate changes behaviour. This project is important because if we can understand the brain mechanisms affected by methylphenidate, we can develop measures that will allow clinicians to predict whether a child is going to respond to this treatment or not. Such a measure would allow clinicians to treat ADHD more effectively and would result in adolescents with ADHD experiencing faster relief from symptoms.

11. Sensory and affected pain responding in a preclinical rat model of Autism is altered in sex-dependent manner and associated alterations in gene expression in the anterior cingulate cortex

Rachel Humphrey, University of Galway

Autism is associated with altered pain responding however, the underlying neurobiology remains poorly understood. This study examined sensory and affective pain responding in a preclinical model of autism, the effect of sex, and associated alterations in gene expression in the anterior cingulate cortex (ACC), a key brain region involved in affective and sensory pain responding. Male and female adolescent rats, prenatally exposed to saline or the antiepileptic valproic acid (VPA), were assessed for mechanical (von Frey) and thermal (hot plate/Hargreaves test) sensory responding prior to, and following, intraplantar administration of complete Freund's adjuvant (CFA). Affective pain responding was assessed using the place/escape avoidance paradigm (PEAP). Expression of c-fos, opioid, and endocannabinoid system-related genes were assessed in the ACC using qRT-PCR. VPA-exposed male and female rats displayed tactile hyposensitivity compared to saline-counterparts. Intraplantar-CFA resulted in mechanical and thermal hypersensitivity in all animals, the time-course and magnitude of which were sex-dependently reduced and shortened by VPA-exposure. VPA-exposed male rats exhibited reduced negative affect in the PEAP, an effect associated with decreased c-fos and proopiomelanocortin (precursor to β-endorphin) expression in the contralateral-ACC. Conclusion: VPA-exposed rats exhibit sex-dependent altered sensory and affective inflammatory pain responding, which is accompanied by neurobiological changes in the ACC.

Oral Presentation Session 2
October 27, 2022, 17:00-18:00
TBSI Tercentenary Hall (Level 2)

#	Presenter	Institution	Career Stage	Abstract Title
1	Janeen Laabei	TCD	PhD	GSK2795039, a novel NOX2 inhibitor, attenuates neuroinflammatory models of microglial activation in vitro
2	Danielle Molly Galvin	UCD	PhD	An investigation of the plant-derived terpene, Ergolide, in in vitro models of neuroinflammation
3	Rebecca Henry	UCC	Other	High fat diet-induced obesity in mice increases neuroinflammation after TBI and worsens cognitive outcomes
4	Nathan Ryzewski Strogulski	TCD	PostDoc	Early modulation of mitochondrial metabolism by trehalose attenuates damage after severe traumatic brain injury.
5	Ciara O'Donoghue	UCC	UG	Why Magnetic Resonance Imaging is Mandatory in Patients Presenting with First Seizures: a Diagnostic Yield of First-Line Investigations
6	Ciara Walsh	UCD	PhD	Investigating the use of gelatin methacrylate (GelMA) hydrogels as an immunomodulatory drug delivery platform for preclinical spinal cord injury
7	Ian Woods	RCSI	PostDoc	Biomimetic 3D-printable hydrogel scaffolds provide immunomodulatory behaviour and promote key regenerative behaviours for spinal cord repair applications.
8	Tara McGuire	RCSI	PhD	Investigating scaffold-mediated non-viral delivery of small-interfering RNA to promote axonal regrowth following spinal cord injury
9	Cian O'Connor	RCSI	PhD	Development of an iPSC loaded biomimetic scaffold for spinal cord applications
10	Rebecca Brady	TUD	PhD	Models of Visual-Vestibular Integration in a Speed Accuracy Task
11	Vanessa Teckentrup	TCD	PostDoc	Smartphone-based assessment of processing speed: evidence from longitudinal measurements in a large general population sample

1. GSK2795039, a novel NOX2 inhibitor, attenuates neuroinflammatory models of microglial activation in vitro

Janeen Laabei, Trinity College Dublin

NADPH oxidase 2 (NOX2) is an enzyme complex responsible for reactive oxygen species (ROS) production in microglia. NOX2 also acts as a priming signal for NLRP3 inflammasome activation, which is implicated in neuroinflammation. GSK2795039 is a novel small molecule drug that inhibits NOX2. The goal of this in vitro study was to characterise GSK2795039 in models of microglial activation. Immortalised Microglial (IMG) cell line or primary microglia from p1 Wistar rat pups were pre-treated with GSK2795039 (1-40μM) or diphenyleneiodonium (DPI; broad antioxidant; 0.005-0.1μM) and stimulated with either lipopolysaccharide (LPS; 100ng/ml) or LPS(100ng/ml) + ATP(1mM; 10 min) to induce NOX2/ROS and NLRP3 inflammasome activation. ROS and cell viability were measured on the cells using CM-H2DCFDA and MTT assays, respectively. The conditioned media was analysed for cytokines by ELISA, and nitric oxide (NO) using a Griess assay. Protein expression of iNOS and NLRP3 were determined by Western immunoblot. GSK2795039 reduced LPS-induced ROS production, iNOS expression, NO and TNF-α. In the LPS/ATP model, GSK2795039 attenuated ROS, IL-1β and NLRP3 expression. Preliminary results suggest that GSK2795039 attenuates pro-inflammatory responses in microglia, including NLRP3 inflammasome activation which may be due to reduced NOX2/ROS signalling. Therefore, GSK2795039 may be a promising therapeutic drug for NOX2-mediated neuroinflammation.

2. An investigation of the plant-derived terpene, Ergolide, in in vitro models of neuroinflammation

Danielle Molly Galvin, University College Dublin

Neuroinflammation is central to the pathology of most neurodegenerative conditions, including epilepsy, AD, and PD. Chronic activation of microglia associated with these conditions often result in the progressive loss in neuronal viability. Microglial activation is widely-reported to mediate the inflammatory changes and neuronal dysfunction and has therefore become an interesting avenue of therapeutic investigation. For many years, naturally-occurring compounds have been exploited for their anti-oxidant and anti-inflammatory properties. Previously, Ergolide has been reported to attenuate the pro-inflammatory activation of macrophages, following exposure to lipopolysaccharide(LPS) and interferon-x. This study examines whether the anti-inflammatory effects of Ergolide extend to the brain, and may offer therapeutic potential for neuroinflammatory disorders. Here we report that the activation of BV2 microglial cells, following exposure to the TLR2 and 4 agonists lipoteichoic acid and LPS respectively, is attenuated by ergolide. Incubation with ergolide significantly reduced the production of the cytokine IL-6, chemokine MCP-1 and nitric oxide from TLR-stimulated microglia. luciferase assays, we further demonstrate that ergolide likely exerts its anti-inflammatory effects in microglia via inhibition of NF-KB. Moreover, we evaluate its capacity to mitigate cell death in a neuronal cell line. Taken together, our findings support the further exploration of ergolide as a promising therapeutic agent for neuroinflammatory conditions.

3. High fat diet-induced obesity in mice increases neuroinflammation after TBI and worsens cognitive outcomes

Rebecca Henry, University College Cork

The present study aimed to examine the effects of sustained high fat diet (HFD) feeding on inflammatory responses (peripheral and central) and neurological outcomes following subsequent exposure to a traumatic brain injury (TBI). Mice were placed on a HFD or a standard diet (SD) for 12 weeks prior to exposure to experimental TBI. Cognitive behavioural tasks were preformed to assess cognitive function up to 1 month following injury. The hippocampus and adipose tissue were isolated for gene expression analysis. Exposure to TBI exacerbated the effects of HFD feeding on inflammatory markers in the adipose tissue. TBI induced a significant increase in hippocampal expression of inflammatory genes; effects of which were exacerbated in the presence of HFD feeding. TBI-SD mice displayed a deficit in the Y maze task; effects of which were not altered by HFD. In contrast, TBI-HFD mice spent significantly less time with the novel object in the NOR, compared to TBI-SD counterparts. Furthermore, TBI-HFD mice utilized an increased random search strategy, compared to TBI-SD counterparts in the MWM. Overall, these findings demonstrate a bi-directional link between the adipose tissue and brain under co-morbid obesogenic and injurious conditions, that may offer a credible therapeutic target.

4. Early modulation of mitochondrial metabolism by trehalose attenuates damage after severe traumatic brain injury.

Nathan Ryzewski Strogulski, Trinity College Dublin

Traumatic brain injury (TBI) is a leading cause of death and disability. Following injury, mitochondrial dysfunction supports long-term neurodegeneration. Here, we investigate potential neuroprotective mechanisms of trehalose over mitochondrial function after severe TBI in mice. Briefly, 60 male adult C57BL6J mice were separated into three groups: one SHAM group, and two severe cortical impact groups; one with free access to water (CCI) and another with a 3% trehalose solution (TRE) until euthanasia. Three days following injury high-resolution mitochondrial respiration, calcium handling, and membrane potential assessments in ipsilateral synaptosomes were performed. Lysosomal and mitochondrial content was assessed through flow cytometry analysis of ipsilateral hemisphere homogenates. To evaluate spatial memory, a separate cohort of mice was euthanized on day 15. Statistical significance was calculated using two-way analysis of variance (ANOVA), considered when $p<0.05$, and all procedures were approved by the local ethics committee. A decrease in the mitochondrial and lysosomal content in CCI was observed, which was attenuated in TRE. Reduced Complex-I and Complex-II respiration, impaired calcium handling, and reduced mitochondrial membrane formation were observed in CCI and were prevented in TRE. Spatial memory was preserved in TRE. Our study suggests mitochondrial metabolism as a component of trehalose neuroprotection following TBI.

5. Why Magnetic Resonance Imaging is Mandatory in Patients Presenting with First Seizures: a Diagnostic Yield of First-Line Investigations

Ciara O’Donoghue, Medical Student, University College Cork, Ireland;
Eimer Maloney, MD, University College Cork, Ireland;
Elijah Chaila, MD, University Hospital Limerick, Ireland;
Eilis O’Reilly, ScD, University College Cork, Ireland ;
Daniel Costello, MD, University Hospital Cork, Ireland

Background: Recent revision of the International League Against Epilepsy’s operational definition of Epilepsy allows a diagnosis to be made after a single seizure with a ≥60% chance of experiencing another in the future. Consequently, detection of epileptogenic lesions on structural brain imaging is important. The difference in diagnostic yield from low resolution computed tomography (CT) compared to a high resolution magnetic resonance imaging (MRI) has not been quantified in a population-based cohort study. Methods: Using multiple overlapping methods of case ascertainment and classification by an epileptologist, all patients who presented with a first seizure (n = 1330) were identified in a defined geographical area (Cork City and County Cork, Ireland; population 550,000) from January 1, 2017 to December 31, 2017. Three cohorts were defined: new onset epilepsy, unprovoked first seizures, provoked first seizures. CT and MRI results were evaluated. Results: When both CT and MRI were performed (n = 127), 24.41% (n = 31) of patients had MRI detection of epileptogenic lesions not evident on CT ($p = 0.0013$). New epilepsy criteria had significantly higher MRI abnormalities than the previous definition ($p = 0.0036$) and single seizure low risk ($p < 0.0001$). Focal seizures had significantly higher yield of epileptogenic lesions on MRI imaging than generalized ($p < 0.0001$). Conclusion: First presentation seizures warrant MRI brain imaging as epileptogenic lesions were not detected in a significant number of patients by CT who were detected by MRI. Furthermore, focal seizures are more associated with epileptogenic lesions on brain imaging than generalized.

6. Investigating the use of gelatin methacrylate (GelMA) hydrogels as an immunomodulatory drug delivery platform for preclinical spinal cord injury

Ciara Walsh, Univesity College Dublin

Spinal cord injury (SCI) is a devastating condition with limited regeneration, and no curative therapy is available. Neuroinflammation is a critical event after SCI, and recent research has focused on immunomodulation as a therapeutic strategy post-injury. Hydrogels are emerging as a promising treatment option as they may offer sustained and localised delivery of immunomodulatory factors. Here, we assess the suitability of gelatin methacrylate (GelMA) hydrogels as a sustained and localised drug delivery system for preclinical SCI. Physical properties of differentially charged GelMA hydrogels were characterized via Anton Paar rheometer and swelling assay. Cytocompatibility and immunomodulatory properties were assessed in vitro using BV2 microglia and RAW264.7 macrophages (n=3), and ex vivo biocompatibility was assessed using primary murine organotypic spinal cord slices (n=6). Microglia exhibit greater survival in negatively-charged versus positively-charged GelMA across all stiffnesses. 3% GelMA demonstrates optimal cytocompatibility and does not affect microglia/macrophage polarization after 48hr, as determined by inflammatory marker expression (TNF-α, iNOS, Arg-1, CD206). Ex vivo, 3% GelMA does not affect reactivity of GFAP+ astrocytes or Iba-1+ microglia. Finally, 3% GelMA can achieve sustained immunomodulatory drug release over 21 days in vitro, suggesting that 3% GelMA may act as a suitable platform for drug delivery in preclinical SCI.

7. Biomimetic 3D-printable hydrogel scaffolds provide immunomodulatory behaviour and promote key regenerative behaviours for spinal cord repair applications.

Ian Woods, Royal College of Surgeons Ireland

Spinal cord injury (SCI) is a debilitating trauma that results in extensive loss of motor and sensory function and lifelong paralysis. The complex pathophysiology of SCI makes a tissue engineering hydrogel scaffold-based approach an attractive prospect. Scaffolds need to be multifunctional and be capable of physically supporting axonal regrowth, minimize inflammatory responses and enable therapeutic delivery. To develop an scaffold optimized for SCI, 2D growth assays of native tissue matrix molecules was conducted and a novel combination of collagen-IV and fibronectin (ColIV/Fn) promoted strong neurite outgrowth ($p < 0.05$) from different neuronal cell types and d induced pro-reparative phenotypes in astrocytes ($p < 0.05$). When combined into 3D Hyaluronic acid (Hya) scaffolds, a synergistic growth promoting effect of Coll-IV/Fn in combination with scaffold stiffness was discovered [1]. Subsequently, neural stem cell spheroids, a potentially potent therapeutic, were cultured in 3D-printed Hya-Coll-IV/Fn hydrogels and exhibited significantly improved ($p<0.05$) outgrowth in printable gels. Together, these data demonstrate the ability of 3D-printable Hya-Coll-IV/Fn hydrogel scaffolds to support CNS cell growth with the potential to 3D print patient injury-specific implants, with significant clinical implications for the design of biomaterial implants for SCI repair. Research was supported by an IRC Postdoctoral fellowship, IRFU-Trust and SFI-Advanced Materials and Bioengineering Research (AMBER) Centre (SFI/12/RC/2278_P2). Reference: [1] Woods et al. (2022) Adv. Healthcare Mater. 2022, 11, 2101663.

8. Investigating scaffold-mediated non-viral delivery of small-interfering RNA to promote axonal regrowth following spinal cord injury

Tara McGuire, Royal College of Surgeons Ireland

After spinal cord injury (SCI), injured neurons lack the intrinsic ability to regrow their axons. An appropriately designed biomaterial scaffold may offer a solution by facilitating the delivery of nucleic acid cargoes to neurons to over-express neuronal growth factors or silence growth-inhibitory molecules. This study sought to investigate whether our novel SCI scaffold (1) could effectively deliver siRNA to neurons to boost regrowth. A novel nanoparticle (2) was used to complex with a fluorescently-tagged siRNA (siGLO) to form siGLO-nanoparticles. Successful siRNA-delivery was obtained as siGLO nanoparticles were seen within the cytoplasm of neurons three days post-delivery. Subsequently, functional knockdown of the growth-inhibiting phosphatase and tensin homolog (PTEN) was achieved in neurons after delivery of PTEN siRNA-nanoparticles demonstrating their therapeutic potential in terms of silencing growth-inhibitory molecules. Finally, an RNA-activated scaffold was developed by combining our scaffold with these siRNA-nanoparticles. This siRNA-activated scaffold was shown to be capable of delivering siRNA to neurons and manipulating their genetic expression, demonstrating potential for future therapeutic applications for SCI repair. Funding: IRFU Charitable Trust and SFI-AMBER Center 1. Woods, I. et al. AHM, e2101663 (2021). 2. Dixon, J.E. et al. PNAS 113, E291-299 (2016).

9. Development of an iPSC loaded biomimetic scaffold for spinal cord applications

Cian O'Connor, Royal College of Surgeons

Following spinal cord injury, a lesion cavity forms preventing axonal regrowth. Despite the ongoing development of stem cell treatments, repair remains a challenge due to the inhibitory environment. Therapeutic implants that bridge the cavity while simultaneously delivering stem cells to restore lost tissue may have potential. We aimed to identify cord-specific growth-promoting proteins, incorporate them into scaffold implants and validate their neurotrophic capacity. By optimizing scaffold stiffness and matrix composition for stem-cell delivery, we aimed to create a therapeutic scaffold in combination with iPSC-derived progenitors to promote cord repair. Screening of extracellular matrix proteins revealed that collagen-IV (Coll-IV) and fibronectin (FN) synergistically enhanced neuronal and astrocyte outgrowth. Next, hyaluronic acid scaffolds functionalized with Coll-IV/FN were manufactured with differing stiffnesses from soft-stiff. Astrocytes cultured in soft, Coll-IV/FN scaffolds exhibited morphologies typical of ‘resting’ cells and upregulated secretion of anti-inflammatory factors while also enhancing neuronal outgrowth. Soft, Coll-IV/FN scaffolds promoted iPSC-progenitor infiltration and growth into large spheroid structures. When spinal cord and dorsal root ganglia explants were cultured on soft Coll-IV/FN iPSC-scaffolds, astrocyte migration and axonal extensions within scaffolds were significantly enhanced. This work shows the successful development of a biomimetic scaffold that when combined with iPSC-progenitors has significant therapeutic potential.

