Biological Psychiatry
AUSTRALIA

2023

Proceedings of the Biological Psychiatry Australia Scientific Meeting 2023

Welcome

The 13th Biological Psychiatry Australia Scientific Meeting

25 – 27th October 2023

Dear Friends and Colleagues,

On behalf of the Local Organising Committee, we warmly welcome you to the 13th Annual Biological Psychiatry Australia 2023 (BPA2023) Scientific Meeting. This year marks our first meeting in tropical Northern Queensland, and we are excited to meet at the Pullman Palm Cove Resort (Wednesday, 25th of October). We will also be using the Whova portal (Whova.com). You can use the app on a computer or mobile device to see the agenda, abstract book, see all the session times, as well as connect with other attendees, either directly via their profiles or in Session Q&As.

On behalf of the Local Organising Committee, we wish you an engaging and stimulating meeting.

Co-Chairs: Prof Zoltan Sarnyai and Dr Tertia Purves-Tyson

Local Organising Committee: Zoltan Sarnyai, Tertia Purves-Tyson**,** Rachel Hill (Scientific Review Committee), Thomas Burne, Lauren Harms, Leigh Walker (Treasurer), Priscila A. Costa, Sabine Finlay, and Carlo Longhitano.

Stay connected with our Twitter accounts: @biolpsychaust @BPA_ECRN

If you have any question, please do not hesitate to contact us at biolpsychaust@gmail.com

All online material can be found at https://whova.com/portal/webapp/biolo_202310/

Contents

Acknowledgement of Country

We acknowledge with respect the Aboriginal and Torres Strait Islander peoples as the first peoples, educators and innovators of this country. We acknowledge that Country was never ceded, and value the accumulation of knowledge and traditions that reflect the wisdom of ancestral lines going back some 60,000 years, and recognise the significance of this in the ways that Aboriginal and Torres Strait Islander peoples are custodians of Country.

We acknowledge the Traditional Owners of the lands on which we are meeting, the Yirrganydji (*Irri-kand-ji*) people and pay our respects to the Elders, past, present and emerging. We would also like to acknowledge the other Traditional Owner groups in the Cairns region. Towards the mountains and rainforest, the Djabugay (*Ja-pur-kai*) people, in the CBD, Gimuy Walubara Yidinji (*Gim-moy Wah-lu-bara Yid-in-ji*) people. We pay our respects to their Elders past, present and emerging.

BPA Equality and Diversity Statement

Biological Psychiatry Australia (BPA) has a mission to promote research and innovation in the field of biological psychiatry within Australia.

Diversity drives quality and innovation, and so BPA strives to develop a strong culture of diversity and inclusivity. We aim for all voices to be heard, regardless of gender, race, disability, age, social class, sexuality, or religion.

We recognise our responsibility to our membership to promote equality of opportunity across all our activities, including developing meeting programs, and bestowing prizes and awards.

We will not tolerate actions or language that discriminates against any person or persons based on gender, race, disability, age, social class, sexuality, religion or otherwise at any event held by or sponsored by BPA.

Through fostering a culture of inclusivity, we aim to promote diversity and provide a forum where researchers of all levels and all backgrounds can freely share ideas and inspiration.

Society Profile

Biological Psychiatry Australia is a society established in 2010 for professionals interested in the advancement of biological research in psychiatry.

The research focus of the Society encompasses the application of biological techniques to investigate and better understand the causes of psychiatric disorders and the translation of neuroscience research to the development of more effective clinical treatments.

The society convenes annually at a meeting designed to promote academic exchange and collaboration between researchers and clinicians working in related fields.

Executive Committee

President	Tertia Purves-Tyson	Neuroscience Research Australia
Vice-president	Rachel Hill	Monash University
Secretary	Yann Quidé	University of New South Wales
Treasurer	Leigh Walker	Florey Institute of Neuroscience and Mental Health
Webmaster	Lauren Harms	University of Newcastle
ECRN rep	Bruna Panizzutti Parry	Deakin University
Committee members		
	Sarah Cohen-Woods	Flinders University
	Vanessa Cropley	University of Melbourne
	Alexandre Guérin	University of Melbourne
	Katrina Green	University of Wollongong
	James Kesby	University of Queensland
	Natalie Matosin	University of Wollongong

ECRN Committee

Chair	Bruna Panizzutti Parry	VIC	Deakin University
Secretary	Cassandra Wanna	VIC	University of Melbourne
Treasurer	Helen Clunas	NSW	University of Wollongong
Social media	Stela Petkova	NSW	University of Sydney
VIC reps	Trevor Steward	VIC	University of Melbourne
	Sylvia Lin	VIC	University of Melbourne
	Eveline Mu	VIC	Monash University
NSW reps	Carl Moller	NSW	University of New South Wales
	Samara Brown	NSW	University of Wollongong
ACT rep	Shaam Al-Abed	ACT	Australian National University

Society Profile

Scientific Review Committee: Chair: Rachel Hill

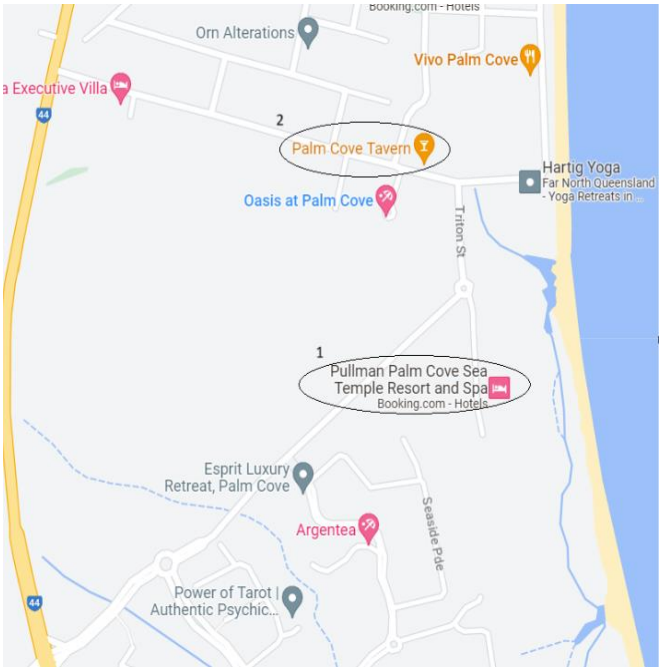
Robyn Brown, Thomas Burne, Rose Chesworth, Kelly Clemens, Jennifer Cornish, Brian Dean, Chao Deng, Eske Derks, Darryl Eyles, Claire Foldi, Andrew Gibbons, Katrina Green, Melissa Green, Alex Guérin, Tony Hannan, Lauren Harms, Tim Karl, Pat Michie, Kelly Newell, Jess Nithianantharajah, Claire O'Callaghan, Iain Perkes, Christina Perry, Tertia Purves-Tyson, Yann Quidé, Luba Sominky, Suresh Sundram, Melissa Tadros, Adam Walker, Andrew Zalesky, Murray Cairns, William Reay, Thibault Renoir, Zoltan Sarnyai, Caroline Gurvich, Wittaya Suwakulsiri, Sandesh Panthi, Augustin Cota-Coronado.

Annual Award Presentations

Isaac Schweitzer Lecture		**Aubrey Lewis Award**	
2010	-	2010	Mark Bellgrove
2011	-	2011	Melissa Green
2012	-	2012	Andrea Gogos
2013	Michael Berk	2013	Michael Breakspear
2014	Paul Fitzgerald	2014	Adam Guastella
2015	John McGrath	2015	Irina Voineagu
2016	Cyndi Shannon Weickert	2016	Andrew Zalesky
2017	Patricia Michie	2017	Jee Kim
2018	Christos Pantelis	2018	Rachel Hill
2019	Brian Dean	2019	Marta Garrido
2020	Susan Rossell	2020	Bronwyn Graham
2021	Anthony Hannan	2021	Lianne Schmaal
2022	Jayashri Kulkarni	2022	Robyn Brown
2023	Suresh Sundram	2023	Wolfgang Marx

Venue Information

1.	**Wednesday 25th-27th of October,**	**Pullman Palm Cove Resort**	**5 Triton Street, Palm Cove**
2.	**Wednesday 25th Welcome Event 7 PM**	**Pullman Palm Cove Resort**	**5 Triton Street, Palm Cove**
3.	**Thursday 26th October, Social Event 6:30 PM**	**Palm Cove Tavern**	**24 Veivers Road, Palm Cove**



Pullman Resort

Program at a glance

BPA2023 Translation in the Tropics 25-27 Oct 2023

	Wed, 25 Oct	Time	Thurs, 26 Oct	Time	Fri, 27 Oct
		8am	Registration Desk open		
		8:15am	Aubrey Lewis Lecture: Dr Wolfgang Marx	8am	Symposium 4 The Markers in Neuropsychiatric Disorders Study
		9:15am	Data blitz 2	9:30am	Data blitz 5
		9:45am	Morning tea and DB2 posters	10:00am	Morning tea DB5 posters
		10:15am	Symposium 2 Human post-mortem techniques to understand Schizophrenia	10:30am	POSTERS
12pm	Registration Desk open. Hang posters	11:45am	Data blitz 3	11:30am	AGM, Discussants Discussion Prizes Wrap up CLOSE
12:20pm	Welcome	12:15pm	Lunch		
12:30pm	11th Isaac Schweitzer Lecture: Prof Suresh Sundram	12:30pm	Lunch cont. and Posters incl DB3 posters	12:45pm	
1:30pm	Data blitz 1	1:45pm	Highest ranked abstracts	NOTES:	
2pm	Afternoon tea and ECRN Mentoring session	2:30pm	Data blitz 4	Please use the WHOVA app to arrange to meet poster presenters at times other than their allocated slot.	
2:45pm	Symposium 1 Treatment Strategies for Eating Disorders	3:00pm	Afternoon tea and DB4 posters		
4:15pm	POSTERS 1 hour And DB1 posters	3:30pm	Symposium 3 Cannabidiol for substance use disorder treatment	Wednesday Welcome Event (Substantial Canapes/Drinks) is a@The Lagoon Bar, Palm Cove Resort and Spa -	
5:30pm	Intro by EMCR Rising Star Lizzie Manning, International Keynote Lecture: Etienne Sibille, GABA and cognitive deficits in depression and ageing	5:00pm	ECRN Plenary 1 and Plenary 2	Thursday Social Event is at Palm Cove Tavern (light canapes/drinks) – 5 minute walk from conference venue Dress: "Tropical Chic"	
		6:00pm			
		6:30pm	Social Event at Palm Cove Tavern (5 min walk from Palm Cove Resort)	Posters to remain up for the duration of the conference.	
6:45 pm	Welcome Event at Palm Cove Resort				

Presentation Guidelines

Lectures, Oral Presentations, Data Blitz

- Please bring your presentation on a USB drive to upload in the morning on the day of your session in the Temple Room/Conference Room
- We will aim to run all presentations from the same PC laptop, but a mac laptop will be available if needed
- You will not be able to connect your own computer to the AV system
- Be sure to run through the presentation after uploading with one of the LOC members to ensure the presentation is displaying properly

Posters

- Posters should be A0 portrait orientation, no more than 90cm wide and 120cm long
- Please hang posters before 12:30 on Wednesday 25th Oct in the Garden Pavilion/Melaleuca Room
- Please take your poster down after 12:45pm on Friday 27th Oct.

Sponsor

Tropical Brain & Mind Foundation

The Tropical Brain and Mind Foundation (TBMF) is a volunteer organization in Townsville made up of academics, medical professionals and researchers, industry and community members. Our work is designed to build a stronger focus on mental wellness for all people across the lifespan which we believe will contribute to a flourishing community. The vision of the TBMF is to work with community stakeholders to identify and support high quality research and build community awareness in the areas of brain health and initiatives likely to improve mental wellness.

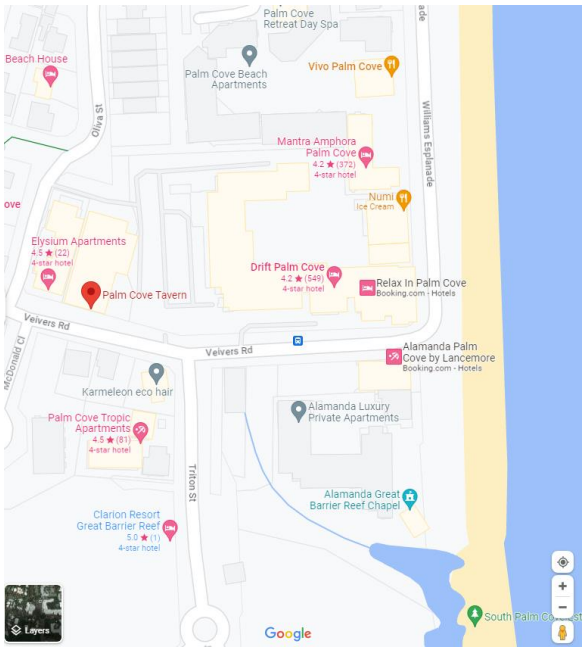
BPA Social Event

Thursday, 26th October at Palm Cove Tavern
At 6:30pm

Dress code: Tropical Chic

Address: 24 Veivers Road, Palm Cove Queensland 4879

Map



Scientific Program
Wednesday, 25 October 2023

Registration desk opens (Outside Temple Room)
12:00 PM
*Hang Posters

Welcome – Temple Room
12:20 PM Dr Tertia Purves-Tyson, BPA President

11th Isaac Schweitzer Plenary Award – Temple Room
12:30 PM
Chair: Prof Brian Dean

Prof Suresh Sundram
Imagining precision medicine for psychiatry: an incomplete template

Data Blitz – Session 1 – Temple Room
1:30 PM – 2:00 PM
Chair: Hayley North

1:30 PM **Suzy A Alexander**
Intranasal clozapine: a viable route of administration that may avoid related side-effects

1:36 PM **Laisa de Siqueira Umpierrez**
Chronic treatment with GOO during abstinence from METH self-administration induces cue-relapse to METH, and does not have any effect on reinstatement, anxiety, and recognition memory

1:42 PM **Xiaoying Cui**
Epitranscriptomic regulation of striatal function: a new biology of schizophrenia?

1:48 PM **Hadis Jameei**
Understanding brain volume heterogeneity through polygenic risk profiling of psychiatric disorders and commonly comorbid medical conditions

1:54 PM **Dylan J. Kiltschewskij**
Epigenetic Scores for Schizophrenia and First Episode Psychosis are Associated with Diagnostic Status

Afternoon tea and ECRN Mentoring Program Meetings (Terrace Area outside Temple Room)
2:00 PM – 2:45 PM

Symposium 1 – Temple Room
2:45 PM – 4:15 PM

A pathway towards improved treatment strategies for eating disorders
Chair/Discussant: Dr Robyn Brown (University of Melbourne/Bio21 Institute) and Prof Phillipa Hay (Western Sydney University)

Speakers: Dr Trevor Steward, Dr Claire Foldi, Dr Robyn Brown, and Prof Phillipa Hay

Poster Viewing - Session 1. Melaleuca Room (Garden Pavilion)

4:15 PM – 5:15 PM

WED_1 **Suzy A Alexander**
Intranasal clozapine: a viable route of administration that may avoid related side-effects

WED_2 **Emma Sampson**
Long-term characterisation of relationship between change in depression severity and change in inflammatory markers following inflammation-stratified treatment with vortioxetine augmented with celecoxib or placebo

WED_3 **Laisa de Siqueira Umpierrez**
Chronic treatment with GOO during abstinence from METH self-administration induces cue-relapse to METH, and does not have any effect on reinstatement, anxiety, and recognition memory

WED_7 **Xiaoying Cui**
Epitranscriptomic regulation of striatal function: a new biology of schizophrenia?

WED_8 **Sylvia Lin**
Parent Emotion Socialization is Associated with Neural Correlates of Emotion Regulation in Early Adolescents

WED_14 **Madison Brooke**
Effects of sex hormones and hormonal contraceptives in adolescent fear extinction

WED_20 **Christine Leonards**
Altered task-induced functional decoupling of the frontocingulate cortex in depression

WED_26 **Emily Jaehne**
The Arx R264Q mouse model of a human mutation identified in a person with schizophrenia recapitulates disease-relevant behavioural and neural network oscillation phenotypes

WED_31 **Hadis Jameei**
Understanding brain volume heterogeneity through polygenic risk profiling of psychiatric disorders and commonly comorbid medical conditions

WED_32 **Sebastian McCullough**
Deciphering Effects of Nucleus Accumbens Deep Brain Stimulation on Effort-Based Decision Making and Local Phasic Dopamine Efflux

WED_38 **Amber Curry**
Expression of hippocampal cortisol receptors in psychiatric disorder patients with trauma histories

WED_41 **Ken Walder**
Drug repurposing to treat bipolar disorder using participant-derived neural progenitor cells

WED_44 **Luke Ney**
Stress induction, fear conditioning, trauma film viewing, and intrusive memories: Relationship between salivary alpha amylase, endocannabinoids, and cortisol

WED_47 **William Reay**
Genetic influences on circulating retinol: implications for mental health

WED_50 **Caitlin Fenech**
Can modulation of glycinergic periaqueductal grey neurons be therapeutic in a chronic pain state?

WED_53 **Gezelle Dali**
Topiramate versus naltrexone for alcohol use disorder: The effect on neural activation during an anticipatory anxiety task

WED_56 **Katrina Z. Edmond**
Lower FKBP5 DNA methylation at key enhancer sites associates with older age and higher gene expression in psychiatric disorders

WED_59 **Luca Cocchi**
Clinical and neurophysiological effects of transcranial magnetic stimulation of the frontal pole in OCD

WED_62 **Elysia Sokolenko**
NMDA receptor antagonist-induced disruptions to oscillatory and aperiodic neural activity

WED_65 **Theresa Salthouse**
Understanding the role of dynorphin in the therapeutic effects of KNX100, a novel clinical stage molecule in development for the treatment of opioid withdrawal.

WED_68 **Megan Ellis**
Mitochondrial function is increased in lithium-treated neural progenitor cells derived from participants with bipolar disorder

WED_71 **Sheida Shadani**
The Effects of Psilocybin on Social Behaviour in Mice

WED_74 **Isobel A R Williams**
Reversing the effect of prenatal opioid exposure: the efficacy of sodium butyrate in animal models

WED_80 **Daisy L Spark**
Clinically predictive modulation of cognitive deficits in a mouse working memory touchscreen task

WED_83 **Abigail Marcus**
Modelling and treating impairments caused by prenatal methamphetamine exposure in rats

WELCOME EVENT (Temple Room and Lagoon Bar)

5:30 – 10pm
Chair: Zoltan Sarnyai

Intro by EMCR – Rising Star (Temple Room)

5:30 PM

Dr Lizzie Manning (University of Newcastle)

International Keynote Speaker (Temple Room)

6:00 PM
Chair: Lizzie Manning

Prof Etienne Sybille
GABA and cognitive deficits in depression and aging: mechanisms and therapeutic targeting

Canapes/Drinks at Lagoon Bar (Palm Cove Resort)

6:45 PM

Thursday, 26 October 2023

Registration desk open
8:00 AM – 8:15 AM

14th Aubrey Lewis Plenary Award – Temple Room
8:15 AM – 9:15 AM
Chair: Dr Robyn Brown

Dr Wolfgang Marx
Recent advances in nutritional psychiatry: novel mechanisms, interventions, and guidelines

Data Blitz Session 2 – Temple Room
9:15 AM – 9:45 AM
Chair: Christina Perry

9:15 AM **Bruna Panizzutti**
Differentially expressed pathways in stem-cell-derived cortical networks of bipolar disorder participants are modulated by drugs commonly used for treatment.

9:21 AM **Bjorn Burgher**
Personalised neurotherapeutics for major depression: Initial clinical findings from the Queensland Neurostimulation Centre

9:27 AM **Brendan Gillespie**
Maternal selenium dietary supplementation recovers sociability and cognitive deficits following in utero exposure to maternal immune activation in mice

9:33 AM **Muskan Khetan**
Investigation of the association between estradiol levels and brain structure and function in early adolescent females

9:39 AM **Vaidy Swaminathan**
BDNF Met allele and hippocampal volume moderate risk of cognitive dysfunction in schizophrenia

Morning tea and Data Blitz Session 2 Posters - Melaleuca Room (Garden Pavilion)
9:45 AM - 10:15 AM

THUR_13 **Brendan Gillespie**
Maternal selenium dietary supplementation recovers sociability and cognitive deficits following in utero exposure to maternal immune activation in mice

THUR_15 **Muskan Khetan**
Investigation of the association between estradiol levels and brain structure and function in early adolescent females.

