Ollscoil na Gaillimhe
University of Galway

Ionad Néareolaíochta na Gaillimhe
Galway Neuroscience Centre

Galway Neuroscience Centre Annual Research Day

Tuesday 28th November 2023

Small Lecture Theatre (B001), Human Biology Building

Time	
09:30	**Dr. Michelle Roche** (*GNC Director)* Welcome to GNC Research Day
09:35	**Prof. Peter Doran:** *Director of Institute for Clinical Trials:* Opening the GNC Research Day
Session 1 Chair: Dr. Michelle Roche & Dr. Eoin McEvoy	
9:45	**Dr. Jeffrey Glennon** *Assistant Professor, School of Medicine, University College Dublin* **"Immune system control in neuropsychiatry"**
10:30	**Shane Crinion,** *PhD Candidate* **"GWAS of subphenotypes within Bipolar Disorder identifies new loci linked to psychosis"**
10:40	**Jacqueline Quirke,** *PhD Candidate* **"Prefrontal and cingulate effective connectivity and emotion inhibition in bipolar disorder"**
10:50	**Katie Healy**, *PhD Candidate* **"Sex dimorphism in pain-related behaviour in the rat hind limb ischemia-reperfusion model, and associated alterations in the endocannabinoid system"**
11:00	***Tea and Coffee Break & Poster Viewing (G001)***

Session 2 Chair: Dr. Siobhan McMahon & Daniela Costa	
11:30	**Dr. Becky Whay** *Vice President International / Professor of Sustainable Global Animal Welfare*
11:40	**Dr. Eoin McEvoy** *Assistant Professor in Biomedical Engineering, School of Engineering* **"Mechanobiology and active cell forces in cancer and immune-mediated diseases"**
12:10	**Duaa Jabrah,** *PhD Candidate* **"White Blood Cell Subtypes and Neutrophil Extracellular Traps Content as Biomarkers for Acute Ischemic Stroke Etiology"**
12:20	**Aodán Laighneach,** *PhD Candidate* **"The Effect of Post-Weaning Social Isolation and Chronic Celecoxib Administration on Gene Expression in the Mouse Hippocampus"**
12:30	**Shane O'Connell ,** *PhD Candidate* **"Shallow de-noising autoencoders for derivation of neuroimaging endophenotypes of Alzheimer's Disease"**
12:40	**Dr. Jamie Concannon** *Assistant Professor in Biomedical Engineering, School of Engineering* **"Experimental and computational analysis of brain tissue"**
13:10	***Lunch Break*** *Poster Session - Seminar Room (G001), Human Biology Building*

Session 3 Chair: Dr. Andrea Kwakowsky & Dr. Jamie Concannon	
14:30	**Prof. Yvonne Nolan** *Professor of Anatomy and Neuroscience, University College Cork* **"The role of gut microbiota and hippocampal plasticity in Alzheimer's disease: lessons from faecal microbiota transplantation studies"**
15:15	**Kaushik Narasimhan,** *PhD Candidate* **"Assessing biomaterial microspheres for sustained GDNF & BDNF delivery in the context of enhancing cell-based brain repair in the Parkinsonian rat brain"**
15:25	**Dr. Catalina Vallejo Giraldo** *Assistant Professor in Biomedical Engineering, School of Engineering* **"Towards cell mechanobiology in neural tissues"**
15:55	**Neuroscience Ireland Panel Discussion** *Prof Eilís Dowd, Prof Karen Doyle, Prof Dara Cannon, Daniela Costa* **"Neuroscience Ireland: Past, Present and Future"**
16:30	**Dr. Michelle Roche** *Prize-giving, meeting close*

The GNC thank Neuronal Signaling for their generous sponsorship of oral and poster prizes:

Speaker Bios

Dr. Jeffrey Glennon

Assistant Professor, School of Medicine, University College Dublin

Dr. Jeffrey C. Glennon is a neuroscientist based in University College Dublin linking experimental psychology to biological mechanisms with a track record in pharmaceutical industry and academic settings. This is centred around rule making / rule breaking processes in cingulate cortex that govern rational versus emotional decision making. As a translational neuroscientist, he seeks to implement basic and preclinical efforts into clinical practice relevant to patients. This work underlies current research into drug-able mechanisms in Huntington's disease, type I myotonic dystrophy, autism and insulin-signalling pathways in type II diabetes as new drug targets relevant to treatment-resistant obsessive compulsive disorder (OCD). It also underlies his interest in loss of inhibitory GABAergic prefrontal cortical control mechanisms in aggression / (anti)social behaviour and psychopathy. As a neurophysiologist / pharmacologist with both EU academic and industry experience, he has led as coordinator / lead-PI two consortia and led work packages on six others ranging in topic from autism, OCD, ADHD, conduct disorder, aggression, and Tourette Syndrome. He has been instrumental in developing novel robot based interventions in autism but his passion lies in linking -omics to both human and animal phenotypic and MRI information to gain new mechanistic insights. He is the chair of the Scientific Advisory Board of the EU Horizon 2020 CANDY consortium on autism and the incoming Section President of the Biomedical Sciences Section of the Royal Academy of Medicine in Ireland.

Prof. Yvonne Nolan

Professor of Anatomy and Neuroscience, University College Cork

Yvonne Nolan is a Professor in Anatomy and Neuroscience, Investigator in APC Microbiome Ireland and Vice Dean of Graduate Studies in the College of Medicine and Health at University College Cork. Yvonne graduated from NUI, Galway with a BSc (Hons) in Biochemistry, and a PhD in Neuropharmacology. She was a visiting scholar at McGill University Montreal, Canada and held postdoctoral positions in Trinity College, Dublin before her appointment to the Department of Anatomy and Neuroscience, University College Cork.

Research in Professor Nolan's team investigates the impact of inflammation and modifiable lifestyle factors such as exercise, stress and diet on memory and mood though the lifespan, at adolescence, middle age and in Alzheimer's disease. The role of the gut microbiome and hippocampal neurogenesis is of particular interest. To date she has supervised >40 PhD/MSc (research)/postdoctoral researchers as well as numerous visiting and undergraduate students. She was awarded UCC's Research Supervisor of the Year Award in 2016. She has secured funding as lead PI from Science Foundation Ireland, Reta Lila Weston Trust, Marigot Ltd, Irish Research Council and Vasogen Inc., Canada and was consortium lead on a recent European Centres of Excellence in Neurodegeneration (COEN) project. She is a member of the Executive Management Team of UCC Futures: Future Ageing and Brain Science.

Dr. Eoin McEvoy

Assistant Professor in Biomedical Engineering, School of Engineering

Dr McEvoy's research group focuses on the development of novel theoretical, experimental, and computational models to explore the feedback between cell mechanics and tissue remodelling for the prediction of disease progression, with a specific interest in cancer mechanobiology and immune-mediated disease. Eoin completed his PhD in cellular biomechanics at the University of Galway, and subsequently worked as a postdoctoral researcher at the University of Pennsylvania, investigating how the tumour microenvironment guides cancer metastasis. In 2020, he returned to the University of Galway as an Assistant Professor in Biomedical Engineering. He was recently been awarded an ERC Starting Grant (2023) to investigate the mechanobiology of tumour growth and therapy resistance.

Dr. Jamie Concannon

Assistant Professor in Biomedical Engineering, School of Engineering

Dr. Jamie Concannon is an Assistant Professor in Biomedical Engineering at the University of Galway. His research interests include medical image based computational modelling, soft-tissue biomechanics, and device-tissue interactions. Currently, his group's research focuses on fundamental, clinical and translational investigations of the response of brain tissue to deformation and injury.

Dr. Catalina Vallejo Giraldo

Assistant Professor in Biomedical Engineering, School of Engineering

Dr. Catalina Vallejo-Giraldo is an early career lecturer at the Dept. of Biomedical Engineering, University of Galway. Her research interests are at the intersection of biomaterials, brain mechanobiology and medicine. Catalina's international training has given her the experience of interacting with and leading multidisciplinary teams that involve members from academia (Antioquia School of Engineering, Colombia, Imperial College London, UK, Cardiff Univ., UK and University of Galway, Ireland), industry (Galvani Bioelectronics, UK, Neurent Medical, Ireland) and the clinic (Mayo Clinic, USA). To date, Dr. Vallejo Giraldo has published more than 22 refereed papers in high impact factor international journals, 3 refereed book chapters, 16 conference proceedings, and one pre-print, with a h-index 16**.** Dr. Vallejo Giraldo has received nine prestigious academic awards, including the Donegan Medal from the Royal Academy of Medicine Ireland, (RAMI, BME Section) and Trainee Award at the 10th World Biomaterials Congress for her contribution to the field of neuronal design of biomaterials, tissue engineering and brain mechanobiology.

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Neuroscience Ireland Panel Discussion

Prof. Eilís Dowd

Prof. Karen Doyle

Prof. Dara Cannon

Daniela Costa

The aim of the Society is to advance research and education in the neurosciences in Ireland, and to represent Irish neuroscience researchers both nationally and internationally. NSI has a membership in the region of 200 scientists and clinicians, and represents Ireland on the Governing Council of the Federation of European Neuroscience Societies (FENS).