10. Models of Visual-Vestibular Integration in a Speed Accuracy Task

Rebecca Brady, Technological University of Dublin

In order to navigate the world the brain seamlessly integrates signals received across multiple sensory modalities. Mathematical models have been used to investigate unisensory decision and reaction tasks, but to date very few have been extended to include multisensory processing. We present an extension of the Wong and Wang (2006) model, a system of non-linear differential equations, that simulates the neuronal and behavioural processes in a visual-vestibular heading speeded reaction time task. To replicate experimental data the model includes noise to account for within participant trial to trial variability and sampling from a parameter space simulating different ‘participants’. Three different architectures were designed to simulate multisensory integration strategies; 1) a winner-take-all model, 2) a linear summation model and 3) a non-linear summation model. Reaction time and accuracy data were analysed using the general drift-diffusion model. To investigate optimal multisensory integration the observed visual-vestibular drift-rates were compared with a prediction calculated using the unisensory drift-rates. All models showed an improvement in the visual-vestibular reaction times in the multisensory condition. Our findings suggest that the linear summation model most resembles the experimental behavioural results for multisensory reaction time tasks and illustrate the sensitivity of drift-rate as a measure of multisensory integration.

11. Smartphone-based assessment of processing speed: evidence from longitudinal measurements in a large general population sample

Vanessa Teckentrup, Trinity College Dublin

Processing speed is a key predictor of a person’s ability to manage their everyday life. Most tests of processing speed are assessed at one time point only. However, cognition has been shown to fluctuate in healthy individuals over relatively short time windows. Thus, we developed a gamified version (Star Racer) of the Trail Making Test (TMT) and assessed its validity, reliability and associations with health risk factors for cognitive decline. A smaller lab-based sample of N=41 completed Star Racer and the TMT. Additionally, a large online general population sample of N=4208 completed Star Racer only. Both versions include A and B trials, reflecting basic processing speed and cognitive flexibility, respectively. Task performance on the TMT was correlated with Star Racer scores (A: r[39]=.37, p=.008; B: r[39]=.54, p<.001). We found moderate to good test-retest reliability (A: ICC [95% CI]=.68 [0.65 0.72], p<.001; B: ICC [95% CI]=.70 [0.67 0.74], p<.001). Crucially, Star Racer scores were sensitive to subjective memory complaints and cognitive fluctuations, as well as risk factors for brain health including education, socioeconomic status, stroke and hearing problems (all p<.001). We conclude that smartphone-based implementations of clinically established measures allow for valid and reliable measures of cognition at scale over time.

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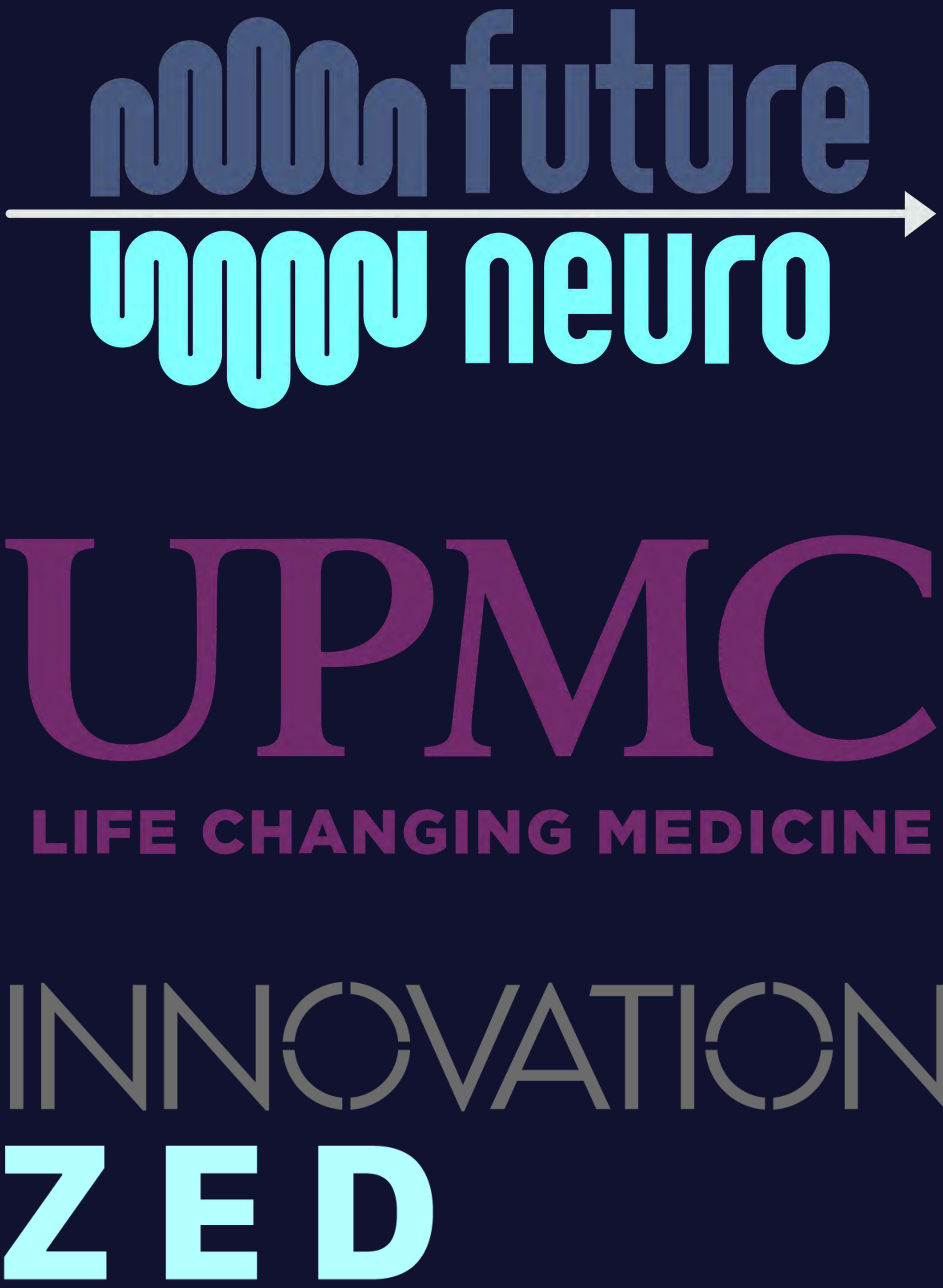

POSTER PRESENTATIONS

Session 1: 12:00-13:00

Session 2: 14:00-15:00

Bullnose & Knowledge Exchange (Level 2)

POSTER PRESENTATION SESSION 1 (#1-20)
TBSI Bullnose & Knowledge Exchange (Level 2)
October 27, 2022, 12:00-13:00

#	Presenter	Institution	Career Stage	Abstract Title
1	Neil Dunne	TCD	RA	HPA Axis Functionality in Alcohol Use Disorder
2	Síle Ní Mhurchú	NUIG	PhD	What's left? How handedness, verbal IQ, and schizophrenia effect white-matter asymmetry?"
3	Shir Dahan	NUIG	MSc	The effect of genetic risk for schizophrenia on cognitive performance – looking for mediators and moderators
4	Cheyenne Brown	NUIG	MSc	The Clinical Associations of Hippocampal Volume Deviation in Bipolar Disorder
5	Jacqueline Quirke	NUIG	PhD	Is bipolar disorder associated with altered or lateralised emotional tone and word processing?
6	Aoife Warren	NUIG	PhD	The Role of Omega-3 and Omega-6 Essential Fatty Acids in Bipolar Disorder Diagnosis and Prediction
7	Catherine Healy	NUIG	PhD	Investigation of sex differences in nociceptive behaviour in a rat model of wound-associated pain, and associated alterations in cutaneous levels of endocannabinoids and N-acylethanolamines
8	Maria Redmond	NUIG	PhD	Characterisation of anxiety and depression-related behaviour and investigation of associated alterations in the endocannabinoid system in a rat incisional wound model
9	Ailís Stevenson	UU	PhD	Shotgun metagenomics reveals taxonomic and functional changes in the salivary microbiome in young adults with depression
10	Alannah Smyth	TCD	PhD	Keep Emotions in Mind: Pharmacological Treatment Outcomes in ADHD with Comorbid Anxiety
11	Tom Farnan	TCD	PhD	Predicting treatment response in ADHD using computational models of decision making
12	Yihe Weng	TCD	PhD	Connectome predictive modelling of sustained attention in adolescents and young adults
13	Leva Vainoraite	NUIG	UG	Inflammation-induced mechanical hypersensitivity is reduced in a preclinical model of Autism and associated with a reduced CFOS expression in the periaqueductal grey and dorsal raphe nucleus
14	Aoife Griffin	QUB	PhD	Dissecting the Genetic Disruptions Underlying Autism Spectrum Disorder Comorbidities
15	Celine Fox	TCD	PhD	Validation of a gamified smartphone assessment of metacognition: Associations with transdiagnostic psychiatric dimensions.
16	Fabiana Traini	TCD	PhD	A neurolinguistic study to assess cognitive abilities and develop composite biomarkers in Fragile X premutation carriers.
17	Oisín C. Joyce	TCD	PhD	The influence of hypertension in middle-aged adults on cognitive function in mid and later life: a systematic review and meta-analysis
18	Anood Sohail	UCD	PostDoc	Discovering neurodevelopmental disruption in an in vivo model of SPG3A associated with Atl M408T
19	Jade Duffy	TCD	PhD	Investigating shared neural mechanisms for working memory and decision-making and loci of their age-related dysfunction.
20	James O'Leary	TCD	PostDoc	Forgetting as a form of adaptive engram plasticity

POSTER PRESENTATION SESSION 1 (#21-38)
TBSI Bullnose & Knowledge Exchange (Level 2)
October 27, 2022, 12:00-13:00

	Presenter	Institution	Career Stage	Abstract Title
21	Livia Autore	TCD	PhD	Interfering with Engram Retrieval: the Neurobiology of Forgetting
22	Camilla Roselli	TCD	PhD	Ataxin-2 dependent control of mRNP granules in development and memory.
23	Clara Ortega-de San Luis	TCD	PostDoc	Connecting the engram dots: role of connectivity mechanism in memory formation
24	Cian Gavin	UCD	PhD	Suppression of mutant huntingtin improves motor symptoms, object recognition memory and the use of allocentric search strategy in the R6/1 mouse model of Huntington's disease.
25	Feng Deng	TCD	PhD	Lifestyle activities contribute to cognitive reserve in mid-life, independently of education, in cognitively healthy middle-aged individuals at risk for late-life Alzheimer's disease
26	Bolin Cao	TCD	PhD	Impact of risk for late-life AD on graph properties of function brain organization and its relationship with cognitive performance
27	Hugh Delaney	TCD	PhD	The Effect of Inflammation on Neuronal Oscillations in Alzheimer's Disease
28	Julia O'Sullivan	TCD	PostDoc	Apolipoprotein-E genotype influences inflammation in Alzheimer's disease
29	Cassandra Dinius	MU	PostDoc	Public and patient involvement (PPI) in neuroscience: Practical considerations and framework
30	Clare McGurk	Ulysses	RA	Alteration of synaptic markers in a preformed fibril (PFF) rat model of synucleinopathy in Parkinson's Disease.
31	Daniel McLoone	TCD	PhD	The effect of formoterol in an alpha-synuclein viral vector and fibril combination model of Parkinson's disease in rats
32	Matthew McAuslan	TCD	PhD	Targeting glial β2-adrenoreceptors for immunomodulation of an inflammatory-driven impairment to attentional and working memory performance
33a	Mairéad Sullivan	UCD	PhD	Altered reward-motivation processing of the TALLYHO/JngJ mouse model is associated with immune signalling mechanisms
33b	Mairéad Sullivan	UCD	PhD	Estrogen signalling: A key upstream regulator of behavioural flexibility
34	Ariyawan Tantipongpiradet	UCD	PhD	Investigation of Bacopa monnieri and Camellia sinensis, alone and in combination, as candidates for potential neurotherapeutic agents.
35	Meimei Yang	NUIG	PhD	Human Stem Cell Modelling for Amyotrophic Lateral Sclerosis
36	Roisin McMackle	TCD	PostDoc	Coil orientation affects the sensitivity of TMS-based measures to ALS cortical pathophysiology
37	Yagmur Bozkurt	NUIG	PhD	Characterisation of Protein N-glycome in Multiple Sclerosis
38	Rosie Giglia	TCD	PhD	ERP markers of cognitive dysfunction in MS

1. HPA Axis Functionality in Alcohol Use Disorder

Neil Dunne, Trinity College Dublin

Stress is a major trigger for relapse in AUD. Investigation into HPA axis functioning in response to stress in AUD may provide a novel drug-target for AUD treatment. This systematic review found 72 studies concerning current AUD, withdrawal from alcohol, early-abstinence (<6 months), late-abstinence (>6months), and genetic factors affecting HPA axis functioning in AUD. Cortisol responses were mixed in ongoing AUD and higher in withdrawal. In early abstinence, significantly lower responses to stress compared to healthy controls were found for ACTH (SMD= -1.47, p= < .001, I2: 35.68%) and cortisol (SMD= -1.32, p= < .001, I2: 38.97). HPA axis functionality may normalise following 6 months of abstinence, though this may be confounded by selection bias. HPA axis hypoactivity was associated with a higher risk of relapse. Individuals with a family history positive status for AUD were shown to have a blunted stress response. Limitations of the present review included inter-study variability and a disproportionate examination of Caucasian male populated studies. Future research should aim to investigate all demographics, increase participant follow up, and use HPA-sensitising drugs during abstinence to assess their effects on relapse rates. Overall, the HPA axis presents strong potential as a novel treatment target in AUD.

2. What's left? How handedness, verbal IQ, and schizophrenia effect white-matter asymmetry?"

Síle Ní Mhurchú, Ciara Egan, Tom Burke, Declan McKernan, Derek W. Morris, John P. Kelly, Brian Hallahan, Colm McDonald, and Gary Donohoe; University of Galway

While language is widely considered left-lateralized, there are a number of factors which influence the extent to which this is true in individuals. Left-handedness is associated with a reduction in leftward language lateralization, and research has shown language-related white matter asymmetry abnormalities in schizophrenia. Here, we investigate the effects of schizophrenia, handedness, and verbal IQ on the asymmetry of three language-related white matter tracts: the uncinate fasciculus (UF), the inferior fronto-occipital fasciculus (IFOF) and superior longitudinal fasciculus (SLF), in a sample of 57 patients diagnosed with schizophrenia and 178 healthy participants. Asymmetry indices were derived from the fractional anisotropy values of each tract, and verbal IQ was measured using WAIS IV vocabulary subtest scores. We found that, irrespective of diagnosis, participants with better verbal IQ displayed greater rightward asymmetry of the UF. A significant interaction between handedness and diagnosis on UF asymmetry was also observed, in that left-handed patients displayed greater rightward asymmetry than right-handed patients and all controls. We posit that this effect of verbal IQ on rightward uncinate asymmetry may reflect the importance of the ventral right hemisphere in semantic processing, and the interaction effect observed could reflect a unique mechanism underlying language lateralization in schizophrenia.

3.The effect of genetic risk for schizophrenia on cognitive performance – looking for mediators and moderators

Shir Dahan, National University of Ireland, Galway

Genetic risk, childhood trauma, and inflammation have been associated with cognitive impairments in schizophrenia. This study aimed to test whether schizophrenia polygenic risk score (i.e., an estimate of schizophrenia genetic liability) would predict performance in episodic memory, emotion recognition, and theory of mind. Furthermore, the study aimed to find if this relationship would be mediated by the pro-inflammatory cytokine interleukin 6 and if childhood trauma and physical neglect would moderate this relationship such that it would be stronger if childhood trauma or physical neglect occurred. A polygenic risk score was calculated for each of the104 schizophrenia patients and 206 healthy participants. Cognitive functions were measured with a battery of cognitive tests. Childhood trauma and physical neglect were measured with the Childhood Trauma Questionnaire. Interleukin 6 was measured in plasma and stimulated toll-like receptors whole blood. Linear regression indicated that schizophrenia polygenic risk score predicted episodic memory but not social cognition performance. Simple mediation analysis revealed that interleukin 6 did not mediate the relationship. Simple moderation analysis revealed that childhood trauma moderated the relationship between schizophrenia polygenic risk score and verbal episodic memory, and physical neglect moderated the relationship of schizophrenia polygenic risk score with episodic memory and theory of mind.