THUR_37 **Vaidy Swaminathan**
BDNF Met allele and hippocampal volume moderate risk of cognitive dysfunction in schizophrenia

Symposium 2 - Temple Room
10:15 AM-11:45 AM

Showcasing advanced human post-mortem techniques to better understand the molecular pathology of schizophrenia: a critical link for translation
Chair/Discussant: Rachel Hill (Monash University)
Speakers: Dr Natalie Matosin, Dr Wittaya Suwakulsiri, Dr Hayley North and Prof Brian Dean

Data Blitz Session 3 – Temple Room
11:45 AM – 12:15 PM
Chair: Elysia Sokolenko

11:45 AM **Mackenzie Rubens**
Biopsychosocial Markers of Posttraumatic Outcomes in a Population of Emergency Responders

11:51 AM **Madeleine Giles**
The Role of Opioid Receptors in the Error Correction Mechanisms Underlying Fear Learning

11:57 AM **Georgia Caruana**
Characterising neural and behavioural correlates of cognitive intra-individual variability in bipolar disorder

12:03 PM **Dominic Kaul**
Dissecting how psychological stress affects human astrocytes in psychiatric disorders

12:09 PM **Andrew Gibbons**
The Btc knockout mouse shares similarities in altered cortical gene expression with individuals with schizophrenia

Lunch - Terrace
12:15 PM – 12:30 PM

Lunch (continued), Posters and Data Blitz Session 3 Posters - Melaleuca Room (Garden Pavilion)
12:30 PM – 1:45 PM

THUR_4 **Alexandre Guerin**
Hippocampal subfield volume as a function of cannabis use and cannabis use disorder

THUR_9 **Andrew Gibbons**
The Btc knockout mouse shares similarities in altered cortical gene expression with individuals with schizophrenia

THUR_10 **Charlotte Bainomugisa**
Genetic overlap between psychiatric disorders and migraine

THUR_16 **Kiran Bagali**
Exploring Cortical Plasticity Changes with TMS-EMG: Differential Effects of High-Definition trans-cranial Direct Current Stimulation (HD-tDCS) Perturbation in Patients with Schizophrenia receiving Clozapine or Other Antipsychotics, and Healthy Controls

THUR_21 **Georgia Caruana**
Characterising neural and behavioural correlates of cognitive intra-individual variability in bipolar disorder

THUR_22 **Sandesh Panthi**
Investigating risk-taking behaviour across multiple mouse models relevant to schizophrenia

THUR_28 **Helen Clunas**
Altered endocannabinoid mRNA expression in the aging human brain in major depressive disorder

THUR_29 **Mackenzie Rubens**
Biopsychosocial Markers of Posttraumatic Outcomes in a Population of Emergency Responders

THUR_34 **Naomi May**
The effect of anthocyanin rich plum on memory and inflammation in MCI

THUR_35 **Dominic Kaul**
Dissecting how psychological stress affects human astrocytes in psychiatric disorders

THUR_39 **Brandon K Richards**
Neurochemically distinct populations of RXFP3+ neurons in the lateral hypothalamus and zona incerta may regulate discrete aspects of behavioural arousal

THUR_42 **Michelle H Shen**
Afferent pathways of RXFP3+ zona incerta cells during threat responses in mice

THUR_45 **Khaizuran Kamarul**
Impact of posttraumatic stress symptoms severity on white matter integrity in chronic pain

THUR_48 **Liza van Eijk**
Can pre-treatment MRI Biomarkers predict treatment outcomes in PTSD?

THUR_51 **Stephanie Hartanto**
The Role of Developmental Timing of Adverse Childhood Experiences in Shaping Brain Structure: A Systematic Review

THUR_54 **Stela P Petkova**
Oxytocin effects on deficits in neonatal ultrasonic vocalizations in a model of prenatal valproic acid exposure

THUR_57 **Jodie Naim-Feil**
Modelling the dynamic brain response to TMS inhibitory perturbations in alcohol dependence during early recovery: A TMS-EEG study

THUR_60 **Calogero Longhitano**
Nutritional approaches in the treatment of Schizophrenia Spectrum Disorders: a Systematic Literature Review

THUR_63 **Lachlan Hamilton**
Distinct contribution of brain geometry and connectivity for whole-cortex communication

THUR_66 **Abdalla Z Mohaned**
Sleep quality associated with altered brain structure and microstructure in the long-term trauma survivors

THUR_69 **Mia J O'Shea**
Investigating the neural correlates of stress-induced binge eating in binge prone versus binge resistant female mice

THUR_72 **Justine Kissane**
Perinatal Sertraline Exposure Induces Changes in Glutamatergic Receptor Gene Expression in Male but Not Female Adolescent Offspring

THUR_75 **Courtney Crawford**
Effect of cannabidiol on neurotransmitter and neuroimmune signalling pathways in a maternal immune (Poly I:C) model of schizophrenia: potential antipsychotic mechanisms

THUR_78 **Aqsa Shahid**
The effect of intergenerational stress exposure on peripheral BDNF levels in adult rats

THUR_81 **Tayla B McCutcheon**
Early life inflammation accelerates the development of emotion regulation in infant rats

Highest Ranked Abstracts – Temple Room

1:45 PM – 2:30 PM
Chair: Prof Suresh Sundram

1:45 PM **Kyna Conn**
Targeting flexible learning to treat anorexia nervosa – insights into the serotonergic effects of psilocybin in animal models

2:00 PM **Nandita Vijayakumar**
Puberty and corticolimbic connectivity: implications for mental health

2:15 PM **Roisin A. Moloney**
Zuranolone as a Neuroprotective Therapy Following Preterm Birth and its Effects on the Dopamine Pathway

Data Blitz Session 4 – Temple Room

2:30 PM – 3:00 PM
Chair: Carlo Longhitano

2:30 PM **Thomas Ferella**
Voluntary Exercise Throughout Abstinence Prevents the Incubation of Craving for Alcohol-Associated Cues in Rats

2:36 PM **Jodie E Pestana**
The effects of diazepam and fluoxetine on models of anxiety differ in female rats depending on their reproductive history

2:42 PM **Priscila A. Costa**
Impact of maternal immune activation on behaviour across adolescence of male and female offspring

2:48 PM **Caspar Muenstermann**
Transcriptomic and Epigenomic regulation in extinction of cocaine and nicotine self-administration

2:54 PM **Yoshito Saito**
Multivariate brain structure-cognition signatures of early psychosis

Afternoon tea and Data Blitz Session 4 Posters - Melaleuca Room (Garden Pavilion)

3:00 PM – 3:30 PM

THUR_17 **Yoshito Saito**
Multivariate brain structure-cognition signatures of early psychosis

THUR_25 **Thomas Ferella**
Voluntary Exercise Throughout Abstinence Prevents the Incubation of Craving for Alcohol-Associated Cues in Rats

THUR_27 **Priscila A. Costa**
Impact of maternal immune activation on behaviour across adolescence of male and female offspring

Symposium 3 - Temple Room

3:30 PM - 5:00 PM

Cannabidiol for substance use disorder treatment: novel mechanistic insights and translation into the clinic

Chair/Discussant: Dr Rose Chesworth (Western Sydney University) and Dr Nicholas Everett (University of Sydney)

Speakers: Dr Alexandre Guerin, Tristan Hurzeler, and Dr Rose Chesworth

ECRN Plenary 1 and Plenary 2

5:00 PM – 6:00 PM

Chair: Bruna Panizzutti

Dr Alex Guerin
Methamphetamine use in adolescence: from laboratory studies to novel treatments

Dr Cassandra Wannan
The impact of psychosocial stress on body, brain, and cognitive ageing across different mental health disorders

Social Event at Palm Cove Tavern

6:30 PM

Friday, 27 October 2023

Symposium 4 (Temple Room)

8:00 AM - 9:30 AM

The Markers in Neuropsychiatric Disorders Study: a simple blood test to improve diagnosis and care for people with cognitive, psychiatric, and neurological symptoms

Chair/Discussant: Dr Christa Dang (National Ageing Research Institute)

Speakers: Dr Dhamidhu Eratne, Wei-Hsuan, Michelle Chiu, and Dr Matthew Kang

Data Blitz Session 5 Temple Room

9:30 AM – 10:00 AM

Chair: James Kesby

9:30 AM **Susan Thomas**
Plasma glutamate levels are higher in individuals with major depressive disorder and correlated with psychopathology

9:36 AM **Fleur Harrison**
Apathy and fatigue, but not depression, associated with inflammatory biomarkers in older adults

9:42 AM **Suzan Maleki**
Effects of chronic cannabis use on brain structural connectivity: Connectome and Fixel-Based analyses

9:48 AM **Carlton Lloyd Pavy**
The Impact of Neurosteroid Therapy on the Cerebellum Following Preterm Birth in a Guinea Pig Model

9:54 AM **Diana Sketriene**
Unravelling an Intriguing Link Between Occasional Overeating, Gut Microbiota, and Behavior: A Tale of Fragmented Sleep and Midnight Munchies

Morning tea and Data Blitz Session 5 Posters - Melaleuca Room (Garden Pavilion)

10:00 AM – 10:30 AM

FRI_5 **Susan Thomas**
Plasma glutamate levels are higher in individuals with major depressive disorder and correlated with psychopathology

FRI_11 **Fleur Harrison**
Apathy and fatigue, but not depression, associated with inflammatory biomarkers in older adults

FRI_19 **Carlton Lloyd Pavy**
The Impact of Neurosteroid Therapy on the Cerebellum Following Preterm Birth in a Guinea Pig Model

FRI_23 **Suzan Maleki**
Effects of chronic cannabis use on brain structural connectivity: Connectome and Fixel-Based analyses

FRI_33 **Diana Sketriene**
Unravelling an Intriguing Link Between Occasional Overeating, Gut Microbiota, and Behavior: A Tale of Fragmented Sleep and Midnight Munchies

Posters - Melaleuca Room (Garden Pavilion)

10:30 AM – 11:30 AM

FRI_6 **Tylah Doolan**
Oxytocin as a treatment for methamphetamine addiction - why is it not translating?

FRI_12 **Christina J Perry**
The ability of cues to precipitate relapse to alcohol-seeking changes across abstinence

FRI_18 **Roger B Varela**
Role of peripheral metabolic changes underlying anhedonia phenotype in rats

FRI_24 **Poppy Watson**
Reward related attentional bias and problematic alcohol use

FRI_30 **Eva Guerrero-Hreins**
Changes in addiction-like behaviour towards palatable food after vertical sleeve gastrectomy in mice

FRI_36 **Riki Dingwall**
Goal-Directed Behaviour under Uncertainty in the NLGN3R451C/Y Mouse Model of Autism

FRI_40 **Sarah Cameron**
Translating Habenula Dysfunction in Depression: A Systematic Review

FRI_43 **Sophie R Debs**
Maternal immune activation and estrogen receptor modulation induce distinct changes in inflammatory-related gene expression in the substantia nigra of female and male offspring

FRI_46 **Shruthi Malappurath Suresh**
Genetic and psychosocial and drivers of mental health and well-being: a comparison of pre and duringCOVID university students

FRI_49 **Morgan C. Bucknor**
A high-fat diet and psychosocial stress mouse model for maternal immune activation

FRI_52 **Trang Cao**
Mode-based morphometry: a new approach to mapping human neuroanatomy

FRI_55 **Jessica Ann May Adams**
Effects of Childhood Maltreatment on Adult Mental Health Outcomes

FRI_58 **Kaixin Huang**
Investigating the role of dorsal striatum in compulsive exercise using the activity-based anorexia (ABA) rat model

FRI_61 **Alexander Athanasopoulos**
Targeting the oxytocin system to promote preference for social interaction over alcohol consumption in rats

FRI_64 **Zoe SJ Liu**

Baicalin enhanced neuroprotection and mitochondrial function in a human neuronal cell model

FRI_67 **Ellen E Towers**
Protocol: Structural brain networks implicated in co-occurring PTSD and alcohol use disorder

FRI_70 **Lauren Barker**
White blood cell proportions predict remission of psychosis risk in Ultra High Risk individuals

FRI_73 **Suhaana Shaik**
Molecular evidence for glial pathology in Schizophrenia and Bipolar Disorder Midbrains

FRI_76 **Ella Parkes**
Investigating the antioxidant potential of medicinal mushrooms and their effect on oxidative stress

FRI_77 **Warren Logge**
Comparing the effects of topiramate versus naltrexone in neural alcohol cue reactivity and intrinsic functional connectivity in alcohol use disorder

FRI_79 **Julianna Lys de Sousa Alves Neri**
Systematic review of effects of flavonoids on adiponectin: Implications for inflammation and brain function

FRI_82 **Jessica Sarah Lim**
Investigating the relationship between inflammation, angiogenesis, the blood brain barrier and neurogenesis in schizophrenia

Conference Discussion - Temple Room
11:30 AM – 12:45 PM

Discussants
Prof Michael Berk

AGM, Prizes and Wrap up
Dr Tertia Purves-Tyson

Conference Close
12:45 PM

Invited Plenary Speakers

11th Isaac Schweitzer Plenary Lecture

Imagining precision medicine for psychiatry: an incomplete template

Prof Suresh Sundram – Chair and Head, Department of Psychiatry, Monash University

Professor Suresh Sundram (MBBS, MMed, FRANZCP, PhD) is a psychiatrist and neuroscientist committed to understanding the biological foundations of schizophrenia and related disorders in order to improve the lives of affected patients and families through the development of relevant biomarkers and ultimately disease modifying treatments.

He is Chair and Head, Department of Psychiatry, School of Clinical Sciences, Monash University; Director of Research, Mental Health Program, Monash Health; and Clinical Director, Cabrini Outreach. He is co-Chair of the Monash Partners Neuroscience and Mental Health Theme. At Monash University and Monash Health, he established and leads the Translational Molecular Psychiatry program with over 25 staff and students which uses a recursive bedside to bench and back philosophy to discover new molecules and genes of relevance to the major psychiatric disorders. Prior to these roles he established and led a molecular laboratory at the Mental Health Research Institute in conjunction with a clinical research laboratory at the Northern Hospital which transferred to the Florey Institute of Neuroscience and Mental Health where he also was appointed as Head of the Statewide Psychotropic Drug Advisory Service.

Professor Sundram has conducted in excess of 40 phase II, IIIA, IIIB and IV industry-sponsored and investigator-initiated clinical trials with multiple pharmaceutical companies. Currently, he co-supervises the Clinical Psychedelic Laboratory at Monash University conducting cutting edge clinical research using psychedelic agents in mental disorders. He has held a number of international roles including current President-elect, Asian College of Neuropsychopharmacology; expert consultant, United Nations High Commissioner for Refugees; Member, Joint Advisory Committee to the Governments of Australia and Nauru on Nauruan Regional Processing; Co-Chair, Asian Schizophrenia Network; Executive Committee Member and Member, Section on Developing Countries, World Psychiatric Association.

Chair: Brian Dean

14th Aubrey Lewis Plenary Award

Recent advances in nutritional psychiatry: novel mechanisms, interventions, and guidelines

Dr Wolfgang Marx – Senior Research Fellow, Food & Mood Centre, Deakin University

Dr Wolfgang Marx is a Senior Research Fellow and an NHMRC Emerging Leader at the Food & Mood Centre where he leads the Nutraceutical Research stream.

Wolfgang is president of the International Society for Nutritional Psychiatry Research as well as an honorary research fellow at The Florey Institute of Neuroscience and Mental Health, La Trobe University, and Bond University.

Wolfgang's current research program covers a broad range of projects involving the development of international guidelines for lifestyle interventions, and the investigation of the efficacy and mechanisms of action of novel food and nutraceutical interventions in mental health.

Chair: Robyn Brown

Invited Plenary Speakers

International Keynote Speaker

GABA and cognitive deficits in depression and aging: mechanisms and therapeutic targeting

Prof Etienne Sybille – Campbell Family Chair, Mental Health Research Institute of CAMH, Toronto, ON, Canada

Prof Etienne Sibille, PhD, is senior scientist and Chair of the Campbell Institute at CAMH, and Professor of Psychiatry, and of Pharmacology and Toxicology at the University of Toronto.

He is a neuroscientist with 25+ of experience in investigating the biological bases of neuropsychiatric disorders. His group has provided key evidence in support of several major hypotheses for biological mechanisms implicated in depression, aging and age-related disorders. He has published close to 150+ research and review papers and has attracted international recognition, being supported by NIH, CIHR and by several foundations for the past 25 years.

Building on breakthrough findings from his group over the past 10 years, he has now developed novel therapeutics that he intends to bring to the clinic for treating and preventing cognitive symptoms in depression and in age-related disorders, but also for healing the brain cells that are affected by these disorders. He is co-Founder and chief scientific officer of DAMONA Pharmaceuticals.

Chair: Lizzie Manning

Early Career Researcher Network Plenary Award

ECRN Speakers

Dr Alex Guerin – University of Melbourne

Methamphetamine use in adolescence: from laboratory studies to novel treatments

Methamphetamine use disorder is a chronic, relapsing condition with adverse health and psychosocial consequences. Methamphetamine use commonly starts in adolescence or early adulthood, adversely impacting the developmental trajectory. New treatment approaches for young people are required. In this plenary, I will provide an overview of my work to date - from the preclinical and human laboratory studies conducted during my PhD, to the clinical trials I currently lead. I will also discuss my research program's future directions.

In the first part of this plenary, I will review the key findings from my PhD research. I will then present preliminary data from two ongoing clinical trials investigating novel pharmacotherapies for young people with methamphetamine use disorder. I will highlight how fundamental and preclinical research have informed the development of these trials and discuss the potential mechanism of actions of these novel treatments. I will briefly discuss results from a recent meta-analysis I conducted, and will conclude this talk by discussing the future directions of my research program and discuss how new treatments may help reduce the marked social deficits observed in this vulnerable and often under researched population.

Dr Cassandra Wannan – Orygen, Parkville, Parkville, Victoria, Australia; Centre for Youth Mental Health, University of Melbourne, Melbourne, Victoria, Australia

The impact of psychosocial stress on body, brain, and cognitive ageing across different mental health disorders

Psychosocial stress, including poverty, childhood neglect and maltreatment, traumatic events, and social isolation, is both a risk factor for and consequence of mental health disorders. However, it is unclear whether particular types of stress are more strongly associated with particular disorders, or whether these stressors represent non-specific risk factors for poorer mental health outcomes. Furthermore, the biological and cognitive impacts of various types of stressors in individuals with mental illness is poorly understood. In this plenary, I will describe my recent work which utilises the UK Biobank to investigate the prevalence of different types of psychosocial stress in individuals with mental health disorders compared to individuals with physical health diagnoses and healthy individuals, and examines relationships between psychosocial stress and physiological ageing across multiple brain and body systems in individuals with mental illness.

Findings of this work revealed that Individuals with mental, but not physical, health diagnoses had significantly higher scores across most stressors compared to healthy individuals. Across diagnoses, total stress burden was most frequently associated with pulmonary, musculoskeletal, hepatic, whole-body, brain, and cognitive ageing. Stressors most associated with body, brain and cognitive system ageing were those reflecting deprivation, including low individual and neighbourhood SES, unemployment, and unmet needs.

Symposia Abstracts

Symposium 1. A pathway towards improved treatment strategies for eating disorders

Eating disorders are complex psychiatric illnesses associated with numerous medical comorbidities and sequelae. They have a population prevalence of approximately 4-5% and are one of the deadliest mental health conditions, with alarmingly high mortality rates. Despite this substantial public health burden, we still know remarkably little about the underlying biology of eating disorders which speaks to the paucity of effective treatment strategies available. Both anorexia nervosa and binge eating disorder are associated with emotional dysregulation, repetitive negative thoughts, compulsive behaviour, and disruptions in reward and cognitive processing that override the homeostatic maintenance of energy balance and survival. In this symposium, we will present data from both humans (Trevor Steward, ECR, Melbourne Neuropsychiatry Centre) and animals (Claire Foldi, EMCR, Monash University; Robyn Brown, EMCR, Bio21 Institute/Unimelb) which delve into the neurobiology underlying these processes. Prof Phillipa Hay (senior psychiatrist, Western Sydney University) will present a pathway for how neuroscientific evidence gained from the biological psychiatry field can be incorporated into treatment strategies to ultimately improve outcomes and the lived experience of those suffering from eating disorders. Existing barriers to this pathway will also be discussed, including the siloing of medical professions, particularly for those individuals with high BMI who may be receiving treatment for both weight loss and eating disorder symptoms in parallel. Our symposium has diversity in terms of career stage (early, mid and senior), gender (75% female), and institute (Monash University, Melbourne University, Bio21 Institute, Western Sydney University), as well as research focus/techniques (animal models, human imaging, clinical trials).

Chairs and Discussants: Dr Robyn Brown (University of Melbourne/Bio21 Institute) and Prof Phillipa Hay (Western Sydney University)

Dr Trevor Steward, University of Melbourne

Biography: Trevor Steward is a NHRMC Emerging Leader Fellow at the University of Melbourne School of Psychological Sciences and Melbourne Neuropsychiatry Centre. His research focuses on using ultra high-field 7-Telsa MRI technology to understand how subcortical regions of the brain contribute to common symptoms found across psychiatric disorders. Although the majority of his research to date has examined the neuropsychopathology of eating disorders, he also conducted studies on mood disorders, PTSD, and obesity. His aim is to leverage neuroimaging tools to inform brain-based treatments and to predict individual clinical outcomes. He is the co-author of over 90 publications, including in journals such as Molecular Psychiatry and Psychological Medicine.