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List of Poster Presentations

Seminar Room G001

Odd number posters presented at 13:10-13:40
Even number poster presented at 13:40-14:20
(Please stand by your poster at this time)

Number	Name	Poster title
1	Alba Diego	Effect of repeated restraint stress and incisional injury on depression- and anxiety-related behaviour in rats and associated alterations in endocannabinoid levels
2	Andrea Fernandes	Neuroanatomical network connectivity underlying memory performance in euthymic bipolar disorder
3	Aoife O'Connell	Investigating the Spatio-Temporal Hippocampal Neuronal Activity Post β-Amyloid Exposure
4	Ariadni Bella	Repeated restraint stress enhances and prolongs mechanical and thermal post-surgical hypersensitivity and increases C3 gene expression in the ipsilateral spinal cord of male rats
5	Cansu Sahin	Albumin is significantly expressed 'blue' in acute ischemic stroke clots and negatively associated with the severity of stroke
6	Chiara Di Marino	Behavioural characterisation of a model of chemotherapy-induced neuropathic pain in rats of both sexes
7	Daniela AD Costa	Defining selective neuronal vulnerabilities in human/rat tissue and hNPCs-derived cortical neurons in an in vitro model
8	Daniele Fusco	Sex differences in chronic pain-related anxiety: identifying the monosynaptic inputs of the locus coeruleus to basolateral amygdala pathway
9	Deema Ali	MEF2C Dysregulation and its Association with Schizophrenia and Cognitive Function in Human Neural Cells

10	Dijana Ostojic	The challenges of Machine Learning models in psychiatry
11	Evie Doherty	Brain Volume and Inflammatory Markers: How Childhood Trauma Influences Social Cognitive Functioning in Patients with Schizophrenia and Healthy Participants
12	Giulia Comini	A twenty weeks assessment of the effect of a GDNF and BDNF-enriched collagen hydrogel on the differentiation of iPSC-derived dopaminergic progenitors in cyclosporine immunosuppressed rats.
13	Jacqueline Quirke	Is Neural Network Functional Dysconnectivity a Trait Feature of Bipolar Disorder & Cognitive Performance?
14	Jonathan Costello	Differential effects of TLR3 activation on social behaviour and prefrontal cortical inflammatory gene expression in the valproic acid model of autism: a role for the endocannabinoid system?
15	Liadhan Farrell	Investigating the Genetic Basis of Cognitive Function
16	Maria Redmond	Characterisation of Anxiety- and Depression-Related Behaviour and the Endocannabinoid System in the Rat Hindlimb Ischemia-Reperfusion Model of Chronic Wounds
17	Mary Hopkins	Endocannabinoid-Associated Alterations in Behavioural and Electrophysiological Parameters of a Rat Model of Low Back Pain
18	Matthew Stevens	Measuring Emotion Recognition correlates in Schizophrenia: Sensitivity and specificity of unbiased hit rates.
19	Mia Casburn	Electrophysiological and pupillary responses to emotional congruency
20	Nazan Guner Sak	Platelet-derived growth factor b is highly expressed in the red blood cell-rich regions of acute ischemic stroke clots and is positively related to stroke severity

21	Patrick Hurley	Towards a microfluidic model of ectopic follicle-like structures in multiple sclerosis
22	Saahithh Redddi Patlola	Altered mRNA expression and elevated Toll-like receptor and cytokine activity in patients with schizophrenia.
23	Bianca Castelli	Measurement of Chitinase-3-Like-1 in Serum and Saliva in a Multiple Sclerosis Cohort
24	Tommy Patton	Development of novel, clinically-relevant rat model of Parkinson's disease via sequential exposure to AAV-α-synuclein and FN075
25	Wenyi Liu	C-reactive protein expression in acute ischemic stroke blood clots
26	Ying Zhai	Investigating the effect of caffeine on β-amyloid induced neurotoxicity in mouse primary hippocampal cultures
27	Malgorzata Dabrowska	Organotypic cortical brain slices from adult rats as an ex-vivo study platform for neurodegenerative diseases
28	Shima Shapoori	Advancing personalized medicine in progressive multiple sclerosis: exploring biomarkers and point-of-care testing
29	Ciara Shortiss	Lentiviral Vectors in combination with Biomaterial Scaffolds for Spinal Cord Injury Regeneration

Oral Presentation Abstracts

1. **Speaker**: Shane Crinion

Title: GWAS of subphenotypes within Bipolar Disorder identifies new loci linked to psychosis

Abstract

Neuropsychiatric disorders (NPDs) are clinically and genetically heterogeneous and have shared and distinct genetic etiologies. GWAS of subphenotypes will improve representation of NPD heterogeneity. GWASs of subphenotypes (psychosis and unipolar mania) within bipolar disorder (BD) were conducted using RICOPILI, with standard Psychiatric Genomics Consortium (PGC) procedures. QC was performed to remove low powered cohorts (N<30), to remove low frequency variants by cohort, and by INFO score for meta-analysis. LD score regression was also performed to assess the inflation and heritability from the GWAS meta-analysis. Meta-analysis results using data from 33 cohorts (N cases = 8094, N controls = 36,611) we identify three genome-wide significant loci linked to psychosis within BD. SNP-h2 was calculated as 0.21 (SE=0.02) and intercept as 1.02 (p = 0.014). Results include SNPs within the range of TRANK1, a known BD gene, and KCNB1, previously linked to epilepsy and autism. No significant loci were identified for unipolar mania. Low power is likely to have limited the ability to identify associations and led to unstable estimates for LD score regression. Further analyses will be performed to assess other subphenotypes within BD and other NPDs (schizophrenia and major depression).

2. **Speaker:** Jacqueline Quirke

Title: Prefrontal and cingulate effective connectivity and emotion inhibition in bipolar disorder

Abstract

Emotion inhibition, the ability to ignore emotional information while focusing on a cognitive task, is impaired bipolar disorder (BD). Based upon fMRI findings, the cingulate and prefrontal cortex are differentially connected in BD and correspond to emotion inhibition deficits (Wessa 2009). Effective connectivity studies, which explain the dynamic, causal effect neural regions exert over others, may increase our neurobiological understanding of altered networks underlying emotion inhibition deficiencies in BD. Here, we used dynamic causal modelling (DCM) to assess effective connectivity differences in emotion inhibition in BD versus healthy controls (HC). Participants with BD met DSM-V criteria for type-I or -II BD. Subjects underwent 3T structural and functional MRI scanning during an emotion inhibition task. Regions included the anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), dorsolateral PFC (dlPFC), and ventrolateral PFC (vlPFC; Wessa 2009). The causal order of the timeseries between regions during emotion inhibition was examined using Bilinear DCM and group-level Bayesian Model Selection (SPM12, DCM12.5, Matlab R2022b). Regions with the highest probability of explaining the fMRI data were compared between groups (SPSSv27). The BD (n=33) and HC (n=49) groups did not differ in age (U=790.50, p=0.87) or gender ($\chi 2$=0.35, p=0.56). Overall, the influence of the PCC on the dlPFC explained the neural activity detected during emotion inhibition, and in BD and HC separately, there was no significant difference in causal order (U=758, p=0.63). Heretofore, the dynamic causal order of regional involvement during emotion inhibition was not known, and these data implicate the PCC in influencing dlPFC activation.

3. **Speaker:** Katie Healy

Title: Sex dimorphism in pain-related behaviour in the rat hind limb ischemia-reperfusion model, and associated alterations in the endocannabinoid system.

Abstract

Ischemia-reperfusion injury (I/R) can contribute to the formation of chronic wounds and persistent pain in conditions like complex regional pain syndrome type-1. The endocannabinoid system (ECS) is involved in pain modulation, and in ischemic preconditioning, an endogenous protective mechanism against I/R. This study characterised pain-related behaviour in the rat hind limb I/R (HLIR) model and investigated potential alterations in the ECS. Male and female Sprague-Dawley rats (220-350g, n=11-12/group) underwent HLIR or sham procedure on the left hind limb. Mechanical, cold and thermal (heat) hypersensitivity were quantified in the ipsilateral and contralateral hind paws at baseline, up to post-HLIR day 29, via electronic von Frey, acetone drop and Hargreaves' tests. The affective component of pain was assessed using the place-escape avoidance paradigm (PEAP) on post-HLIR day 23. Levels of endocannabinoids 2-AG and AEA, and N-acylethanolamines PEA and OEA was analysed in discrete brain regions via LC-MS/MS. Persistent cold and mechanical hypersensitivity were observed in male but not female I/R rats vs sham post I/R injury ($p<0.05$). Both male and female HLIR rats had higher percent positive response to ipsilateral (vs sham) paw stimulation in the PEAP ($p<0.05$). Levels of PEA in the thalamus were higher in female I/R rats vs sham ($p<0.05$). These results indicate sexual dimorphism in persistent pain-related behaviour post I/R. Analysis of discrete brain regions indicates no alterations in levels of AEA, 2-AG or OEA at 30 days post I/R, however further investigation into other potential ECS alterations is warranted.