4. The Clinical Associations of Hippocampal Volume Deviation in Bipolar Disorder

Cheyenne Brown; National University of Ireland Galway

Background: This dissertation presents novel clinical hypotheses surrounding the relationship between existing neuroimaging volumetric findings in the hippocampus, clinical symptoms and severity in bipolar disorder, and replications of current neuroimaging findings. The objectives of this study were to analyze the number of episodes (manic and depressive) in bipolar disorder and see if there is a relationship to hippocampal volume. Also, to examine the medication effects of lithium and antiepileptics to know if they moderate the relationship between the number of episodes and hippocampal volume. Next, to analyze bipolar disorder subtypes to see if there is a relationship between hippocampal volume and calculate hippocampal asymmetry and compare it between cases and controls. Methods: This dissertation was a secondary analysis of multisite data through the ENIGMA Consortium involving clinical and neuroimaging data collected from 27 sites. This study utilized various mixed linear regressions with a sample of 4,791 subjects, of which 2,208 were cases, and 2,583 were controls. Results: This study's results indicated no relationship between the number of manic or depressive episodes and hippocampal volume. Also, that lithium and antiepileptics are non- moderators for the relationship between hippocampal volume and the number of episodes. Exploratory analysis revealed that antiepileptics are associated with a greater number of depressive episodes. Bipolar subtype was not related to hippocampal volume, and there was no significant hippocampal asymmetry between patients and controls. One finding revealed a difference between bipolar subtype and hippocampal asymmetry, suggesting more substantial asymmetry in bipolar I compared to bipolar II. Discussion: The study replicated existing literature on medication effects and interactions in the hippocampus. It also found no association between hippocampal volume and bipolar subtype; however, it did present a novel finding indicating a relationship between hippocampal asymmetry and bipolar subtype. Another novel finding suggested that antiepileptic use is associated with more depressive episodes in patients.

5. Is bipolar disorder associated with altered or lateralised emotional tone and word processing?

Jacqueline Quirke, University of Galway

Abnormal emotion processing is a core feature in bipolar disorder (BD) and regularly contributes to impaired daily functioning. Emotion processing is typically lateralised and appears atypical in BD. We aim to investigate differences in emotion processing lateralisation in BD relative to controls using a dichotic listening paradigm. In a dichotic listening test, where two distinct auditory stimuli are presented concurrently, subjects attend to emotional tones of words or words themselves. Accuracy, response time and a laterality index were computed. A multivariate analysis of covariance examined interactions between emotion, language processing and diagnosis. Attending to emotive tones (mean±SD: 1088±270) resulted in higher latency to response, relative to detecting words (930±220, F=14.7, p=1x104). However, contrary to the overall hypothesis, BD subjects (n=35, age=41.8±13.1) did not perform significantly less accurately when detecting emotional tones (0.6±0.2) relative to controls (n=40, age=40.3±13.9, accuracy=0.6±0.3, F=0.60, p=0.2). No evidence of hemispheric advantage/lateralisation (F=0.2, p=0.9) was present. While individuals appear slower on identifying emotional tones, this did not extend to evidence of differential/lateralised processing in BD relative to controls. Extending our findings of lateralised processing in BD to incorporate functional connectivity analyses may provide more neurobiological understanding of abnormal emotional processing extant in BD.

6. The Role of Omega-3 and Omega-6 Essential Fatty Acids in Bipolar Disorder Diagnosis and Prediction

Aoife Warren, University of Galway

Bipolar disorder is a complex psychiatric condition characterised by (hypo)manic and depressive episodes. Blood levels of omega-3 and omega-6 essential fatty acids have been demonstrated to be altered in bipolar disorder compared to healthy controls. This paper aimed to examine if baseline omega-3 and omega-6 essential fatty acid levels were altered in bipolar disorder dependent on the type and frequency of mood episodes experienced. Eighty patients (n=40 in control and placebo groups) with bipolar disorder were recruited for this 12-month randomized, double-blind, placebo-controlled trial. Blood samples were drawn at screening, 6- and 12-months for essential fatty acid analysis. Psychometric measures were recorded at screening, randomisation, 3-, 6-, 9-, 12-months and 3-month follow-up. Eicosopentanoeic acid ($p = .034$) and linoleic acid levels ($p = .021$) were significantly different between patients experiencing equal numbers of (hypo)manic and depressive episodes and those experiencing more (hypo)manic than depressive episodes. There was a significant difference in docosapentanoeic acid dependent on the number of previous episodes experienced ($p = .004$). Variation existed in essential fatty acid levels dependent on the type and frequency of episodes experienced, indicating potential for prediction of illness course from these levels. Furthermore, reduced levels of docosapentaenoic acid suggested reduced mood stability.

7. Investigation of sex differences in nociceptive behaviour in a rat model of wound-associated pain, and associated alterations in cutaneous levels of endocannabinoids and N-acylethanolamines

Catherine Healy, University of Galway

Chronic, wound-associated pain is a significant unmet clinical need. The endocannabinoid system (ECS) is involved in the maintenance of skin homeostasis and regulation of nociception. This study aimed to characterise pain-related behaviour following incisional injury and investigate levels of endocannabinoids and N-acylethanolamines in skin. Male and female Sprague-Dawley rats (210g-320g, 4-5 per group) underwent back incision (BI) or sham surgery. BI involved a 1.2 cm incision on the left side of the dorsum. Mechanical hypersensitivity (MH) was assessed at baseline, and post-surgery days 1-33. LC-MS/MS was used to measure endocannabinoids and N-acylethanolamines in skin from the site of incision, or equivalent in sham animals. Male BI rats showed primary and secondary MH vs male sham ($p<0.05$). No BI-induced nociceptive behaviour was observed in female rats. Levels of 2-AG were significantly higher in female vs male sham rats in the left skin sample. BI had no effect on cutaneous levels of 2-arachidonoylglycerol, anandamide, N-palmitoylethanolamide or N-oleoylethanolamide in either sex. Results from this investigation indicate potential sex differences in 1) pain-related behaviour post-incision and 2) the cutaneous ECS and provide a basis for further investigation of the mechanisms underlying these sex differences.

8. Characterisation of anxiety and depression-related behaviour and investigation of associated alterations in the endocannabinoid system in a rat incisional wound model

Maria Redmond, University of Galway

Anxiety and depression are common comorbidities in individuals with chronic wounds. This study characterised the rat back hairy skin incisional wound (BI) model behavioural phenotype and investigated associated alterations in the endocannabinoid system (ECS). Male and female Sprague-Dawley rats (210-320g, n=4-5/group) underwent BI or sham surgery. Anxiety-related behaviour was assessed using elevated plus maze (EPM), light-dark box, and open field tests on post-surgery days (PSDs) 6, 9, 13, 26, 29 and 32. The sucrose preference test assessed depression-related behaviour on PSDs 30-31. Endocannabinoids and N-acylethanolamines were quantified using LC-MS/MS. Hippocampal and striatal gene expression of CB1, CB2, FAAH, and MAGL was assessed via qRT-PCR. BI rats displayed anxiety-related behaviour in the EPM on PSD6, persisting to PSD26 in females only. Female incision and male sham rats had lower N-palmitoylethanolamide levels in the right hippocampus vs female shams. Incisional wound did not affect rat sucrose preference. Left hippocampal CB1, CB2, and MAGL expression were lower in female vs male shams. Female incision rats had lower striatal FAAH expression than female sham and male incision rats. BI rats exhibit anxiety-related behaviour, which persists in females to PSD26. Further work will determine the implications of ECS alterations on anxiety-related behaviour in BI rats.

9. Shotgun metagenomics reveals taxonomic and functional changes in the salivary microbiome in young adults with depression

Ailís Stevenson, Ulster University

Aims: Oral dysbiosis has been associated with the pathophysiology of a number of systemic diseases with underlying inflammatory components, including psychiatric disorders, with growing evidence linking the oral microbiome and depression. The aim of this study was to conduct shotgun metagenomic sequencing (SMS) to characterise the composition and examine functional differences in the oral microbiome in individuals with depression compared to controls. Methods: Microbial DNA was extracted from saliva samples from young adults with depression (n=13) and healthy controls (n=19). Microbiome analysis was conducted using SMS. Kraken 2 was used to isolate all the non-human reads. The taxonomic and functional profiling for the depressed and healthy cohorts was obtained separately using the co-assembly method from the SqueezeMeta pipeline v.1.1.2. Results: SMS analysis found depression to be associated with significantly decreased alpha diversity ($p=0.047$) in comparison to healthy controls. Significant differences were also found in one phylum, four genera and seven species between the two cohorts, with two of the species identified being almost exclusively present in the depressed cohort. Functional differential abundance analysis revealed a higher abundance in Kegg Orthologies (KOs) related to eleven molecular functions, including xenobiotic biodegradation and environmental information processing. Conclusions: Overall, characteristic differences in the composition of the oral microbiome have been identified in young adults with depression. The clinical importance and their link with pathogenesis of depression require further SMS studies in larger cohorts.

10. Keep Emotions in Mind: Pharmacological Treatment Outcomes in ADHD with Comorbid Anxiety

Alannah Smyth, Trinity College Dublin

25% of young people with a diagnosis of ADHD will also receive a diagnosis of comorbid anxiety. Literature shows that ADHD with comorbid anxiety can be extremely debilitating, affecting quality of life. This project will test patients before they begin their routine treatment on methylphenidate and again one month after they begin treatment. Participants for this study will be aged between 10 -18 and a conscious effort will be made to recruit females as this group has been under-represented in ADHD research in the past. Brain activity will be recorded remotely using dry mobile EEG headsets and gamified cognitive tasks. Participants will also complete anxiety questionnaires. Behavioural and EEG data will be combined with computational modelling in an attempt to find biomarkers that will predict whether a given patient will respond to treatment with methylphenidate. It is currently unclear whether treatment with methylphenidate alleviates anxiety symptoms or instead aggravates them. The ability to predict whether a patient will have a clinically meaningful response to methylphenidate and understanding the role anxiety plays in this interaction will hugely improve treatment outcomes and the quality of life of patients with ADHD as well as creating a method for more efficient treatment planning for clinicians.

11. Predicting treatment response in ADHD using computational models of decision making

Tom Fernan, Trinity College Dublin

Attention-Deficit/Hyperactivity Disorder (ADHD) is a highly prevalent neurodevelopmental disorder affecting ~5% of children/adolescents and 2.5% of adults worldwide. It is associated with many adverse outcomes. Including increased risk of other psychiatric disorders, such as anxiety and depression; addiction and substance misuse disorders; poor academic performance and occupational failure. First-line treatment for ADHD is usually stimulant medication, typically methylphenidate. Although treatment response is favourable at ~70%, Many cognitive domains have been implicated in ADHD, however it is often best characterised by altered or impaired decision making. We aim to use computational models of such decision making, namely the Drift Diffusion Model, neurally constrained via electroencephalography (EEG) and fit to behavioural data. Estimation of model parameters obtained from model fits allow for the identification of cognitive characteristics associated with ADHD across conditions (on/off MPH). These parameters can be used to derive machine-learning driven predictions of treatment response to methylphenidate that are clinically relevant.

12. Connectome predictive modelling of sustained attention in adolescents and young adults

Yihe Weng, Trinity College Dublin

Introduction Sustained attention is essential to daily life. Although prior studies characterized predictive models of sustained attention in adults, the trajectory of predictive models from adolescents to young adults is still unclear. This study aims to identify the trajectory of predictive networks predicting sustained attention from adolescents and young adults using a data-driven approach, connectome-based predictive modeling (CPM). Method Task-fMRI data at ages 14,19,23 (n=717/1071/1120) were used from a longitudinal IMAGEN dataset. Sustained attention was measured using the intra-individual coefficient of variation (ICV) from the stop-signal task. A general psychophysiological interaction approach was performed to yield a task-related connectivity matrix and CPM was applied to predict ICV across three timepoints. We examined the model's generalization and calculated the correlation between predictive network strength and inattention, measured from Strengths and Difficulties Questionnaire. Result We established predictive models predicting ICV for each timepoint. The predictive networks generalized to external datasets. Inattention correlated with network strength at ages 14 and 19. Inattention at age 14 predicted network strength at ages 19 and 23. Conclusion We identified the trajectory of predictive models predicting sustained attention from ages 14 to 23. Inattention both correlates with and predicts brain activity associated with sustained attention.

13. Inflammation-induced mechanical hypersensitivity is reduced in a preclinical model of Autism and associated with a reduced CFOS expression in the periaqueductal grey and dorsal raphe nucleus

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Up to 95% of individuals with autism exhibit sensory abnormalities, including altered pain responding. However the underlying neurobiology mediating these behavioural changes remains poorly understood. This study examined nociceptive responding in response to a chronic inflammatory pain stimulus in the Valproic acid (VPA) rat model of autism, the effect of morphine and associated alterations in protein expression of immediate early gene and neuronal activation marker cFOS in discrete brain regions Male adolescent rats, prenatally exposed to saline- or VPA, were assessed for mechanical hypersensitivity using the von Frey test seven days following intraplantar administration of complete Freund's adjuvant (CFA). A subgroup of VPA-exposed male rats received morphine (3mg/kg s.c.) 1h prior to testing. Immunohistochemistry was used to identify cFOS protein expression and quantified using Qpath software. Mechanical hypersensitivity was significantly reduced in VPA-exposed rats 7 days post CFA. Morphine attenuated the CFA-induced mechanical hypersensitivity in VPA exposed rats. VPA exposed rats exhibited reduced cFOS expression in the ipsilateral primary motor cortex, ipsilateral lateral PAG and dorsal raphe nucleus following CFA, an effect not further modified by morphine. There was no effect of VPA or VPA+morphine on cFOS expression in the nucleus accumbens, lateral septum or other regions of the PAG. These data indicate a possible role for discrete brain regions in mediating and modulating alterations in inflammation-induced mechanical hypersensitivity observed in this preclinical animal model of autism. Acknowledgements: This research was supported by the Galway Neuroscience Centre Summer Research Scholarship (to IV), the Undergraduate Research Opportunities Programme (to AD), the Hardiman Postgraduate Scholarship (to RH) and College of Medicine, Nursing and Health Sciences, University of Galway.

14. Dissecting the Genetic Disruptions Underlying Autism Spectrum Disorder Comorbidities

Aoife Griffin, Queen's University Belfast

Up to 80% of children with autism spectrum disorder (ASD) have at least one other neuropsychiatric co-morbidity. Among the most common, at 30-70%, are attention-deficit hyperactivity disorder, epilepsy, and depression. The causes of such disorders are known to be highly genetic and have recently been shown to involve disruptions to gene expression programmes in important cell-types. Therefore, we here analysed a single-cell RNA sequencing dataset from ASD prefrontal cortex samples including each co-morbidity of interest for differentially expressed genes in excitatory neurons. The top most significant genes were then plotted in a single-cell RNA sequencing dataset of the fetal developing prefrontal cortex to shortlist novel genes with relevant expression trajectories in developing excitatory neurons. Our ongoing work involves knocking down our candidate genes in an iPSC system of rapid neurogenesis with the intention of taking a few interesting targets to knockout in cortical organoids. The overall goal is to unveil novel gene expression signatures involved in important neurodevelopmental processes that, when disrupted, lead to each of the ASD comorbidities of interest. This will help to provide a better understanding of co-occurring conditions at a transcriptomic and cell-type level and thereby aid in providing better diagnostics, care and, intervention.

15. Validation of a gamified smartphone assessment of metacognition: Associations with transdiagnostic psychiatric dimensions.

Celine Fox, Trinity College Dublin

Introduction: Dysfunction across the metacognitive hierarchy, including local and global confidence, has been associated with anxious-depression (AD) and compulsivity and intrusive thoughts (CIT). However, individuals often describe traditional metacognitive tasks as tedious and unengaging. To address this, we developed Meta Mind, a gamified version of a metacognitive task. Methods: Meta Mind was implemented in a free smartphone app called Neureka. Fifty-two paid individuals [median age=22(range=18-57), 75% female] completed both Meta Mind (80 trials) and a traditional visuo-perceptual metacognitive task (210 trials). We additionally analysed data from 860 unpaid Neureka citizen scientists [mean age=49.8(14.34), 69% female] who completed Meta Mind and self-reported clinical questionnaires pertaining to AD and CIT. Results: Confidence bias was moderately associated across tasks ($r(50)=0.64$, $p<0.001$). Split-half reliability for confidence bias was high in Meta Mind ($r(50)=0.91$, $p<0.001$). Among citizen scientists, AD was negatively associated with confidence bias ($\beta=-0.18$, $SE=0.03$, $p<0.001$), while CIT was positively associated ($\beta=0.11$, $SE=0.04$, $p=0.003$). Global confidence was negatively linked to AD ($\beta=-0.19$, $SE=0.04$, $p<0.001$), but not CIT ($\beta=0.07$, $SE=0.04$, $p=0.120$). Conclusion: Meta Mind demonstrated adequate validity and reliability. This brief gamified task was able to replicate the recent finding of disruption to metacognition at different levels of the hierarchy across transdiagnostic psychiatric dimensions.

16. A neurolinguistic study to assess cognitive abilities and develop composite biomarkers in Fragile X premutation carriers.

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Fragile X Premutation Carriers (FXPCs) carry an expanded CGG trinucleotide repeat in the 5' untranslated region of the Fmr1 gene (Fragile X Messenger Ribonucleoprotein 1; 55-200 repeats). While the full mutation of Fmr1 (>200 CGG repeats) leads to the neurodevelopmental disorder Fragile X Syndrome (FXS), the premutation can lead to various conditions, including the neurodegenerative disorder Fragile X Tremor-Ataxia Syndrome (FXTAS). Typically, naming objects or actions is an automatic process. In an ageing population completing this task can be challenging and impairment or delay to this process can be a hallmark of cognitive decline. In individuals at risk of developing FXTAS, deficits in naming objects or actions may be used to detect pathology early on in its progression. This study will use naming via an analysis of language abilities (linguistic biomarker) along with measures of psychomotor coordination (digital biomarker) and plasma protein alterations (peripheral molecular biomarker).We aim to recruit 25 FXPCs and 25 healthy controls, with the aim of developing a non-invasive composite biomarker with language abilities at its core. The results are expected to provide the foundation for future studies aimed at researching early intervention for FXPCs and providing novel treatments and interventions for the full mutation disorder, FXS.