Abstract: Binge eating disorder is the most prevalent eating disorder, and less than 50% of binge eating disorder patients respond to currently available treatments. Binge eating episodes are characterized by recurrent episodes of excessive food consumption, loss of control and feelings of shame. Most human neuroimaging research to date on binge eating has focused on alterations in the cortex and basal ganglia, while overlooking possible contributions from smaller regions in the brainstem and subcortex. Advanced imaging technology like 7-Tesla MRI provide an opportunity to obtain detailed structural and functional information about subcortical systems involved in binge eating. This presentation will highlight recent findings from two processes known to play a crucial role in triggering binge eating: stress reactivity and repetitive negative thinking. The extended amygdala, thalamic nuclei and the hypothalamus are known to modulate stress response during food cue presentation and receipt. Dysfunctions in these regions can disrupt the balance between emotion regulation and eating behaviours, leading to increased food intake. Likewise, repetitive negative thinking, defined by persistent negative thoughts and rumination, increases vulnerability to binge eating. New evidence will be presented on how thalamo-cortical pathways are involved in generating and maintaining repetitive negative thinking, thereby perpetuating binge eating behaviours. In summary,

there is growing evidence to support the subcortex playing a vital role in maintaining binge eating episodes. Integrating these findings in neurobiological models of binge eating advances our understanding of the complex interplay between neurobiology, psychology, and behaviour in BED, informing the development of more effective interventions.

Dr Claire Foldi, Monash University

Biography: Dr Claire Foldi is a Laboratory Head at the Monash Biomedicine Discovery Institute (BDI), where she leads a program of research focused on the neurobiological underpinnings of anorexia nervosa. Much of this work has centred on how cognition, behaviour and activity within specific neural circuits are involved in the development of compulsive exercise and pathological weight loss in the activity-based anorexia (ABA) rat model. The Foldi Lab is now investigating how psilocybin acts in the brain to modify behaviour in order to gain insight into its therapeutic potential for anorexia nervosa with funding from the National Health and Medical Research Council of Australia. Dr Foldi also co-leads the Workforce Development stream of the Australian Eating Disorders Research and Translation Centre (AEDR&TC) and is an affiliate of the Monash Centre for Consciousness and Contemplative Studies (M3CS) and the Monash Neuromedicines Discovery Centre (NDC).

Abstract: AN is the deadliest of all eating disorders, and there are currently no effective and durable treatment options. Those with AN and compulsive exercise (up to 80%) are at risk of poorer response to standard treatment. One barrier to the treatment of compulsive exercise in the context of AN is that the standard protocol requires strict prohibition in the face of the medical acuity associated with this disorder. In order to systematically investigate the neuronal underpinnings of compulsive exercise we use the activity-based anorexia (ABA) rat model, which remains the only experimental approach whereby laboratory rats will choose self-starvation over homeostatic energy balance (that will lead to death if left unchecked). There are multiple similarities between ABA in rats and individuals with AN, including a predominance of phenotype in young females, altered hormonal and neuronal function and compulsive exercise. In this presentation, I will describe a series of experiments in which we used chemogenetics in combination with the ABA model to determine the involvement of cortico-striatal circuitry in the development of compulsive wheel running in female rats and aligned these with operant measures of cognitive flexibility and compulsive behaviour. These data are complemented by studies using fiber photometry to record changes in activity in medial and lateral sub compartments of the dorsal striatum during value-based decision-making. Together, our studies contribute to an understanding of why ABA rats develop compulsive exercise in the context of limited access to food and will allow detailed insight into how this behaviour arises in humans.

Dr Robyn Brown, University of Melbourne/Bio21 Institute

Biography: Robyn Brown is an ARC DECRA Fellow and head of the Behavioural Neuropharmacology Laboratory in the Department of Biochemistry and Pharmacology, University of Melbourne/Bio21 institute. She completed a PhD in 2010 (Monash University) and Bachelor of Commerce/Science (honours) in 2004 (University of Melbourne). She completed her postdoctoral training with Peter Kalivas (USA). During her postdoc Robyn established an independent line of research investigating the parallels between drug addiction and overeating. Her laboratory studies use preclinical models to investigate the neural mechanisms underlying compulsive forms of motivated behaviour such as loss-of-control eating, binge eating and addiction using a multi-disciplinary approach involving behaviour, electrophysiology, fibre photometry, chemo genetics, mutiomic approaches and transgenics.

Abstract: Binge eating disorder is the most prevalent eating disorder and is associated with significant comorbidities. A hallmark feature of binge eating is a loss of control overeating insomuch that eating behaviour is compulsive in nature, persisting in the face of negative consequences. Disorders of compulsion

are often associated with deficits in corticostriatal circuitry. Striatal glutamatergic dysfunction in particular is associated with addictive behaviour towards drugs of abuse. We used an intermittent access model of binge eating to determine whether similar glutamatergic deficits exist in an animal model of binge eating. Rats provided intermittent access to high-fat/high-sugar 'western diet' 1h x 3 per week in a stochastic nature for 8 weeks showed increased compulsive-like eating of this diet compared to both rats provided the diet continuously, as well as rats provided only standard chow (note: animals were not food restricted at any point during the protocol). Intermittent access 'binge' rats also showed changes in glutamate receptors and proteins in the dorsal, not ventral striatum, synonymous with glutamate dysfunction observed in animal models of drug addiction in ventral striatum. Collectively these data point to glutamatergic dysfunction in dorsal striatum as a mechanism underlying compulsive eating in binge eating disorder. These data also point to parallels in the neurobiology underlying binge eating disorder and substance use disorder. Lastly, this data suggests that sporadic and intermittent access to 'junk food' (even just 1h, 3 times per week) is sufficient to promote binge eating symptoms and associated neuroplastic changes.

Prof Phillipa Hay, University of Western Sydney

Biography: Professor Phillipa Hay DPhil, FAED, MD, is a leading mental health researcher, educator, and practicing Psychiatrist. Her research has been translational, guided policy and practice and award winning, e.g., in 2015 she received the Lifetime Leadership Award from the ANZ Academy for Eating Disorders, and in 2020 she was awarded the RANZCP Senior Research Award. She laid the foundations for mental health programs in two new medical schools James Cook and Western Sydney. She has published over 400 indexed scientific papers. She has led major Australian epidemiological surveys, been a leading Investigator on all major randomised Australian controlled trials of therapy for adults with anorexia nervosa, as well as others in bulimia nervosa and binge eating disorder, and has led many Cochrane and other systematic reviews distilling the research evidence.

Abstract: Eating disorders are mental health problems characterised by dysregulation of appetite systems with diverse intra and inter-personal psychological constructs that drive behaviours such as binge eating and compulsive exercise. Advances in neuroscience, particularly genome wide association studies are pointing to new conceptualisations of phenotypic groups of people with symptoms that may be delineated along dimensions of compulsivity/impulsivity and reward sensitivity. Contemporary treatments are often transdiagnostic and/or show similar efficacy of diverse approaches for the same disorder, particularly for people with anorexia nervosa. Neuroscience, such as the understanding of how disrupted thalamo-cortical pathways may play a specific role in negative thinking and binge eating behaviours, or how cortico-striatal circuits can drive both compulsive eating in binge eating models and compulsive exercise in anorexia nervosa, has the capacity to inform a more nuanced approach to treatments. Instead of "one size fit all" people may be offered a neurocognitive assessment to derive a personal profile and then offered an individualised nuanced treatment package. This may include a range of psychological and other approaches to e.g., reduce impulsivity, enhance self-effectiveness and/or modulate compulsivity. This would be in alignment with the recognition that person cantered and preferenced treatment is urgently needed to improve outcomes and the lived experience of people with eating disorders.

Symposia Abstracts

Symposium 2. Showcasing advanced human post-mortem techniques to better understand the molecular pathology of schizophrenia: a critical link for translation

A major challenge in psychiatry is to identify reproducible pathologies and targets for new drugs and biomarkers. Human postmortem tissue from people with psychiatric disorders are a highly valuable resource used to gain insight into the pathologies of psychiatric disorders as a first step toward drug and biomarker discovery. However, several challenging factors have plagued this field including heterogeneity of the disorder and limited access to brain tissue. Importantly, previous studies have largely used bulk homogenates of brain tissue to assess gene expression changes meaning cell-specific changes critical to the pathology of the psychiatric disorder could not be identified. This symposium will showcase the latest application of innovative single cell omics technologies that has enabled the discovery of cell specific pathologies in severe psychiatric disorders across multiple labs in Australia. Novel findings in astrocytes, microglia, oligodendrocytes neural stem cells, and GABAergic interneurons will be presented by rising stars in the field, Natalie Matosin (Wollongong), Hayley North (NeuRA) and Wittaya Suwakulsiri (Monash). Senior leader in the field, Prof. Brian Dean (Florey Institute) will then present a translational journey of post-mortem findings to clinical application with insight into sub-groups of schizophrenia that speak to the heterogeneity of the disorder. Eminent post-mortem leader in the field, Prof. Cyndi Weickert will act as discussant, ensuring a vigorous and exciting discussion on these world leading topics. The symposium is balanced by a mixture of ECRs (North and Suwakulsiri), mid-career (Matosin and Hill) and senior researchers (Dean and Weickert) with diverse cultural and gender backgrounds.

Chair and Discussant: Rachel Hill (Monash University)

Dr Natalie Matosin, University of Wollongong

Biography: Dr Natalie Matosin is an Al & Val Rosenstrauss Senior Fellow (Rebecca L Cooper Medical Research Foundation) and Head of the MINDS Lab at the University of Wollongong UOW, Australia. Natalie was awarded her PhD in Neuroscience at UOW, and subsequently undertook early postdoc training at the University of New South Wales. Natalie then received Fellowships from the NHMRC (CJ Martin), Humboldt Foundation, and the International Brain Research Organisation to undertake international training at the Max Planck Institute of Psychiatry, Munich, with Prof Elisabeth Binder, a global leader in psychiatry, stress and genetics. Natalie developed highly specialised expertise in single cell genomics technologies and state-of-the-art histology approaches. Natalie returned to her alma mater UOW in 2018 to establish the Mental Illness, Neurobiology and Disorders of Stress (MINDS) Lab. The MINDS Lab's mission is to understand the complexity of the human brain and the processes that lead to brain disorders. To do this, we merge cutting edge single nucleus and spatial omics technologies with histological approaches in postmortem and ex-vivo human brain tissues, animal and cell models, to contextualise cell-type specific molecular changes at the cellular level. We work as part of an international team with world-leaders at research institutes, universities and brain banks spanning Australia, Canada, Germany, Iceland, Sweden, and the USA

Abstract: Early life stress is a major societal problem due to the unacceptably high prevalence that transdiagnostically increases risk to psychopathology. Neuroglia, commonly referred to as "nerve glue," are crucial for literally holding the brain together, shaping its intricate structure and function. Consequently, neuroglia are implicated in various psychopathologies with global dysfunction, including schizophrenia, depression, and bipolar disorder. Animal and cell studies have shown that neuroglia are highly stress responsive, and alterations to their function generates psychiatric-like symptoms; however glia are relatively understudied in humans, presenting a critical knowledge gap given glia are often poorly conserved between rodents and humans. My lab has been combining single-cell sequencing, spatial transcriptomics, and

histology to identify and characterise human neuroglia and how they are impacted by stress/psychopathology. We examine postmortem samples from individuals across a range of psychiatric disorders exposed to childhood versus adulthood stress, as well as 2D and 3D human pluripotent stem cell-derived glia treated with dexamethasone, a cortisol analogue, to mimic the stress response in a dish. In this symposium, I will give an overview of our work focusing on characterising astrocytes and microglia in the human prefrontal cortex. Our studies have shown, for the first time, that there are many subtypes of molecularly-defined astrocytes. Furthermore, these astrocyte subtypes in combination with previously defined microglia subtypes, are overrepresented in individuals with transdiagnostic psychiatric disorders that were exposed to severe childhood stress. Lastly, we suggest that changes in astrocytes and microglia may culminate in neuropathologies related to neuroinflammation and the blood brain barrier.

Dr Wittaya Suwakulsiri, Monash University

Biography: Dr. Suwakulsiri is an early career postdoctoral researcher and a computational biologist at the Translational Molecular Psychiatry laboratory, Monash University. Since 2016, he has focused on advanced Molecular Biology techniques and Bioinformatics. As a computational biologist, he has gained experience in multi-omic data analysis such as proteomics, transcriptomics, fusion genes, DNA methylation and multi-sample single-nuclei (sn) RNA sequencing data analysis using high performance computer (HPC) clusters. He has been invited to share his analysis on snRNA sequencing data from people with Schizophrenia (SCZ) and Major Depressive Disorder (MDD) as an invited speaker at the 2023 Single-Cell User Meeting Group, Melbourne along with other laboratory heads in Australia. In Neuroscience, he has established a pipeline to isolate single nuclei and live cells from post-mortem brain tissues from people with SCZ and MDD and mouse brain tissues (schizophrenia-like mouse models), respectively. Furthermore, he is the only researcher from Australasia who was selected to attend the prestigious advanced 2022 Neuroscience CAJAL Training program, Neuroepigenetics at the Bordeaux School of Neuroscience in Bordeaux, France with a travel award from the Federation of European Neuroscience Societies (FENS) and Australasia Neuroscience Society (ANS). Already, his research articles, review articles and a book chapter have received over 1,189 citations during his PhD study and early research career.

Abstract: Cortical GABAergic dysfunction in schizophrenia is thought to contribute significantly to the cognitive impairments associated with the disorder. GABAergic interneurons inhibit the firing of neurons and consist of multiple subtypes that differ in their innervation (axonal or dendritic), electrophysiological properties, morphology and the expression of specific peptides or calcium binding proteins. Given the distinct role of each GABAergic subtype, it is important to understand which subtypes are altered in schizophrenia and how. Altered expression of parvalbumin and somatostatin subtypes have been reported in schizophrenia. To gain insight into how GABAergic subtypes may be altered, cell-specific gene expression was performed using innovative single nuclei RNA sequencing in human post-mortem prefrontal cortex from people with schizophrenia (n=47,896 cells from 6 samples) compared to controls (n=31,717 cells from 5 samples). We identified multiple clusters of GABAergic neurons including parvalbumin (PV)-, somatostatin (SST)- and vasoactive intestinal polypeptide (VIP)-expressing neurons. We further identified several GWAS genes previously associated with schizophrenia, such as CACNA1A, MAPT and LRRC4B, that were altered across all interneuron subtypes. Further interneuron specific gene expression changes were also noted, including upregulation of GRIN2D, NTRK3 and MEG3 in PV interneurons, and GRIN3A and NRXN2 in SST interneurons in people with schizophrenia compared to control. We are currently analysing a larger dataset of 15 people with schizophrenia, 16 controls and 19 with major depressive disorder (MDD) (over 400,000 nuclei). We will present altered genes and functional pathways in schizophrenia and MDD compared to control and distinguish schizophrenia and MDD at the interneuron-specific cellular level.

Dr Hayley North, NeuRA

Biography: Dr Hayley North is a post-doctoral researcher at NeuRA and conjoint lecturer at UNSW focussed on the neurobiology of schizophrenia. Her publications in high impact journals primarily involve the topics of inflammation and neurogenesis in schizophrenia and bipolar disorder. Outside of the lab, Hayley founded an organisation called Understand Your Brain to communicate neuroscience research to help non-scientists improve their well-being and mental health. Her PhD titled 'Discovering links between inflammation, neurogenesis, brain structure and brain function in schizophrenia' earned the UNSW Dean's Award for Outstanding PhD Theses. Some other awards include the BPA best early career data-blitz 2022, The Don and Warwick McDonald Award for Schizophrenia Research 2018 and 2021, The Chris Hunter Scholarship for Schizophrenia Research 2019 and 2020 and The Neil McConaghy Prize For Best Seminar 2019.

Abstract: The subependymal zone (SEZ; also termed subventricular zone) constitutes a neurogenic niche that persists during post-natal life. In humans, the neurogenesis declines after the first year of life and recent debate has questioned the existence of adult neurogenesis. However, studies discovering markers of stem and progenitors cells highlight the neurogenic capacity in the adult human SEZ, with altered neurogenesis markers in psychiatric conditions. Here we characterised the adult human SEZ using singlenucleus RNA sequencing (snRNAseq) comparing 4 youth (age 16-22) and 4 middle-aged adults (age 44-53). We identified 11 cellular clusters, including clusters representing neural stem cells (NSCs), neuroblasts, immature neurons and oligodendrocyte progenitor cells. The relative abundance of NSC and neuroblast clusters did not differ between the two age groups, indicating that neurogenesis persists. The relative abundance of oligodendrocyte progenitors and microglia decreased in middle-age, indicating that non-neuronal cell composition differs into adulthood. The expression of genes related to nervous system development was higher in youth suggesting ongoing central nervous system plasticity in youth, which may somewhat decline by middle age. We are currently undertaking deep snRNAseq in the SEZ from 8 controls, 8 low- and 8 high-inflammation schizophrenia cases. We hope that by BPA we can share preliminary findings from this study because our previous bulk RNAseq studies suggest that neurogenesis is altered in schizophrenia, especially in those with elevated inflammation.

Prof Brian Dean, Florey Institute for Neuroscience and Mental Health

Biography: Brian Dean is an internationally recognised expert on muscarinic receptors and their role in the molecular pathology and treatment of schizophrenia. Additionally, Brian has made a significant contribution to understanding the differences in the molecular pathologies of psychiatric disorders by showing marked differences in gene expression across the cortex in schizophrenia and in the same cortical regions from people with schizophrenia, major depressive disorder and bipolar disorder. Brian's research has become translational by using PET imaging to measure levels of muscarinic M1/M4 receptors in the living brain. Brian's contribution to understanding the molecular pathology of psychiatric disorders has been recognised by the Schizophrenia International Research Society (Outstanding Basic Scientist Award) and Lundbeck / AsCNP (Outstanding Basic Scientist Award). Brian has been an author on over 300 papers and book chapters, many in high impact journals. Brian has a significant role in the dissemination of psychiatric research data by acting as Deputy Editor for Psychiatry Research and Associate Editor for Comprehensive Psychiatry. Brian has had leading roles in learned societies including acting as the Foundation President for BPA (2 terms) and Treasurer for the World Psychiatry Society (CINP) (2 terms). Brian has also served on committees of many funding bodies and has had multiple roles in the peer review process of the NHMRC. In his role as Board Member and Head of the Rebecca Cooper Foundation Scientific Advisory Committee, Brian has ensured significant funding is available for early and mid-career scientists to aid their career development

Abstract: Multiple research findings suggest a role for muscarinic receptors in the molecular pathology and treatment of schizophrenia1 and argued that activating muscarinic M1 / M4 receptors would give clinical benefits for those with the disorder2. This hypothesis may be proven with a coformulation based on the M1 / M4 agonist, xanomeline, producing better than placebo outcomes in 3 phase three clinical trials3. These trials argue that the coformulation will be an affective antipsychotic and reduce the severity of the negative symptoms of schizophrenia. Significantly, a sub-group within the syndrome of schizophrenia can be separated because they have a marked deficit in cortical muscarinic M1 receptors 4,5. Notably, in replicating the presence of the sub-group within schizophrenia we have reported that the sub-group appears to be less cognitively impaired compared to others with the disorder5. In addition, the subgroup has a number of differences in their cortical molecular cytoarchitecture compared to controls, people with schizophrenia and those with other psychiatric disorders1. These data argue their may be unique biochemical pathways affected within the cortex of the deficit sub-group that may contain targets for drug treatments. In this presentation their will be an update on progress on targeting muscarinic receptors to treat schizophrenia and the growing understanding of the molecular pathology of the muscarinic receptor deficit sub-group within schizophrenia.
1. Dean et al. Front.Mol.Neurosci. (2023) 17, 1124333, 2. Dean et al. Curr.Mol.Med. (2003) 3, 419-426, 3. Paul Am.J.Psychiatry (2022) 179, 611-627, 4. Scarr Mol.Psychiatr. (2009) 14, 1017-1023, 5. Dean Schizophr.Res. (2023) 255, 174-282.

Symposia Abstracts

Symposium 3. Cannabidiol for substance use disorder treatment: novel mechanistic insights and translation into the clinic

Substance use disorder affects 1 in 20 people in Australia, costs >$80 billion annually, and relapse rates remain high. There is an urgent need for novel pharmacotherapies for substance use disorders. Cannabidiol (CBD) is a promising treatment for substance use disorder, demonstrating efficacy in preclinical models for alcohol, opioids and psychostimulants. Recent clinical trials have started to assess CBD for cocaine use disorder, but other drug classes have not been investigated. This symposia brings together male and female PhD candidates and postdoctoral fellows from several Australian Universities working on clinical and preclinical CBD-based research for substance use disorder. We will present data from the first clinical trials evaluating CBD for alcohol and methamphetamine use disorder, and describe functional impacts of CBD using neuroimaging and psychophysiology (Dr Alex Guerin, University of Melbourne; Tristan Hurzeler, University of Sydney). We will also present preclinical discoveries of novel mechanisms of CBD for opioid and cocaine use disorder, for despite the swift implementation of CBD into clinical trials, the mechanism/s of action of CBD in reducing substance use disorder behaviours is poorly understood (Dr Rose Chesworth, Western Sydney University; Ms Rhianne Scicluna, University of Sydney). Together, this symposia will provide critical insights into CBD's translation into the clinic (i.e. how preclinical outcomes influence clinical trials) and highlight mechanistic questions from clinical data that can be addressed with preclinical work, facilitating reverse translation. We will debate psychological and physiological mechanisms of CBD, enabling a targeted approach in future translational CBD research across several drug classes.