4. **Speaker:** Duaa Jabrah

Title: White Blood Cell Subtypes and Neutrophil Extracellular Traps Content as Biomarkers for Acute Ischemic Stroke Etiology

Abstract

Lymphocytes, macrophages, neutrophils, and neutrophil extracellular traps (NETs) associate with stroke risk-factors and form a thrombus through different mechanisms. We aim to investigate the total white blood cells, WBC-subtypes, and NETs composition in acute ischemic stroke (AIS) clots to identify possible etiological differences and whether procedural passes and thrombolysis might affect NETs composition to help us further understand the process of thrombosis that leads to AIS. AIS clots from 100 cases each of large artery atherosclerosis (LAA), cardioembolic (CE) and cryptogenic etiology were collected per-pass as part of the RESTORE-registry. Martius Scarlet Blue stain used to identify the main histological clot components. Immunohistochemical staining was used to identify neutrophils, lymphocytes, macrophages, and NETs patterns. Cellular and histological components were quantified using Orbit Image Analysis software. LAA clots had more RBCs (48.2[68-31]) compared to CE (38.3 [54-20]) and cryptogenic clots (42.3 [56-21]) and fewer WBCs (2.8[5-2]vs 4.6[7-2] and 3.6[7-1.3]). LAA clots had more lymphocytes and cryptogenic clots had fewer macrophages than other etiologies. Most significantly, CE clots showed higher expression of neutrophils and extracellular web-like NETs (7.5 [12-3], 1[2-0.7]) compared to LAA (5.5 [9.4-3.4], 0.6[1.4-0.4]) and cryptogenic clots (5[8-2], 0.9[1.7-0.5]). A significantly higher distribution of web-like NETs was found around the periphery of CE clots while a mixed distribution was observed in LAA clots. No effect of procedural passes or thrombolysis on NETs expression or distribution. The difference in neutrophil and NETs expression in clots from different etiologies may provide insight into the mechanism of clot formation.

5. **Speaker:** Aodán Laighneach

Title: The Effect of Post-Weaning Social Isolation and Chronic Celecoxib Administration on Gene Expression in the Mouse Hippocampus.

Abstract

Two risk factors for neuropsychiatric disorder are early life stress and chronic inflammation. Here we model these factors in mice using post-weaning social isolation (SI) and chronic anti-inflammatory administration. We investigate how these factors alter gene expression in the hippocampus and investigate the biological relevance of these changes. A total of 32 female C57Bl6 mice were split between chronic celecoxib-treated (CEL) and vehicle-treated controls. Half of the animals were also subject to post-weaning SI from postnatal day (PD) 21 for a total of 40 days for an n = 8 per group. RNA was extracted from the hippocampus and subject to paired-end RNA-seq. Differentially-expressed genes (DEGs) were defined at FDR < 0.05 using DEseq2. SI induced a total of 55 DEGs in the hippocampus, while CEL administration induced 355 DEGs. Five genes (Adamtsl5, Neurod1, Hrasls, Kcnab3, Cdh6) were differentially -expressed by both factors. The most significantly-enriched GO terms for SI DEGs were gamma-aminobutyric acid:sodium symporter activity (GO:0005332), calcium ion binding (GO:0005509). For CEL administration, the top GO terms were neuron part (GO:0097458), neuron projection (GO:0043005) and locomotory behaviour (GO:0007626). Neither set were enriched for common risk genes contributing to neurodevelopmental or neuropsychiatric disorder. When cell type enrichment analysis was performed, SI-induced DEGs were enriched in a population of astro-ependymal cells, while CEL-induced DEGs were enriched in four populations of medium spiny neurons (MSNs). Overall, both factors induced transcriptomic changes in the brain. These changes were related to neurodevelopment and some showed concordance with human psychiatric disorders through cell type enrichment analysis.

6. **Speaker:** Shane O'Connell

Title: Shallow de-noising autoencoders for derivation of neuroimaging endophenotypes of Alzheimer's Disease

Abstract

Alzheimer's disease (AD) is a debilitating neurodegenerative condition marked by memory loss, cognitive impairment, and large patterns of brain atrophy. To date, several patterns of neuroanatomical variation have been repeatedly observed, including temporal lobe volumetric reductions and ventricular enlargement. However, such observations have historically focused on regions in isolation, which is likely not reflective of AD neuroanatomical manifestations. Additionally, such relationships have been described in linear terms, which may be a prohibitive modelling assumption. Here, we present the use of interpretable unsupervised de-noising autoencoders to model the neuroanatomical variation of 533 AD participants and controls from the Alzheimer's Disease Neuroimaging Initiative. We condition our latent node values on AD status to determine the node with the most statistically significant differential values in AD participants relative to controls (adj.P = 4e − 6). Further, we investigate the genetic properties of our discriminative node by carrying out a genome-wide association (GWA) study. Results from this association study identify three significant loci located in long non-coding RNA transcripts (RP11-239H6.2, RP11-509J21.1, and RP11-707M1.1) aligning with an emerging body of literature linking non-coding RNA expression to AD progression. We further demonstrate that the regions with the largest contribution to node output are consistent with previous neuroanatomical findings, including atrophy in several temporal gyrus structures. This method offers a

flexible non-linear modelling approach to deriving composite biomarkers of neuropsychiatric phenotypes and examining their genetic properties.

7. **Speaker:** Kaushik Narasimhan

Title: Assessing biomaterial microspheres for sustained GDNF & BDNF delivery in the context of enhancing cell-based brain repair in the Parkinsonian rat brain.

Abstract

Cell replacement-based therapeutic approaches for Parkinson's disease has long faced hindrance by the poor cell survival post-transplantation, in part due to growth factor deprivation experienced in the adult, diseased brain relative to their pre-implantation levels in the embryonic brain (for primary cell transplants) or in tissue culture (for stem cell-derived transplants). In this context, we investigated the suitability of PEGDA-SPA cryogel microcarriers (MCs) (loaded with hGDNF or hBDNF) as potential biomaterial systems for neurotrophin (NT) delivery. Initial in vitro assessment of their morphology was done by microscopy, followed by NT loading efficiency and kinetics of NT release (using ELISA), and their cytocompatibility (using AlamarBlue® assay). Preliminary early in vivo assessment of their biocompatibility and NT delivery, retention & release profiles was done (using IHC). In vitro assessment confirmed their spongy spherical structure, and their capability for loading and sustained release of NTs, as well as their cytocompatibility with neurons (SH-SY5Y cell line), microglia (HMC3 cell line), and trophic effect in primary neural (E14 VM cell) cultures. In vivo assessment confirmed their biocompatibility, and their intact presence in rat brains even at day 14 post-implantation, as well as their ability to have NTs retained within the MC structure, and released into the surrounding brain tissue even at day 14 post-implantation. These findings offer promising potential of the MCs for sustained delivery of NTs to engrafted cells in the context of enhancing cell-based brain repair in PD.

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Poster Presentation Abstracts

1. **Presenter:** Alba Diego

Title: Effect of repeated restraint stress and incisional injury on depression- and anxiety-related behaviour in rats and associated alterations in endocannabinoid levels

Abstract

The endocannabinoid system (ECS) has a role in the modulation of both stress and nociception. However, both the effect of chronic stress on affective behavioural responding post-surgery and the role of the ECS in stress-induced exacerbation of post-surgical pain warrant further study. Aim: Investigate the effect of restraint stress (RRS) and hind paw incisional injury on pain, depression- and anxiety-related behaviour in rats, and its effect on the ECS. Male Sprague-Dawley rats underwent either RRS (6h per day) or no stress (noRRS) for 21 days. Paw withdrawal thresholds were assessed using Von Frey and Hargreaves tests. Anxiety- and depressive-related behaviours were assessed using open field (OFT), elevated plus maze (EMP) and sucrose splash (ST) tests. Spinal cord and brain regional levels of endocannabinoids and N-acylethanolamines were analysed via LC-MS/MS. RRS rats exhibited a depressive-like phenotype with higher duration of partial and total immobility behaviours in FST1 and lower duration of swimming in both FST1 and FST2 compared to noRRS. RRS+Incision showed lower thermal and mechanical hypersensitivity thresholds compared to the noRRS+Incision group. No significant differences between groups were found in the OFT, EPM, or ST. Finally, surgery and stress-related alterations were found in spinal cord and brain regional endocannabinoid and N-acylethanolamine levels. RRS prior to incisional injury elicits a depressive-like phenotype in male rats, and enhances and prolongs surgery-induced somatosensory hypersensitivity.

2. **Presenter:** Andrea Fernandes

Title: Neuroanatomical network connectivity underlying memory performance in euthymic bipolar disorder

Abstract

Aberrant intrinsic network connectivity and impaired visuo-spatial memory performance has been demonstrated in euthymic Bipolar Disease (BD) patients (Bellani et al., 2020; Brady Jr. et al., 2017; McPhilemy et al., 2020; Olley et al., 2005; Rubinsztein et al., 2000). This study aims to investigate the relationship between intrinsic connectivity and memory performance in euthymic BD patients compared to healthy controls (HC). All participants underwent a 3T structural and resting-state fMRI. Thirty-eight resting-state average components were decomposed into 16 independent components via independent component analysis (ICA, GIFT software) (Calhoun et al., 2001) and sorted into 6 resting-state networks. Visuo-spatial memory was assessed utilizing subtest of the CANTAB (Cambridge Cognition, 2018). Interaction effects between intra-network connectivity, memory performance and diagnosis was assessed with a MANCOVA accounting for age and gender (GIFT) (Allen et al., 2011). Memory was impaired in the BD group (n=34, mean age ±SD, 43±2) relative to the controls (n=45, 41±2, Pillai's trace=2.613 p=.03). Significant differences were observed in the functional connectivity involving all components between groups. Similarly, altered intra-network connectivity of the medial and lateral fronto-parietal related to visuo-spatial memory performance overall in BD compared to controls. Episodic memory performance was also associated to significant differences in the intra-network connectivity of the midcingulo-insular network between groups. A main effect of diagnosis was detected in the intra-network connectivity of the midcingulo-insular, lateral and medial fronto-parietal networks. Multivariate analysis suggested a diagnosis effect on memory performance (F=2.61, p=0.03). These memory impairments and connectivity alterations in euthymic states may reflect

challenges in processing, encoding and stimulus inhibition (Shing et al., 2010), suggesting the importance of examining the intrinsic connectivity underlying cognition in this population.