17. The influence of hypertension in middle-aged adults on cognitive function in mid and later life: a systematic review and meta-analysis

Oisín C. Joyce, Trinity College Dublin

Management of midlife blood pressure and hypertensive status may provide a window of intervention to mitigate cognitive decline with advancing age. The aim of this review was to investigate the relationship between midlife hypertension and cognition in both midlife and later life. Methods: Online electronic databases EMBASE, MEDLINE, PubMed, Web of Science, and CINAHL were searched from their inception to May 2022. Studies that assessed midlife (40-65 years) hypertension status and cognition at mid and/or later-life were eligible for inclusion. Data extraction was carried out in accordance with the STROBE guidelines. Methodological study quality was evaluated using the Appraisal Tool for Cross sectional Studies (AXIS). A random effects meta-analysis was deemed appropriate. Results: 150 studies across 26 countries were included (129,845 participants, weighted mean age: 54.5 ± 3.9 yrs), of which 56 were deemed high-quality. Qualitative synthesis found a negative relationship between midlife hypertension and later life cognition in the domains of memory, executive function, and global cognition, irrespective of study design and quality. However, no relationship with attention, psychomotor speed and visuospatial organisation was found. Conflicting metanalytical evidence was found on the relationship between hypertension and cognition at midlife with high levels of heterogeneity (I2 ≥75%). Hypertension was found to negatively impact memory (MD = -0.19; 95% CI = -0.21 to -0.17; I2 = 97%) and global cognition (MD = -0.55; 95% CI = -0.74 to 0.35; I2 = 96%) but had no apparent effect observed effect on attention (MD = 0.73; 95% CI = 0.20 to 1.26; I2 = 92%) and executive function (MD = 0.14; 95% CI = -0.07 to 0.34; I2 = 98%). Conclusion: Hypertension at midlife has a significant negative impact on on cognition in later life, but only in some cognitive domains, namely memory and global cognition. This evidence of domain specific cognitive variability may be accounted for by biological, environmental, and/or lifestyle factors leading to imminent onset of midlife hypertension and negative sequalae to select cognitive domains. Future studies are warranted to better understand the temporal nature of hypertension from midlife onwards on cognitive decline with advancing age.

18. Discovering neurodevelopmental disruption in an in vivo model of SPG3A associated with Atl M408T

Anood Sohail; University College Dublni

Hereditary Spastic Paraplegias (HSPs) are a group of neurodegenerative disorders caused by mutations in endoplasmic reticulum (ER)-shaping proteins; these proteins function to organize tubular ER in motor neuron axons, highlighting the importance of the role of ER in neuronal maintenance and function. However, the extent and mechanisms by which ER-shaping proteins contribute to axonal ER organization and dynamics are unclear. Recently, a missense mutation in the ER shaping-protein atlastin-1 (Atl M408T), an ER shaping protein has been identified that causes a highly severe form of HSP. The aim of my project is to understand the role of this mutation in organization of axonal ER and how it causes neurodegeneration in an in vivo model of SPG3A in the fruit fly Drosophila melanogaster. Using CRISPR gene-edited Drosophila melanogaster, in which the analogous missense mutation (Atl M383T) is present, we have investigated the effect of this variant on motor neuron organization and function. We have found that homozygous Atl M383T flies are severely disrupted with drastically reduced survival. Moreover, we found that a single copy of Atl M383T (replicating the genotype of the affected patient) results in altered motor neuron development in addition to disruption of the tubular ER and mitochondrial organization within motor neurons. Specifically, tubular ER at the ends of long motor neurons appears fragmented while axonal mitochondria are elongated, perhaps pointing to disruption in mitochondrial fission, which is regulated by tubular ER. Through this project, we are exploring the pathogenic mechanisms underpinning degeneration in a novel in vivo model that will lead to a better understanding of this neurodegenerative disease.

19. Investigating shared neural mechanisms for working memory and decision-making and loci of their age-related dysfunction.

Jade Duffy, Trinity College Dublin

As the global population continues to age, a major imperative exists to pinpoint cognitive mechanisms that explain the wide-ranging detrimental effects of cognitive ageing. Working memory (WM) and decision-making (DM) are building blocks of cognition that decline across the lifespan. While typically studied in isolation, several lines of evidence suggest a shared neural mechanism underpinning both processes. Specifically, attractor models account well for behaviour on a wide range of WM and DM tasks. The present study leverages insights from attractor models to study WM and DM, and their decline with cognitive ageing, in a unified way. Young and older adults completed behavioural tasks purposely designed to be able to pinpoint sources of shared and unique variance in WM and DM behaviour, and the possible reliance of both functions on a common neural circuit. We analysed human behaviour and electroencephalography (EEG) data recorded while participants completed the behavioural tasks. Results from both modalities converged to suggest a shared mechanism for WM and DM, as well as a single locus of age-related dysfunction – degraded sensory encoding – that gives rise to specific patterns of deficit in both domains.

20. Forgetting as a form of adaptive engram plasticity

James O'Leary, Trinity Colllege Dublin

Memories are stored as ensembles of engram neurons and their successful recall involves reactivation of these cellular networks. While progress has been made in understanding the biology of engrams, there remain significant gaps in connecting these cell ensembles with the process of forgetting. We developed a forgetting paradigm based on an object recognition task and characterised the forgetting curve of wild-type mice. Using engram labelling technology, active neurons within the dentate gyrus of c-fos-tTA transgenic mice were labelled during the initial encoding of an object memory. Mice that recalled the memory at 24 hrs showed a higher level of overlap between ChR2-EYFP+ and c-Fos+ cells, compared to mice that failed to recall the memory at two weeks, suggesting that the level of engram reactivation decreased as the memory was forgotten. Similarly, morphological analysis indicated that engram spine density decreased with the level of forgetting and engram activation. Furthermore, optogenetic reactivation of dentate gyrus engram cells facilitated the recall of a previously forgotten object memory, while their inhibition prevented memory recall. Together, these findings suggest that forgetting is an adaptive form of engram plasticity that involves circuit remodeling that allows engrams to switch from an accessible state to an inaccessible state.

21. Interfering with Engram Retrieval: the Neurobiology of Forgetting

Livia Autore, Trinity College Dublin

While investigation of engram cell properties and functionality during memory formation and recall has been extensive, less is known about how engram cells are affected by forgetting. We sought to elucidate the behavioural and neurobiological correlates of retroactive interference. We characterized a form of interference-based forgetting using an object memory behavioural paradigm. Using this behaviour, we labelled dentate gyrus (DG) engram cells in mice during object exposure, and studied the effect of retroactive interference on engram cell function, showing that interference results in decreased engram cell reactivation during recall trials. We found that, following interference, a brief re-exposure to the original stimulus is sufficient to restore access to the missing information evidenced by reactivation of the originally labelled ensemble. Moreover, exposure to a misleading cue drives the reconsolidation of a ‘false’ memory. Furthermore, through optogenetic stimulation of engram cells we were able to elicit the artificial retrieval of the forgotten memory. Together, these findings indicate that retroactive interference modulates the accessibility of engram cells in a manner that is both reversible and updatable. Retroactive interference may constitute a form of adaptive forgetting, where in everyday life new perceptual and environmental inputs modulate the natural forgetting process.

22. Ataxin-2 dependent control of mRNP granules in development and memory.

Camilla Roselli, Triinity College Dublin

Experience-induced protein translation is required for long-term memory (LTM) formation. But how this process is regulated and how broadly it occurs in neuronal elements of a memory encoding circuit remains unclear. Previous work has shown that a C-terminal intrinsically disordered domain (cIDR) of Ataxin-2 required for ribonucleoprotein protein (mRNP) granule assembly plays a key role in long-term olfactory habituation (LTH). Here we further analyse roles and mechanisms by which Ataxin-2 influences mRNP assemblies, translational control in different biological and mnemonic systems. Using genetically modified flies in which FLP recombinase expression can be used to exclude either the entire Atx2 locus or its cIDR, we show that: (a) Ataxin-2 and its cIDR are required for assembly of “sponge bodies,” ovarian mRNP granules containing IMP, Me31B and Cup, required for translational control of maternal mRNAs including gurken (b) required for the assembly of related IMP and Me31B on neuronal granules in vivo. We show that Atx2 is required in Kenyon cells for appetitive long-term memory (LTM) but not STM and will present additional data addressing related and/or synergistic functions of Atx2 and other RNP granules components in translational control in neurons required for appetitive LTM and LTH formation.

23. Connecting the engram dots: role of connectivity mechanism in memory formation

Clara Ortega-de San Luis, School of Biochemistry and Immunology, Trinity College Dublin, Dublin, Ireland

Engram cells are a subset of neurons that experience plasticity during learning, allowing them to store long-term memory information. The connectivity pattern between these ‘building blocks’ of memory has been proposed as a candidate mechanism through which to hold the information in a stable state. However, the mechanisms of the formation and maintenance of engram cell connectivity are poorly understood. We combine inducible Cre recombinase-dependent labeling and doxycycline controlled tTA/TRE system to achieve simultaneous engram labeling of two experiences that are either separated or become associated by natural learning. The association of the memories induces a physical link between the previously-separated engrams, across the monosynaptic connection ventral CA1 to amygdala, indicating that learning translates perceptual information from the outside into a change in the connectivity pattern between engram cells. We further explore how this change in the connectivity pattern is required for the memory to be expressed, by optogenetically silencing the reactivation of the second engram. Finally, we explore the molecular correlates of the association and describe the modulation of plasticity-related mechanisms as a consequence of the connectivity pattern change. Overall, our research supports that learning experiences translate the information from the outside into the connectivity pattern between engram cells.

24. Suppression of mutant huntingtin improves motor symptoms, object recognition memory and the use of allocentric search strategy in the R6/1 mouse model of Huntington’s disease.

Cian Gavin, University College Dublin

Introduction: Huntington’s disease (HD) is a monogenic neurodegenerative disorder caused by a mutation in the huntingtin (HTT) gene. Although HD is typically considered a motor disorder, cognitive symptoms often appear first and are the primary cause of functional decline. Aim: To explore whether HTT-lowering can improve memory in transgenic HD mice. Methods: R6/1 mice were treated with antisense oligonucleotide (ASO) or vehicle by injecting into the right lateral ventricle. Spatial and recognition memory were assessed using Barnes maze and novel object tests respectively. Motor symptoms were evaluated with rotarod and elevated beam apparatus. Results: We show that ASO-treated mice learn to use the optimal spatial search strategy to escape the Barnes maze while vehicle treated controls do not. Relocation of the escape hole resulted in significant reversal effect in ASO-treated but not vehicle-treated mice, indicating improved memory. However, long-term memory consolidation of escape location was not restored. Conversely, novel object tests show rescue of recognition memory by ASO. Motor symptoms and hyperactivity are also ameliorated by HTT suppression. Conclusions: ASO mediated gene suppression partially improves cognition and motor symptoms in the acute R6/1 model of HD. However, additional experiments are required to reveal the optimal approach for therapeutic efficacy.

25. Lifestyle activities contribute to cognitive reserve in mid-life, independently of education, in cognitively healthy middle-aged individuals at risk for late-life Alzheimer's disease

Feng Deng, Trinity College Dublin

Introduction
Stimulating lifestyle activities are associated with maintenance of late-life cognitive abilities, and lower cognitive impairment in Alzheimer's disease (AD), but it remains unknown whether such activities contribute to cognitive reserve (CR) from mid-life, in cognitively healthy individuals who are at risk for late-life AD. Methods: Middle-aged individuals (40–59 years) from the PREVENT Dementia study (www.preventdementia.co.uk) were assessed at baseline (N=210) and two-year follow-up (N=188), with cognitive ability (multi-domain battery) and brain health (grey matter volume, functional brain network segregation) measures. Mid-life activities (MA) were measured using the Lifetime of Experiences Questionnaire. The Dementia Risk Score (DRS) was calculated for each participant using the Cardiovascular Risk Factors, Ageing, and Incidence of Dementia score. Results: Multivariable linear regression found that MA made a unique contribution to mid-life cognitive ability independent of education, occupation, sex and age. Furthermore, MA moderated the relationship between cognitive ability and brain health, with the cognitive ability of people with higher MA less dependent on their brain functional integrity, both at baseline and follow-up, consistent with the concept of CR. Critically, more frequent engagement in these activities was associated with stronger cognition in individuals with high DRS, and MA moderated the relationship between cognitive ability and brain health in this group. Conclusion: These findings suggest that modifiable lifestyle activities contribute uniquely to CR and offset cognitive decrements due to AD risk in mid-life. They support the targeting of modifiable lifestyle activities for the prevention of Alzheimer's disease.

26. Impact of risk for late-life AD on graph properties of function brain organization and its relationship with cognitive performance

Bolin Cao, Trinity College Dublin

Although it is well accepted that Alzheimer's Disease (AD) processes start decades before the onset of clinical symptoms, limited understanding of brain mechanisms and biomarkers of AD in midlife limits early intervention. Here we asked whether risk for late-life AD impact graph theoretical properties of the brain's functional organization and its association with cognitive performance. We used data from 701 cognitively-healthy individuals aged 40 to 59 years from Dublin, Cambridge, West London, Oxford and Edinburgh PREVENT sites. After preprocessing the fMRI data, we used the Dosenbach atlas to extract the mean timeseries and constructed functional connectivity matrices. Then, the small-world propensity, clustering coefficient and path length were estimated and compared between the APOE Ɛ4 carriers and non-carriers. In addition, we also analyzed the association of these graph metrics with cognition. APOE Ɛ4 had a positive impact on the small-world propensity. The CAIDE score was significantly positively associated with path length. Additionally, path length was positively associated with visual short-memory. Our findings suggest a beneficial effect of APOE ε4 genotype in midlife, and that cognitive disruption due to AD risk are reflected on graph properties of function brain organization in this age group.

27. The Effect of Inflammation on Neuronal Oscillations in Alzheimer's Disease

Hugh Delaney, Trinity College Dublin

Neuronal oscillations are rhythmic activities that occur at a range of frequencies in the brain. Oscillations in the frequency range 20 – 80 Hz are referred to as gamma frequency oscillations. Gamma frequency oscillations have been associated with cognitive processes, such as working memory and selective attention. Alzheimer's disease is associated with loss in cognitive function and changes in the immune environment of the brain. In a mouse model of Alzheimer's disease (APP/PS1), using ex vivo brain slice electrophysiology, gamma frequency oscillations were shown to be disrupted across at 9-11 months and at 20-24 months. Inhibitory interneurons are essential for generating gamma frequency oscillations; a reduction in a specific class of inhibitory interneurons (parvalbumin interneurons) was also observed in APP/PS1 animals across the course of disease. Given the profound immune changes seen in Alzheimer's disease, the effect of pro-inflammatory mediators on gamma frequency oscillations was examined. Exposing ongoing oscillations in young wildtype animals to a range of pro-inflammatory mediators (TNFα, CCL2, IL-1β) reduced the growth of the oscillation amplitude over time. This reduction in oscillation growth was also observed in older wildtype animals when treated with IL-1β, but this response was lost in APP/PS1 animals. Additionally, tissue from young wildtype animals which was incubated in various inflammatory mediators had a reduced ability to generate gamma frequency oscillations. These data suggest that changes in the immune system can drive changes in neuronal network activity in both health and disease. In the context of Alzheimer's disease, they are a possible link between immune related changes and the loss in cognition experienced by individuals with the disease.

28. Apolipoprotein-E genotype influences inflammation in Alzheimer's disease

Julia O'Sullivan, Trinity College Dublin

Objectives: It is estimated that over 50 million people suffer from dementia, up to 70% of these are diagnosed with Alzheimer's disease (AD). The apolipoprotein E (APOE) gene has been linked risk of developing sporadic late-onset AD (LOAD). There are 3 APOE allelic variants of interest for AD; APOE2, APOE3 and APOE4. APOE4/E4 has been associated with a 14-fold risk increase for AD development compared to APOE3/E3. In the brain, APOE is expressed by glial cells, predominantly astrocytes, and at lower concentrations microglia. Interestingly another risk factor for AD is neuroinflammation which is the purview of glial cells. As such we aim to explore the effects of APOE on the function of glial cells and their responses to neuroinflammation. Methods: Using an APOE4/E4 hiPSC line and its isogenic controls we will differentiate glutamatergic neurons, astrocytes, and microglia. These will be used to explore the interaction of microglia and astrocytes and how in so doing induces neuronal dysfunction. Results: Our previous work identified some alterations in gene expression and glutamate uptake between E3 and E4 in reactive astrocytes. We aim to repeat these studies in our isogenic lines to confirm the responses are a result of APOE variance.