Chairs and Discussants: Dr Rose Chesworth (Western Sydney University) and Dr Nicholas Everett (University of Sydney)

Dr Alexandre Guerin, University of Melbourne

Biography: Dr Alexandre Guerin is a Research Fellow and Project Manager at the Centre for Youth Mental Health (University of Melbourne) and Orygen. Dr Guerin completed his PhD at the Florey Institute of Neuroscience and Mental Health in 2021. Under the supervision of A/Prof Jee Hyun Kim, he investigated risk factors associated with adolescent-onset methamphetamine use in people with methamphetamine use disorder. He has since joined Orygen's Substance Use Research Group led by A/Prof Gill Bedi. He has a keen interest in psychostimulants and their effect on the developing brain. Dr Guerin currently manages several clinical trials of novel psycho- and pharmacotherapies for young people with substance use problems, including the Integrated Treatment for Young People with Psychological Distress (INTEGRATE) study, and the MASKOT and CALM studies - two open-label trials investigating new treatments for methamphetamine use disorder in youth.

Abstract: Methamphetamine use disorder can be a chronic, relapsing condition with adverse health and psychosocial consequences. Methamphetamine use commonly starts in adolescence or early adulthood, adversely impacting the developmental trajectory. New treatment approaches for young people are required. One possibility not yet investigated in humans is the non-intoxicating cannabinoid cannabidiol (CBD). CBD interacts with multiple neural systems and has a range of potentially therapeutic effects including anxiolytic, anti-psychotic and anti-depressant properties. Preclinical research also supports a therapeutic potential for methamphetamine use disorder, with CBD reducing methamphetamine self-administration and drug-primed reinstatement in rodents, which has directly motivated this clinical trial. The aim of this open-label study is to assess the safety and tolerability of CBD in young people (15 to 25 years-old) with methamphetamine use disorder. Participants (N = 12) in the CALM study (Cannabidiol – A novel pharmacotherapy for Lowering Methamphetamine use) will complete 8 weeks of oral CBD (800-1000mg/day), with follow-ups at weeks 4, 8,

and 12. Primary endpoints are safety (assessed with liver function tests) and tolerability (assessed by the number of participants withdrawing from the study due to adverse effects). Secondary endpoints are preliminary efficacy of CBD, assessed by reduction of methamphetamine use and craving in young people with methamphetamine use disorder. Recruitment will commence in mid-2023, and this study will provide feasibility and tolerability data for future fully powered clinical trials of CBD for young people with methamphetamine use disorder. The measures used in clinical trials, and their preclinical models (and lack thereof) will be also discussed.

Tristan Hurzeler, University of Sydney

Biography: Tristan Hurzeler is a Medicine and Health PhD candidate in his final year at The University of Sydney and is working at the Edith Colins Centre. As an undergraduate, Tristan completed a Bachelor of Psychological Sciences at UNSW and then continued to complete a Masters of Brain and Mind Sciences in which he undertook a geospatial analysis of alcohol-related suicide occurrences. Subsequently, his research interests span psychology, epidemiology and neuroscience disciplines and is primarily focused on substance use disorder. Tristan's PhD research program is conducted at the Royal Prince Alfred Hospital and is aimed at elucidating the therapeutic mechanisms of CBD in the management of Alcohol Use Disorder. Due to his interdisciplinary background, Tristan uses a vast array of neuro psychophysiological measurement techniques including fMRI (task-based and resting state), MRS, psychophysiological testing, and neuropsychological cognitive testing. The major aims of his PhD are to examine CBD's effects on cue-induced craving though physiological and neurobiological indices. Since commencing his PhD in late 2020, Tristan has been involved in 11 publications and is intending to complete his PhD early to mid-2024.

Abstract: Current treatments for alcohol use disorders (AUD) have limited efficacy. Recently, cannabidiol (CBD) has been examined in a multitude of clinical settings. Preclinical and clinical results suggest that CBD might be particularly well-suited for the treatment of AUD and may reduce alcohol cue and stress-induced craving and alcohol-seeking. Preclinical studies have shown that CBD mitigates withdrawal symptoms, reduces voluntary alcohol consumption, and alcohol-induced relapse behaviours in preclinical models of alcohol dependence. Most recently, an 800 mg regime of CBD was found to be more effective than 400 mg in reducing craving and anxiety in heroin users using a psychophysiology 3-day dosing paradigm. In this symposium, I will discuss a research program that investigates CBD as a new and potentially effective pharmacotherapy for alcohol use disorder, with a particular focus on neuro psychophysiological indices of alcohol and stress cue-induced craving. We will consider the results and implications from psychophysiological and neuroimaging paradigms applied in a double-blind, randomised, placebo-controlled, cross-over study in which non-treatment seekers were randomly allocated three days of four 200 mg CBD gel capsules (800 mg/day) or matched placebo. I will discuss the need for preclinical methods which model these clinical neural and psychophysiological manifestations of AUD, to improve clinical translation. Additionally, I will discuss the implications of these results on our understanding of the therapeutic mechanisms of CBD in reducing cue-induced craving.

Rhianne Scicluna, University of Sydney

Biography: Rhianne is a final year PhD candidate at the University of Sydney, researching new pharmacotherapies for opioid addiction using preclinical models. Rhianne has a bachelor's degree in psychology and neuroscience (with honours) and 6 years of research experience in psychopharmacology, neuroscience, and drug development. Her passion lies in translational research to improve treatments for psychiatric illnesses, particularly substance use disorders. Rhianne's PhD focuses on CBD's influence on physical dependence to opioids, including tolerance development and the withdrawal syndrome. She found that although CBD alleviates gastrointestinal symptoms in opioid withdrawal, combining CBD with opioids accelerates tolerance development and necessitates higher doses over time. In collaboration with Kinoxis

Therapeutics, Rhianne evaluated a novel small molecule for opioid addiction.Her research demonstrated efficacy in reducing negative psychological aspects of spontaneous opioid withdrawal and suggests potential for relapse prevention after long-term abstinence. This work has contributed to the advancement of the compound to phaseI clinical trials, informed phase II design, and secured external funding. Rhianne has one first author publication, 3 first author manuscripts, and co-authored several manuscripts. She has received 10 national and international awards and presented at 12 conferences. Rhianne will deliver a preclinical perspective with a translational focus, delving into the mechanisms underlying the effects of CBD on opioid use. She will shed light on the intricate interplay between CBD and opioids, offering insights for clinical practice.

Abstract: The potential of CBD as an adjuvant therapy for chronic pain management alongside opioids has gained attention, and CBD/opioid co-use is now widespread globally, despite lacking the evidence base to support this combined usage. It is therefore essential to identify how these drugs interact. We evaluated CBD's effectiveness in reducing oxycodone withdrawal and the impact of coadministration on short- and long-term oxycodone analgesia. We found that CBD reduces gastrointestinal upset associated with opioid withdrawal, but has no effect on negative affective symptoms, which is the key driver for drug seeking. Surprisingly, we discovered that CBD delays the metabolism of oxycodone into its less active metabolites and extends the analgesic efficacy of oxycodone. However, this delayed metabolism problematically accelerates the development of tolerance to oxycodone's analgesic 8 / 17 properties when administered sub-chronically. This acceleration in tolerance development wasn't observed with morphine, suggesting a unique interaction between CBD and the enzymes (CYP2D6 and CYP3A4) involved in oxycodone but not morphine metabolism, which CBD has been shown to inhibit in vitro. Further, CBD upregulated mu-opioid and cannabinoid-1 receptor mRNAs in the periaqueductal gray in oxycodone-, but not morphine-treated mice. Together this suggests a potentially dangerous drug-drug interaction between CBD and oxycodone, and given CBD's widespread availability and the common prescription of oxycodone, this discovery needs to be considered by patients and healthcare providers to be aware of the possible dangers associated with CBD/oxycodone co-use. The implications of this should also be considered when designing clinical trials using CBD to treat opioid use disorder.

Dr Rose Chesworth, Western Sydney University

Biography: Rose is an emerging leader in behavioural neuroscience investigating mental health and healthy aging (H-index: 18, 35 publications). Rose completed her PhD at the Florey in the Addiction Neuroscience laboratory under the supervision of Prof Andrew Lawrence, and now works as a postdoctoral fellow in the Behaviour Neuroscience Laboratory at Western Sydney University under the guidance of Prof Tim Karl. Rose’s research interests span animal models of drug-taking behaviour, Alzheimer’s disease and schizophrenia, and she has more than 10 years' experience in animal models of drug-taking behaviour. She has explored the potential of cannabidiol (CBD) for both substance use problems and schizophrenia using mouse models, and has investigated behavioural, brain and gut-based mechanisms for protective effects of CBD in these models. Rose collaborates with leading Australian researchers in the schizophrenia and dementia fields, supervises several PhD, Masters and Honours students, and teaches undergraduate medical students.

Abstract: Cocaine use disorder (CUD) is a global health problem with no approved medications. One potential treatment target is the gut microbiome, but it is unknown if cocaine induces long-lasting effects on the gut microbiome. Also, a novel therapeutic candidate for CUD, cannabidiol (CBD), can improve gut function in rodent models, and it is possible that protective effects of CBD against cocaine use in animal models may be regulated in part by improving gut health. We examined this question in the present experiment. Cocaine conditioned place preference (CPP) was conducted in 48 adult male C57BL/6JArc mice. Mice were treated with vehicle or 20 mg/kg CBD prior to all cocaine CPP sessions. Mice were tested drug

free 1, 14 and 28 days after cessation of cocaine and CBD treatment. Fecal samples were collected prior to drug treatment and after each test session. Gut microbiome analyses (i.e. microbe richness, diversity, species abundance) were conducted using 16s rRNA sequencing, and correlated with behavioural parameters. We found a persistent preference for a cocaine-environment in mice, which corresponded with long-lasting changes to gut microbe alpha diversity. CBD treatment reduced cocaine-environment preference, and returned gut beta diversity measures to control levels, while cocaine caused a persistent change to beta diversity which lasted for 4 weeks. Here we show that CBD reverses persistent cocaine-induced changes to gut microbe diversity. This suggests that CBD may act via the gut to reduce the memory of cocaine reward. Our data supports improving gut health and using CBD to limit cocaine abuse.

Symposia Abstracts

Symposium 4. The Markers in Neuropsychiatric Disorders Study: a simple blood test to improve diagnosis and care for people with cognitive, psychiatric, and neurological symptoms

Accurate diagnosis of psychiatric and neurological disorders poses a formidable challenge due to overlapping symptoms, despite the available investigations. Psychiatry has an urgent need for blood biomarkers which will improve accurate diagnosis and outcomes. Using ultrasensitive technology, we can now measure small fragments of neurofilament light (NfL) in blood, which correlates with neurodegeneration. The utilisation of NfL as a blood test holds promise for aiding clinicians in distinguishing between psychiatric and neurological disorders. By providing objective measures of neuronal damage, these biomarkers including NfL could contribute to more accurate diagnostic processes and personalised treatment. Additionally, their correlations with clinical markers may offer valuable insights into disease progression and treatment outcomes.

Clinical translation of these biomarkers requires research into its validity, reliability and clinical utility. This is the core aim of the Markers in Neuropsychiatric Disorders (MiND) Study. The MiND Study team presenting at the symposium is represented equally by gender, and are diverse in age, disciplines (psychiatry, neuropsychiatry, speech pathology, neuropsychology in the symposium team), and career stages (head of department, PhD student, postdoctoral fellow, psychiatrist, clinicians). Despite hailing from a range of backgrounds including Tasmania, Melbourne, Canada, USA and New Zealand, the team's affiliated institutes include Royal Melbourne Hospital, University of Melbourne, National Ageing Research Institute, Epworth Health, Ramsay Clinic Albert Road and Melbourne Neuropsychiatry Centre. Our collective success stems from the unique perspectives, expertise, and experiences contributed by each team member, representing an inclusive collaboration that enriches the MiND Study\'s outcomes and ensures its broader applicability to diverse populations.

Chair and Discussant: Dr Christa Dang (National Ageing Research Institute)

Dr Dhamidhu Eratne, Neuropsychiatry, The Royal Melbourne Hospital

Biography: Dr Dhamidhu Eratne graduated in medicine from the University of Auckland in 2007. After extensive experience in consultation liaison psychiatry and psychiatry of old age, he completed his two years of advanced training at Neuropsychiatry, obtaining his Fellowship of the Royal Australian and New Zealand College of Psychiatrists in 2016. After working as an old age psychiatrist and senior lecturer, Dhamidhu was proud to join Neuropsychiatry in 2017, working in the younger-onset and neuropsychiatry outpatient and inpatient, and epilepsy services. Dhamidhu's interests include younger-onset dementia, biomarkers, clinical reasoning, education, and the interface between psychiatry, neurology, and the rest of general medicine. He completed his certificate of advanced training in consultation-liaison psychiatry of advanced training and is completing the certificate in old age psychiatry. In addition, he is an Honorary Fellow at the Walter and Elizabeth Hall Institute of Medical Research and the University of Melbourne, and is a keen clinician researcher, and enjoys lecturing and supervising students. Dhamidhu is undertaking a PhD and is the clinical/research fellow on the Markers in Neuropsychiatric Disorders Study (The MiND Study), investigating biomarkers and other markers in neurodegenerative and psychiatric disorders, with a view to clinical translation to improve outcomes for patients, their families and clinicians, and the healthcare system.

Abstract: Background: Accurate, timely diagnosis of neuropsychiatric symptoms, in particular distinguishing primary psychiatric from neurological disorders and in younger people, can be challenging. NfL and other blood biomarkers have shown promise to reduce the diagnostic odyssey. Objectives: To investigate the diagnostic utility of NfL and other markers, to distinguish neurological/neurodegenerative from psychiatric disorders, to lead to a widely available screening blood test. Methods: We assessed NfL, P-tau181 and GFAP

in broad cohorts, including patients assessed for neurocognitive/psychiatric symptoms at Neuropsychiatry and memory clinics, in a range of disorders including Alzheimer disease, frontotemporal dementia, schizophrenia, 1 / 17 bipolar disorder, depression, functional neurological disorders, Niemann-Pick Type C, epilepsy. Findings: Updates on The MiND Study progress and findings that NfL differentiated diverse neurodegenerative from psychiatric disorders, with 90+% accuracy, from over 800 patients/participants, will be presented, with real patient and family stories to demonstrate the challenges and potential clinical impact of The MiND Study. P-tau181 and GFAP distinguished Alzheimer disease (mainly younger sporadic), from Non Alzheimer. As recruitment, sample analysis, and data collection is ongoing, the most up to date results including cognitive and neuroimaging markers, will be presented. Conclusions: NfL shows great promise as a diagnostic screening blood test, to identify neurological causes of neuropsychiatric symptoms. P-tau181 and GFAP show strong diagnostic utility in younger-onset Alzheimer disease. NfL could dramatically alter clinical care of patients with neuropsychiatric and neurological symptoms, improving outcomes for patients, their families, the healthcare system, and clinical trials, facilitating precision medicine algorithmic diagnostics incorporating other biomarkers and clinical/cognitive markers, for real-world clinical settings.

Wei-Hsuan Michelle Chiu, University of Melbourne

Biography: Michelle is also a PhD candidate at the Melbourne Medical School of the University of Melbourne and holds an honorary position at Neuropsychiatry of the Royal Melbourne Hospital. Her research focuses on the interrelationship between neuropsychiatric symptoms, cognition and biomarkers in neurocognitive disorders. She has experience working with people living with young onset neurodegenerative disorders and primary psychiatric disorders. She is a current executive committee member and student representative of the National Younger Onset Dementia Special Interest Group.

Abstract: Title: The interactions between negative symptoms and neurofilament light levels on cognitive domains in treatment-resistant schizophrenia (TRS) Background: TRS is defined as the persistence of symptoms in people with schizophrenia despite adequate treatment trials, with hypothesis that TRS may be the consequence of neurodegenerative process. To investigate, the interaction effects between clinical symptoms and levels of NfL on cognitive domains in TRS. Methods We obtained data for 95 patients with TRS including neuropsychiatric symptoms, cognitive functioning (memory, attention, processing speed, executive function, visuospatial function) and plasma NfL levels. GLMs were used to identify associations between neuropsychiatric symptoms and NfL, and their interaction effects on cognitive domains. Results We did not identify any direct relationship between NfL levels and neuropsychiatric symptoms or cognitive functions. Negative symptoms were negatively correlated with memory (r = -0.37, 95% confidence interval [CI]: [-0.6,-0.15]) and executive function (r=-0.45, 95% CI: [-0.66,-0.24]). Inattentiveness, a specific domain of negative symptoms, predicted impairments in all cognitive functions. NfL levels moderated the negative associations between inattentiveness and visuospatial (B = 0.29, 95% CI: [0.06,0.62]) and executive function (B = 0.28, 95% CI: [0.08, 0.67]) after adjustment for age and weight. Conclusions Our findings suggest that neuropsychiatric symptoms and cognitive impairments in TRS do not directly relate to neurodegeneration as measured by plasma NfL levels. NfL levels within the normal reference limits may have reflected some protective mechanisms that act to preserve visuospatial and executive function indirectly. Longitudinal and neuroimaging studies are required to elucidate the role of NfL in TRS

Dr Matthew Kang, The Royal Melbourne Hospital

Biography: Dr Matthew Kang is a clinician-researcher who recently obtained his Fellowship of the Royal Australian and New Zealand College of Psychiatrists. He is currently a research fellow for the MiND Study, Royal Melbourne Hospital Neuropsychiatry and Ramsay Clinic Albert Road, and is working on completing his PhD at the University of Melbourne. Through his research, he aims to gain a better understanding of the complex relationship between the brain and the mind, with the goal of improving assessment and care for patients with mental illness.

Abstract: Title: Neurofilament light and glial fibrillary acidic protein as a diagnostic and prognostic biomarker for mood disorders: A systematic review and meta-analysis Blood-based biomarkers of neuronal injury (NfL) and neuroinflammation (GFAP) are being increasingly used for diagnosis and prognosis in neurodegenerative conditions including multiple sclerosis. However, current literature is mixed as to whether these biomarkers are mildly elevated in mood and anxiety disorders. This is important to clarify given 2 / 17 neurodegenerative diseases can present with psychiatric presentations especially in the prodromal phase. The aim of this systematic review is to identify the association between neuronal and glial biomarkers in patients with mood and anxiety disorders compared to healthy controls. If appropriate, we will perform meta-regression analyses of comparing severity of mood and anxiety disorders with biomarker levels, as well as performing subgroup analyses of those with later-onset illness. A protocol for a systematic review has been submitted to PROSPERO, with the initial literature search identify 832 papers. We plan to complete the review and present the findings at BPA2023. Our findings will be important for the translation of these biomarkers to clinical practice, as it will either validate the use to differentiate neurodegenerative and psychiatric disorders, or potentially identify prognostic and diagnostic blood-based biomarkers for these prevalent psychiatric conditions.

Highest Ranked Abstracts

Targeting flexible learning to treat anorexia nervosa – insights into the serotonergic effects of psilocybin in animal models

Presenting Author: Kyna Conn

Kyna Conn - Biomedicine Discovery Institute, Monash University, Clayton, VIC 3800

Laura Milton - Biomedicine Discovery Institute, Monash University, Clayton, VIC 3800

Kaixin Huang - Biomedicine Discovery Institute, Monash University, Clayton, VIC 3800

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Erika Greaves - Biomedicine Discovery Institute, Monash University, Clayton, VIC 3800

Jihane Homman-Ludiye - Monash Micro Imaging Facility, Monash University, Clayton, VIC 3800

Claire Foldi - Biomedicine Discovery Institute, Monash University, Clayton, VIC 3800

Chair: Suresh Sundram

Background
Psilocybin is being explored as a novel therapeutic for anorexia nervosa (AN), and is proposed to act by alleviating cognitive inflexibility, a transdiagnostic characteristic examinable in preclinical animal models. Accordingly, we have previously shown that a single dose of psilocybin (1.5mg/kg) attenuates the development of pathological weight loss in the activity-based anorexia (ABA) rat model. In the present study, we examined the direct effects of psilocybin on cognitive flexibility using a reversal learning task in combination with selective serotonin receptor (5-HTR) antagonism, and assessed acute cellular activation and 5-HTR mRNA expression in the medial prefrontal cortex (mPFC).

Methods
Female Sprague-Dawley rats were trained to nose-poke into one of two operant ports to obtain sucrose rewards and administered psilocybin or saline 24h prior to reversal of the reward-paired port. The action of psilocybin via 5-HTR subtypes (5-HT1A or 5-HT2A) was antagonised with pre-administration of compounds ketanserin (non-selective 5-HT2A; n=23), MDL100907 (selective 5-HT2A; n=18) or WAY100635 (selective 5-HT1A; n=26). The time course-specific effects of a single dose of psilocybin on neuronal activity and 5-HTR abundance was examined with both acute cFos expression (a marker for cellular activation), and the in-situ hybridization assay, RNAscope, at 6h, 12h and 24h post-administration (n=5/group).

Results
Psilocybin enhanced cognitive flexibility by increasing accuracy at the initial reversal of reward contingencies (p=.031), which was abolished with antagonism of 5HT1A (p=.001) but not 5-HT2A (ketanserin; p=.071, MDL; p=.194) receptor subtypes. Intriguingly, 5HT2A antagonism impaired flexibility in control rats (ketanserin; p=.049, MDL; p=.006), whereas 5-HT1A antagonism did not (p=.747). Acute cFos expression was decreased in both the prelimbic (p<.001) and infralimbic (p=.001) cortices. In the infralimbic cortex specifically, psilocybin transiently increased the number of 5-HT1A-expressing cells which was normalised to control levels by 24h (p=.028). The number of cells expressing 5HT2A showed a trend towards the opposite pattern (p=.072).