3. **Presenter:** Aoife O'Connell

Title: Investigating the Spatio-Temporal Hippocampal Neuronal Activity Post β-Amyloid Exposure

Abstract

Alzheimer's disease is a progressive neurodegenerative disease, accounting for ~70% of dementia cases. The cognitive decline seen in Alzheimer's disease patients is accompanied by a disrupted neuronal network and an excitatory/inhibitory neurotransmission imbalance, especially in the hippocampus. These effects are hypothesised to be caused by β-amyloids' neurotoxicity which is mediated by changes in the excitatory (glutamate) and inhibitory (GABA) neurotransmitter systems. However, how β-amyloid affects the spatio-temporal functional activity of the excitatory/inhibitory neuronal network in the mouse hippocampus remains unclear. The Kwakowsky laboratory has previously shown that β-amyloid alters GABAergic tonic inhibition through the α5-GABAA receptor. α5-GABAA receptors are activated by low GABA levels generating tonic inhibition, which is involved in learning and memory. β-amyloid can increase GABA levels and upregulate α5-GABAA receptor expression resulting in increased receptor activation, tonic inhibition and dysregulated the excitatory/inhibitory balance. This causes network dysfunction and cell death which may contribute to cognitive decline. Thus, α5-GABAA receptors are potential targets for disease treatment. When treated with α5IA, an inverse agonist of α5-GABAA receptors, tonic inhibition and cognitive abilities were restored in β-amyloid injected mice. The neuronal mechanism underlying this cognitive improvement remains unknown. Therefore, this project plans to advance our understanding of the neuronal changes induced by Aβ and investigate if a novel therapeutic strategy can reverse these changes. To do this mouse hippocampal brain slices will be utilized for in vitro electrophysiology. Spatio-temporal electrical activity will be recorded using microelectrode arrays following Aβ administration.

4. **Presenter:** Ariadni Bella

Title: Repeated restraint stress enhances and prolongs mechanical and thermal post-surgical hypersensitivity and increases C3 gene expression in the ipsilateral spinal cord of male rats

Abstract

Pre-surgical stress is recognised as a risk factor for the development of chronic post-surgical pain. The neuroimmune system plays a key role in pain, depression and their interactions. Here, we investigated the effect of repeated restraint stress on post-surgical hypersensitivity and the expression of spinal neuroinflammatory markers in a model of chronic stress-induced enhancement of post-surgical pain. Male 6-week-old Sprague-Dawley rats were exposed to repeated restraint stress (RRS, 6h/day for 21 days) or no restraint stress (handling). Behavioural despair was assessed on day 21 (FST1) and 22 (FST2) using the Forced Swim Test, after which animals underwent paw incision or sham surgery. Mechanical and thermal hypersensitivity (electronic Von Frey [eVF] and Hargreaves [HG] test, respectively) were assessed periodically for 17 days post-surgery, while affective behaviour was assessed on days 19 (Elevated Plus Maze, Open Field) and 21 (Splash Test). On post-surical days 23 and 26 when hypersensitivity had resolved, naloxone (3 mg/kg) was administered to the rats and paw withdrawal thresholds and latencies were determined over a 2h period. Expression of Itgam, Gfap, C3, S100a10, Bdnf, Glt1 and Glast was evaluated in the dorsal horn using RT-qPCR. RRS exposure resulted in increased immobility and decreased swimming in FST1, but had no effect on baseline mechanical and thermal sensitivity. In addition, RRS exacerbated ipsilateral mechanical and

thermal hypersensitivity on days 1-5 post-surgery, and prolonged both for 1-2 weeks. No effect of surgery or stress was observed on affective behaviour. In addition, RRS prolonged naloxone-mediated latent sensitization to thermal stimuli for 90 minutes post-injection. Naloxone failed to reveal latent sensitization to mechanical stimuli. Lastly, RRS increased the expression of C3, a marker of proinflammatory astrocytes, in the ipsilateral dorsal horn of incised animals. RRS increased despair-like behaviour and enhanced post-surgical mechanical and thermal post-surgical hypersensitivity. Moreover, RRS resulted in prolonged opioid-mediated latent sensitization to thermal stimuli, as well as elevated levels of pro-inflammatory astrocytes in the ipsilateral dorsal horn of animals exposed to surgery.

5. **Presenter:** Cansu Sahin

Title: Albumin is significantly expressed 'blue' in acute ischemic stroke clots and negatively associated with the severity of stroke

Abstract

Studies have shown that low serum level of albumin is a blood-based predictor associated with poor clinical outcome following Acute Ischemic Stroke (AIS). In plasma, albumin is known to decrease platelet aggregation and has an antithrombotic effect. This study aimed to investigate the expression of albumin in AIS clot subsets based on histopathology, its relationship with other clot components, and stroke severity. 300 blood clots were analysed in the Clotbase International registry. Clots were stained with Martius Scarlett Blue (MSB), which differentiates the major clot components. Some clots were seen to have an unusual 'blue' appearance that was not related to any usual clot component. In this study, 48 representative clot samples (12 from each group, RBC-rich (>45% RBCs), fibrin-rich (>45% fibrin), platelets/other-rich (>45% platelets confirmed by anti-CD42b immunohistochemistry (IHC)) and a final group confirmed as other, referred to as blue clots) were selected to investigate the differences between clots. IHC was performed using anti-albumin (ab207327, abcam). Clot components and albumin were quantified via Orbit Image Analysis. Non-parametric statistical tests were used. Clots were grouped according to the results from MSB. Albumin was significantly higher in blue clots compared to RBC-rich ($p=0.001$) and platelet-rich ($p=0.004$) but not fibrin-rich ($p=0.2$) clots. It was higher in the clots than mild stroke cases compared to both moderate and severe stroke ($p=0.007$ and $p=0.02$). Regions identified in blue clots on MSB contain high expression levels of albumin. The involvement of albumin in thrombus formation needs to be further explored.

6. **Presenter:** Chiara Di Marino

Title: Behavioural characterisation of a model of chemotherapy-induced neuropathic pain in rats of both sexes

Abstract

Paclitaxel is one the most widely used chemotherapeutic agents against cancer, however, it can induce chronic neuropathic pain in up to 80% of human patients, as well as other adverse effects. Evidence suggests that the prevalence of chemotherapy-induced neuropathic pain is higher in women compared to men. The neurobiological mechanisms underlying this sex difference are poorly understood and may be advanced with the aid of preclinical models. Therefore, the aim of this study was to characterise pain-, cognition-, anxiety- and depression-related behaviour in male and female rats following Paclitaxel administration. Forty male and female Sprague-Dawley rats (N=10 per group) received intraperitoneal injections of Paclitaxel (2 mg/kg in 1:1:18 ethanol:cremophore:saline) or vehicle on four alternate days.

Von Frey, Acetone Drop and Hargreaves' were used to assess sensitivity to mechanical, cold and heat stimuli, respectively, pre-Paclitaxel administration and over days 7-69 post-first Paclitaxel administration. Animals were exposed to cognition-related tests during week 5 and 6, anxiety-related tests during week 8, and depression-related tests during week 9 and 10 post-Paclitaxel administration. The results from these tests suggest Paclitaxel induced hypersensitivity to mechanical and cold stimuli, but not heat, post-treatment in both sexes at each time point analysed, compared with vehicle-treated controls. Female rats exhibit greater mechanical hypersensitivity at discrete time points post-Paclitaxel administration compared to male rats. Paclitaxel did not elicit alterations in the other behaviours with the tests and time points studied here. Studies are ongoing to investigate the neurobiological mechanisms that may underlie the sex dimorphism in Paclitaxel-induced mechanical hypersensitivity observed.