29. Public and patient involvement (PPI) in neuroscience: Practical considerations and framework

Cassandra Dinius, Maynooth University, Ireland

Public and Patient Involvement (PPI) is focused on embedding contributors with lived experience into the research process. Funding bodies increasingly recognise PPI as a necessary phase in the research process for studies involving human participants. PPI can encompass a broad array of community input from advising on participant-facing materials or constructing recruitment plans, to co-designing elements of research methodology (Ní Shé et al., 2020). Here we present a collection of three case studies that utilise a PPI approach with unique samples of human contributors (healthy-older, people with dementia, dementia carers). Given the diversity of approaches, there is no singular involvement strategy for PPI. Our sessions included agenda-setting, recruitment, introductions, consultancy, conclusions and maintenance. Practical considerations of implementing these sessions are science communication, accessibility, flexibility and inclusivity. Here we present a practical framework that may be applied broadly to various research methods that concern PPI. Outcomes from these case study sessions significantly impacted our recruitment strategy, research methodology, study design and dissemination practices. We wish to facilitate dialogue about PPI in the research process and to collaboratively share experiences with other researchers and contributors, particularly in neuroscience. Strengths, limitations, and best practices of PPI will be discussed.

30. Alteration of synaptic markers in a preformed fibril (PFF) rat model of synucleinopathy in Parkinson's Disease

Clare McGurk1, Aimée Freeburn1, Disha Disha1, Johana Tello1, James B. Koprich2, Jonathan M. Brotchie2, Arianne Pusung2, Michael P. Hill2, Massimiliano Bianchi1. 1Ulysses Neuroscience Limited, Trinity College Institute of Neuroscience, Lloyd Institute, Trinity College Dublin, Ireland. 2Atuka Inc. Toronto, ON, Canada

Parkinson's Disease (PD) is the second most common neurodegenerative disorder. Impairments in synaptic plasticity are a crucial feature in the onset and the progression of motor and cognitive symptoms of PD. The preformed fibril (PFF) synucleinopathy model in rodents recapitulates the molecular and nigrostriatal pathology associated with PD, as well as the progressive decline in dopaminergic function. However, its use as a tool to examine synaptic dysfunction in PD has not been deeply explored. We analysed the progression of synaptic pathology by using a PFF model in female rats and evaluated endpoints at three time points following injection of alpha-synuclein-PFF (aSyn-PFF; PD) or αSyn-monomer (control) into the striatum (Day 30, Day 60, and Day 120, all groups n=8). Using Multiplex Infrared Western Blotting (IFWB), relative levels of synaptic markers (Synaptophysin, PSD-95 and Spinophilin) were analysed in the ventral midbrain and hippocampus. In the ventral midbrain, PSD-95 expression was decreased in the αSyn group at Day 120 and also in the hippocampus at Day 30 and D120. Hippocampal synaptophysin was also decreased at D120, suggesting altered synaptic plasticity. These results form the basis of a preclinical platform using the PFF rat model to identify novel biomarkers of synaptic integrity in PD.

31. The effect of formoterol in an alpha-synuclein viral vector and fibril combination model of Parkinson’s disease in rats

Daniel McLoone, Trinity College Dublin

Animal models of Parkinson’s disease which incorporate alpha-synuclein pathology are considered to be the most relevant model of the human condition and the most suitable for testing neuroprotective interventions. The β2-adrenoreceptor agonist formoterol has previously been shown to have neuroprotective effects. Therefore, the aim of this study is to determine if combining a viral vector expressing A53T-alpha-synuclein with A53T-alpha-synuclein preformed fibrils results in nigral neurodegeneration and motor deficits, and to determine if formoterol can attenuate these motor deficits. Female and male Wistar rats underwent intranigral administration of an AAV1/2 vector expressing A53T-alpha-synuclein in combination with A53T-alpha-synuclein fibrils. Rats then underwent motor performance testing and were sacrificed for immunohistological assessment at 6 weeks. In a separate experiment using the same model, rats were treated with formoterol for 7 days, starting 14 days after model induction. Deficits in motor performance in the stepping and cylinder test were observed. However, formoterol treatment did not attenuate motor deficits at any time point. In conclusion, combining an A53T-alpha-synuclein expressing viral vector with A53T-alpha-synuclein fibrils holds significant promise as an approach to produce motor deficits and evoke Parkinson’s like neuropathology. However, further studies are required to assess the neuroprotective effects of formoterol.

32. Targeting glial β2-adrenoreceptors for immunomodulation of an inflammatory-driven impairment to attentional and working memory performance

Matthew McAuslan, Trinity College Dublin, Institute of Neuroscience

Disruption of Locus-Coeruleus-Noradrenergic (LC-NA) transmission is associated with multiple psychiatric and neurodegenerative disorders in humans including Alzheimer's Disease. The LC-NA system regulates various cognitive and executive domains that are impaired in Alzheimer's disease like attention and working memory, however the degeneration of the LC-NA system has a two-fold contribution to pathology in that noradrenaline additionally has the propensity to regulate the inflammatory phenotype in the brain and modulate microglial activities facilitating amyloid and tau clearance. The β2-adrenoreceptor subtype, highly expressed on cortical glial cells, mediates the anti-inflammatory action of noradrenaline and presents as a viable disease modifying target in Alzheimer's and related dementia's. For these investigations a delayed non-matching to position (DNMTP) protocol was employed to assess rodents’ attention and working memory performance. Pharmacological validation of this assay consisted of observing deficits in working memory following administration of the muscarinic antagonist scopolamine and reversal of these effects with the acetylcholinesterase inhibitor donepezil. Subsequently systemic administration of the bacterial endotoxin and inflammogen, lipopolysaccharide (LPS), induced a sickness like behaviour followed by sustained deficits to working memory in the DNMTP task 24-hrs post-administration, attributed to mnemonic performance alone. Subsequent co-treatment of LPS with the long-acting brain-penetrant β2-adrenoreceptor agonist, formoterol, attenuated the effects of LPS on working memory performance.

33a. Altered reward-motivation processing of the TALLYHO/JngJ mouse model is associated with immune signalling mechanisms

Mairéad Sullivan, University College Dublin

Insulin signalling was previously identified as a key network involved in OCD symptomology, with impaired reversal learning (ability to switch behaviour depending on changed stimulus-reward associations) and spontaneous alternation observed in TALLYHO/JngJ mouse models of Type 2 diabetes/obesity. Insulin regulates not only metabolism but also inflammation. Here, we aimed to establish the causative mechanisms through which aberrant insulin signalling impacts behaviour through proteomic analysis of TALLYHO/JngJ blood using the Olink Mouse Exploratory panel and bioinformatic analysis of available OCD GWAS studies. Reactome and Webgestalt pathway analyses of proteomic results highlight immune-related mechanisms at play. Furthermore, Ingenuity Pathway Analysis reports interleukin-17 (Il-17) signalling, a pro-inflammatory cytokine that mediates neutrophil recruitment during the innate immune response, as a highly significant pathway, amongst other interleukins. This is confirmed also as a significant pathway across OCD GWAS studies (p<;0.01). Further validation analysis of TALLYHO/JngJ blood samples via Mass Spectrometry show altered expression of targets that further confirm that an immune dysregulation may be at play. These results indicate a role of aberrant immune/inflammatory signalling as a causative mechanism for the behaviourally inflexible phenotype in insulin resistant mouse models.

33b. Estrogen signalling: A key upstream regulator of behavioural flexibility

Mairéad Sullivan, University College Dublin

Previous investigations of OCD symptomology indicated that insulin signalling may be a central mechanism. Indeed, TALLYHO/JngJ mouse models of Type 2 diabetes/obesity demonstrate impaired reward-response relationships and reduced spontaneous alternation, a proxy for behavioural flexibility. Here, we sought to identify core upstream regulatory networks responsible for their behaviourally inflexible phenotype. We compared genetic studies of compulsive disorders (Autism, Depression, Alzheimer's and OCD) and Type 2 diabetes and examined common upstream regulators. Results were validated via proteomic analysis. Beta-estradiol and estrogen receptor agonists featured amongst the most significant shared upstream regulators. Pairwise analysis was then performed between immune and microbiome-related somatic disorders (Psoriasis, Crohn's, Ulcerative Colitis, IBS, Anoerexia) vs behavioural disorders (Autism, OCD, Depression) due to links between immune and microbiome changes in behaviour. This also showed beta-estradiol as the most significant recurring upstream regulator. Proteomic analysis of blood from TALLYHO/JngJ mouse models showed a significant decrease in Follistatin (FST) compared to controls, relevant for estrogen release, with levels significantly correlated with appetitive extinction % response in TALLYHO/JngJ and controls, a measure of reward-response inhibition. We conclude from this that, in agreement with current literature, estrogen may serve a neuroprotective function and is a key upstream regulator of behavioural circuitry.

34. Investigation of Bacopa monnieri and Camellia sinensis, alone and in combination, as candidates for potential neurotherapeutic agents.

Ariyawan Tantipongpiradet, 1- Dipartimento di Farmacia Università degli studi di Napoli Federico II 2- Conway Institute, University College Dublin

Bacopa monnieri (BM) and Camellia sinensis (CS) are natural plants used as nutraceutical products with neuroprotective properties. BM is a memory and learning enhancer, while CS is a supplement with high antioxidant activity. Several previous studies have investigated the neurotherapeutic effect on a single extract, but there is currently no evidence regarding the combination of BM and CS. This study was a preliminary investigation to explore the effects of BM and CS, both alone and in combination, on microglial activation. Using lipopolysaccharide (LPS)-stimulated BV2 microglia as an in vitro model of neuroinflammation, we report that both extracts can significantly attenuate the expression of pro-inflammatory cytokines TNFα and Interleukin-6, and the chemokine MCP-1, in a concentration-dependent manner as well as the combination of BM and CS. Further, nitrite concentration (Griess assay) and iNOS expression (Western immunoblot analysis) reveal that both test agents, alone and in combination, can significantly attenuate microglial nitric oxide (NO) production in response to LPS. Interestingly, the anti-inflammatory effects of each extract do not appear to be consistently enhanced when cells are exposed to both agents in combination, compared with CS alone.

35. Human Stem Cell Modelling for Amyotrophic lateral sclerosis

Meimei Yang, University of Galway

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by losing motor neurons (MNs). Most ALS cases are sporadic with no familial history or known genetic association. Therefore, a large collection of sporadic ALS models is required to identify pathological mechanisms and develop new therapeutics. Induced pluripotent stem cells (iPSCs) are a valuable tool for disease modelling, drug screening and cell therapy, especially for sporadic cases as there is no animal model. In combination with small molecules cocktail, we established a rapid, simple, and efficient protocol of spinal MN differentiation. >95% CHAT+ and 98% MAP2+ MNs can be derived in 18 days and are functionally mature in 28 days as evidenced by firing strong multiple action potentials, typical calcium transients, extensive network bursts. Using this new protocol, we observed hyperexcitability in MNs derived from sporadic ALS in comparison to healthy control neurons. Above all, a rapid, simple, and efficient spinal MNs differentiation protocol was established and applied to a model of ALS. This new protocol enables the generation of large quantities of MN with high purity and maturity, which will provide a basis for modelling ALS and other MN diseases, drug screening and cell therapy.

36. Coil orientation affects the sensitivity of TMS-based measures to ALS cortical pathophysiology

Roisin McMackin, Trinity College Dublin

Background: Short intracortical inhibition (SICI) is a non-invasive measure of motor cortical GABAergic inhibition, evoked using transcranial magnetic stimulation (TMS). Lowering/absence of SICI has been proposed as a diagnostic biomarker of amyotrophic lateral sclerosis (ALS), however all prior studies applied stimulation with induced current flowing in posteroanterior (PA) direction across the motor cortex, despite evidence that SICI is more potently evoked using an anteroposterior (AP) orientation. Objective: To determine if coil orientation affects sensitivity of SICI to ALS. Methods: EMG was recorded from abductor pollicis brevis while TMS was applied over the contralateral motor cortex using a 50mm figure-of-eight coil to induce PA and AP directions of current flow across the precentral gyrus. SICI was recorded by applying pairs of pulses with 1ms (PA ALS n: 24, control n: 34) or 3ms (PA ALS n: 34, control n: 26, AP ALS n: 11, control n: 18) interstimulus intervals. Results: SICI was significantly lower in ALS across conditions, but effect size was greater (Cohen's d=-0.96, 3ms ISI) when AP orientation was used compared to PA orientation (Cohen's d=-0.62/-0.66 for 1/3ms ISI). Conclusion: Using AP orientation while measuring SICI in ALS can provide greater discrimination from controls compared to PA orientation.

37. Characterisation of Protein N-glycome in Multiple Sclerosis

Yagmur Bozkurt1, Ana Lucia Rebelo1, Kieran Joyce1,2, Jill McMahon1, Una FitzGerald1, and Abhay Pandit1; Univesity of Galway, Ireland

Protein N-glycosylation, one of the most common mammalian post-translational modifications, plays a significant role in the structural integrity and functions of the glycoproteins in the formation of myelin in neural cells. Protein N-glycome can be altered due to mitochondrial dysfunction in neuronal cells in MS patients. Therefore, the study of N-glycans can give insights into their role in regulating and establishing the neurodegenerative pathophysiological cues of the disease. A high throughput screen was performed using a lectin microarray for the characterisation of overall glycome across the three post-mortem relapsing-remitting MS, eight progressive MS, age- and sex-matched control cases. This assay included 48 lectins specific for different N- and O-glycan epitopes—significant increase in sialylation, complex antennary Gal and LacNAc, and GlcNAc residues. Our data suggest that the complexity of glycome increase with the disease, and overall glycome is altered with the disease progression. Acknowledgement This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 813263. We thank the U.K. MS Society Tissue Bank for the supply of post-mortem tissues.

38. ERP markers of cognitive dysfunction in MS

Rosie Giglia, Trinity College Dublin

Background: Cognitive dysfunction is a commonly reported but under-addressed symptom of multiple sclerosis (MS). Radiological measures of disease progression do not always correspond to the clinical presentation of symptoms, including cognitive symptoms (the clinic-radiological paradox). This work aims to identify electroencephalographic biomarkers of the nature and progression of cognitive dysfunction in MS.
Methods: 128-channel EEG data was recorded from 41 participants with MS and 43 neurologically healthy controls during an auditory oddball task and the sustained attention to response task (SART). Mismatch negativity (MMN) and P300 event-related potentials (ERPs) were identified from the auditory oddball and SART data, respectively. Results: This work is in progress. Additional participants and results will be available by the symposium. Preliminary results suggest that the MMN does not distinguish patients and controls in the sensor domain. Conclusions: Pre-cognitive ERP measures like the MMN in the EEG sensor domain may not distinguish patients with MS and healthy controls. Transformation of the signal into the source domain may improve the discriminatory power of these measures. Further work is necessary to determine whether ERP measures of attention and inhibitory control are altered in people with MS.

POSTER PRESENTATION SESSION 2 (#1-18)
TBSI Bullnose & Knowledge Exchange (Level 2)
October 27, 2022, 14:00-15:00

#	Presenter	Institution	Career Stage	Abstract Title
1	Niamh Moreton	UCD	PhD	Targeting prolyl hydroxylase domain inhibition as a neuroprotective strategy against hypoxia in isolated rat hippocampal slices and organotypic slice cultures.
2	Aoife Cosgrave	UCD	PhD	Investigating a novel phytocannabinoid compound in models of acute neuroinflammation
3	Roisin Winters	TCD	PostDoc	An evaluation of i.p. administration of lipopolysaccharide (LPS) across 96 hours as a mouse model of neuroinflammation
4	Adina MacMahon Copas	TCD	PhD	Peripheral Immune Cells Induce A Reactive Phenotype in Human iPSC-derived Midbrain Astrocytes
5	Dara O'Boyle	TCD	UG	A novel Immunofluorescent analysis of the mechanisms of action of IGF-1 and its derivatives in Neurons.
6	Sarah McComish	TCD	PostDoc	Human iPSC-derived reactive astrocytes display an altered metabolic profile compared to quiescent-like astrocytes
7	Jessica White	QUB	PhD	The role of MHC-II in CNS remyelination
8	Sheffinea Koshy	NUIG	UG	The influence of commonly used medications on Central Nervous System blood biomarkers in young healthy athletes
9	Emily Knox	UCC	PhD	The Gut Microbiota is Important for the Maintenance of Blood-Cerebrospinal Fluid Barrier Integrity
10	Colin Simon	TCD	PhD	Neural Mechanisms underlying self-regulation of corticospinal excitability; a TEP pilot study
11	Ciara Connolly	TCD	RA	Investigating Peripheral Microtubule Proteins in Human CDKL5 Deficiency Disorder (CDD) Patients
12	Martyna Stasiewicz	RCSI	PhD	Non-viral targeting of junctional proteins in a 3D model of the fibroglial sar formed after spinal cord injury
13	Liam M. Leahy	RCSI	PhD	Development of an Electroconductive, 3D-Printed Scaffold Designed to Promote Axonal Regrowth after Spinal Cord Injury
14	Ross O'Carroll	UCD	Other	Investigating microglial behaviour in Spinal Cord Injury (SCI) - Development of a cheap, open-source in vitro live-cell imaging system
15	Ailbhe Conway	TCD	UG	To identify proteins that interact with Ataxin-2 in mRNP granules
16	Leticia Villalba Benito	UCD	PhD	Analysis of m6A modification of microRNAs in epileptogenesis and in chronic epilepsy reveals specific m6A microRNA pattern involvement in disease
17	Theresa Auer	UCD	PhD	Investigation of long non-coding RNAs as mediators of aberrant gene expression in epilepsy
18	Martina Puzio	UCD	PhD	Targeting oxidative stress and prolyl hydroxylase inhibition as therapeutic strategies in an in vitro rat stroke model