Conclusions
Taken together, these findings support the potential of psilocybin to treat cognitive inflexibility in AN. While much focus in psychedelic neuroscience has been on the 5-HT2A receptor subtype, due to its necessity for their acute “hallucinogenic” effects, these results suggest its actions at the 5-HT1AR may be more relevant for therapeutic outcomes related to cognitive flexibility. This is brought into sharper focus considering that changes in the balance between 5-HT1A and 5-HT2A receptor binding have been observed in the PFC of patients with AN. Future studies will examine the functional consequences of psilocybin acting via 5-HTR subtypes using fiber photometry.

Highest Ranked Abstracts

Puberty and corticolimbic connectivity: implications for mental health

Presenting Author: Nandita Vijayakumar

Nandita Vijayakumar - School of Psychology, Deakin University; Centre for Adolescent Health, Murdoch Children's Research Institute

Sarah Whittle - Melbourne Neuropsychiatry Centre, University of Melbourne

Timothy Silk - School of Psychology, Deakin University; Developmental Neuroimaging, Murdoch Children's Research Institute

Chair: Suresh Sundram

Background
Undergoing puberty ahead of peers ("earlier pubertal timing") is a risk factor for adolescent mental health problems. Puberty also influences the maturation of brain regions implicated in mental health problems, including limbic and cortical regions. Functional connectivity between these regions (i.e., corticolimbic connectivity) thus represents a potential pathway between earlier pubertal timing and mental health problems. Understanding this pathway will aid identification of intervention targets to support adolescent mental health. Therefore, the current study examined pathways between pubertal timing and mental health via corticolimbic connectivity in 9-to-14-year-olds. We also explored whether family environments moderate these neural risk pathways.

Methods
Sample was derived from the Adolescent Brain Cognitive Development Study (N = 10,501). Puberty was measured with the Pubertal Development Scale. Connectivity was based on resting state MRI, extracting correlations between time courses for limbic regions (amygdala, hippocampus) and cortical networks (Gordon parcellation). Mental health (depressive and rule-breaking) problems were measured with the Child Behavior Checklist, and family environment was based on reports of family conflict and parental acceptance. Bayesian multilevel models examined corticolimbic connections as mediators of the relationship between pubertal timing and mental health problems, with family environments as moderators.

Results
Earlier pubertal timing was associated with decreased corticolimbic connectivity. Robust effects (with split-half sample replication) were identified for six connections, between limbic structures (bilateral amygdala and right hippocampus) and the cingulo-opercular network (CON), left amygdala and somatomotor (mouth) network, as well as between the left hippocampus and ventral attention network (VAN) and visual network. Five of six of these connections mediated the relationship between earlier pubertal timing and increased depressive problems. Finally, higher levels of parental acceptance buffered against these risk patterns in amygdala-CON, being related to less reductions in connectivity in those with earlier pubertal timing.

Conclusions
This study highlights neural mechanisms that partially account for the increased risk for depressive problems in adolescents experiencing puberty earlier than peers. In particular, findings implicated decreased connectivity between limbic structures and the cingulo-opercular network involved in higher-order cognitive control. Exploratory analyses provided preliminary support for the role of positive family environments in buffering against neural risk patterns in earlier pubertal maturers, highlighting protective pathways that those at heightened vulnerability during the early adolescent years.

Highest Ranked Abstracts

Zuranolone as a Neuroprotective Therapy Following Preterm Birth and its Effects on the Dopamine Pathway

Presenting Author: Roisin A. Moloney

Roisin A. Moloney - 1. School of Biomedical Sciences and Pharmacy, University of Newcastle, Newcastle, Australia 2. Hunter Medical Research Institute, Mothers and Babies Research Centre, Newcastle, Australia

Carlton L. Pavy - 1. School of Biomedical Sciences and Pharmacy, University of Newcastle, Newcastle, Australia 2. Hunter Medical Research Institute, Mothers and Babies Research Centre, Newcastle, Australia

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Julia C. Shaw - 1. School of Biomedical Sciences and Pharmacy, University of Newcastle, Newcastle, Australia 2. Hunter Medical Research Institute, Mothers and Babies Research Centre, Newcastle, Australia

Jonathon J. Hirst - 1. School of Biomedical Sciences and Pharmacy, University of Newcastle, Newcastle, Australia 2. Hunter Medical Research Institute, Mothers and Babies Research Centre, Newcastle, Australia

Chair: Suresh Sundram

Background
Preterm birth results in an increased likelihood of developing neurobehavioural disorders, with two of the most prevalent being ADHD and anxiety. These disorders are both underpinned by disruptions to dopaminergic pathways, however knowledge of the effects of preterm birth on this system is limited. When infants are born preterm, they prematurely lose the support of the placental neurosteroid, allopregnanolone. This increases the risk of excitotoxic damage to the brain which we propose harms the dopamine pathway. We propose that postnatal restoration of neurosteroid action through Zuranolone therapy will prevent disruption of dopaminergic transmission and reduce neurological impairments following preterm birth.

Methods
Guinea pig dams underwent survival C-section surgery to deliver pups prematurely (GA64) or delivered spontaneously at term (GA70). For the period between birth and term equivalence age (TEA), preterm pups received either vehicle (15% B-cyclodextrin) or the allopregnanolone analogue, Zuranolone (1mg/kg/day) orally. Behavioural analysis was performed at PND7 and PND40. Pups were maintained until PND42 before tissue collection. Relative mRNA expression of dopamine synthesis enzyme (TH) and dopamine receptor D1 (DRD1) were quantified by RT-PCR.

Results
Preterm born males had a significantly reduced expression of TH expression, which was restored to control levels in the male Zuranolone treated preterm group ($p=0.04$; $p=0.001$ respectively). Conversely, preterm born females had a significantly increased expression of TH, which was again restored following treatment ($p=0.0004$; $p=0.002$ respectively). Preterm birth also significantly reduced the expression of DRD1 in males, and these levels were restored to control in the Zuranolone treated group ($p=0.02$; $p=0.007$ respectively). Behavioural analysis was performed, and results will be presented.

Conclusions
Preterm born males show a reduction in expression of the key dopamine synthesis enzyme TH, as well as a reduction of the key dopamine receptor DRD1, which may contribute to hyperactive behaviour commonly seen following preterm birth. These changes were reversed to control levels following Zuranolone treatment, indicating neurosteroid stimulating action is key in maintaining normal dopaminergic transmission. Additionally, preterm born females showed contrasting results to males, which were also improved by neurosteroid analogue treatment. These findings suggest sex-dependent differences play a role in the development of preterm birth associated neurobehavioural disorders.

Data Blitz Abstracts

Data Blitz Session 1

WED_1 Intranasal clozapine: a viable route of administration that may avoid related side-effects

Presenting Author: Suzy A Alexander

Suzy A Alexander - Queensland Brain Institute, The University of Queensland, St Lucia, QLD 4072. Queensland Centre for Mental Health Research, Wacol, QLD, 4076

Darryl W Eyles - Queensland Brain Institute, The University of Queensland, St Lucia, QLD 4072. Queensland Centre for Mental Health Research, Wacol, QLD, 4076

Chair: Hayley North

Background
Clozapine is the most effective antipsychotic drug (APD) for Treatment Resistant Schizophrenia (TRS), yet it has severe debilitating metabolic and potentially lethal immune-related side effects. Most of these side effects are peripherally mediated. Intranasal (IN) drug delivery offers a direct route to the brain and may largely avoid the periphery. Suppression of the Conditioned Avoidance Reaction (CAR) is a unique feature of all antipsychotic agents. The aim of this study was to determine if IN Clozapine suspended in a patented Sol-Gel nanoemulsion could suppress CAR.

Methods
Training: Male Sprague-Dawley Rats underwent 40 trials once a day for 5-7 days in a two-way shuttle box. Each trial started with the presentation of a tone (Conditioned Stimulus, CS, 10s), followed by mild footshock (Unconditioned Stimulus, US, 10s). Movement between sides during the CS resulted in an “Avoidance”, and during the US an “Escape”. Failure to move during both CS & US counted as an “Escape failure”. Testing: The rats underwent a baseline CAR session and then received drug / control (IN / Oral). Additional CAR testing occurred at 20, 90, 240 min and 24 hour post admin.

Results
IN+Cloz (0.7mg/kg) produced a similar degree of CAR suppression over time as 20mg/kg Oral Cloz with minimal escape failures, indicating a standard antipsychotic action. These doses were selected based on CAR suppression without inducing cataleptic / tranquilizing effects. Additional results (not presented) showed that higher doses IN+Cloz at 1.16mg/kg, or oral Cloz at 30mg/kg had undesirable cataleptic outcomes so were not further explored. Brain and blood collected 30 minutes post IN+Cloz or IN+Sol-Gel administration were analysed using HPLC and shows 5.5 times higher Cloz in the brain vs the blood.

Conclusions
This study shows we can achieve an antipsychotic behavioural effect when Clozapine is administered intranasally. Furthermore, we get this effect using only 3.5% of the Oral dose required to achieve the same level of CAR suppression. Chronic studies are now required in rats prior to clinical trials. Given the greatly diminished dose required for IN administration to achieve a therapeutic effect, we predict IN administration will greatly diminish clozapine-related side-effects. Additionally, as the IN route completely avoids the gut we further predict virtual absence of debilitating extreme constipation and immune-related side-effects of oral therapy.

Data Blitz Abstracts

Data Blitz Session 1

WED_3 Chronic treatment with GOO during abstinence from METH self-administration induces cue-relapse to METH, and does not have any effect on reinstatement, anxiety, and recognition memory.

Presenting Author: Laisa de Siqueira Umpierrez

Laisa de Siqueira Umpierrez - Macquarie University, School of Psychological Sciences, Sydney, Australia

Priscila Almeida Costa - Macquarie University, School of Psychological Sciences, Sydney, Australia

Maral Jkorkozian - Macquarie University, School of Psychological Sciences, Sydney, Australia

Jacqueline Brown - Macquarie University, School of Psychological Sciences, Sydney, Australia

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Iain McGregor - Brain and Mind Centre, Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Jonathon Arnold - Brain and Mind Centre, Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Sarah Baracz - Macquarie University, School of Psychological Sciences, Sydney, Australia

Christina Perry - Macquarie University, School of Psychological Sciences, Sydney, Australia

Jennifer Cornish - Macquarie University, School of Psychological Sciences, Sydney, Australia

Chair: Hayley North

Background
There is increasing interest in medicinal applications of cannabinoids for psychiatric conditions such as substance use disorder. Using a validated rodent model, we recently found that acute treatment with a cannabis extract (GOO) prevents METH-relapse in rats. Although this is promising, clinical treatment schedules generally involve administering anti-relapse pharmacotherapies on a chronic or repeated basis during the period of abstinence. Therefore, the aim of this study was to verify the anti-relapse properties of chronic treatment with GOO during abstinence from METH self-administration, as well as establish the effect of this schedule on anxiety and short-term memory.

Methods
Male Sprague-Dawley rats underwent METH intravenous self-administration (IVSA) training on FR1, followed by a phase of 3-hour intermittent availability (three drug-available periods of 40 min + three non-drug-available periods of 20 min). Subsequently, rats underwent 60 days of forced abstinence (in home cages). Rats received GOO (intraperitoneal) from day 13 to 23. On day 2, 30 and 60 they were tested for cue-induced reinstatement of METH-seeking, on day 25 on the elevated plus maze (EPM), and on day 28 they were subjected to the novel object recognition (NOR) test. After abstinence, they underwent extinction sessions, followed by METH-primed reinstatement tests.

Results
In direct contrast to the acute effect, chronic treatment with GOO enhanced cue-relapse to METH on day 30 of abstinence, and this effect was dose-sensitive. The chronic schedule did not have any effect on relapse to METH-seeking after a priming injection of METH. Furthermore, there were no changes in performance in the EPM and NOR tests. Finally, rats treated with GOO were more resistant to extinction after undergoing a cue-relapse test.

Conclusions
This is the first study to examine the effects of treatment with GOO during abstinence from METH self-administration on relapse, anxiety, and memory function in rats. Rather than decreasing relapse, chronic treatment with GOO resulted in an increase in METH-relapse triggered by cues, as well as resistance to extinction. There were no demonstrable improvements in anxiety-like behaviour nor cognition. While these findings represent important limitations for its use as chronic treatment for METH use disorder in humans, the contrast between acute and chronic effects of GOO administration are important for understanding the mechanism by which cannabinoids can alter METH-related behaviours.

Data Blitz Abstracts

Data Blitz Session 1

WED_7 Epitranscriptomic regulation of striatal function: a new biology of schizophrenia?

Presenting Author: Xiaoying Cui

Xiaoying Cui - Queensland Centre for Mental Health Research, Wacol, Qld 4076, Australia,Queensland Brain Institute, University of Queensland, Qld 4072, Australia. Queensland Brain Institute, University of Queensland, Qld 4072, Australia

Alice Petty - Imperial College London, United Kingdom

Ning Wang - Queensland Brain Institute, University of Queensland, Qld 4072, Australia

Darryl Eyles - Queensland Centre for Mental Health Research, Wacol, Qld 4076, Australia,Queensland Brain Institute, University of Queensland, Qld 4072, Australia. Queensland Brain Institute, University of Queensland, Qld 4072, Australia

Chair: Hayley North

Background
We developed an animal model called "Enhanced Dopamine in Prodromal Schizophrenia" (EDiPS) based on the clinical finding in schizophrenia of increased dopamine activity in the dorsal striatum. EDiPS animals display schizophrenia-relevant behavioural phenotypes and enhanced dopamine release in the dorsal striatum in response to amphetamine. RNA modification (the epitranscriptome) is an additional layer of control over gene expression and has been found to regulate dopamine-mediated behaviours. Epitranscriptomic modification is also implicated in schizophrenia pathophysiology. Here, we used the EDiPS model to explore how an increase in dopamine synthesis and release alters the epitranscriptome in the striatum.

Methods
EDiPS animals were produced by overexpressing human tyrosine hydroxylase and GTP cyclohydrolase I - critical enzymes for dopamine synthesis - in the nigro-striatal pathway via injection of an AAV-packaged construct. Six weeks following construct delivery, the dorsal striatum was collected, and methylated RNAs (N6-methyladenosine,m6A) were assessed by m6A-RNA immunoprecipitation(IP)-sequencing. Candidate m6A-modified RNAs were validated using qPCR. To determine the specific roles of m6A-containing RNAs, an m6A-RNA editing system, a Crispr-inspired RNA targeting system (CIRTS), was developed. CIRTS contained a guided RNA against methylation sites on RNAs of interest and an m6A demethylase FTO to manipulate specific endogenous transcripts.

Results
Our findings revealed that enhancing dopamine synthesis in EDiPS led to increased expression of m6A methyltransferase Mettl14. M6A-RNA IP-sequencing identified 119 transcripts with differential methylation status in EDiPS striatum, predominantly hypermethylation, consistent with heightened Mett14 expression. GeneCard analysis highlighted 13 m6A-marked transcripts linked to schizophrenia. Among these, the schizophrenia-associated gene phospholipase (PLC)-β1 exhibited hypermethylation, contributing to elevated protein levels in the EDiPS striatum. A guide RNA within CIRTS-FTO construct effectively removed m6A from PLC-β1 mRNA, reducing mRNA and protein expression in cultured neurons. Future investigation aims to assess whether targeting PLC-β1 m6A methylation mitigates schizophrenia-related behavioural phenotypes in EDiPS animals.

Conclusions
Hyper-dopaminergia in the dorsal striatum is a robust marker that provides a highly plausible neurochemical prophylactic target. We have provided the first evidence that increased dopamine synthesis capacity in the dorsal striatum alters RNA methylation. We engineered a CIRTS m6A-RNA editing system that can effectively manipulate m6A on RNAs of interest. In future studies, we will use CIRTS to determine the causative role of m6A accumulation on schizophrenia-related genes in dopamine-related behaviour in the EDiPS model. Our findings will not only provide etiological insight but also help to identify novel treatment targets for schizophrenia.

Data Blitz Abstracts

Data Blitz Session 1

WED_31 Understanding brain volume heterogeneity through polygenic risk profiling of psychiatric disorders and commonly comorbid medical conditions

Presenting Author: Hadis Jameei

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Chair: Hayley North

Background
A common feature of neuropsychiatric disorders is reduced regional brain volumes, yet the extent and spatial distribution of these reductions are heterogeneous, even within diagnostic groups. To understand this variability from an etiological standpoint, recent studies examined common genetic risk variants of distinct psychiatric disorders, revealing significant, albeit weak, associations with brain volume. We speculate that variability is better explained by genetic risk profiles for diverse psychiatric and non-psychiatric conditions overrepresented in psychiatric populations. Here, we evaluate polygenic risk correlations between psychiatric disorders and commonly comorbid chronic diseases and test their effects on deviations in brain volume.

Methods
This study comprises healthy adults with available genotype and magnetic resonance imaging data from the UK Biobank (N=7,908, age=56±8, 45% male). Polygenic risk scores (PRSs) were computed for 5 psychiatric traits (ADHD, autism, depression, and bipolar disorder and schizophrenia) and 16 chronic medical conditions overrepresented amongst individuals with a psychiatric diagnosis. Normative models calculated person-specific brain volume deviations from the median for a given age/sex. Linear regressions tested pair-wise correlations between disorder PRS, and associations between each PRS with regional volume deviations. Spatial correspondence (Spin) tests evaluated overlap between traits in terms of their PRS associations with regional deviation profiles.

Results
As expected, polygenic risk for chronic conditions exhibited smaller pair-wise correlations across individuals compared to psychiatric disorders, suggesting greater diagnostic specificity and/or more distinct aetiologies. Despite several traits being clinically and genetically distinct (n=69 disease-pairs), 12 (17%) of these same trait pairs exhibited similar associations with brain regional deviation profiles (r range=0.21-0.41; p<0.05). In contrast, of 141 disease-pairs that were genetically correlated, only 33 (23%) revealed significant spatial correspondence in their regional distributions of brain volume deviations (r range=0.17-0.42; p<0.05).

Conclusion

We demonstrated that chronic diseases with distinct genetic bases to psychiatric disorders can map to similar deviation profiles of brain volume. Conversely, psychiatric disorders with shared genetic components can exhibit varied deviation profiles, consistent with pleiotropic-like effects. Moving beyond analyses of single genetic traits leads to improved characterisation of complex relationships between genetic architecture and phenotypic variability in brain volume. These advancements can help toward developing predictive models of neuro-phenotypic outcomes in psychiatry.

Data Blitz Abstracts

Data Blitz Session 1

Epigenetic Scores for Schizophrenia and First Episode Psychosis are Associated with Diagnostic Status

Presenting Author: Dylan J. Kiltschewskij

Authors:
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Chair: Hayley North

Background
Epigenome-wide association studies (EWAS) of schizophrenia and psychosis have identified a vast array of disorder-associated DNA methylation changes at CpG dinucleotides, which may functionally contribute to phenotypic heterogeneity. Since DNA methylation could index a component of an individual's life-time burden of genetic and environmental risk factors, there is likely to be important utility in leveraging this information in risk stratification. In the present study, we derived epigenetic scores (ES) encapsulating genetic and environmental risk for schizophrenia and psychosis to examine whether this personalised information can inform diagnostic status for these conditions.

Methods
ES for schizophrenia (ESsz) and first episode psychosis (ESfep) were derived and tested using three large, publicly available schizophrenia cohorts, and two first episode psychosis cohorts. Across all cohorts, DNA methylation was profiled from the blood of 1,680 cases and 1,387 non-psychiatric controls using Illumina 450K or EPIC DNA methylation arrays. EWAS were firstly conducted for each trait in a hold-out cohort and utilised to construct ES in the remaining cohorts using CpGs at multiple P-value thresholds. Logistic regression models were employed to identify, test and validate (schizophrenia only) the best fit ES with appropriate covariates.

Results
Strikingly, the best fit ESsz (124 CpGs, P < 1x10–11) and ESfep (1,593 CpGs, P < 1x10–3) were significantly associated increased odds of their respective diagnoses (ORsz = 1.64–1.94, Psz ≤ 2.76x10–3; ORfep = 1.85, Pfep = 2.08x10–5). However, no association was identified between ESsz and first episode psychosis, nor ESfep and schizophrenia. Individuals with a top decile ESSZ or ESFEP exhibited significantly increased odds of a schizophrenia (ORsz = 4.05–7.03, Psz < 1.25x10–4; ORfep = 4.28, Pfep = 1.44x10–5) or first episode psychosis diagnosis, respectively, versus individuals with bottom decile ES.

Conclusion
These findings suggest elevated epigenetic burden for schizophrenia and first episode psychosis, encapsulated in epigenetic scores, is associated with diagnostic status for these conditions. Although schizophrenia is often associated with psychotic symptoms, our results additionally indicate there is limited overlap of epigenetic risk between these conditions, necessitating further instigation in large, independent cohorts. Nonetheless, our results suggest epigenetic scores may assist in the classification of affected individuals in a manner which addresses individual-to-individual molecular heterogeneity, and may therefore offer utility for development of personalised risk stratification and intervention strategies together with existing genetic methods.

Data Blitz Abstracts

Data Blitz Session 2

Differentially expressed pathways in stem-cell-derived cortical networks of bipolar disorder participants are modulated by drugs commonly used for treatment.