7. **Presenter:** Daniela AD Costa

Title: Defining selective neuronal vulnerabilities in human/rat tissue and hNPCs-derived cortical neurons in an in vitro model

Abstract

Chronic neuronal degeneration is the prime substrate of cognitive abnormalities in progressive multiple sclerosis (PMS). In MS lesions, cortical demyelination is sustained by deficient remyelination mechanisms, and its extent may be determined by meningeal inflammation, further correlating with neuronal damage and loss. Moreover, pathological changes are widespread across the upper cortical layers, with heightened vulnerability of Cux2-, RORβ-, PV-expressing pyramidal neurons (PNs) and SST-expressing interneurons (INs). Thus, labelling and tracking cortical neuronal subtypes may provide invaluable data for the development of improved models of PMS-like pathology. We therefore aimed to establish in vitro human models of excitotoxicity, with particular focus on neurons from layers II/III and V. To facilitate the monitoring of different cortical cell populations, a panel of antibodies against 14 cortical neuron markers was tested and validated in rat and human (non-MS) paraffin-embedded tissue, using colorimetric staining. In parallel, human stem cell-derived cortical neurons were obtained via small molecule-induced differentiation. The cortical cultures were characterized by their neuronal heterogeneity at 24 days in vitro after the neuronal progenitor (NPC) stage. Immunocytochemistry allowed the evaluation of the relative expression of PNs and INs, accounting for approximately 20% and 55% of the cell population, respectively. Full validation of cortical markers revealed the expression of mixed cortical neurons, including the upper layer cortical subpopulation Cux2. To test neuronal vulnerability to excitotoxicity, NPC-derived monocultures were treated with 1 mM glutamate for 24h and axonal damage was screened using the antibodies validated in human paraffin tissue.

8. **Presenter:** Daniele Fusco

Title: Sex differences in chronic pain-related anxiety: identifying the monosynaptic inputs of the locus coeruleus to basolateral amygdala pathway

Abstract

The Locus Coeruleus (LC) is a small brainstem nucleus that represents the main source of noradrenaline within the entire CNS. This nucleus plays an active role in the modulation of chronic pain and its related psychopathologies. Some recent preclinical studies, using a DREADDs-based approach in a neuropathic pain model, have shown that the hyperactivation of the noradrenergic LC neurons projecting to the basolateral amygdala (BLA) leads to an anxiety-like phenotype. The aim of this study was to identify the brain regions that send monosynaptic inputs to the LC-BLA pathway and detect potential neuroanatomical differences

between sexes. The cTRIO approach (cell-type-specific tracing of the relationship between input and output) was used to evaluate the inputs to the LC within the LC-BLA pathway in male and female B6.129X1-Th tm1(cre)Te/Kieg (TH-Cre) transgenic mice (N=8). A histological study was performed to verify and quantify the expression of mCherry+ and GFP neurons (starter cells) in the LC and GFP+ neurons projecting to the LC-BLA pathway (input cells). Both sexes showed the highest input density in the caudal regions of the rostral axis (bregma -6.12mm to -3.80mm). Specifically, in both sexes, a high number of inputs cells were observed from the gigantocellularis nuclei at the pons level and from the raphe and PAG nuclei at the midbrain level. These results suggest that caudal regions would presumably be more involved in upstream modulation of LC-BLA pathway activity. It would be interesting to assess whether these inputs are activated differently in males and females after stressful/painful stimuli.

9. **Presenter:** Deema Ali

Title: MEF2C Dysregulation and its Association with Schizophrenia and Cognitive Function in Human Neural Cells

Abstract

Myocyte Enhancer Factor 2C (MEF2C) is a transcription factor that plays a crucial role in neurogenesis and synapse development. Genetic studies have identified MEF2C as a gene that influences cognition and risk for neuropsychiatric disorders, including autism spectrum disorder (ASD) and schizophrenia (SCZ). Here, we investigated the involvement of MEF2C in these phenotypes using human-derived neural stem cells (NSCs) and induced neurons (iNs), which represented early and late neurodevelopmental stages. For these cellular models, MEF2C function had previously been disrupted, either by direct or indirect mutation, and gene expression assayed using RNA-seq. We integrated these RNA-seq data with MEF2C ChIP-seq data to identify dysregulated direct target genes of MEF2C in the NSCs and iNs models. Several MEF2C direct target gene-sets were enriched for SNP-based heritability for intelligence, educational attainment and SCZ, as well as being enriched for genes containing rare de novo mutations reported in ASD and/or developmental disorders. Analysis of single-cell RNA sequencing data revealed that several excitatory glutamatergic neurons in the hippocampus and cortex, including deep layer pyramidal cells, CA1 principal cells, and entorhinal cortex, were enriched for MEF2C direct-target genes. Overall, our results suggest that genes dysregulated as a consequence of either direct or indirect MEF2C disruption contribute to SCZ development and cognitive function from early stages of neurodevelopment. These genes are involved in a wide range of biological processes including neural/glial cell differentiation, protein modification and catabolism in NSCs, as well as mitochondrial function and energy production in iNs.

10. **Presenter:** Dijana Ostojic

Title: The challenges of Machine Learning models in psychiatry

Abstract

Machine learning (ML) offers the opportunity to enhance and potentially revolutionise the diagnosis, treatment and comprehension of psychiatric disorders. ML focuses on the development of computer systems that are able to learn the patterns in datasets and make educated guesses based on the greatest probability without being explicitly programmed to do so (Panat & Kumar, 2019).

The current review provides an in-depth examination and offers practical guidance of the challenges encountered in the application of ML models in psychiatric research. The challenges discussed in this review include the curse of dimensionality, data quality issues, black box problem, hyperparameter tuning, external validation, class imbalance, and data representativeness issues. These challenges are particularly critical in the context of psychiatry as it is expected that researchers will encounter these issues during the stages of ML model development and deployment. Practical solutions and best practices are provided to effectively mitigate the outlined challenges. These recommendations are of great importance as they can improve reliability and interpretability of the prediction models in psychiatry.

In summary, this review provides a comprehensive overview of the common challenges faced during the development and validation of ML models. By addressing these issues, it aims to facilitate the integration of ML into psychiatric research and practice in order to provide reliable models that perform exceptionally well on the new, unseen datasets drawn from the population of interest.

11. **Presenter:** Evie Doherty

Title: Brain Volume and Inflammatory Markers: How Childhood Trauma Influences Social Cognitive Functioning in Patients with Schizophrenia and Healthy Participants

Abstract

Exposure to childhood trauma has been repeatedly linked to impaired social cognition in both clinical and non-clinical populations, including those with schizophrenia. Investigations have shown that this relationship is mediated by immune response involving proinflammatory cytokines, interleukin-6, C-reactive protein, and tumour necrosis factor alpha. Early-life adversity has also been linked to grey matter atrophy in the amygdala, hippocampus, and anterior cingulate cortex. These neural alterations also appear to partially mediate the relationship between childhood trauma and social cognitive dysfunction. However, the mechanism by which these alterations mediate the association has not yet been explored. Here, we sought to examine whether a combined immune response measure (IL-6, CRP, TNF-α) and brain structural alterations (global grey matter, amygdala, hippocampus, anterior cingulate cortex) sequentially mediate the association between childhood trauma and emotion recognition. The sample included 188 schizophrenia patients (n= 44) and healthy individuals (n= 144). Social cognition was assessed using the CANTAB emotion recognition task, while the childhood trauma questionnaire measured early-life adversity. Cytokine levels were obtained from plasma and brain volumes were assessed using T1-weighted structural magnetic resonance imaging. In line with previous research, we observed that immune response mediated the association between childhood trauma and emotion recognition. We also found that global grey matter atrophy mediated this relationship. No sequentially mediating effects of the immune response and brain volumes on the association were observed. We conclude that the mediating roles of immune response and grey matter in the relationship between early-life adversity and social cognition occur independently and not relatedly.

12. **Presenter:** Giulia Comini

Title: A twenty weeks assessment of the effect of a GDNF and BDNF-enriched collagen hydrogel on the differentiation of iPSC-derived dopaminergic progenitors in cyclosporine immunosuppressed rats.

Abstract

iPSC-derived brain repair has a considerable potential in the treatment of Parkinson's disease. However, this is limited by the poor graft survival and differentiation once the iPSC-derived dopaminergic progenitors

(iPSC-DAPs) are lifted from cell culture and transplanted into the neurotrophins-depleted adult rat brain. Therefore, the aim of this study was to assess the effect of a GDNF and BDNF-enriched collagen hydrogel on the survival and maturation of the iPSC-DAPs in the Parkinsonian rat brain. After 6-hydroxydopamine lesion, rats received unilateral intra-striatal transplantation of iPSC-DAPs either alone, with neurotrophins, in a collagen hydrogel or in a neurotrophins-enriched collagen hydrogel. Rats were sacrificed at 20 weeks post-transplantation for histological assessment of survival and maturation of the iPSC-DAPs. Although survival of the cells, which was assessed with immunostaining for human nuclei (HuNu), did not show any improvement when the iPSC-DAPs were transplanted in a neurotrophins-enriched hydrogel, the maturation of the progenitors, assessed with immunostaining for tyrosine hydroxylase (TH), seems to benefit from the combination of the neurotrophins and the collagen hydrogel. These findings support further investigations on the benefits of this GDNF and BDNF-enriched collagen hydrogel in the field of cell-derived brain repair for Parkinson's disease.

13. **Presenter:** Jacqueline Quirke

Title: Is Neural Network Functional Dysconnectivity a Trait Feature of Bipolar Disorder & Cognitive Performance?