POSTER PRESENTATION SESSION 2 (#19-35)
TBSI Bullnose & Knowledge Exchange (Level 2)
October 27, 2022, 14:00-15:00

#	Presenter	Institution	Career Stage	Abstract Title
19	Beatriz Gil	RCSI	PostDoc	The role of P2X7 receptors in TBI-induced brain pathology: a pre-clinical evaluation
20	David Lee	TCD	PhD	Investigating the Effects of Ketolytic Metabolism on Neuroblastoma Growth and Viability
21	Elin Strachan	UCL	PhD	Developing Zebrafish and Drosophila Models for Optic Atrophy
22	Amirhossein Chalehchaleh	TCD	PhD	Speech Comprehension and Semantic Encoding
23	Sara Carta	TCD	PhD	Cortical encoding of phonetic features of both attended and ignored speech in hearing impaired individuals
24	Paul Conway	TCD	PhD	Overwriting an instinct: how innate circuitry can be modified with experience
25	Jivesh Ramduny	TCD	PhD	Towards data salvage in high-movement cohorts: bagging yields robust and reproducible brain-behaviour relationships
26	Henry Potter	TCD	PhD	Naturalising Agent Causation
27	Sowmya Vijayakumar	TUS	PhD	BiLSTM-based Quality of Experience Prediction using Physiological Signals
28	Jack Maughan	TCD	PhD	Collagen/Pristine Graphene as an Electroconductive Interface Material for Neuronal Medical Device Applications
29	Kelly Donegan	TCD	PhD	Cannon Blast: A Novel Gamified Tool For Measuring Model-Based Planning In The Wild
30	Huiqing Hu	TCD	PhD	The development of functional small-world architecture in early infancy
31	Ciara McMahon	UCD	PhD	Generation and characterisation of an induced pluripotent stem cell derived cerebral organoid model of foetal cocaine exposure
32	Aisling Leavy	TCD	PhD	Altered Microglia Morphology at Acute and Chronic Timepoints following Neonatal Hypoxia
33	Disha Disha	Ulysses	RA	Acetylated alpha-tubulin and Neurofilament Light Chain as clinical plasma biomarkers in Charcot-Marie-Tooth disease.
34	Magdalena Imiolek	TCD	PhD	The effect of cannabidiol treatment on reactive human-induced pluripotent stem cell-derived astrocytes
35	Janelle Stanton	UL	PhD	Patient-derived cellular models as tools to elucidate the pathophysiology of Hao-Fountain syndrome - Using iPS cell-based model systems to understand the pathophysiology of USP7 mutations

1. Targeting prolyl hydroxylase domain inhibition as a neuroprotective strategy against hypoxia in isolated rat hippocampal slices and organotypic slice cultures.

Niamh Moreton, University College Dublin

The contribution of hypoxia to the pathophysiology of acute ischemic stroke (AIS) is well established and lead to disruptions in synaptic signaling. Hypoxia can lead to the stabilization of hypoxia inducible factors. Prolyl-4-hydroxylase domain enzyme inhibitors (PHDI) have been shown to have a preconditioning and neuroprotective effect post-ischemia. Therefore, this study explores the effects of DMOG, JNJ and Roxadustat on synaptic transmission post hypoxia in isolated rat hippocampal slices using electrophysiological techniques and their ability to protect cell viability post hypoxia using organotypic hippocampal slice cultures. We report that the application of DMOG (1mM) and JNJ (10uM) significantly attenuated the extent of the synaptic transmission depression during acute hypoxia in the CA1, an effect that appears to be post-synaptic. In addition, DMOG, JNJ and Roxadustat significantly rescue the iLTP post intermittent hypoxia in the CA1. Our organotypic data demonstrates a neuroprotective role for both JNJ and Roxadustat, where slices had significantly less cell death post hypoxia compared to controls. Our results suggest a neuroprotective role for PHDIs in maintaining synaptic integrity and cell viability during hypoxic stress. These new findings may help to disambiguate the complex interaction between synaptic signaling and hypoxia informing novel therapies for the treatment of AIS.

2. Investigating a novel phytocannabinoid compound in models of acute neuroinflammation

Aoife Cosgrave, University College Dublin-University College London

Neuroinflammation is a key hallmark of many neurological diseases and is initiated by glial cells in response to inflammatory challenges, such a bacterial and viral pathogens, and endogenous damage signals. Glial activation is largely mediated by the activation of specific Toll-like receptors (TLRs) and is shown to lead to subsequent neuronal dysfunction. Activation of subtypes TLR2 and 4 has been associated with neuroinflammatory disorders and therefore offers an attractive target for therapeutic intervention. Phytocannabinoids derived from the Cannabis sativa plant, such as Cannabidiol, have shown to act as modulators of neuroinflammation. While several compounds have been identified from the plant many have been poorly investigated to date. This study examines the properties of a lesser-explored phytocannabinoid “GL4a” (identity blinded for research purposes) in TLR-mediated models of acute neuroinflammation. GL4a was found to attenuate pro-inflammatory cytokine release in microglial BV2 cells exposed to the TLR2 agonist lipoteichoic acid (LTA). These effects were extended to the mitigation of TLR-mediated inflammatory responses on a neuronal cell line. Furthermore, the impact of GL4a on neuronal excitability and firing under control conditions and on potassium currents that are important determinants of neuronal excitability was examined in CA1 pyramidal cells using whole-cell electrophysiology techniques. This exploratory study reveals anti-inflammatory and neuroprotective effects of a novel, plant-based compound “GL4a”, and supports further interrogation of potential neurotherapeutic properties.

3. An evaluation of i.p. administration of lipopolysaccharide (LPS) across 96 hours as a mouse model of neuroinflammation

Roisin Winters, Trinity College Dublin

Dysregulated immune signaling is implicated in CNS disease and neuroinflammation has been linked to the pathogenesis of multiple neurodegenerative and psychiatric disorders (Salazar et.al., 2012). LPS administration is a well-established model of acute neuroinflammation in rodents (Domínguez-Rivas et. al., 2022). This study further investigates this model through an analysis of the effects of LPS administration on brain tissue and plasma over a 96 hour time frame. Male C57BL/6J mice (n=50) were administered LPS (0.25mg/kg, i.p.) and sacrificed at 24h, 48h, 72h or 96h post injection. Cytokine and chemokine (IFN-γ, IL-10, IL-1β, CCL2, IL-6, KC/GRO, TNF-α, CCL3, CCL4) concentrations were determined by MESO QuickPlex SQ 120 for both plasma and brain homogenate. At the 24h time point a significant increase was observed in the plasma samples across all cytokines and chemokines. In plasma, IL-10, IL-1β, IL-6, CCL2, TNFα, CCL3 and CCL4 showed a significant increase in concentrations at the 48hr time point, with Il-10 and CCL3 maintaining a significant increase up to the 96hr time point. In brain tissue, IL-1β, TNFα, CCL2, CCL3 and KC-GRO were significantly increased at the 24h time point. KC/GRO and CCL2 showed a significant increase at the 48hr timepoint also. Only CCL3 showed a significant increase at the 72hr timepoint in brain tissue. There was no significant increase in IL-6, IFN-γ and IL-10 in the brain at any time point. This study demonstrates that LPS administration by i.p. injection induces a robust inflammatory response in plasma and brain. These data indicate that 24h post LPS treatment is the optimal time point to observe inflammation across the time points investigated here. This model can be utilised to further explore neuroinflammatory mechanisms and to assess novel anti-inflammatory agents relevant to the treatment of a number of diseases.

4. Peripheral Immune Cells Induce A Reactive Phenotype in Human iPSC-derived Midbrain Astrocytes

Adina MacMahon Copas, Trinity College Dublin

Parkinson's disease (PD) is characterised by accumulation of misfolded alpha-synuclein protein and loss of dopaminergic neurons in the substantia nigra pars compacta. Involvement of astrogliosis and microgliosis in PD is well established. Recently infiltration of CD4+ T cells, facilitated by a disrupted blood brain barrier was demonstrated in post-mortem brain tissue of PD patients and linked to neurodegeneration. The implications of this infiltration on astrocytes remains to be elucidated. iPSC-derived midbrain astrocytes (iPSC-Astros) were stimulated with CD4+ T cell conditioned media (CD4CM). Following evidence of induced reactivity we aimed to determine the probable origin of this response.Increasing evidence supports the role Th17 cells in PD. IL-17, their main secreted cytokine is demonstrated to synergise with TNFα, commonly secreted by activated microglia and known to induce reactive astrocytes.Hence, iPSC-Astros were stimulated with IL-17, TNFα or both combined. A synergistic increase in IL-6 was observed with combined IL-17 and TNFα. To investigate the implications of chronic cytokine exposure, responses at 72 hrs and 7 days were assessed. Results suggest that time had no effect on astrocyte reactivity however, cellular integrity may be comprised. This provides a novel insight into the effect of peripheral immune cell infiltration in PD.

5. A novel Immunofluorescent analysis of the mechanisms of action of IGF-1 and its derivatives in Neurons.

Dara O'Boyle, Trinity College Dublin

Within the central nervous system, Insulin-like growth factor 1 (IGF-1) is converted into GPE, a tripeptide composed of the final three amino acids (Glycine-Proline-Glutamate) from the N-terminal tail of IGF-1. For decades, IGF-1 and GPE have been studied for their neuroprotective effects, and the GPE analogue Trofinetide has recently passed a Phase III clinical trial for the treatment of Rett Syndrome, a neurodevelopmental disorder. However, the mechanisms of action by which these molecules induce neuroprotection are poorly understood. The goal of this experiment was to determine the effect of IGF-1 and GPE treatment on the localisation of the Insulin-like growth factor 1 receptor (IGF1R) and the activation of its downstream effectors under various conditions of time and concentration. Using a novel method for immunofluorescent quantification, 1,187 neurons were analysed with the following endpoint measurements: cytosolic IGF1R, nuclear IGF1R, cytosolic GLUT4, cytosolic pAKT, cytosolic pMAPK, and nuclear pCREB. The results indicate that 2 days of GPE 4ng/ml treatment induces the nuclear translocation of IGF1R and that persistent, but not transient, activation of IGF1R by IGF-1 induces the cytosolic degradation of the receptor. There also appeared to be a time-dependent relationship between GPE treatment and MAPK signalling.

6. Human iPSC-derived reactive astrocytes display an altered metabolic profile compared to quiescent-like astrocytes

Sarah McComish, Trinity College Dublin

Astrocytes are the most abundant cell type in the CNS and play a central role in the development and homeostasis of the healthy brain. However, astrocytes have the potential to become activated and reactive in neurodegenerative diseases such as Alzheimer's disease. Our study aimed to investigate the impact of astrocyte reactivity on gene and protein expression, and function using human induced pluripotent stem cell (iPSC)-derived astrocytes. Human iPSC were patterned towards a neural fate using dual SMAD inhibition. Astrocytes were derived using epidermal growth and human leukemia inhibitory factors to produce mature astrocytes after 90 days. They were characterised then stimulated with IL-1 , TNF and C1q to induce a reactive phenotype. iPSC-derived astrocytes were positive for astrocyte markers GFAP, S100β, Connexin-43 and EAAT1 confirming cell fate. Stimulation resulted in increased IL-6 secretion, coupled with increased expression of genes associated with reactive astrocytes (e.g., C3, CXCL10, PTX3). Reactive astrocytes were also shown to have an altered metabolic profile with significantly elevated glycolysis and glycolytic capacity compared to controls as assessed by Seahorse Assay. In conclusion, the ability to produce reactive astrocytes from human cells in vitro provides a powerful model for investigating the mechanisms that underpin the role of astrocytes in neurodegenerative diseases.

7. The role of MHC-II in CNS remyelination

Jessica White, Queens University Belfast

Multiple sclerosis is an immune-mediated inflammatory disease of the central nervous system (CNS), characterised by the loss of myelin and oligodendroglia. Our lab has previously shown that regulatory T cells (Treg) can drive oligodendrocyte progenitor cell (OPC) differentiation and remyelination—a pro-regenerative response known to be mostly dependent on MHC-II. As MHC-II is upregulated in the CNS by glial cells important to myelin regeneration, we hypothesised that MHC-II is required for efficient OPC differentiation and remyelination. To test this hypothesis, we used in vitro pure OPC cultures and an in vivo model of lysolecithin-induced demyelination in WT and MHC-II-deficient mice. Surprisingly, we found that Treg cells significantly drive OPC differentiation independent of MHC-II in vitro. Immunofluorescence staining of demyelinated spinal cord sections also revealed the absence of MHC-II does not significantly affect the number of oligodendrocyte lineage cells, proliferating OPCs and differentiated oligodendrocytes, but did impair the density of proliferating microglia and astrocytes. Together, these findings suggest a novel MHC-II-independent mechanism of Treg-driven OPC differentiation, and a possible requirement for MHC-II in glial proliferation. Ongoing work is investigating whether MHC-II is required for remyelination in vivo and the mechanism(s) by which Treg function beyond what is classically known in regeneration.

8. The influence of commonly used medications on Central Nervous System blood biomarkers in young healthy athletes

Sheffinea Koshy, National University of Ireland Galway

Background: Annually, 3.8 million sports-related concussions (SRC) occur in the United States alone. Current SRC diagnosis is based on subjective clinical measures, but the addition of blood biomarkers may augment clinical decision-making. Prior to the validation of these biomarkers, influence of confounding factors such as commonly used medications will be important. Objective: To investigate the influence of medications on candidate blood biomarkers of SRC. Methods: This is a cross-sectional analysis of healthy athletes enrolled in the Canadian SHRED Concussions study. One hundred and forty-nine athletes (male 51%, 11-17 years) provided blood samples and self-reported medication data. Select plasma biomarkers were analyzed by ultra-sensitive single molecular array immunoassay (SIMOA). Independent t-tests were preformed to examine difference in means. Results: Twenty-six athletes reported using medications. Medications such as birth control, non-steroidal anti-inflammatory, acetaminophen, birth control, Accutane and CNS stimulant resulted in significant changes in biomarkers GFAP and UCH-L1 levels. Conclusion: This study suggests commonly used medications may influence candidate blood biomarkers of SRC in healthy athletes, but further research is needed.

9. The Gut Microbiota is Important for the Maintenance of Blood-Cerebrospinal Fluid Barrier Integrity

Emily Knox, Univesity College Cork

The gut microbiome communicates with the brain though several communication pathways including the vagus nerve, immune system, microbial metabolites, and through endocrine pathways. These pathways along the humoral/immune gut-microbiota-brain axis include a series of vascular and epithelial barriers such as the intestinal epithelial barrier, gut-vascular barrier, blood brain barrier, and blood-cerebrospinal fluid barrier. Of these barriers, the relationship between the gut microbiota and blood- cerebrospinal fluid barrier is yet to be fully defined. Here, using a germ-free mouse model, we aim to assess the relationship between the gut microbiota and the integrity of the blood- cerebrospinal fluid barrier which is localized to the choroid plexus epithelium. We visualized the tight junction protein zonula occludens-1, an integral aspect of choroid plexus integrity, as well as the choroid plexus fenestrated capillaries using confocal microscopy. Quantification of tight junction proteins via a network analysis revealed a disruption in the zonula occludens-1 network organization in germ-free mice, however, we did not observe any differences in capillary structure. Future studies are required to elucidate its relative contribution in signaling from microbiota to the brain.

10. Neural Mechanisms underlying self-regulation of corticospinal excitability; a TEP pilot study

Colin Simon, Trinity College Dublin

Neurofeedback based on responses to Transcranial Magnetic Stimulation (TMS-NF) can be used to train individuals to upregulate or downregulate the amplitudes of their Motor Evoked Potentials (MEPs). This is achieved with mental strategies to increase (UP) or decrease (DOWN) corticospinal excitability of motor projections to the target muscles. The distinct, trained brain-states for regulating excitability are associated with differences in neurophysiological correlates. In the current pilot experiment we investigated differences in TMS-evoked potentials (TEPs) recorded over motor cortex while using TMS-NF to self-regulate brain-state. We recorded TEPs while 5 healthy participants used TMS-NF to regulate the amplitude of their MEPs, with a game rewarding regulated MEPs and providing real-time feedback immediately following each TMS pulse. Background muscle activity was monitored and displayed in real-time. Elevations above 7 microvolts in the target muscle or surrounding muscles caused the trial to halt until sufficient relaxation was achieved. TEPs recorded during UP, DOWN, and REST trials demonstrated different patterns of evoked positivity and negativity around the P180. DOWN trials produced a very minimal P180 component compared with UP trials or baseline REST trials. As TMS-NF may be help promote functional recovery in stroke survivors, understanding the self-regulation mechanisms of corticospinal excitability is important.