Presenting Author: Bruna Panizzutti

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Chair: Christina Perry

Background

Bipolar disorder is a complex psychiatric condition characterised by recurring episodes of manic and depressive states. While substantial progress has been made in understanding its clinical manifestations, the underlying biological mechanisms remain incompletely understood. Therefore, this study aimed to investigate differentially expressed pathways between individuals with bipolar disorder and healthy controls using stem-cell-derived cortical networks (a mixture of neurons and astrocytes).

Methods

Fifteen research participants (8 with bipolar disorder and 7 matched (age, sex) healthy controls) were recruited for this

study. Peripheral blood mononuclear cells isolated from blood samples were reprogrammed into induced pluripotent cells (iPSCs) using episomal vectors. iPSCs were differentiated into cortical networks using commercially available reagents (Stem Cell Technologies). Genome-wide RNA expression in cortical networks was measured using next-generation sequencing (NGS). The differentially expressed genes were used for gene set enrichment (GSEA) analysis using the KEGG database as a reference.

Results

Cortical networks from participants with bipolar disorder showed 69 differentially expressed pathways. Downregulated pathways included metabolism (e.g., fatty acid metabolism q=0.019, genetic information processing (e.g., protein processing in endoplasmic reticulum q=0.009), and cellular processes (e.g., apoptosis q=0.030. Upregulated pathways were associated with organismal systems (e.g., glutamatergic synapse q=0.009) and environmental processing (e.g., Hippo signalling pathway q=0.044). We have shown that commonly prescribed drugs (e.g., lithium, quetiapine) affect these pathways, including cell signalling, fatty acid metabolism, and ribosome/protein synthesis.

Conclusion

The use of stem-cell-derived neurons and astrocytes provides a valuable platform to study the disorder in a more controlled and representative manner. Overall, this study contributes to our understanding of the biological underpinnings of bipolar disorder by identifying specific pathways that are differentially expressed in affected individuals. The findings may lead to the development of targeted treatments and further research into the complex nature of this psychiatric condition.

Data Blitz Abstracts

Data Blitz Session 2

Personalised neurotherapeutics for major depression: Initial clinical findings from the Queensland Neurostimulation Centre

Presenting Author: Bjorn Burgher

Luke Hearne - QIMR Berghofer

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Bjorn Burgher - QIMR Berghofer, Queensland Neurostimulation Centre

Luca Cocchi - QIMR Berghofer

Chair: Christina Perry

Background
Neuroimaging-guided personalisation of rTMS for everyday clinical use is relatively complex (e.g., requiring neuroimaging expertise) and costly (e.g., MRI scan). Thus, it is necessary to evaluate whether this strategy provides a notable clinical benefit compared to the conventional one-size-fits-all rTMS approach. Here we report the clinical outcomes of our personalised protocol in the first 70 clients with MDD treated at QNC, benchmarking them against the 44.6% response rate typically observed in clinical trials for DLPFC rTMS (Cao et al., 2018).

Methods
Psychiatrists and general practitioners in the Brisbane metropolitan area referred clients, with either a primary or secondary diagnosis of MDD. Change in Montgomery–Åsberg Depression Rating Scale (Montgomery and Åsberg, 1979) were used as the primary clinical outcome. Clients undertook neuroimaging comprising of a structural-functional MRI. The client's TMS target was defined as the coordinate in the DLPFC with the largest negative correlation value to the subgenus cingulate at rest (see Cash et al., 2021). Clients undertook 20 sessions of intermittent theta burst stimulation. TMS procedures were carried out using a TMS-robot and a MagPro R30.

Results
Clients were a priori assigned to one of three 'tiers': Tier 1) clients with MDD meeting criteria for randomised-controlled clinical trials, n=17, Tier 2) clients with MDD and complex co-morbidity, n=40, Tier 3) clients with bipolar depression and/or structural neurological disorder, n=13. Clinical response and remission were defined as a >50% and >80% symptom reduction in the MADRS, respectively. A clinical response was found in 66.7% of Tier 1, 43.2% of Tier 2, and 23.1% of Tier 3 clients. Furthermore, a remission was found in 50% of Tier 1, 22% of Tier 2 and 0% of Tier 3 clients.

Conclusions
Overall, our results support previous retrospective evidence suggesting that personalized rTMS has the potential to deliver superior clinical efficacy compared to standard rTMS in individuals with MDD. However, the effectiveness of our approach appears limited when treating individuals with more complex clinical presentations of MDD. These findings provide strong motivation for future prospective randomized controlled trials to comprehensively evaluate the clinical benefits of robotically delivered personalized TMS for MDD.

Data Blitz Abstracts

Data Blitz Session 2

THUR_13 Maternal selenium dietary supplementation recovers sociability and cognitive deficits following in utero exposure to maternal immune activation in mice

Presenting Author: Brendan Gillespie

Brendan Gillespie – Monash University

Michael J. Houghton - Monash University

Rachel A. Hill - Monash University

Katherine Ganio - University of Melbourne

Christopher A. McDevitt – University of Melbourne

Daniel Bennett - Monash University

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Anna Schroeder - Monash University

Barbara R. Cardoso - Monash University

Chair: Christina Perry

Background
Infections during pregnancy are a risk factor for the unborn foetus to develop autism spectrum disorder (ASD) later in life. This is thought to be driven by maternal immune activation (MIA) that crosses the foetal compartment. MIA mouse model recapitulates a spectrum of behavioural and biological phenotypes relevant to ASD, making it a valuable model to test novel treatment approaches. The dietary supplement, selenium has anti-inflammatory properties that make it a promising candidate for preventative interventions. The aim of this study was to determine if selenium supplementation during pregnancy can prevent adverse effects of MIA on offspring brain and behaviour.

Methods
Pregnant mice were given selenium selenate (0.15 mg/100 mL) from Gestational day(GD) 9 until birth, and the viral mimetic, poly-I:C, or saline during late gestation(GD17). Foetal brains(n=7-12/group) and placenta (n=3-6/group) were assessed for changes in inflammatory markers using a Luminex assay, and for changes in the elemental nutrients magnesium-24, calcium-44, iron-56, copper-63 and zinc-66 using inductively coupled plasma- mass spectrometry. Adult offspring exposed to MIA and/or selenium were assessed for behavioural changes in a reinforcement learning paradigm (n=10-22/group), which was analysed using computational modelling (Q-learning) techniques. Sociability, pre-pulse inhibition, anxiety-like behaviour, and working memory were also assessed (n=5-23/group).

Results
MIA elevated placental IL-17 (p<0.01), and selenium supplementation successfully prevented this elevation (p<0.01). MIA increased foetal brain calcium (p<0.05), which was recovered by selenium treatment (p<0.001). MIA impaired offspring performance in the reinforcement learning paradigm (p<0.05), which was driven in part by a reduced rate of learning the location of the food reward (p=0.05), but primarily by an increased tendency to explore options other than the reward (p<0.01). Selenium normalised this increased exploration in MIA exposed offspring (p<0.01) but promoted exploration in non-MIA exposed offspring (p<0.01). MIA caused reduced sociability in female offspring (p=0.06), which was recovered by selenium (p<0.05).

Conclusion

As expected, MIA elevated IL-17, and impaired performance in a reinforcement learning task. Surprisingly, this impairment was primarily driven by increased exploratory behaviour, challenging the established belief that such performance impairments are driven by deficits in learning. Selenium supplementation increased exploration in this task, which may be due to selenium induced dyshomeostatis in multiple elemental micronutrients that play key roles in neurodevelopment. Increased exploration induced by selenium may also explain its ability to recover the reduced sociability phenotype in female mice exposed to MIA. Overall these data provide novel insights into potential preventative strategies for women exposed to MIA.

Data Blitz Abstracts

Data Blitz Session 2

THUR_15 Investigation of the association between estradiol levels and brain structure and function in early adolescent females.

Presenting Author: Muskan Khetan

Muskan Khetan - University of Melbourne

Nandita Vijayakumar - Deakin University

Ye Tian - University of Melbourne

Sarah Whittle - University of Melbourne

Chair: Christina Perry

Background
During adolescence, about one-third of young people are diagnosed with an internalizing disorder like depression or anxiety, with these disorders being more common in females than males. Sex difference in incidence rates may be related to pubertal factors, such as the influence of pubertal hormones on brain development. While some studies have examined the correlation between sex hormone levels and brain structure in adolescents, more research is needed to investigate the associations between sex hormone levels and both brain structure and function in adolescent females, particularly during early adolescence when hormone levels begin to surge.

Methods
We used the Adolescent Brain Cognitive Development (ABCD) study baseline (9-10 years) and two-year follow-up (11-12 years) brain-imaging and oestradiol hormone data (N = 2204; females). Using elastic-net regression, we investigated associations between brain features and oestradiol levels (with separate models for gray matter Volume, cortical thickness, surface area, sulcal depth, white matter microstructure, resting-state connectivity, emotional n-back task-related function). Regions with non-zero beta values from these models separately were then included as predictors of oestradiol in a multi-modality model. Confirmatory univariate mixed effect models were then run for all brain features with non-zero beta values to establish strength of effects.

Results
Single modality models resulted in 304 brain features with non-zero beta values (out of 1707 total brain features) and in multi-modality model, 276 of these features had non-zero beta values (R-squared = 0.012; r = 0.21). Confirmatory univariate analyses showed that 34 brain features significantly predicted oestradiol levels (p < 0.05). From both multi-modality and confirmatory analyses, we found that structural features were predominantly implicated, for example insula, superior temporal sulcus, ventrolateral pre-frontal cortex, precuneus, and ventral anterior cingulate cortex gray matter, in addition to while white matter connections between temporal and frontal areas). Emotion-related hippocampal activity was also implicated.

Conclusion
Analyses suggested that the structure of brain regions underlying social and emotional processes were associated with oestradiol levels in 9–12-year-old female adolescents. Oestradial levels have been linked with both emotion regulation and social cognition. As such, our findings might reflect a neurodevelopmental mechanism of these associations. Predominant involvement of brain structure rather than function might reflect an organisational role of oestradiol on the developing brain.

Data Blitz Abstracts

Data Blitz Session 2

THUR_37 BDNF Met allele and hippocampal volume moderate risk of cognitive dysfunction in schizophrenia

Presenting Author: Vaidy Swaminathan

Holly Peacock - Monash University

Vaidy Swaminathan - Monash University

Rachel Hill - Monash University

Vanessa Cropley - University of Melbourne

Suresh Sundram - Monash University

Chair: Christina Perry

Background
Cognitive impairment impacts the functioning and quality of life for people with schizophrenia (SCZ). Cognitive clustering strategies and their relationship to biomarkers to predict models of illness and severity have been attempted, for example treatment resistant schizophrenia (TRS). The aim of this study was to investigate if specific biomarkers, including the Brain Derived Neurotrophic Factor (BDNF) Val66Met polymorphism, and hippocampal volume are associated with defined cognitive clusters in people with SCZ and healthy participants (HC). A further aim was to investigate if specific cognitive clusters and/or biomarkers were able to predict treatment resistance in the SCZ group.

Methods
Clinical, neuropsychological, genetic and neuroimaging data from 449 persons with SCZ and 646 HC (aged 18-65) was obtained from the Australian Schizophrenia Research Bank (ASRB). 183 HC and 210 persons with SCZ underwent Magnetic Resonance Imaging (MRI) scanning of their brains. A hierarchical clustering strategy identified cognitive clusters. Genotyping was performed by a multiplex assay. Structural MRI scanning was performed with a Siemens 1.5 Tesla scanner to obtain T1 images of participant brains and processed with Freesurfer Imaging Suite to extract grey matter metrics. Left and right hippocampus volumes were summed to derive a total variable. Routine statistics were performed.

Results
Clustering identified 3 cognitive clusters. Cluster 1 was cognitively normal; Cluster 2 had a current functioning of 0.75 standard deviations (SD) and Cluster 3, 2.75 SD below HC. Within SCZ, Met carriers associated with Cluster 2 compared to Cluster 1 (p<0.05). Hippocampal volumes (HV) were lower in SCZ compared to HC (p<0.001), but no effect of Genotype. HV was lower in Cluster 3 (p<0.01). There were no significant interaction effects of Val66Met genotype and cognitive clusters on HV. No difference in allele frequency and TRS status was observed for Val66Met overall (p=0.54), Met carriers and Val homozygotes (p=0.373).

Conclusion
These results have strong implications for the Met allele to be characterised as a potential risk factor for cognitive dysfunction with persons with SCZ. Importantly, cluster 2 showed a declining cognitive function, while cluster 3 showed a consistent and sustained low functioning. Therefore, the Met allele may be associated with declining cognitive function in people with SCZ. Results also show that hippocampal volume was lowest for cluster 3 – the lowest performing group. Therefore, both biomarkers were able to identify discrete clusters of cognitive function.

Data Blitz Abstracts

Data Blitz Session 3

THUR_29 Biopsychosocial Markers of Posttraumatic Outcomes in a Population of Emergency Responders

Presenting Author: Mackenzie Rubens

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Caroline Nievergelt - Department of Psychiatry, University of California

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Jane Shakespeare-Finch - School of Psychology and Counselling, Queensland University of Technology

Divya Mehta - Centre for Genomics and Personalised Health, School of Biomedical Sciences, Faculty of Health, Queensland University of Technology

Chair: Elysia Sokolenko

Background
Between 70-80% of people are exposed to a potentially traumatic event in their lifetime. Contrary to popular belief, adverse outcomes such as posttraumatic stress disorder (PTSD) are not the only result of such exposures. Most people return to pre-traumatic functioning or undergo positive, transformative change referred to as posttraumatic growth (PTG). This project examined the genetic underpinnings and biomarkers of holistic posttraumatic outcomes in Australian emergency service workers.

Methods
The project employed a repeated-measures study design, gathering data from participants in the first week of their training as a baseline and again 6-12 months later for longitudinal data. Participants completed a survey at each timepoint that collected psychosocial data and provided a saliva sample for genetic and epigenetic information. Analyses included a genome-wide association study (GWAS), and genome-by-environment (GxE). Psychosocial factors included belongingness and social support. Posttraumatic outcomes included PTSD, PTG, and psychological distress. The project was funded by the NHMRC (#2004536).

Results
We found significant GxE interactions (after genome-wide corrections) between thirty-four SNPs and protective environmental factors (n = 19 SNPs for social support, n = 15 for belongingness) on measures of posttraumatic outcomes. These SNPs were within several genes including DLGAP2, DNCIC1, DRGX, GCNT3, MAML3, PAX5, PRR5L, RFTN1, SHROOM3, and STAM.

Conclusions
This is the first genome-wide study to identify GxE effects associated with PTG. Replication of these preliminary results in an independent sample and longitudinal DNA methylation data analyses is underway. These results provide novel insights into the aetiology and biological underpinnings of posttraumatic outcomes.

Data Blitz Abstracts

Data Blitz Session 3

The Role of Opioid Receptors in the Error Correction Mechanisms Underlying Fear Learning

Presenting Author: Madeleine Giles

Madeleine Giles - UNSW

Fred Westbrook - UNSW

Nathan Holmes - UNSW

Chair: Elysia Sokolenko

Background
Organisms learn to fear conditioned stimuli (CSs; e.g., a tone) that signal innate sources of danger (e.g.,shock), and to extinguish this fear when the CS is repeatedly presented in the absence of danger– first-order conditioned fear. Opioid receptors are thought to code for the error signal that regulates the acquisition and extinction of first-order fear. We examined whether they regulate the acquisition and extinction of fear to a CS (e.g., a light) that signals a learned source of danger (e.g., the fear-conditioned tone)– second-order conditioned fear; and whether any regulation varies as a function of the predictive relationship between stimuli.

Methods
In experiment 1, rats received first-order conditioning (tone-shock pairings) in stage 1, standard second-order conditioning (sequential light-tone pairings) in stage 2, second-order extinction (light-alone presentations) in stage 3, and finally a test of fear to the light and the tone. The opioid-receptor antagonist, naloxone, or vehicle was injected subcutaneously prior to stage 2 and stage 3. In experiment 2, rats received first-order conditioning (tone-shock pairings) in stage 1, second-order conditioning (either sequential or simultaneous light-tone pairings) in stage 2, and a test of fear to the light and the tone. Naloxone or vehicle was injected subcutaneously prior to stage 2.

Results
Naloxone enhanced the acquisition and impaired the extinction of second-order conditioned fear in experiment 1. That is, opioid-mediated error-correction mechanisms appear to regulate the acquisition and extinction of fear to stimuli that signal a learned source of danger, much like they do for stimuli that signal an innate source of danger (i.e., first-order conditioned fear). In experiment 2, naloxone enhanced the acquisition of second-order conditioned fear both when the stimuli were presented sequentially and simultaneously, suggesting that opioid receptors may play a general role in learning about both predictive (sequential) and non-predictive (simultaneous) associations.

Conclusions
Opioid-mediated error-correction mechanisms appear to regulate fear to stimuli that signal innate sources of danger (i.e., first-order conditioned fear) and fear to stimuli that signal learned sources of danger (i.e., second-order conditioned fear). Further, the facilitative effect of naloxone on simultaneous second-order fear conditioning suggests opioid receptors are doing more than simply regulating predictive relationships; for example, they may also regulate within-event relationships (simultaneous presentations).

Data Blitz Abstracts

Data Blitz Session 3

THUR_21 Characterising neural and behavioural correlates of cognitive intra-individual variability in bipolar disorder

Presenting Author: Georgia Caruana

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James Karantonis - Melbourne Neuropsychiatry Centre, Department of Psychiatry, University of Melbourne and Melbourne Health, Melbourne, Australia

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Chair: Elysia Sokolenko

Background
Intra-individual variability (IIV), a construct describing within-person performance fluctuations when completing a cognitive task, is becoming increasingly understood as a robust behavioural indicator of neuropathology and aging. But it's relevance to mental illnesses that feature heterogeneous cognitive functioning, such as bipolar disorder (BD), is lesser known. Further, the biological mechanisms underpinning IIV are yet to be identified. Therefore, this study sought to characterise IIV in BD; explore if it is increased in patients, investigate its relationships to overarching cognitive performance, and probe its associated neurobiology.

Methods
Two hundred and seventeen adults, including 100 people living with BD and 117 healthy controls participated in this study. BD participants were euthymic at the time of testing. IIV was operationalised as the individual standard deviation in reaction time on the Computerised Performance Test-Identical Pairs task, with raw performance scores of processing speed, sustained attention, working memory, and executive function assessments also collected. A subsample of 55 BD participants underwent diffusion tensor imaging, to investigate underlying white matter microstructure. Group differences in IIV and cognition were established using ANOVA, with correlational analyses applied to study associations.

Results
Despite being matched on criteria such as age and premorbid intelligence, BD participants had significantly greater IIV than controls. IIV was only associated with cognition in the BD group, with greater IIV conferring poorer performance across all domains tested. IIV was also significantly correlated with the white matter measures of fractional anisotropy and radial diffusivity.

Conclusion
IIV may be a core behavioural feature of BD and linked to established brain structural changes. The significant increase in IIV, and its diagnosis specific associations with performance may suggest that people living with BD have greater sensitivity to cognitive inconsistencies. IIV was also related to white matter measures that represent reduced structural integrity and increased demyelination, key age-related brain changes. Taken together, this study presents novel evidence of links between brain structure and behaviour in BD and could provide support to broader hypotheses that BD involves an accelerated aging process.

Data Blitz Abstracts

Data Blitz Session 3

THUR_35 Dissecting how psychological stress affects human astrocytes in psychiatric disorders

Presenting Author: Dominic Kaul

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Chair: Elysia Sokolenko

Background

Severe stress is the strongest environmental risk factor across psychiatric disorders, yet we have limited evidence of this association at the cellular and molecular level in the human brain. This knowledge is essential for future development of effective and precise interventions. Astrocytes, a cell type sensitive to stress, have been shown to be altered in psychiatric disorders and in rodent models of stress. However, astrocytes are poorly conserved between rodents and humans and the heterogeneity of human astrocytes is not well-defined. Both high dimensional and human-relevant approaches to study these cells in stress-associated psychiatric disorders are necessary, but currently lacking.

Methods

We combined cutting-edge bioinformatic techniques (single nucleus RNAseq, n=87, spatial transcriptomics (n=13)) on postmortem prefrontal cortices. Functional and spatial annotation of these cells was conducted using gene set enrichment analysis and label transfer algorithms. Diversity formed a basis to explore case-control differences. Findings were complemented using fluorescent immunohistochemistry. The functional response of astrocytes to ‘stress’, was considered using human astrocytes differentiated from pluripotent stem cells (iAsts). iAsts were exposed to 100nM

dexamethasone to mimic the action of cortisol for 1-7 days. Neurotransmission function was assessed using clearance assays (ELISA), glutamate receptor expression (qPCR), and signalling response (whole-well ratiometric Ca2+ imaging).

Results

Our transcriptomic dataset of >100,000 human astrocytes detected functionally and regionally distinct groups of astrocytes. Case-control analysis highlighted astrocytes in the grey matter involved in clearing glutamate were increased across cases. Immunohistochemical morphology analysis of over 10,000 EAAT2+ cells, the glutamate transporter on astrocytes, demonstrated that all cases had a significant increase in the size of these cells (Padj<0.001). Cases with a history of childhood stress also had increased density across the grey matter (P<0.05). Dexamethasone stimulation of iAsts transiently reduced glutamate transport (P<0.001) and altered expression of neurotransmitter receptors (P<0.05), most notably reducing subunit 3/4 of the AMPA receptor.