Abstract

Cognitive impairment in bipolar disorder (BD) significantly impacts quality of life. In bipolar depression or mania, neural network dysconnectivity is relatively consistent, correlated with theory of mind (ToM), executive function (EF), and memory deficits. In euthymia, resting-state functional MRI (rsfMRI) studies examining cognition and network disruptions are rare. We aim to investigate cognitive intrinsic, intra- and inter-network connectivity in bipolar euthymia relative to healthy controls using rsfMRI. BD participants met DSM-V criteria for type-I or -II BD. Cognitive assessments included Reading the Eyes in the Mind, and The Cambridge Neuropsychological Test Automated Battery (CANTAB). Subjects underwent 3T structural and rsfMRI. Motion correction, registration, segmentation, normalization, and smoothing (SPM12) preceded spatial independent component analysis (ICA, GIFT). Defined networks include occipital, pericentral, midcingulo-insular and dorsal, lateral and medial frontoparietal networks. Intra- and inter-network connectivity of neuroanatomical networks was compared between groups on cognitive variables, accounting for age, gender, IQ (Mancovan Toolbox, GIFT). The euthymic BD (n=34) and healthy control (n=45) groups did not differ in age ($U=699.00, p=0.51$), gender ($\chi 2=0.18, p=0.67$), IQ ($F=3.37, p=0.07$). Compared with controls, the BD group performed more poorly on cognitive tasks ($F=2.2, p=0.03$). A main effect of diagnosis was observed in intra-network connectivity for all defined networks. Interactions between diagnosis and EF and diagnosis and memory revealed alterations within the lateral frontoparietal network. The BD group demonstrated altered intra- and inter-network connectivity within the lateral frontoparietal network, correlated with worse EF and memory performance. These findings may show cognitive-related connectivity disruptions contribute to persistent features of bipolar euthymia.

14. **Presenter:** Jonathan Costello

Title: Differential effects of TLR3 activation on social behaviour and prefrontal cortical inflammatory gene expression in the valproic acid model of autism: a role for the endocannabinoid system?

Abstract

Autism is associated with immune alterations and neuroinflammation. Increasing endocannabinoid tone attenuates autism-related behavioural changes in models and modulates TLR-induced neuro-immune

responses. This study examined TLR3 activation, in the presence or absence of a FAAH inhibitor, on behaviour, neuroinflammatory gene expression and endocannabinoid levels, in a preclinical rodent model of autism. Female Sprague-Dawley rats prenatally exposed to saline or VPA received 1) polyI:C (3mg/kg i.p.) or saline vehicle and were euthanised 4h later OR 2) the FAAH inhibitor PF3845 (10mg/kg i.p.) or vehicle, prior to polyI:C, and underwent nociceptive and social behaviour testing 24h later before euthanasia. The PFC from both cohorts was assessed for endocannabinoid and N-acylethanolamines levels using LC-MS/MS and inflammatory gene expression using RT-qPCR. PFC inflammatory gene expression was increased in saline-exposed rats at 4h & 24h post polyI:C. In comparison, in VPA-exposed rats, polyI:C-induced increases in IL-1β and CCL2 expression were blunted at 4h, while inflammatory gene expression returned to baseline levels at 24h. PFC 2-AG levels were reduced in saline-exposed poly I:C-treated and VPA-exposed vehicle-treated rats, when compared to saline-exposed vehicle-treated counterparts. PF3845 increased N-acylethanolamine levels in saline- and VPA-exposed rats, an effect associated with blunted poly I:C-induced inflammatory gene expression in saline-exposed rats only. Nociceptive responding did not differ between the groups, however polyI:C reduced social novelty preference of VPA-, but not saline,-exposed rats, an effect unaltered by PF3845. VPA-exposed female rats display differential behavioural and neuroimmune responses to a viral immune challenge, which were unaltered by FAAH inhibition.

15. **Presenter:** Liadhan Farrell

Title: Investigating the Genetic Basis of Cognitive Function

Abstract

Rare protein truncating variants in ADGRB2, KDM5B, GIGYF1, ANKRD12, SLC8A1, RC3H2, CACNA1A and BCAS3 have an impact on adult cognitive function. The aim of this study was to investigate if common variants at these genes also influence cognitive function, specifically the domains of general IQ, episodic memory, working memory, attentional control and social cognition. SNPs were selected at each gene for analysis if they represented eQTL in brain tissues, missense variants or variants that have been associated with cognitive function or schizophrenia from GWAS. Genotypic data for these SNPs and phenotypic data for the cognitive domains were extracted from our Irish psychosis case-control (1540 = 1005 cases and 535 controls) and analyzed using linear regressions. Twenty-three LD independent SNPs were analyzed across all genes. No SNPs were associated after the Bonferroni correction. Among the nominally significant results, two missense variants (rs7243088 and rs34996750) at ANKRD12 were associated with IQ and social cognition respectively. In addition, eQTL SNP rs12607307 was associated with IQ and working memory, where the G allele was associated with poorer cognitive function and increased gene expression. At CACNA1A eQTL SNP rs2302080 was associated with IQ and working memory (C allele was associated with poorer cognitive function and increased gene expression). At SLC8A1 eQTL SNP rs62149405 was associated with IQ and social cognition (T allele was associated with poorer cognitive function and decreased gene expression). We detected some evidence that common variants at these genes are associated with cognitive function but further analysis is required in larger samples.

16. **Presenter:** Maria Redmond

Title: Characterisation of Anxiety- and Depression-Related Behaviour and the Endocannabinoid System in the Rat Hindlimb Ischemia-Reperfusion Model of Chronic Wounds

Abstract

Ischemia-reperfusion injury can be an aetiology underlying the formation of chronic wounds, which are associated with a high incidence of comorbid anxiety and depression. The endocannabinoid system (ECS) may have a role in ischemia-reperfusion injury and is involved in the modulation of mood and anxiety. This study characterised anxiety- and depression-related behaviour in a rat model of hindlimb ischemia-reperfusion (HLIR) injury and investigated alterations in the ECS in discrete brain regions. Male and female Sprague-Dawley rats (220-350g, n=11-12/group) underwent HLIR injury or sham procedure on the left hind limb. Anxiety-related behaviour was assessed using elevated plus maze, light-dark box, and open field tests between post-HLIR days 16 and 26. Sucrose preference and splash tests assessed depression-related behaviour between post-HLIR days 17 and 20. Quantification of endocannabinoids (2-AG and AEA) and N-acylethanolamines (PEA and OEA) in brain tissue was carried out by LC-MS/MS. There was no effect of HLIR injury on anxiety- or depression-related behaviour. Female HLIR animals reared for longer than male HLIR animals in the open field test. Lower levels of 2-AG were found in the amygdala of female HLIR animals compared to female shams, with no differences in AEA, PEA or OEA levels. No differences existed in levels of analysed endocannabinoids or N-acylethanolamines in the hippocampus or striatum. These results indicate sex differences in locomotor activity and the ECS in discrete brain regions following HLIR injury. Further work is required to determine the implications of reduced 2-AG levels in the amygdala of female HLIR rats.

17. **Presenter:** Mary Hopkins

Title: Endocannabinoid-Associated Alterations in Behavioural and Electrophysiological Parameters of a Rat Model of Low Back Pain

Abstract

Chronic low back pain (CLBP) is a major unmet clinical need. The endocannabinoid system is involved in the modulation of nociception and has been shown to be altered in patients with CLBP. The prefrontal cortex (PFC) is a crucial region for top-down modulation of nociceptive processing. Male 12-week-old Sprague-Dawley rats underwent intervertebral disc injury (IVDI) or sham surgery (n=10/group). Mechanical (electronic von Frey-eVF) and heat (Hargreaves-HG) hypersensitivity were assessed at the base-of-the-tail 48/72hrs, respectively, and weekly thereafter, until post-surgery day (PSD)20. Following euthanasia on PSD21, levels of endocannabinoids/N-acylethanolamines (ECBs/NAEs) were analysed in the spinal cord and plasma via LC-MS/MS. The acute ex-vivo brain slice preparation was used to investigate cellular and synaptic properties of layer 5 (L5) pyramidal neurons in the PFC. IVDI rats displayed hypersensitivity to radiant heat and mechanical stimuli, compared to sham rats, from PSD3 and PSD7, respectively, which was sustained until euthanasia. Post-mortem analysis revealed lower levels of plasma 2-AG in IVDI rats compared to shams. Plasma 2-AG levels correlated positively with PSD19/20 eVF/HG thresholds, while HG latencies from PSD3 onwards (AUC) correlated negatively with NAE levels in the lumbar spinal cord. L5 pyramids were more excitable in the IVDI model compared to sham. Depolarisation-induced suppression of excitation (DSE), a phenomenon depending on presynaptic activation of cannabinoid receptor-1 was present in both conditions, but significantly enhanced in IVDI animals in terms of amplitude and duration. Results reveal endocannabinoid-associated alterations in nociceptive behaviour, and endocannabinoid-mediated synaptic activity in a brain region implicated in emotional processing of pain.

18. **Presenter:** Matthew Stevens

Title: Measuring Emotion Recognition correlates in Schizophrenia: Sensitivity and specificity of unbiased hit rates.