11. Investigating Peripheral Microtubule Proteins in Human CDKL5 Deficiency Disorder (CDD) Patients

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CDKL5 Deficiency Disorder (CDD) is a rare X-linked brain disorder caused by a heterogeneous mutation in the CDKL5 gene, resulting in severe early-onset seizures, intellectual disability, motor, and social impairments. Alterations in microtubule dynamics have been implicated in the pathogenesis of CDD. Alpha-tubulin post-translational modifications (PTMs) modulate changes in microtubule dynamics, reflecting changes in neuroplasticity. These alpha-tubulin PTMs can be detected in peripheral fluids, making them potential biomarkers for CDD. Here, alpha-tubulin PTMs were measured using Infrared Western Blot in the plasma of CDD patients (n=8) vs. healthy controls (n=9). Acetylated alpha-tubulin (Acet-Tub) and delta-2 alpha tubulin (Δ2-Tub) were analysed as ratios of total alpha-tubulin (Tot-Tub) and tyrosinated alpha-tubulin (Tyr-Tub) was analysed as a ratio of detyrosinated alpha-tubulin (Glu-Tub). The results showed significant Acet-Tub/Tot-Tub overexpression in CDD patients compared to controls, indicating less dynamic microtubules, and therefore reduced synaptic plasticity. Tyr-Tub/Glu-Tub and Δ2-Tub/Tot-Tub ratios were not significantly different in the plasma of CDD patients compared to controls. These results suggest that CDD patients exhibit overexpressed plasma Acet-Tub/Tot-Tub consistent with dysregulated microtubule dynamics. In conclusion, this data indicates that Acet-Tub/Tot-Tub may represent a potential plasma biomarker of disease progression in CDD, and microtubules may represent a novel therapeutic target for CDD.

12. Non-viral targeting of junctional proteins in a 3D model of the fibroglial sar formed after spinal cord injury

Martyna Stasiewicz; Royal College of Surgeons Ireland

One of the outcomes of spinal cord injury is the formation of an inhibitory scar around a lesion cavity in the damaged tissue. Consisting of astrocytes and invading fibroblasts, this potent barrier impedes axonal regrowth, but also functions to impede macrophage-mediated inflammation and expansion of the injury site. We hypothesised that by reducing junctional protein connections between scar-forming cells we will destabilize the scar, subsequently enabling the diffusion of therapeutics into the damaged tissue. To do so we developed a gene-activated biomaterial scaffold capable of releasing nanoparticles complexed with silencing RNA for non-viral delivery to scar-forming cells. Soft hyaluronic acid and collagen IV porous scaffolds designed specifically for SCI research, were fabricated , seeded with human astrocytes and meningeal fibroblasts and treated with TGFβ to induce scar-forming behaviours and replicate the scar in-vitro. Reactive cells significantly upregulated the Connexin43 (Cx43) gap junctional protein compared to controls. Subsequent silencing of Cx43 using scaffold-loaded Cx43-siRNA nanoparticles, reduced Cx43 expression allowing scar cells to separate from each other. In summary, this work outlines the development of a novel, three-dimensional in-vitro scar model and identification of a cell-junctional target to induce a reduction in cell-to-cell adherence in scar forming cells. Funding sources: IRC & AMBER-SFI-IRFU-Charitable-Trust

13. Development of an Electroconductive, 3D-Printed Scaffold Designed to Promote Axonal Regrowth after Spinal Cord Injury

Liam M. Leahy, Royal College of Surgeons Ireland

Electrical stimulation (ES) is a promising method of stimulating neurons to promote axonal regrowth following spinal cord injury (SCI), and its efficacy may be enhanced when applied through an implantable, electroconductive scaffold. To effectively stimulate all injured axons, a novel, electroconductive scaffold for SCI repair was developed by coating 3D-printed polycaprolactone (PCL) with electroconductive polypyrrole (PPy). Coated via in situ polymerisation, the evenly distributed PPy layer exhibited conductivity 30 times higher than neuronal tissue. Neurons grown directly on PPy/PCL and PCL substrates exhibited robust neurite outgrowth, indicating healthy development, and demonstrating the suitability of PPy/PCL as a material for neural tissue engineering. PCL/PPy scaffolds were then developed as a collection of interlocking cylindrical channels, mimicking cord axonal tract structure and size tuned to optimise ES efficacy. The scaffolds were then filled freeze-dried extracellular matrix mixture with aligned-pores to further promote axonal growth. Ongoing work is focused on optimising neuronal growth under ES on the 3D scaffolds substrates to further promote their development. In conclusion, a novel, biocompatible, 3D EC scaffold with complex architecture was developed for SCI repair. Research was funded by Irish Rugby Football Union Charitable Trust and Science Foundation Ireland Advanced Materials and Bioengineering Research (AMBER) Centre (SFI/12/RC/2278_P2).

14. Investigating microglial behaviour in Spinal Cord Injury (SCI) - Development of a cheap, open-source in vitro live-cell imaging system

Ross O'Carroll, University College Dublin

Traumatic Spinal Cord Injury (SCI) is a significant medical problem, diminishing quality of life and functional ability. SCI is characterised by the loss of motor, sensory and autonomic function below the lesion. After an initial mechanical injury phase, a chronic phase consisting of inflammatory cytokine signalling, axonal dieback, and astroglial scar formation persists. Microglia play a pivotal role in SCI pathology, as resident phagocytes of the CNS. Imaging these cells in real-time is of vital importance to our understanding of SCI lesion evolution. Here we present a prototype live-cell optical imaging system, which operates on the bench-top. BV2 microglia were maintained at 32-37 °C using a temperature controller and peristaltic pump to circulate medium. pH, osmolality & flow rate were controlled for the duration of each experiment. Time lapse images were acquired using a brightfield microscope. In our system, BV2 microglia remain morphologically normal, and retain their motility. As a result, image analysis techniques such as motion tracking and morphological analysis are being employed for a comprehensive quantification of cell behaviour. Although more optimisation is needed, this system remains a cheap, effective solution for live-cell imaging, allowing longitudinal image analysis in near-physiological conditions. References: 1. Dooley, D. et al. (2016) Cell-Based Delivery of Interleukin-13 Directs Alternative Activation of Macrophages Resulting in Improved Functional Outcome after Spinal Cord Injury. Stem Cell Reports, 7(6), pp.1099-1115 2. Rust, R. and Kaiser, J. (2017) Insights into the Dual Role of Inflammation after Spinal Cord Injury. The Journal of Neuroscience, 37(18), pp.4658-4660.

15. To identify proteins that interact with Ataxin-2 in mRNP granules

Ailbhe Conway, Trinity College Dublin

Stress granules (SGs) are assemblies of translationally repressed mRNAs and associated proteins that form in response to stress in the cellular environment. Persistence or aberrant formation of SGs has been implicated in the pathophysiology of neurodegenerative disease, including Amyotrophic Lateral Sclerosis (ALS). The protein Ataxin-2 is of interest as a therapeutic target for treatment of ALS. This project details several experiments to investigate the response of four proteins to oxidative stress in cultured cells. We report that ectopically and endogenously expressed Insulin-like Growth Factor 2 mRNA-Binding Protein (Imp) assembles into stress-induced foci in response to stress. These foci are found to colocalize with Ataxin-2 protein in SGs. We also investigate the response of Imp to oxidative stress in vivo employing Drosophila as a model organism. Previous studies in Prof. Ramaswami’s Laboratory have elucidated the functions and mechanisms of action of the domains of the Ataxin-2 protein. Understanding the relevance of each domain is of interest in the development of Ataxin-2 as a druggable target. Through expression of mutant Ataxin-2 constructs and plasmid encoding Imp-HA fusions in cultured cells we report that the cIDR of Ataxin-2 appears to be essential for the recruitment of Imp to ectopic Ataxin-2 granules.

16. Analysis of m6A modification of microRNAs in epileptogenesis and in chronic epilepsy reveals specific m6A microRNA pattern involvement in disease

Leticia Villalba Benito, University College Dublin

Epilepsy is one of the most common neurological conditions, affecting ~50 million people worldwide. Evidence is emerging that persistent changes in gene expression regulation and post-transcriptional regulation underlies the epileptogenic process. MicroRNAs have recently been identified as key regulators of epileptogenesis via altered regulation of gene expression at the post-transcriptional level, however their regulation during epileptogenesis remains obscure. Preliminary data suggests that microRNAs may be subjected to m6A, and that this process may also be disrupted in epilepsy, representing an unexplored layer of gene expression regulation likely to influence neuronal activity and seizures. In order to evaluate the effect of m6A-microRNAs on normal brain behaviour and epileptogenesis, we have profiled hippocampal m6A-tagged microRNAs during epileptogenesis using an adapted m6A-seq approach in the intra-amygdala kainic acid mouse model. Our analysis revealed extensive differential methylation of microRNAs during epilepsy development suggesting this may be linked the gene dysregulation which characterises epilepsy. Next, we will determine the physiological relevance of m6A-microRNAs, its potential role in disease development and whether it may be therapeutically targeted to prevent neurological disease. This study represents the first microRNA methylation study in the brain, which is hoped will illuminate novel therapeutic strategies for the treatment of epilepsy.

17. Investigation of long non-coding RNAs as mediators of aberrant gene expression in epilepsy

Theresa Auer, University College Dublin

Temporal lobe epilepsy (TLE) is a chronic brain disorder characterised by spontaneous recurrent seizures. It is an acquired condition, where neuronal excitability and aberrant circuitry formation increase after an initial insult during a plastic process called epileptogenesis. LncRNAs as epigenetic modulators are known to contribute to network reconstruction via their large-scale influence on gene expression, however, their functional involvement in epilepsy pathogenesis remains unexplored. Here, we aim to investigate the contribution of lncRNA dysregulation to epileptogenesis and explore their potential as novel drug targets. Performing genome-wide transcriptomic sequencing we comprehensively profiled lncRNA abundance at key timepoints during epileptogenesis in kainic acid-induced post-Status Epilepticus mouse models. Analysis revealed significant, timepoint-dependent changes in numerous lncRNAs, some already known for their importance during embryonic development and in plasticity (e.g. H19), which suggests lncRNA-mediated effects on major epileptogenic disease mechanisms. Applying stringent bioinformatic filtering we predicted those lncRNAs with the highest pro-epileptogenic potential and selected the most promising candidates for further in vitro and in vivo examination. Next, we will use antisense oligonucleotide-mediated inhibition to screen the effects of lncRNAs on TLE development and progression, assess their disease-modifying and therapeutic potential, and explore the underlying mechanisms of action.

18. Targeting oxidative stress and prolyl hydroxylase inhibition as therapeutic strategies in an in vitro rat stroke model

Martina Puzio, Conway Institute, University College Dublin

Targeting oxidative stress and prolyl-hydroxylase inhibition has been shown to be a promising treatment in ischemia. Therefore, this study investigated the effects of the SOD mimetic, MnTMPyP and the prolyl-hydroxylase inhibitor Roxadustat on synaptic transmission and neuronal viability in an oxygen-glucose deprivation (OGD) stroke model. Field excitatory post-synaptic potentials were elicited by stimulation of the Schaffer collateral pathway. During OGD, hippocampal tissue was perfused with glucose-free aCSF bubbled with 95% N2/5% CO2. Organotypic hippocampal slices were exposed to 1hr of OGD before staining with propidium iodide. MnTMPyP did not attenuate the OGD-induced depression (24.4±6.6% vs controls 21.2±3.0%) but fully reverted synaptic transmission after OGD (89.0±9.0% vs controls 70.0±11.3%, n=5). Incubation with Roxadustat did not modulate the OGD-induced depression (16.5±1.0% vs controls 21.2±3.0%, n=6) but improved the recovery of synaptic transmission (120.3±18.1% vs controls 70.0±11.3%). In the organotypic slice cultures, MnTMPyP improved neuronal viability after 1hr OGD compared to untreated slices 40min after the insult (25.0±5.4% vs controls 60.0±9.0%). Roxadustat improved neuronal viability compared to untreated slices 40min (19.5±2.7% vs OGD 41.0±7.0%) and 24hr after OGD (34.6±2.1% vs OGD 62.0±8.1%, n=9). Antioxidants and prolyl-hydroxylase inhibition appear to have promising effect. However, more research will determine whether they can play a role in ischemia.

19. The role of P2X7 receptors in TBI-induced brain pathology: a pre-clinical evaluation

Beatriz Gil, Royal College of Surgeons Ireland

Epilepsy is a neurological disorder that affects millions of people worldwide and is characterized by recurrent emergence of unprovoked seizures. Post-traumatic epilepsy (PTE), which is developed following traumatic brain injury (TBI), accounts for 10-20% of symptomatic epilepsy and is associated with a particularly high percentage of pharmacoresistance. Epileptogenesis, the process leading to epilepsy development, is associated with pathological processes, such as neuronal loss, neuronal plasticity changes, and gliosis. Despite currently available anti-seizure drugs (ASDs) successfully controlling seizures, they have no impact upon the underlying causes of the disease, and around 30% of patients do not respond to treatment. The ATP-gated P2X7 receptor (P2X7R) expression and function have been demonstrated to increase following status epilepticus and during epilepsy, both in animal models and patients; while P2X7 antagonism reduces seizure severity and brain damage in such conditions. In addition, these anti-epileptogenic effects persist beyond drug-washout, suggesting a disease-modifying potential. Using a controlled cortical impact (CCI) mouse model of TBI-induced epilepsy, we aim to further study the effectiveness of P2X7 antagonism (at optimal treatment window and concentration) in suppressing epileptogenesis and brain damage, and restoring cognition impairments, compared to mice treated with a commonly used ASD.

20. Investigating the Effects of Ketolytic Metabolism on Neuroblastoma Growth and Viability

David Lee and Dr. Denis Barry, Discipline of Anatomy, Trinity Biomedical Sciences Institute, TCD

Background: Neuroblastoma (NB) is a childhood malignancy of the sympathetic nervous system. Its neoplastic and neurodevelopmental manifestations are characterised by a high glucose demand, which maintains its high proliferative capacity. This metabolic phenotype may be exploited in dietary therapies such as the ketogenic diet which alter substrate availability through oxidative phosphorylation and may starve NB cells of their preferred biosynthetic requirements. However, the effects of ketone metabolism on cancer growth remain poorly understood due to the involvement of other metabolic substrates in experimental paradigms and complexities underlying the Warburg effect. To investigate this, we tested the effects of ketone metabolism on NB using genomic and in vitro methodologies. Material and methods: The expression of glycolytic and ketolytic genes in the context of MYCN amplification, tumour staging, and survival was investigated in six NB genomics datasets using the R2: Genomics analysis and visualisation platform (http://r2.amc.nl). We next investigated how the primary ketone body β-hydroxybutyrate (βOHB) affects the growth and metabolic viability of SH-SY5Y NB in vitro using MTT assays and immunocytochemistry. Results: Our genomic data revealed that elevated levels of glycolytic genes are correlated with tumorigenicity and a low probability of survival, while ketolytic gene expression is lower in metastatic tumours and is associated with better survivability. In vitro data demonstrated that while glucose deprivation reduced the viability of SH-SY5Y NB cells, a growth response to βOHB was only revealed in media deprived of glucose and pyruvate. Conclusions: These data show that ketogenic metabolism may be exploited to prevent NB growth and shed new light on the roles of metabolic substrate availability as key determinants of the responses of NB cells to ketone supplementation.

21. Developing Zebrafish and Drosophila Models for Optic Atrophy

Elin Strachan, University College London

Purpose Optic atrophy (OA) is an inherited optic neuropathy characterised by the irreversible degeneration of the retinal ganglion cells (RGCs) - associated with vision loss. Most OA patients have mutations in the mitochondrial fusion protein OPA1. It’s unclear why OPA1 mutations lead to RGC death, and subsequently to vision loss. Methods CRISPR-Cas9 gene editing was used to knockout the Opa1 homologs in the fruit fly (Drosophila melanogaster) and zebrafish (Danio rerio) generating putative novel models of OA in two model systems. PCR, qPCR, optokinetic response assays and survival assays were used to evaluate phenotypic changes in these models. Results Drosophila Opa1 neuronal- KO animals have a significant reduction in lifespan ($p<0.0001$) and severe motor impairment. OKR assays on zebrafish larvae revealed a significant ($p<0.01$) loss of visual acuity in Opa1 mutants. I have preliminarily identified that a small cohort of Opa1 mutant flies demonstrate a slight rescue in mortality upon treatment the Q10 analogue Idebenone. Conclusions I have successfully generated 2 novel in vivo Opa1 KO models. Opa1 has highly conserved roles in neuronal function with neurodegenerative and visual and survival phenotypes observed in OA model flies and fish. These models can be used to screen potential therapeutics for OA.

22. Speech Comprehension and Semantic Encoding

Amirhossein Chalehchaleh, Trinity College Dublin

Speech comprehension requires our brains to process acoustic features of sounds, such as the broadband amplitude and spectrogram into more abstract semantic information. Crucially, each speech token is interpreted based on the available semantic context However, the neural mechanisms allowing for the integration of context during speech perception remain poorly understood. Recent work could successfully probe the neural mechanism at the interface between word perception and context by using non-invasive electroencephalography (EEG) and experiments involving the listening of natural speech (e.g., audio-books). In this study, we hypothesise that, while previous studies were based on a single context model, the neural process integrating context builds multiple models for the different topics in a conversation. The most relevant model would be used at each given time. We study this question by performing a computational analysis of EEG data recorded as participants listened to natural speech from audio-books. Word embeddings were used to estimate the semantic dissimilarity of each word compared with the proximal context by using either a single context model or by dynamically switching to context models that are tailored to the given topic. A temporal response function analysis was then conducted to determine the physiologically plausibility of those models.