Conclusion

This study provides one of the most in-depth studies of astrocytes in human psychiatric disorders and, for the first time, indicates that stress history contributes to detectable changes to these cells in postmortem human brain analysis. These approaches converge on evidence that the homeostatic roles of astrocytes at the synapse are altered in psychiatric cases and exacerbated in cases with childhood trauma. Dexamethasone treated iAsts demonstrate that these functions are actively impacted by ‘stress’ signalling, an effect rarely observed in previous studies of neurons. This suggests that astrocytes are likely important to the molecular contributions of stress towards psychiatric disorders.

Data Blitz Abstracts

Data Blitz Session 3

THUR_9 The Btc knockout mouse shares similarities in altered cortical gene expression with individuals with schizophrenia.

Presenting Author: Andrew Gibbons

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Chair: Elysia Sokolenko

Background
Individuals with schizophrenia have lower levels of the Epidermal Growth Factor Receptor family ligand, Betacellulin (BTC), in Brodmann's Area (BA) 46 of the dorsolateral prefrontal cortex. The Btc knockout mouse displays several schizophrenia-relevant behaviours, including anxiety-related disturbances, abnormal social interaction and cognitive deficits. This mouse also shows increased dendrite spine density in the medial prefrontal cortex. We hypothesised that individuals with schizophrenia and the Btc knockout mouse would share similarities in disrupted gene expression and sought to determine whether the genes that are altered in the Btc knockout mouse are also differentially expressed in BA 46 from individuals with schizophrenia.

Methods
RNA was isolated from the medial prefrontal cortex of 10-week-old Btc knockout and wildtype mice (n=10) and RNA-Seq analysis was performed using 30 million reads/sample. Following analysis, the top 20 upregulated and 20 downregulated genes, 10 differentially expressed genes identified from neuron/axon developmental pathways, and 10 genes involved in psychiatric illness were selected for high throughput qPCR analysis in human post-mortem subjects. Gene expression was measured in BA 46 tissue from 16 subjects with schizophrenia, 21 subjects with mood disorders and 16 control subjects using Taqman-based assays on Fluidigm Integrated Fluidic Circuits with a Biomark HD system.

Results
Following false discovery rate correction, 5 genes: MTHFR (q <0.001), MT-ND1 (q <0.001), MT-ND6 (q <0.001), GRB2 (q =0.01), TNFRSF18 (q =0.05) were differentially expressed between subjects with schizophrenia and controls with no differentially expressed genes detected between mood disorders and controls. When the cohort was stratified into "low-BTC" and "control-level-BTC" cases, based on previously measured BA 46 BTC protein levels, 25% of the assayed genes were differentially expressed in subjects with low BTC, with the most significantly different genes being MTHFR (q <0.001), MIAT (q <0.01), PLPP4 (q <0.01), TNFRSF18 (q =0.01) and RREB1 (q =0.01).

Conclusion
Our data validates the Btc knockout mouse as both a behavioural and molecular model for understanding the mechanisms underlying BTC deficits in schizophrenia. Our data also suggest that BTC deficits in psychiatric illness are associated with changes in molecular pathways that are distinct from the pathways that are altered in non-BTC deficit individuals. This has important implications for the potential stratification of patients based upon BTC levels and the development of novel therapeutics.

Data Blitz Abstracts

Data Blitz Session 4

THUR_25 Voluntary Exercise Throughout Abstinence Prevents the Incubation of Craving for Alcohol-Associated Cues in Rats

Presenting Author: Thomas Ferella

Thomas Ferella - Macquarie University

Amy Lin - Macquarie University

Mia Swinsburg - Macquarie University

Andrew Lawrence - Florey Institute of Neuroscience and Mental Health

Jennifer Cornish - Macquarie University

Christina Perry - Macquarie University

Chair: Carlo Longhitano

Background
Craving – the powerful urge to seek and consume alcohol in response to alcohol-associated cues does not diminish after drinking cessation, but rather is magnified throughout abstinence. This phenomenon, termed "incubation of craving", contributes to the relapsing nature of alcohol use disorder. Despite its occurrence in human populations and being well-studied in rodent models of psychostimulant drug relapse, this phenomenon, the underlying neural mechanisms, and potential treatments remain largely unexplored for alcohol. The present study aimed to investigate neural activation underlying the incubation of craving for alcohol-associated cues and assess whether exercise could prevent increased relapse propensity in rats.

Methods
Male Long Evans rats were trained to lever press for an alcohol reward delivered with simultaneous presentation of a discrete cue. This response was then extinguished and subsequently reinstated by presentation of the discrete cue alone upon lever press. Cue-induced reinstatement occurred either at day 1 following extinction (No Abstinence), or at day 29 (Abstinence). A third group was tested on day 29 and had 4-hour daily voluntary running wheel access throughout this abstinence period (Exercise). All rats were perfused 90 mins following the test, and relative activation across multiple reward-associated regions was estimated by quantifying c-Fos protein immunoreactivity.

Results
Rats in group Abstinence performed more alcohol-seeking lever press at cue-induced reinstatement when compared with group No Abstinence, however this time-dependent increase was not evident in group Exercise. Furthermore, brains of rats from group Abstinence had higher c-Fos immunoreactivity compared to No Abstinence in multiple reinstatement-related brain regions and again, this effect was reduced in group Exercise.

Conclusions
We have shown, for the first time, that voluntary exercise throughout abstinence prevents incubation of craving for alcohol-associated cues. Taken together, the findings suggest that ongoing abstinence from alcohol actively causes neural adaptations leading to increased recruitment of the reinstatement circuitry and hence enhanced craving in response to alcohol associated cues. Furthermore, exercise treatment acts to prevent, or reverse these changes. The present investigation is the first to characterise the neural underpinnings of the incubation of craving for alcohol-associated cues and offers a readily implementable treatment to help individuals seeking treatment for alcohol use disorder.

Data Blitz Abstracts

Data Blitz Session 4

The effects of diazepam and fluoxetine on models of anxiety differ in female rats depending on their reproductive history

Presenting Author: Jodie E Pestana

Jodie E Pestana - School of Psychology, UNSW

Bronwyn M Graham - School of Psychology, UNSW

Chair: Carlo Longhitano

Background
Recent research from our lab shows that pregnancy leads to long-term changes in the neurobiological and hormonal features of anxiety in rats and humans. Yet, treatments for anxiety have mostly been tested in male or virgin female animals only. This study examined the effects of two common anti-anxiety medications, a benzodiazepine (diazepam) and a selective serotonin reuptake inhibitor (fluoxetine), on models of anxiety in female rats pre- versus post-pregnancy.

Methods
In Experiment 1, virgin (n=47) and age-matched mother rats 1-month post-weaning (n=50), were injected with diazepam (1.3mg/kg or 1.7mg/kg) or vehicle, during the proestrus (high estradiol/progesterone) or metestrus (low estradiol/progesterone) phases of the estrous cycle. 30 min later, rats were tested on the elevated plus maze (EPM) for anxiety-like behaviour. In Experiment 2, virgin (n=25) and mother rats (n=20) were chronically administered fluoxetine (10mg/kg) or vehicle for 2 weeks prior to a fear conditioning and extinction protocol, and the EPM. Rats were euthanised 30 min post-EPM to measure plasma corticosterone, as a physiological index of the stress response.

Results
Replicating past research, in virgin rats, the low dose of diazepam produced anxiolytic-like effects in proestrus, but only the high dose was anxiolytic in metestrus. In contrast, in mother rats, both doses of diazepam were anxiolytic irrespective of estrous phase. Fluoxetine produced anxiogenic-like effects in virgin rats during extinction and the EPM, but had no effects in mothers. In contrast, fluoxetine increased corticosterone levels post-EPM in mothers, but not virgin rats.

Conclusion
This study demonstrates that reproductive experience alters the dose response and efficacy of two common anti-anxiety medications in female rats. These findings highlight the importance of considering reproductive status in studies on anxiety in females. Doing so may lead to more effective evidence-based treatments that are specifically tailored towards women both with and without reproductive history.

Data Blitz Abstracts

Data Blitz Session 4

THUR_27 Impact of maternal immune activation on behaviour across adolescence of male and female offspring

Presenting Author: Priscila A. Costa

Priscila A. Costa - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia (NeuRA), Sydney-NSW, Australia

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Tertia Purves-Tyson - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia (NeuRA), Sydney-NSW, Australia

Chair: Carlo Longhitano

Background
Adolescence is a critical period of vulnerability for behavioural changes in schizophrenia, and psychotic symptoms frequently occur at this age. Maternal immune activation (MIA) induced by a viral mimetic polyinosinic:polycytidylic acid [Poly(I:C)], is a preclinical model of dopamine dysregulation resulting in behavioural alterations including sensorimotor deficits and increased psychostimulant sensitivity precipitating in late adolescence/early adulthood (>PND60), with few studies including females. In order to consider sex-specific early interventions, a comprehensive understanding of sex differences in how MIA alters behaviour over adolescence is needed. To test this, we measured dopamine-related and anxiety-related behaviours over adolescence in male and female MIA offspring.

Methods
Wistar pregnant dams were MIA-induced on gestational day 19 with 4 mg/kg high molecular weight poly(I:C) or saline as controls (n=2/group) via tail injection, recording sickness behaviour afterwards. Maternal care was recorded for 30 minutes on six postnatal days (PND) between PND1-21. Adolescent offspring performed the prepulse inhibition (PPI) test on PND40-43 (n=9F/16M/group). Half the offspring (n=5F/8M/group) were tested for amphetamine-induced locomotion on PND47-48 and the rest (n=4F/8M/group) on PND56-57, followed by intraperitoneal injection of 1.0mg/kg in females and 1.5mg/kg in males. All animals performed the elevated plus-maze (EPM) on PND62. Data were analysed using one/two-way ANOVAs and/or repeated measures.

Results
Preliminary data shows no PPI deficit at early adolescence (PND40-43) in male or female MIA-offspring. Contrary to our prediction, a trend toward increased %PPI was observed in female MIA-offspring. Male and female controls and male MIA-offspring travelled further in response to amphetamine at PND56-57 compared to PND47-48. No increased locomotor activity was observed as a result of MIA at either age in males. In females, MIA-offspring trended toward increased distance travelled in response to AMPH at each age, which reached significance when ages were combined (P=0.014). MIA had no significant effect on anxiety-like behaviour at PND62 in males or females.

Conclusions
Our study suggests that the changes in dopamine-related behaviours may be sex- and age-specific in MIA-offspring. At the early stages (PND40-43) of adolescence, sensorimotor deficits were not visible in MIA-offspring, in fact, in female MIA offspring, were in the opposite direction. Only MIA female rats had an increase in amphetamine sensitivity over adolescence, suggesting that dopamine dysregulation occurs earlier in females than males. This study suggests the window of opportunity for pharmacological interventions to prevent the onset of these behaviours and the age of molecular changes in the brain that underpin the precipitation of altered behaviour may be sexually dimorphic.

Data Blitz Abstracts

Data Blitz Session 4

Transcriptomic and Epigenomic regulation in extinction of cocaine and nicotine self-administration

Presenting Author: Caspar Muenstermann

Caspar Muenstermann - School of Psychology, UNSW

Sarah Baracz - School of Psychology, UNSW

Eilish Heffernan - School of Psychology, UNSW

Nicholas Lister - School of Biotechnology & Biomolecular Science, UNSW

Paul Waters - School of Biotechnology & Biomolecular Science, UNSW

Kelly Clemens - School of Psychology, UNSW

Chair: Carlo Longhitano

Background
Epigenomic and transcriptional alterations induced by drugs of abuse underlie long lasting neuronal changes contributing to addiction. Neural adaptations in the ventromedial prefrontal cortex of the brain are critical for inhibitory learning and expression of extinction. While drug induced epigenetic and transcriptional changes have been investigated in response to acute drug administration, it is unclear whether these persist in the absence of acute drug exposure, across extinction.

Methods
Rats were taught to intravenously self-administer nicotine, cocaine or saline, following which they went through 1 or 6 days of extinction. Ventromedial prefrontal cortices were dissected to perform RNA-sequencing and ATAC-sequencing, determining transcriptional changes and underlying accessibility changes in chromatin during extinction of drug seeking.

Results
We found that extinction from nicotine and cocaine self-administration led to distinct epigenetic and transcriptomic changes in the prefrontal cortex that were maintained between day 1 and day 6 of extinction. Transcriptional changes showed converging regulation of gene expression in cocaine and nicotine animals, network analyses implicating a role for pathways involved in protein phosphorylation and regulation of intracellular MAPK pathways. Similarly, epigenomic changes show consistent changes in chromatin accessibility between nicotine and cocaine animals, as well as day 1 and 6 of extinction. However regulation of chromatin accessibility is not consistent with changes in gene expression.

Conclusion
In conclusion, abstinence of nicotine and cocaine self-administration lead to long lasting transcriptomic and epigenomic changes that are maintained across time and therefore may play a role in lasting vulnerability to relapse. Funded by ARC Discovery Project to KC (DP200102087).

Data Blitz Abstracts

Data Blitz Session 4

THUR_17 Multivariate brain structure-cognition signatures of early psychosis

Presenting Author: Yoshito Saito

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Chair: Carlo Longhitano

Background
Cognitive impairment is one of the major symptoms of recent-onset psychosis (ROP), not improving with medications and affecting functional outcomes. ROP individuals present widespread grey matter (GM) reductions mainly in frontal and temporal regions and widespread and subtle white matter (WM) abnormalities, but their association with cognitive impairment remains unclear. This study examined multivariate GM-WM patterns using novel, multiblock partial least squares correlation analyses (MB-PLS-C) and assessed their relationship with cognitive abilities in ROP individuals. We hypothesised that MB-PLS-C would show differential GM-WM patterns between controls and ROP individuals and that these patterns would be correlated with disease-specific cognitive abilities.

Methods
We used the Human Connectome Project for Early psychosis and the Human Connectome Project Development datasets, including the results of cognitive assessments, T1 and diffusion-weighted MRI data from 71 nonaffective ROP patients (age 22.1±3.1) and 71 matched healthy controls (HC) (age 22.0±3.2). We performed MB-PLS-C analyses using GM thickness and surface area (Desikan-Killiany atlas) and fractional anisotropy (FA) from WM tracts (JHU atlas) to identify multivariate GM-WM patterns. We analysed correlations between the GM-WM patterns and cognitive abilities including cognitive flexibility, attention, working memory, episodic memory, processing speed, reading and vocabulary.

Results
MB-PLS-C between cortical thickness and FA identified HC-specific and ROP-specific GM-WM patterns, explaining 16.92% and 12.38% of the total covariance. The ROP-specific pattern was related to frontal and temporal regions and anterior limbs of internal capsule. MB-PLS-C between cortical surface area and FA pinpointed shared and differential GM-WM patterns between groups, explaining 53.21% and 18.97% covariance. The differential pattern was associated with cingulate, frontal, and parietal regions and inferior cerebellar peduncles and posterior coronae radiatae. The thickness-FA ROP-specific pattern was associated with processing speed, working memory, and episodic memory, while the surface area-FA differential pattern was related to reading abilities.

Conclusions
MB-PLS-C identified patient-specific and differential GM-WM patterns significantly associated with GM regions and WM tracts reportedly affected in ROP individuals. This research suggests that GM-WM correlation patterns differ between controls and those with ROP, emphasising the importance of GM-WM couplings in schizophrenia. The differential pattern with surface area was correlated with crystallised intelligence, whereas the ROP-specific pattern with thickness was correlated with fluid intelligence, indicating the different pathological processes for surface area and thickness. These differential and ROP-specific GM-WM patterns indicate potential signatures of brain alterations contributing to multidomain cognitive dysfunction in the early stages of schizophrenia.

Data Blitz Abstracts

Data Blitz Session 5

FRI_5 Plasma glutamate levels are higher in individuals with major depressive disorder and correlated with psychopathology.

Presenting Author: Susan Thomas

Susan Thomas - Graduate School of Medicine, University of Wollongong

Theresa Larkin - Graduate School of Medicine, University of Wollongong

Chair: James Kesby

Background
There is accumulating evidence of involvement of glutamate in the pathophysiology of MDD, both in the brain and in peripheral sites such as the gastrointestinal track. Glutamate is the main excitatory neurotransmitter in the brain, however excessive glutamate signalling can be neurotoxic and has been proposed as a cause of MDD. Recently, elevated plasma glutamate levels have been reported in individuals with MDD, however the relationship between peripheral glutamate levels and psychopathological symptoms is unclear. We aimed to investigate plasma glutamate levels in individuals with MDD and healthy controls, and relationships with psychopathology and quality of life.

Methods
Sixty untreated individuals meeting DSM-5 MDD criteria were recruited, along with sixty healthy controls. Diagnoses were confirmed using semi-structured interviews. Blood samples were taken and plasma glutamate was measured using a standard enzyme linked immunosorbent assay (ELISA) method. Samples and standards were run in triplicate. Participants completed psychometric measures of mental health symptoms including the Depression, Anxiety and Stress Scales and the Brief Symptom Inventory, and the World Health Quality of Life Brief questionnaire. Analysis of variance was used to assess differences by sex and diagnostic status. Correlations were performed to assess relationships between the variables.

Results
Groups did not differ significantly on age or sex ratios. Plasma glutamate levels were significantly higher in participants with MDD than healthy controls, and also higher in males than females. Plasma glutamate levels correlated significantly with a wide range of psychopathology including depression, anxiety, suicidal ideation, obsessive-compulsive and psychotic symptoms. Additionally, there were significant negative correlations between glutamate levels and all domains of quality of life.

Conclusions
The current results add to a growing body of studies reporting elevated peripheral glutamate levels in depression. Additionally, our results indicate that plasma glutamate levels are meaningfully and broadly related to psychopathology, and negatively related to quality of life. While further research is needed to understand relationships between peripheral and brain glutamate levels, our results suggest that peripheral levels are important to mental health. Growing indications that there may be dysregulation of peripheral as well as brain glutamate indicate the need for further study, including consideration of multidirectional gut-brain communication, to better understand the role of glutamate in depression.

Data Blitz Abstracts

Data Blitz Session 5

FRI_11 Apathy and fatigue, but not depression, associated with inflammatory biomarkers in older adults

Presenting Author: Fleur Harrison

Fleur Harrison - Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney

Moyra Mortby - School of Psychology, UNSW Sydney; Neuroscience Research Australia, Sydney

Adam Guastella - Brain & Mind Centre, The University of Sydney; Children's Hospital Westmead Clinical School, The University of Sydney

Perminder Sachdev - Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney

Henry Brodaty - Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney

Chair: James Kesby

Background
Major depressive disorder is highly heterogenous. Deconstructing depression into individual symptoms or clusters may provide insight into its underlying biological dysregulation, including systemic inflammation. However, this has received little attention, particularly in older adults where depression may present differently. Symptoms of loss of motivation or interest (known as apathy), fatigue, and physical symptoms are more common in older adults. Further, these symptoms are among the most debilitating, according to lived experience of depression. The current research aims to investigate whether inflammatory biomarkers are differentially associated with apathy, depression and fatigue in older adults.

Methods
In 1,037 community-dwelling older adults without dementia (aged 70-90, 55% women), completed self-report assessments including measures of apathy and depression from the Geriatric Depression Scale, and fatigue from Assessment of Quality of Life-6D. Inflammatory biomarkers from early morning fasting blood collection included C-reactive protein (CRP) and interleukin-6. Logistic regressions examined associations between levels of biomarkers and apathy, depression and fatigue separately, and then included all in the same model as concurrent predictors. Analyses were initially unadjusted. The fully adjusted model controlled for baseline age, sex, education, global cognition (MMSE), health conditions, medications and BMI.

Results
Interleukin-6 was associated with apathy, depression and fatigue in unadjusted models (odds ratio [OR] per natural log unit increase in IL-6: 1.73, 95% confidence interval [CI] 1.38-2.22; OR 1.56, 95% CI 1.12-2.15; OR 1.72, 95% CI 1.14-2.59 respectively). The association with apathy remained significant after adjustment for other symptoms, socio-demographics, cognition and health-related covariates, but findings for depression and fatigue were attenuated. CRP was associated with apathy and fatigue (OR 1.10, 95% CI 1.00-1.21; OR 1.34, 95% CI 1.11-1.60 respectively) although the former was attenuated by adjustment for covariates. Previous associations between CRP and depression were not replicated.

Conclusion
In older persons, apathy and fatigue were differentially linked with inflammatory biomarkers, whereas previous associations with depression were not replicated. Findings support the symptom-specific rather than generalised nature of the depression-inflammation relationship. They confirm the importance of fatigue, and provide novel insight into apathy, as prevalent and impairing symptoms which map to immune dysregulation.

Data Blitz Abstracts

Data Blitz Session 5

FRI_23 Effects of chronic cannabis use on brain structural connectivity: Connectome and Fixel-Based analyses

Presenting Author: Suzan Maleki

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Chao Suo - Turner Institute for Brain and Mental Health, Monash University
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Karen Caeyenberghs - Deakin University, Melbourne, Victoria
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Chair: James Kesby

Background
Cannabis is the most commonly used illicit substance. Chronic cannabis use causes deficits in memory, learning, executive functions. Diffusion MRI studies on white matter (WM) integrity in regular cannabis use is under-examined, with studies reporting altered WM tracts connecting hippocampus, frontal regions, and cerebellum. In this study, we used structural Connectome and Fixel-Based analyses to investigate WM integrity in people with Cannabis Use Disorder (CUD). These techniques are complementary to study the whole brain network, with the advantages of overcome the limitation of crossing fibre in DTI.