Abstract

Schizophrenia (SCZ) is a complex neurodevelopmental disorder characterized by disturbances in perception, cognition, emotion, and social functioning. Early adversity such as childhood trauma is linked with a greater risk of later developing schizophrenia and impairments in social cognitive functioning. In the present study, we investigated whether microstructural organization of the uncinate fasciculus (UF) was associated with emotion recognition outcomes. Additionally, we investigated the usefulness of an unbiased hit-rate (UHR) score to control for response biases (i.e., participant guessing) during an emotion recognition task (ERT). Fifty-eight individuals diagnosed with SCZ were included. The CANTAB ERT was used to measure social cognition. We found that the microstructural organization of the UF was significantly correlated with physical neglect, and emotion recognition outcomes. Furthermore, we found that the UHR score was more sensitive to ERT subscale emotion items than the standard HR score. Finally, a mediation analysis considered the influence of physical neglect, and the relationship between UF microstructural organization and emotion recognition outcomes. Results demonstrated that trauma is associated with brain development, which in turn impacts social cognition in SCZ.

19. **Presenter:** Mia Casburn

Title: Electrophysiological and pupillary responses to emotional congruency

Abstract

Little is known about the neurophysiological underpinnings of emotion processing. The N170 is a face sensitive ERP component, and debate exists as to whether it is responsive to facial emotion. The N400 is an ERP component that responds to semantic incongruency, and a similar debate exists as to how emotional incongruency modulates this. Finally, a large body of research exists as to whether pupil dilation (PD) discriminates between facial emotions, and whether it is sensitive to emotional congruency. A word-prime face-target task was utilised to investigate all three of these responses in the context of emotional processing. Participants were shown a word that was positively, negatively, or neutrally valanced followed by a face that was either happy, angry, or neutral. Each trial was either incongruent (e.g. positive word [e.g. “sunshine”] – angry face) or congruent (e.g. positive word [e.g. “sunshine”] – happy face). Participants had to judge whether or not the face and emotion matched in each case, while having their EEG and PD recorded. Testing is ongoing until a sample of 30 participants is reached. It is predicted that facial emotion will modulate the N170 (with largest amplitudes to angry, then happy faces). Emotional congruency is predicted to modulate the N400 (larger amplitude to incongruent items). Finally, PD will be modulated by both facial emotion and congruency, leading to an interaction effect. These results will shed light on the physiological underpinnings of emotion recognition, and future research will utilize this paradigm in populations with social cognition deficits.

20. **Presenter:** Nazan Guner Sak

Title: Platelet-derived growth factor B is highly expressed in the red blood cell-rich regions of acute ischemic stroke clots and is positively related to stroke severity

Abstract

Platelet-derived growth factors (PDGFs; PDGF-A, -B, -C, and -D) and their receptors are implicated in vascular pathologies such as atherosclerosis, restenosis, and pulmonary arterial hypertension, resulting in ischemia, myocardial infarction, and stroke. They also play a role in erythropoiesis, facilitating the differentiation of erythroid progenitors and the formation of primitive red blood cells (RBC). Considering the highest content of Acute Ischemic Stroke (AIS) clots are RBCs, it was of interest to explore expression of PDGFs in AIS clots.

This study investigated the expression of PDGF-B, its relationship with stroke etiology and severity (NIHSS). 80 blood clot samples from Clotbase International Registry (large artery atherosclerosis (LAA) (n=39) and cardioembolic (CE) (n=41) patients) were cut into 3 µm-sections and stained with Martius Scarlett Blue (MSB). Immunohistochemistry was performed using anti-PDGF-B (1:100, ab23914, abcam) and anti-Glycophorin-A (1:100, ab212432, abcam). Slides were scanned using a slide scanner (VS120, Olympus) and confocal laser scanning microscope (FV3000, Olympus) was used to visualise colocalization. The components were quantified via Orbit Image Analysis. Non-parametric statistical tests were used. The results show that PDGF-B colocalized with RBCs. Moreover, expression of PDGF-B was higher in CE than in LAA samples, but there was no statistically significant difference (p=0.3, U=688). Severe stroke cases (n=54, NHISS>15) had significantly higher PDGF-B expression compared to moderate cases (n=23, NIHSS 6-15) (p=0.046*, U=442). Regions identified as RBC-rich on MSB contain PDGF-B. High PDGF-B expression in AIS clots was associated with severe stroke. Further investigation role of PDGFs in AIS is warranted.

21. **Presenter:** Patrick Hurley

Title: Towards a microfluidic model of ectopic follicle-like structures in multiple sclerosis

Abstract

Multiple sclerosis (MS) is a progressive chronic inflammatory disease affecting the CNS. An immunological hallmark of MS is the presence of oligoclonal bands in the cerebrospinal fluid (CSF). They are detected when fragments of IgG antibodies are present in the CNS. Their persistence throughout disease course suggests a survival niche for B-cells within the CNS. The description of highly organised follicle-like structures have been detected in several chronic inflammatory diseases and a large proportion of patients with MS. We aim to do the following: 1) use MRI and post-mortem tissue images to define physical properties of brain regions commonly found to harbour these structures: 2) validate the utility of COMSOL software in modelling CSF flow. Outputs will assist in developing an in vitro microfluidic device that mimics the meningeal surface present in MS. Analysis of already-published PM images indicated that the majority (56%) of follicle-like structures are located in the exterior regions of the brain, specifically the pre-central and cingulate sulci. Characterisation of these sulci suggested a physical ratio of 3:1 (width: depth). Our COMSOL-generated model showed minimal flow into the sulci and a range of shear rates that could impact meningeal cell biology. Initial testing of meningeal cells seeded into prototype devices have shown no detectable changes in cell morphology following application of fluid flow. The work described is the first step in developing a novel testing platform for compounds that could prevent formation of the toxic B cell niche.

22. **Presenter:** Saahithh Redddi Patlola

Title: Altered mRNA expression and elevated Toll-like receptor and cytokine activity in patients with schizophrenia.

Abstract

Schizophrenia is a psychiatric disorder with a complex aetiology. There has been a growing interest in the role of Toll-like receptors (TLRs) and cytokines in the pathophysiology of schizophrenia. TLRs are pattern recognition receptors primarily involved in immune mediation. We aim to investigate if there is an altered expression and activity of peripheral cytokines and TLRs in patients with schizophrenia. A total of 279 participants were included in this study. We used high-sensitive ELISA kits to detect the peripheral levels (plasma) of cytokines in healthy volunteers (N=189) and patients with schizophrenia (N=90). Whole blood was stimulated with TLR2-4 agonists to investigate cytokine activity. cDNA synthesised from purified mRNA

(whole blood) was used to perform qRT-PCR to analyse the relative expression of cytokines and TLRs. Results from ELISAs show significantly elevated levels of IL6, IL8, IL10, TNFα and CRP ($p < 0.01$) but not IL12 and IFNγ in patients with schizophrenia compared to controls. Higher levels of IL6 and IL8 in patients were observed post-TLR2 and TLR4 receptor stimulation. The mRNA expression analysis illustrated a significantly higher expression of IL6 (1.3-fold, $p<0.06$) and IL-8 (1.44-fold, $p<0.001$) and not with TNFα. A significant upregulation in the mRNA expression of TLR2 (1.1-fold, $p<0.05$), TLR4 (1.3-fold, $p<0.01$) and TLR6 (1.07-fold, $p<0.01$) was observed but not with TLR1, 3 and 5. These results suggest that patients with schizophrenia show altered inflammatory activity. These results also point in the direction of the possible role of toll-like receptors in mediating neuroinflammatory response in schizophrenia.

23. **Presenter:** Bianca Castelli

Title: Measurement of Chitinase-3-Like-1 in Serum and Saliva in a Multiple Sclerosis Cohort

Abstract

Multiple sclerosis (MS) exhibits a diverse and unpredictable disease course, necessitating reliable biomarkers for prognosis. Chitinase-3-Like-1 (CHI3L1), a secreted glycoprotein associated with inflammation and disease progression, holds promise as a potential biomarker. This study sought to evaluate CHI3L1 levels in serum and saliva from a cohort of MS individuals and explore their correlation with hand dexterity. The study included 27 MS patients (17 relapsing-remitting, 10 progressive) and 18 healthy controls. Medical history was recorded through self-assessed questionnaires, and serum and saliva were collected simultaneously. CHI3L1 levels were assessed via ELISA, while hand dexterity was measured using the 9-Hole Peg Test (9HPT). Individuals with MS exhibited elevated CHI3L1 levels in both serum and saliva, with progressive MS (PMS) patients displaying higher levels than relapsing-remitting MS (RRMS) patients. Notably, saliva CHI3L1 levels in PMS patients were significantly higher than in RRMS patients and healthy controls, whereas serum levels showed no significant intergroup differences. Intriguingly, CHI3L1 levels did not exhibit a correlation between serum and saliva samples. Although 9HPT scores were generally higher in MS patients, no correlation was observed between these scores and CHI3L1 levels in either serum or saliva. These findings suggest that saliva may serve as a promising fluid for CHI3L1 detection, offering potential insights into monitoring MS progression. Additionally, the study challenges the conventional emphasis on serum biomarker detection in neurodegenerative diseases, highlighting the importance of exploring alternative bodily fluids for enhanced diagnostic accuracy and disease tracking.