23. Cortical encoding of phonetic features of both attended and ignored speech in hearing impaired individuals

Sara Carta, Trinity College Dublin

Speech comprehension involves the simultaneous processing of increasingly more abstract properties, from acoustics to phonetic and semantic features. Previous studies probed the hierarchical nature of speech processing, by measuring neural activity with electroencephalography (EEG), resulting in objective neural indices of speech and language comprehension. Importantly, these neural metrics have been found to be impacted by the attentional focus of the listener, in realistic noisy and multi-talker scenarios. Building up on this body of knowledge, we assessed how attentional selection impacts cortical representations of speech in environments with competing talkers. This study investigates cortical responses to acoustic and phonetic features of speech, in a cohort of older participants with hearing impairment. Participants were immersed in a multi-talker auditory scene, which is particularly challenging for people with hearing impairment, even when using hearing-aids. Specifically, participants were asked to selectively attend to one speaker, while ignoring other competing speakers. We fit linear models to characterise the brain encoding of both attended and ignored speech streams. By doing so, we could determine how strongly acoustic and phonetic features are encoded in the listeners' EEG signals, across two different hearing-aid noise reduction schemes. Cortical signals were shown to reflect phonetic features of both attended and unattended speakers, regardless of the noise-reduction strategy used. In doing so, these results indicate that categorical perception of phonetic features contributes to the neural representation of speech.

24. Overwriting an instinct: how innate circuitry can be modified with experience

Paul Conway, Trinity College Dublin

Behavioural neuroscience is implicitly divided into the study of innate behaviour (instinct) and the learned behaviour (memory). However, it is becoming increasingly understood that instincts are not set in stone. Here, used multiple training paradigms to alter behavioural responses to a visual looming stimuli, including extinction, reinstatement, and counterconditioning. Our experiments demonstrate a remarkable plasticity of the innate looming/sweeping responses. We investigated how activity in the superior colliculus (SC) changes in response to these experiences by quantifying overlap of c-Fos expressing cells in the naïve and experienced behavioural states. We then manipulated SC activity using optogenetics and investigated the behavioural outcomes, demonstrating a strong defensive response to stimulation of the SC. This was further examined in the context of learning to determine how the activation of the SC post-extinction alters behaviour. We then considered the role of other brain regions using whole-brain histological analysis to identify new candidate regions that modulate innate and learned behavioural responses to looming stimuli. These findings indicate that the mouse visual looming response is highly plastic, and the complexity of this behaviour can only be explained by understanding the role of several regions, including but not limited to the SC.

25. Towards data salvage in high-movement cohorts: bagging yields robust and reproducible brain-behaviour relationships

Jivesh Ramduny, Trinity College Dublin

In functional connectivity (FC) brain-behaviour studies, many participants are excluded due to excessive head motion based on a threshold (rmsFD). Bagging is a machine learning technique that has been proposed to reduce variance and increase the robustness of estimates derived from noisy data. We assessed whether bagging could be applied to estimate FC from a restricted number of timepoints sampled for each individual from those showing the least motion. We used the Healthy Brain Network (N=423, 153 females, 6-20y) to compute the confidence intervals (CIs) derived from Spearman's Rank correlation (R) for FC-age relationships as a function of N by treating sex and rmsFD as covariates. By retaining participants whose rmsFD<0.20mm, i.e., "standard approach", we obtained comparable brain-behaviour relationships using the standard approach (R=0.35) and bagging (R=0.37). The 95% CIs tightened as the sample size increased from N=20 to N=239. By salvaging "high-motion" participants based on their least motion-corrupted timepoints (e.g., only 20), N=379, R=0.24, and 95% CIs narrowed with increasing N. Bagging offers a promising avenue to salvage "high-motion" participants that would otherwise be discarded and maximise sample sizes for robust and reproducible brain-behaviour relationships.

26. Naturalising Agent Causation

Henry Potter, Trinity College Dublin

The idea of agent causation - that a system, such as an organism, can be a cause of things in the world - is often seen as mysterious and deemed to be at odds with the physicalist thesis that is commonly embraced in science and philosophy. Instead, an organism's apparent causal power is ascribed to its mechanistic components or derived from causal activity at the lowest level of physical description. In either case, the 'agent' (i.e., the system as a whole) is left out of the picture entirely, and agent causation is explained away. We argue that this is not the right way to think about causation in biology or in systems more generally. We present a framework of eight criteria that we argue, collectively, describe a system that overcomes the challenges concerning agent causality in an entirely naturalistic and non-mysterious way. They are: (1) thermodynamic autonomy, (2) persistence, (3) endogenous activity, (4) holistic integration, (5) low-level indeterminacy, (6) multiple realisability, (7) historicity, (8) agent-level normativity. Each criterion is taken to be dimensional rather than categorical, and thus we conclude by highlighting how researchers working on quantifying agency may use this multidimensional framework to situate and guide their research.

27. BiLSTM-based Quality of Experience Prediction using Physiological Signals

Sowmya Vijayakumar; Technological University of the Shannon

Multimedia technologies are now pervasive across entertainment, business, healthcare, education and communication. This has led to increased service demand and competencies to provide better multimedia services. Performing user quality of experience (QoE) evaluations is crucial for multimedia service providers to improve their services. QoE can be assessed through explicit and implicit metrics. Several recent studies have suggested that understanding QoE can be achieved through processing physiological signals. This work presents the analysis of physiological responses in relation to different perceptual quality factors using a publicly available multimodal dataset (SoPMD). This paper presents an evaluation of the deep learning (DL) model to predict the user quality of experience (QoE) from physiological signals using a publicly available multimodal dataset, SoPMD. The subjective scores related to QoE factors, namely, perceptual video quality, immersion level, surrounding awareness, interest in video content and audio content are evaluated. A DL model, Bidirectional Long-short term memory (BiLSTM), is trained on the fusion of electrocardiogram (ECG) and respiration features to predict subjective scores for the five QoE factors. This study achieved classification accuracies and F1-scores ranging between 58% and 67% for different QoE factors. The results of the BiLSTM model were compared with machine learning techniques. The experimental results demonstrated that the proposed BiLSTM network has the potential to predict QoE from physiological signals.

28. Collagen/Pristine Graphene as an Electroconductive Interface Material for Neuronal Medical Device Applications

Jack Maughan, Trinity College Dublin

Bioelectricity is an integral mechanism in neuronal tissue function, playing a central role in communication across central nervous system (CNS) neuronal networks. Interrogating function through stimulation and/or recording has diverse applications in human health and disease. The neural tissue engineering demand for stimulation-based solutions requires the development of medical device biomaterials that balance conductivity, biocompatibility, and mechanical performance. However, traditional materials often induce scarring, due to their stiffness and toxicity, presenting barriers to clinical translation. To address this, we report the development of a pristine graphene (pG)-based composite material. Consisting of collagen loaded with 60wt% pG to yield conductivities (~1.2 S/m) necessary for electrostimulation, CpG is biocompatible and closer in stiffness to the CNS than traditional materials. Neurons and glial cells grown on composite films exhibited robust growth, with no change in inflammatory markers, and electrostimulated mouse primary neurons showed enhanced neurite outgrowth, viability and morphology on composites. CpG is readily processable and can produce different neural-interfacing structures - porous scaffolds for CNS repair, microneedle arrays for electrostimulation/recording, and 3D-printed circuits for bioelectronics. These results show that CpG is versatile, with strong biocompatibility, and balances physiological conductivity with the robust mechanical properties necessary for the development of next-generation medical devices.

29. Cannon Blast: A Novel Gamified Tool For Measuring Model-Based Planning In The Wild

Kelly Donegan, Trinity College Dublin

Deficits in model-based planning have consistently been linked to compulsivity, characterized by maladaptive and rigid patterns of behaviour, but effect sizes are small and to estimate them accurately we need large Ns. As well as, questions surrounding the validity and reliability of this measure abound. Several studies have shown that model-based planning estimates are sensitive to variations in task set-up, including transition probabilities, reward rates and more but remains untested whether these changes affect its reliability and validity. To address this gap, we developed Cannon Blast, a highly gamified version of the traditional two-step reinforcement learning task to test the impact of task-optimizations. In experiment 1, N=57 paid participants completed Cannon Blast via a smartphone app, Neureka and the traditional task on a computer. We found Cannon Blast reproduced the classic findings and that estimates of model-based planning from the two tasks showed fair correlation (r=.4) with comparable internal consistency (traditional task: r=.81, Cannon Blast: r=.79). In experiment 2, N=4484 unpaid citizen scientists completed Cannon Blast and provided self-report demographic information. Of those, N=1450 also completed an extensive battery of self-report psychiatric questionnaires. Consistent with prior research, model-based planning in Cannon Blast was reduced in older adults, female, less educated and those with high self-reported compulsivity. In line with prior research, we found that adjustments to task parameters affected mean model-based planning levels, but this had little-to-no effect on their association with individual difference measures or reliability. We conclude that model-based planning can be estimated in a highly gamified context with similar fidelity to in-lab versions.

30. The development of functional small-world architecture in early infancy

Huiqing Hu, Trinity College Institute of Neuroscience, School of Psychology, Trinity College Dublin, Dublin, Ireland

Functional adult brain networks exhibit a small-world architecture, which is critical in supporting integrating information from discrete but interconnected modules across the brain, and therefore theoretically fits in with the conceptual understanding of brain processes that support consciousness. It remains unclear whether or not the small-world architecture is instantiated in neonates at birth. Premature birth most commonly happens during the third trimester of gestation, a critical phase for functional brain development. However, the effect of premature birth on the development of small-world architecture in early infancy remains poorly understood. Rs-fMRI data for full-term neonates (N = 282), preterm neonates at term-equivalent age (TEA, N = 72), or before TEA (N = 70) were obtained from the developing human connectome project, and for a reference adult group (N = 176). Graph theoretical methods were used to estimate functional brain architecture in each participant. We found that 1) small-world architecture develops in neonates as they reach TEA; 2) premature birth was associated with reduced small-world characteristics, independent of neonate age; 3) prematurity-related disruptions were predominantly located in the sensory/somatomotor network. These findings improve understanding of the development of functional brain architecture supporting consciousness at birth and its disruption by premature birth.

31. Generation and characterisation of an induced pluripotent stem cell derived cerebral organoid model of foetal cocaine exposure

Ciara McMahon, University College Dublin

Cocaine is a strong, addictive stimulant that can induce a range of debilitating side effects including cognitive impairments. The impact this illicit drug has on neurodevelopment is still unclear. Due to a lack of in utero models of human prenatal substance abuse, we established a prenatal model to recapitulate the transcriptional responses of cocaine exposure on neurodevelopment. Induced pluripotent stem cell (iPSCs) derived cerebral organoids were generated over 36 days. Cerebral organoids were treated with 25µM Cocaine for 48h, with a repeated dose after 24h. Initial characterisation was carried out by haematoxylin and eosin staining and indirect immunofluorescence. Single-cell RNA sequencing (scRNA-seq) and Assay for Transposase Accessible Chromatin with high- throughput sequencing (scATAC-seq) was used to further analyse the heterogeneous cerebral organoid tissue and identify transcriptional responses induced by cocaine. Immunofluorescent characterisation of cerebral organoids showed evident expression of both radial glial and neuronal markers. Cerebral organoids treated with cocaine also displayed increased exptression of FOSB. scRNA-seq confirmed a diverse array of neural progenitors, immature neurons as well as glial populations within the cerebral organoid. Treatment of organoids with cocaine induced marked changes in transcription in multiple cell types and elicited a reinforcement of the neural phenotype. Genome-wide profiling of chromatin by scATAC-seq revealed some differences in accessibility in specific clusters; however, the power of the integrated data is best observed for individual enhancer and regulatory loci.

32. Altered Microglia Morphology at Acute and Chronic Timepoints following Neonatal Hypoxia

Aisling Leavy, Trinity College Dublin

Hypoxic-Ischaemic Encephalopathy (HIE), caused by lack of oxygen during the perinatal period, is a detrimental condition in newborns; associated with neonatal seizures, infant mortality and a high risk of long-term neurological deficits in surviving neonates, including learning deficits. Many studies have implicated neuroinflammation, particularly microglia, in both adverse neurological outcomes and in neuroprotective strategies. Microglia carry out maintenance of neurons and neural circuitry; however, once activated, they mediate the neuroinflammatory response. Studies in rodent models of severe HIE have shown increased numbers of microglia in the hippocampus post-hypoxia, however, the mechanism of action is not fully understood. This study aimed to identify the role of microglia in a moderate murine model of neonatal hypoxia using behaviour testing (neonatal reflex tests and in adults) and immunofluorescence staining of the hippocampus for Iba1 (microglial marker). We characterised microglia by analysing anatomical functional phenotypes 72 hours and 6 weeks post-hypoxia. Increased numbers of Iba1+ cells and active microglia phenotypes were found at both 72 hours and 6 weeks post-hypoxia compared to controls. The results show that the acute neuroinflammatory activation post-hypoxia persists long after the original insult, supporting the hypothesis that treatments targeting neuroinflammation hold promise for attenuation of post-HIE neurological sequelae.

33. Acetylated alpha-tubulin and Neurofilament Light Chain as clinical plasma biomarkers in Charcot-Marie-Tooth disease.

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Charcot-Marie-Tooth disease (CMT) is a progressive peripheral neuropathy affecting 2.6 million people worldwide with limited treatment options available. It is divided into demyelinating (Type 1), axonal damaging forms (Type 2), and other more complex forms. We investigated Acetylated-Tubulin (Acet-Tub), a marker of microtubule dynamics, and neurofilament light (NfL), a marker of axonal damage, as potential biomarkers of neuronal health to track CMT progression and severity. Plasma was collected from CMT patients (n=13) with mutations either in PMP22 (duplication; CMT1A; n=10) or MFN2 (CMT2A; n=3). Comparisons were made with hereditary neuropathy with liability to pressure palsies (HNPP) patients (PMP22 deletion; n=5), and healthy volunteers (n=16). Acet-Tub was analysed as a ratio of Total-Tubulin using infrared western blot, and significant decreases were found in the Acet-Tub/Total-Tubulin ratio of CMT1A and HNPP patients and trending towards a decrease was found in CMT2A versus healthy controls. NfL was measured using an R-Plex Mesoscale assay. NfL levels were significantly higher in CMT2A and HNPP patients, and trending towards an increase in CMT1A patients compared to healthy controls. These data suggest that plasma-based biomarkers may be beneficial to drug discovery in CMT and related neuropathies. All work was performed following ethical approval from Tallaght University Hospital, Dublin.

34. The effect of cannabidiol treatment on reactive human-induced pluripotent stem cell-derived astrocytes

Magdalena Imiolek, Trinity College Dublin

There is growing evidence that inflammation plays a role in many neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Glial cells, including astrocytes and microglia, are thought to play a central role in neuronal dysfunction and/or death. This study utilises a human model of inflammation which involves differentiating astrocytes from human-induced pluripotent stem cells (iPSC), followed by stimulation with microglial secreted factors, TNFα, IL-1α and C1q. This treatment promotes a reactive phenotype in astrocytes which permits testing of possible neuroprotective candidates. One family of potential candidates are cannabinoids. These are a group of compounds found in the Cannabis sativa L. plant. The two main plant-derived cannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD), both of which can easily cross the blood-brain barrier due to their high lipophilicity. The astrocytes were treated with various concentrations of CBD (+/- TNFα, IL-1α and C1q) to assess its potential to prevent astrocyte reactivity. Astrocyte reactivity profile was examined via RT-qPCR and ELISA. AlamarBlue and LDH cytotoxicity assays were also performed to assess cell viability. This is an ongoing study, but early results will be presented. So far, our data suggest that CBD alone does not affect astrocyte viability and we anticipate that when given with an inflammatory signal it can modulate astrocyte reactivity. Authors: Magdalena D. Imiolek1,2, Sarah F. Mc Comish1,2, Eric J. Downer1, Maeve A. Caldwell1,2 1Department of Physiology, School of Medicine, Trinity College Dublin, Dublin, Ireland 2Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin, Ireland

35. Patient-derived cellular models as tools to elucidate the pathophysiology of Hao-Fountain syndrome - Using iPS cell-based model systems to understand the pathophysiology of USP7 mutations

Janelle Stanton, Bernal Institute, University of Limerick

Synaptic plasticity (SP) plays a key role in the human ability to adapt to environmental input, along with the processes of learning and memory. Altered SP significantly contributes to neurological and psychiatric disorders, including Autism Spectrum Disorders (ASD). Mutations in essential proteins facilitating SP have also been identified in human patients with intellectual disabilities. Recently, loss of function mutations in ubiquitin-specific protease 7 (USP7, also called herpes virus-associated ubiquitin-specific protease, HAUSP), have been identified as disorder causing variants, specifically linked to Hao-Fountain syndrome, a neurodevelopmental disorder manifesting intellectual disability, ASD, and seizures. Located at chromosome 16p13.2, USP7 encodes a deubiquitinating proteolytic enzyme that can cleave multiple ubiquitin chain linkages. Previously, USP7 was shown to regulate the ubiquitination of proteins, including the MDM2-p53 pathway, important for DNA repair, transcription, and cancer. However, so far, the precise mechanisms how USP7 mutation cause the clinical phenotype on a cellular level are missing. In this collaborative project, using patient-derived human induced pluripotent stem cells in combination with omics approaches and targeted biochemical analyses, we aim to understand the functions of USP7 in neuronal development and SP by recapitulating neurodevelopmental processes using in vitro model systems.

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