24. **Presenter:** Tommy Patton

Title: Development of novel, clinically-relevant rat model of Parkinson's disease via sequential exposure to AAV-α-synuclein and FN075

Abstract

There are many issues impeding the development of neuroprotective treatments for Parkinson's disease (PD), but consistently identified is the lack of clinically-relevant animal models. Viral vector overexpression of α-synuclein is widely considered the most relevant model, however this has been limited by high variability and inconsistency. One potential method of optimizing this model is pairing it with a secondary insult such as FN075, a synthetic molecule demonstrated to accelerate α-synucleinopathy. Thus, we investigate if sequential exposure of AAV-α-synuclein and FN075 into the rat brain can replicate the features of PD. 40 female Sprague-Dawley rats received a dual unilateral injection of AAV-WT-α-synuclein or AAV-GFP into the

substantia nigra. Followed 4 weeks later by unilateral injection of FN075 or vehicle control into four sites in the striatum. Animals underwent behavioural testing (corridor, stepping, and whiskers) every 4 weeks until sacrificed at 20 weeks, followed by immunohistochemistry post-mortem analysis. In the behavioural assessments AAV-α-synuclein, administered either alone or sequentially with FN075, did not induce any impairment in contralateral motor function in the Corridor, Stepping, or Whisker test. Post-mortem analysis showed a significant increase in α-synuclein and ps129-α-synuclein in both AAV-α-synuclein groups, however there was no additive effect when combined with FN075. Furthermore, neither administration of FN075 or AAV-α-synuclein alone nor combined lead to any significant difference in the amount of dopaminergic degeneration. Although this experiment did not replicate the key characteristics of PD further studies are required to create more representational models for testing of novel compounds and treatments for PD.

25. **Presenter:** Wenyi Liu

Title: C-reactive protein expression in acute ischemic stroke blood clots

Abstract

C-reactive protein (CRP) is a prototypic marker of inflammation. Elevated plasma CRP concentration is associated with an increased risk of cerebrovascular events. To determine whether CRP can become a potential biomarker of stroke etiology, we investigated CRP expression in AIS clots from cardio embolism (CE), large artery atherosclerosis (LAA) and cryptogenic subtypes. We collected blood clot samples from AIS patients of different etiologies, including CE (n=50), LAA (n=39) and cryptogenic (n=29). Assessment of clot composition was carried out using Martius Scarlet Blue stain. Immunohistochemistry was used to investigate CRP expression. Colocalization studies were carried out for the detection of interaction between CRP and platelets as well as fibrin. Data was analysed using Graphpad Prism.Overall, 30% (38% of CE, 21% of LAA, 28% of Cryptogenic) of clot samples expressed CRP. The proportion of CRP expressed in CE was higher than LAA samples ($X2(1,n=89)=3.170,P=0.07$). Significantly higher expression of CRP was observed in clots from female patients compared to males ($X2(1,n=114)=5.094,P=0.02$). Clots expressing CRP had significantly higher fibrin content than clots with no CRP expression ($P=0.0357$). Confocal microscopy showed the colocalization of CRP and fibrin but not platelets. AIS clots of CE origin expressed higher CRP compared to LAA clots, suggesting CE related strokes may be more strongly linked to inflammation. Our study found some differences in CRP expression due to sex in AIS. Studying the relationship between fibrin and CRP in the clots may improve our understanding of the processes of thromboinflammation.

26. **Presenter:** Ying Zhai

Title: Investigating the effect of caffeine on β-amyloid induced neurotoxicity in mouse primary hippocampal cultures

Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the widespread loss of synapse density and remodelling of neurotransmitter systems, underlying cognitive deficits. A hallmark of AD is the formation of toxic extracellular β-amyloid (Aβ) plaques associated with neuronal loss. At present, the efficacy of the pharmacological treatments available for AD is very limited as a consequence of its sophisticated pathophysiology. Thus, research is shifting focus on dietary interventions or nutraceuticals. Caffeine is a widely consumed psychoactive substance that has been shown to exert controversial biomedical effects in AD models. The main inhibitory neurotransmitter gamma-aminobutyric acid (GABA) plays a key role in a number of pathological conditions affecting the nervous system, including AD. Defects in GABA

molecular pathways are involved in the cause of AD but the exact molecular mechanism is unknown. This study aimed to characterise the effect of caffeine on Aβ -mediated changes in hippocampal neuronal loss and adenosine receptor 1 (A1R) expression using an in vitro AD model. We reported significant decreases in neuronal death in caffeine-treated primary hippocampal neurons at all concentrations examined (0.1, 1, 25, and 50 µM) 5 days post- Aβ treatment. The 25 µM caffeine concentration was also effective in acute (6h) caffeine treatment conditions. We also observed a decrease in A1R expression 5 days after Aβ application on primary hippocampal neurons and caffeine was able to ameliorate this decrease. These findings indicate Aβ-induced neurotoxicity might be associated with the downregulation of A1R expression, and this reduction is attenuated by caffeine exposure.

27. **Presenter:** Malgorzata Dabrowska

Title: Organotypic cortical brain slices from adult rats as an ex-vivo study platform for neurodegenerative diseases

Abstract

Adult rat brains, having fully developed central nervous systems, make better ex vivo models for studying neurodegenerative disease than neonates and, in mimicking human brain sulci, can provide a representation of the natural cell interaction and 3D orientation, with signalling pathways intact. However, previous reports suggest that adult tissue slices do not remain viable after 7 days. We aimed to obtain an intact interhemispheric fissure from coronal brain slices and to determine metabolic activity and survival of slices from different anatomical areas. Sequential coronal slices (300µm) were cultured and the effect of FBS (0-10%) on viability measured. Cortical slices were significantly more metabolically active ($p<0.001$, N=4) in media enriched with 10% FBS compared those cultured with lower FBS concentrations, allowing viable slices up to 21 days in vitro. Results were supported by a viability/cytotoxicity assay. As an acute response to the culture environment, the tissue slices were seen to swell, and slice area was monitored over time. The first 7 days in vitro (DIV) were marked as crucial for the recovery and establishment of a sustainable system, so any further experimental manipulations took place after that period. Caudal slices (~Bregma point -1,33mm) were significantly more metabolically active ($p<0.05$) than rostral regions. Our model introduces a novel use of adult rat brain slices for ex vivo investigation of neurodegenerative disease, allowing drug testing and analysis of cortical pathology in conditions such as multiple sclerosis. Furthermore, the variation in metabolic activity along the rostral-caudal axis emphasises the significance of tracking anatomical origin.

28. **Presenter:** Shima Shapoori

Title: Advancing personalized medicine in progressive multiple sclerosis: exploring biomarkers and point-of-care testing

Abstract

Understanding the pathology of progressive multiple sclerosis (PMS) and developing reliable biomarkers are crucial for monitoring the disease and advancing new therapeutics. Our hypothesis centers on elevated levels of neurofilament light chain (NFL), kappa free light chain (KFLP), glial fibrillary acidic protein (GFAP), and other biomarkers of interest in the biofluid samples of people with PMS (pwPMS) compared to the other groups. Moreover, it has been proved that olfactory dysfunction in people with MS (pwMS) is correlated with the progression of the disease and severity of the disability. So, smell can be used as a clinical marker in MS patients. Measurement of these potential biomarkers, along with cognitive and smell tests will help us design a point-of-care (POC) device to allow disease monitoring in MS patients non-invasively, quickly,

and simultaneously, without needing a healthcare professional. This study aims to ascertain biomarker reliability across various samples and explore correlations with disease progression and functional testing, while also aiming to develop a non-invasive POC device for monitoring MS. Our methodology involves recruiting over 30 participants each from relapsing-remitting MS (RRMS), PMS, and a control group. Sample such as tears, nasal secretions, saliva, and blood have been collected, processed, and are undergoing assay optimization for biomarkers using various technologies. While our preliminary findings have not yet demonstrated significant differences, it is important to note that with the recruitment of more patients and further optimization of biomarker assays, we anticipate that more meaningful results will be revealed.

29. **Presenter:** Ciara Shortiss

Title: Lentiviral Vectors in combination with Biomaterial Scaffolds for Spinal Cord Injury Regeneration

Abstract

Spinal cord injury (SCI) causes chronic pathological processes that persist for months to years preventing neural regeneration and recovery. The varying nature and prolonged timespan of these processes calls for combinatory strategies to promote repair. Lentiviral vectors (LVs) provide sustained therapeutic effects more efficiently than repeated biomolecule/drug administration due to integration of therapeutic genes into the DNA of host cell genome. LV delivery via biomaterials after SCI can target additional pathological processes, increase LV persistence through controlled release, improve LV localization, stability, transduction efficiency and reduce immune clearance producing superior therapeutic effects. In this study, LVs were combined with Hyaluronic acid (HA) and Oligo(poly(ethylene glycol) fumarate) (OPF) hydrogels. HA is ubiquitous in neural tissue and can help regulate angiogenesis and inflammation after injury. OPF hydrogels have been shown to improve regenerative markers in SCI models. LVs encoding GFP were loaded into hydrogels prior to/post crosslinking. Hydrogels were incubated in cell culture media at 37℃ and LV release/function was evaluated through GFP expression in cells cultured in hydrogel incubation media. Few functional LVs were released from gels at any timepoint investigated (up to 120hrs) despite evidence for some functional LVs remaining in HA gels at 48hrs. To determine whether interaction with HA or OPF biomaterial affects LV functionality, LVs were incubated in solutions containing HA or ground OPF gels. LV functionality was initially increased but decreased faster in HA solutions. Incubation with positively-charged OPF decreased LV functionality. In conclusion, careful consideration must be given to biomaterial selection when approaching this treatment modality.