Methods
MRI data (anatomical T1 and DTI) were collected from 56 subjects with CUD and 38 healthy controls. T1 images were preprocessed using FreeSurfer and Diffusion images were preprocessed in MRtrix3. Next, WM fiber orientation distribution (FOD) maps were estimated using single-shell 3-tissue constrained spherical deconvolution method. Individual anatomically constrained tractography (ACT) was performed to generate 20M tracts at whole brain level. Connectome analysis was performed on ACT using using Desikan Killiany atlas (84 nodes). Between-group differences were tested using NBS method. Individual fixels were generated, reoriented and assigned to the FOD template to compute fibre density and cross-section metrics.

Results
Participants with cannabis use disorder had higher WM connectivity weights across 13 edges compared to healthy non-users at whole brain level, p=0.04 FDR corrected. The altered connection included left Orbitofrontal to right Inferior-Parietal, left Amygdala to right Inferior-Parietal and Parstriangularis. The network differences were observed in frontoparietal network and basal ganglia. Regarding the fixel-based metrics, CUDs had higher fibre density and cross-section in the splenium of corpus callosum (Fig 2B), but lower FDC in the right cerebellum compared to healthy controls.

Conclusions
We present an advanced diffusion model to investigate altered WM connectivity in people with cannabis use disorder. Using anatomically constrained tractography and fixel- based analysis, we demonstrated altered WM connectivity compared to healthy subjects mainly across Frontoparietal network, Basal ganglia and Cerebellum. Our results imply that chronic cannabis use adversely affects brain structural connectivity in regions associated with memory, learning, reward processing and cognitive functions. Also, thesis findings align with previous volumetric, morphometric and diffusion studies on chronic cannabis users.

Data Blitz Abstracts

Data Blitz Session 5

FRI_19 The Impact of Neurosteroid Therapy on the Cerebellum Following Preterm Birth in a Guinea Pig Model

Presenting Author: Carlton Lloyd Pavy

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Julia C Shaw -

Hannah K Palliser - School of Biomedical Sciences and Pharmacy, University of Newcastle, Newcastle, Australia. Hunter Medical Research Institute, Mothers and Babies Research Centre, Newcastle, Australia

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Chair: James Kesby

Background
Preterm birth causes a premature loss of the placentally-derived inhibitory neurosteroid, allopregnanolone. Allopregnanolone is known to contribute to the formation of myelin and premature loss of this neurosteroid due to preterm birth impairs myelin formation. Impaired myelination results in decreased neuronal conductibility and irregular myelination has been associated with neurobehavioral pathologies (ADHD and anxiety) which occur more prevalently in children who are born preterm. This study aimed to determine whether administration of ganaxolone, a synthetic allopregnanolone analogue, in the immediate postnatal period following preterm birth can restore myelination to a term-born developmental phenotype.

Methods
Time-mated Dunkin Hartley guinea pigs delivered preterm (induced at GA62) or term (spontaneous at ~GA69) and offspring were allocated to neonatal or juvenile collection. Preterm neonates received vehicle or ganaxolone (1mg/kg/day) until term equivalent age (TEA, 7 days postnatal). Tissues were collected at term equivalent age (preterm=7 days postnatal; term=24hrs post-delivery), or at the equivalence of late childhood (preterm=TEA+40 days; term=40 days). Immunohistochemical staining for myelin basic protein (MBP) and oligodendrocyte transcription factor 2 (OLIG2) was performed in cerebellar lobes IX, X and DWM (deep white matter) and results analysed using ImageJ software.

Results
OLIG2 staining of lobes IX and DWM in males was significantly lower in term-born (n=7) than vehicle treated preterm-born juveniles (n=5) (p=0.0001 and p=0.0338 respectively). Importantly, MBP staining of lobes IX, X and the DWM was found to be significantly higher in ganaxolone treated preterm-born male juveniles (n=6) than vehicle treated preterm-born juveniles (p=0.0006, p=00024 and p=0.00010 respectively). For females there was significantly lower OLIG2 staining in lobe X and the DWM for term-born juveniles (n=6) compared to vehicle treated preterm-born juveniles (n=5) (p=0.0414 and p=0.0008 respectively). No other significant differences identified at juvenile age or neonatal age.

Conclusion
The lateral hemisphere of the posterior cerebellum, which includes lobes IX and X, has been implicated in cognitive functions. Preterm birth was found to increase total oligodendrocyte numbers (OLIG2) likely through hypoxic excitotoxic

mechanisms. Ganaxolone treatment, which increases GABAergic tone, protecting against excessive excitation, was shown to increase MBP staining, inferring an increase in oligodendrocyte maturation, returning cerebellar development to a term-born phenotype. This study highlights the potential of neurosteroid-based therapies in restoring oligodendrocyte maturation and myelination to a term born phenotype and the possibility of mitigating the increased risk of neurobehavioral conditions developing following preterm birth.

Data Blitz Abstracts

Data Blitz Session 5

FRI_33 Unravelling an Intriguing Link Between Occasional Overeating, Gut Microbiota, and Behavior: A Tale of Fragmented Sleep and Midnight Munchies

Presenting Author: Diana Sketriene

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Laddawan Lalert - Department of Medical Science, School of Medicine, Walailak University, Thailand.

Puspha Sinnayah - Institute for Health and Sport, Victoria University, Melbourne, Australia

Robyn Brown - Department of Biochemistry and Pharmacology, University of Melbourne, Australia

Chair: James Kesby

Background
Intermittent limited access to high-fat/high-sugar ("junk") foods has been shown to increase risk of developing binge eating and obesity. Dysregulated eating and sleeping patterns are also more common in both binge eating disorder and obesity. It is well established that chronic consumption of high-fat/high-sugar foods has a negative impact on gut microbiota; however, it is unclear whether this is the case when these foods are eaten occasionally. As such, this study aimed to determine the impact of intermittent limited access (1h, 3 x per week) of high-fat/high-sugar food gut microbiota as well as eating and sleeping patterns.

Methods
Male Sprague-Dawley rats were given either continuous access (24h) or limited intermittent access to a highly palatable diet (45% kcal from fat; 1h/day, Mon/Wed/Fri) and compared to a control group that only had access to standard rodent chow. Sleeping and eating patterns over 24h before and after the diet were manually scored by two individuals blinded to the experiment. Social behaviour was measured by the social interaction test. 16S rRNA gene amplicon sequencing was performed on fecal samples from rats collected before and after the diet period. Microbiota data were correlated with behaviour, sleep and eating, and food intake measurements.

Results
Rats that received intermittent access to the high-fat/high-sugar diet developed binge-like eating over the 10-week protocol, consuming X% of their weekly kcal intake in the 3x1h sessions. Despite this, their body weight remained similar to controls. This group also showed disturbed sleep and a pronounced spike in eating during the inactive period (lights-on). This group also displayed impaired social interaction, showing increased aggressive behaviour. Notably, only 1h access to 'junk food' 3x per/week in lean animals is sufficient to decrease microbiota diversity to levels comparable to obese animals. Significant correlations between behaviour, microbiota modifications and food intake were also observed.

Conclusion
Our study suggests that even occasional access to junk food can lead to profound changes in gut microbiota diversity, disrupted sleep patterns, and trigger night-eating episodes even before obesity sets in. These findings underscore the importance of early interventions to tackle the complex interplay between dietary habits, gut microbiota, and behavior, ultimately offering new insights into the prevention of adverse health outcomes.

Poster Abstracts

Please note that Poster Abstracts are displayed in alphabetical order.

Poster Abstracts

Poster Session 2: Thursday

THUR_66 Sleep quality associated with altered brain structure and microstructure in the long-term trauma survivors.

Presenting Author: Abdalla Z Mohaned

Abdalla Z Mohaned – Thompson Institute, University of the Sunshine Coast, Sunshine Coast, QLD 4575, Australia.

Background
Disturbed sleep is a hallmark feature of posttraumatic stress disorder (PTSD). However, limited studies examined sleep in long-term trauma survivors' decades following trauma. This study compared sleep quality in trauma-exposed Vietnam War veterans with and without PTSD.

Methods
Trauma-exposed veterans with and without PTSD were recruited as part of the Alzheimer's Disease Neuroimaging Initiative- Department of Defense (ADNI-DOD). Participants filled the Pittsburgh Sleep Quality Index PSQI questionnaires and underwent neuroimaging investigations including diffusion weighted imaging. The sleep quality was correlated with the diffusion measures in the white-matter tracts.

Results
A total of 62 PTSD, and 44 PTSD patients with traumatic brain injury (TBI+PTSD) were included in the study. The total PSQI scores were correlated positively with the diffusion measure including axial (AD), radial (RD), and Apparent diffusion coefficient (ADC), while negatively correlated with the fractional an isotropy (FA) in the PTSD group (PFWE ≤ 0.05). for the TBI+PTSD, negative correlations between PSQI scores and the FA and AD, while positive correlations were observed in the RD (PFWE ≤ 0.05).

Conclusion
This suggests the sleep quality within the trauma survivors to be associated with the white-matter alterations observed in different brain white-matter tracts. Future studies with objective sleep measures using actigraphy watches or Polysomnography would be required to ensure the observed sleep quality changes are not due to subjective bias.

Poster Abstracts

Poster Session 3: Friday

FRI_61 Targeting the oxytocin system to promote preference for social interaction over alcohol consumption in rats.

Presenting Author: Alexander Athanasopoulos

Alexander Athanasopoulos - Brain and Mind Centre, University of Sydney, NSW, Australia. School of Psychology, Faculty of Science, University of Sydney, NSW, Australia.

Tylah J. Doolan - Brain and Mind Centre, University of Sydney, NSW, Australia. School of Psychology, Faculty of Science, University of Sydney, NSW, Australia.

Nicholas A. Everett - Brain and Mind Centre, University of Sydney, NSW, Australia. School of Psychology, Faculty of Science, University of Sydney, NSW, Australia. Kinoxis Therapeutics Pty Ltd, VIC, Australia.

Michael T. Bowen - Brain and Mind Centre, University of Sydney, NSW, Australia. School of Psychology, Faculty of Science, University of Sydney, NSW, Australia. Kinoxis Therapeutics Pty Ltd, VIC, Australia.

Background
Alcohol use disorder (AUD) is associated with deficits to social motivation, which may worsen craving, bingeing, and relapse. Yet, social influences have not been integrated into models of addiction, potentially contributing to the limited clinical success of AUD pharmacotherapies. A new social vs. alcohol choice procedure discovered rats prefer alcohol over social interaction, providing an ideal model for developing pharmacotherapies. The neuropeptide oxytocin is theorised to 'rebalance' the addicted brain, promoting social interaction over drug consumption, although this has been previously untestable. Our study explores whether oxytocin treatment can increase the preference for social interaction over alcohol consumption in rats.

Methods
Male and female Sprague-Dawley rats were provided 24hr home-cage access to 20% ethanol for 6 sessions (2/week). Rats were then trained to self-administer 0.1mL of 20% ethanol (15 days), 30-sec of social interaction (7 days), and to make mutually exclusive choices between alcohol and social interaction. Initially, rats were social preferring, so we tested the role of endogenous oxytocin signalling in this phenotype by administering an oxytocin receptor antagonist (L368,899, 5 mg/kg i.p.) or saline prior to choice. Subsequently, through systematic variation of parameters, rats were encouraged to prefer alcohol, and underwent treatment with oxytocin (0.1 - 1 mg/kg i.p.).

Results
The outcomes of oxytocin receptor antagonism (in socially preferring rats) and oxytocin treatment (in alcohol-preferring rats) will be reported, for both male and female rats.

Conclusion
There is a need for pharmacological interventions addressing both the social and drugs factors implicated in alcohol use; these findings may provide critical knowledge for the development and application of oxytocin-based therapeutics for alcohol use disorder. The antagonist experiment will identify whether endogenous oxytocin signalling contributes to preferring social interaction over alcohol, which is significant given endogenous oxytocin tone and expression are reduced in many psychiatric conditions, including substance use disorders. The oxytocin treatment experiment will identify whether stimulating oxytocin receptors can promote non-alcohol reward choices, which would be impactful for the design of oxytocin-based therapies as adjuncts to psycho-social interventions.

Poster Abstracts

Poster Session 2: Thursday

THUR_4 Hippocampal subfield volume as a function of cannabis use and cannabis use disorder

Presenting Author: Alexandre Guerin

Alexandre Guerin - University of Melbourne

Cassandra Wannan - University of Melbourne

Xuejun Hao - Columbia University Irving Medical Center

Margaret Haney - Columbia University Irving Medical Center

Suzette Evans - Columbia University Irving Medical Center

Gillinder Bedi - University of Melbourne

Background
People who regularly smoke cannabis have decreased volume in bilateral hippocampus relative to controls. Few studies have investigated hippocampal subfield volumes in relation to cannabis use or cannabis use disorder, with conflicting results: some found a link between hippocampal subfield volume and cannabis use itself, while others found an association between volume and cannabis dependence, but not use. The current analyses employed a novel automated subfield segmentation method to assess differences in hippocampal cornu ammonis (CA1-3) subfield volume between 1) people with near daily cannabis use compared to controls; and 2) people with no, mild, or moderate/severe cannabis use disorder.

Methods
Study 1: People with near-daily cannabis use (n=21; 2F, 19M) and demographically matched controls (n=19; 2F, 17M) were recruited. Study 2: People who smoke cannabis ≥4x/month with mild (n=19; 4F, 15M) or moderate/severe (n=23; 5F, 18M) cannabis use disorder and people who smoke cannabis but did not have current cannabis use disorder (n=20; 8F, 12M) were recruited. MRI T2-weighted scans were collected. Subfield data were processed using the Automatic Segmentation of Hippocampal Subfields package (UPenn). The analytic plan was preregistered (https://osf.io/2gj6b). Differences in CA1 to 3 subfield volumes between groups were analyzed using mixed within-between ANOVAs, with Bonferroni corrected follow-up analyses.

Results
In Study 1, there was a Group x CA subfield interaction [$F(2,72) = 5.453$, $p = 0.006$, $\eta p2 = 0.132$], after controlling for education years and number of daily cigarettes smoked. CA1 volume was smaller in people who use cannabis relative to controls [$F(1,36) = 5.433$, $p = 0.025$, $\eta p2 = 0.131$], although this did not survive Bonferroni correction. In Study 2, there was no main effect of Group or Group x CA subfield interaction on CA volumes interaction [$F(4,118) = 0.247$, $p = 0.911$, $\eta p2 = 0.008$].

Conclusion
Near-daily cannabis use, but not cannabis use disorder, was marginally associated with smaller CA1 volume. This suggests that hippocampal subfield volume differences may be related to cannabis use rather than cannabis use disorder. Hippocampal subfields play distinct roles in cognition and are differentially affected in psychiatric conditions. Further investigation of the relationship between hippocampal subfield volumes and cognitive functions as a function of cannabis use is warranted.

Poster Abstracts

Poster Session 1: Wednesday

WED_38 Expression of hippocampal cortisol receptors in psychiatric disorder patients with trauma histories

Presenting Author: Amber Curry

Amber Curry - School of Chemistry and Molecular Biosciences and Molecular Horizons, Faculty of Science, Medicine and Health, University of Wollongong, Australia

Dominic Kaul - School of Chemistry and Molecular Biosciences and Molecular Horizons, Faculty of Science, Medicine and Health, University of Wollongong, Australia

Lezanne Ooi - School of Chemistry and Molecular Biosciences and Molecular Horizons, Faculty of Science, Medicine and Health, University of Wollongong, Australia

Natalie Matosin - School of Chemistry and Molecular Biosciences and Molecular Horizons, Faculty of Science, Medicine and Health, University of Wollongong, Australia

Background
Environmental factors, such as psychological trauma, raise the risk of psychiatric disorder development. Dysfunction of the typical stress response is a major system interfacing this risk with psychopathology; however, human evidence of this association is limited.

Hippocampal cortisol activity is central to regulating the stress response, with the function of cortisol receptors being highly cell-type and region specific. If and how the receptors are altered by stress exposure in psychopathology directly in the human brain at single-cell and spatial resolution is yet to be explored. This information is fundamental to understanding the lasting dysregulation of the stress response in psychiatric disorders.

Methods
Postmortem hippocampus tissue was acquired from the NSW Brain Tissue Resource Centre. The cohort of schizophrenia, bipolar disorder, and major depressive disorder cases was grouped based on lifetime trauma exposure; childhood (n=3), adulthood (n=5), no stress (n=3) and controls (n=3).

Spatial transcriptomics (Visium, 10x Genomics) was used to measure differential gene expression between groups. The datasets were integrated and clusters for each array capture spot were determined. The major cell type in each capture spot was annotated using single nucleus RNA sequencing data from controls (n=2). Spatial- and cell type expression of the cortisol receptors was then compared between groups.

Results
Spatial transcriptomics effectively identified well-established spatial domains including the dentate gyrus and CA1-4. Preliminary data analysis of differential gene expression within hippocampal spatial domains revealed stress related alterations to gene expression between cases and controls. The cortisol receptor gene expression levels (e.g. glucocorticoid receptors, mineralocorticoid receptors) also demonstrated spatial- and cell type-specific alterations in cases compared to controls.

Conclusion
The data indicates specific cells in hippocampal subregions contribute to the dysfunctions stress response in mental illness. However, follow up experiments, such as immunohistochemistry and validation in larger, independent datasets, are needed to validate these findings. Nevertheless, this is an important first study to investigate stress related psychopathology of the hippocampus at a spatial transcriptomic level and provides promising results for future studies.

Poster Abstracts

Poster Session 2: Thursday

THUR_39 Neurochemically distinct populations of RXFP3+ neurons in the lateral hypothalamus and zona incerta may regulate discrete aspects of behavioural arousal

Presenting Author: Brandon K Richards

Brandon K Richards - Macquarie University

Jennifer L Cornish - Macquarie University

Jee Hyun Kim - Deakin University

Andrew J Lawrence - The Florey Institute of Neuroscience and Mental Health

Christina J Perry - Macquarie University

Background
Many psychiatric disorders involve disordered regulation of arousal. The lateral hypothalamus (LH) and zona incerta (ZI) regulate arousal via complex networks that link cortical areas with downstream motor nuclei. The LH/ZI highly expresses RXFP3, a neuropeptide receptor that regulates behavioural arousal via ascending pontine relaxin-3 projections. Activating specific LH/ZI RXFP3+ cells increased locomotion and decreased learned fear expression, but induced escape-like jumping in some mice. Given the known neurochemical diversity of these nuclei, we posited that activating neurochemically variable RXFP3+ subpopulations between mice may have generated different responses. Therefore, we examined the spatiomolecular properties of these cells throughout the LH/ZI.

Methods
RNAscope fluorescent in situ hybridisation was performed to examine the co-expression of RXFP3 with vGlut2, GAD1, tyrosine hydroxylase (TH), parvalbumin (PV), and somatostatin (SST) throughout the entire LH/ZI of RXFP3-Cre mice (n = 4). Co-expression analysis was performed semi-automatically by training and applying supervised machine learning classifiers using QuPath software. To illustrate the spatial distribution of co-expression between RXFP3 and markers of interest, cell classification masks from QuPath were transposed onto Mouse Brain Atlas plates using Adobe Illustrator.

Results
Most ZI RXFP3+ cells (~77%) were GAD1+. Large clusters of TH+/RXFP3+, SST+/RXFP3+, and PV+/RXFP3+ cells populated spatially segregated areas of the ZI. LH RXFP3+ cells were GAD1+ and vGlut2+ in relatively equal proportions (~33% and ~39%, respectively). Spatial mapping revealed partially overlapping GAD1+/RXFP3+ and vGlut2+/RXFP3+ populations in the anterior LH, though were intermingled otherwise. RXFP3+ LH cells were shown to sparsely co-express TH, SST, and PV, though no obvious patterns of co-expression were evident.

Conclusion
Collectively, these results indicate that LH/ZI RXFP3+ cells are a neurochemically heterogeneous cell population, comprising both excitatory and inhibitory subpopulations. These findings inform future functional interrogation studies to address the involvement of identified RXFP3 subpopulations in threat- and arousal-related behaviours.

Poster Abstracts

Poster Session 1: Wednesday

WED_50 Can modulation of glycinergic periaqueductal grey neurons be therapeutic in a chronic pain state?

Presenting Author: Caitlin Fenech

Caitlin Fenech - Pain Management Research Institute, Kolling Institute, University of Sydney

Neda Assareh - Pain Management Research Institute, Kolling Institute, University of Sydney

Karin Aubrey - Pain Management Research Institute, Kolling Institute, University of Sydney

Background
Chronic pain is a significant health issue affecting an estimated 3.4 million Australians and is associated with many comorbidities such as depression, anxiety, and sleep disorders. A population of glycinergic neurons have been reported in the midbrain ventrolateral periaqueductal grey (vlPAG), a key area involved with descending pain modulation. Using behavioural models of pain and chemogenetics, we have demonstrated that glycine-PAG neurons can bidirectionally modulate acute nociception in mice, with their inhibition promoting analgesia. This study aims to investigate if inhibition of glycine-PAG neurons reduces the sensory and potentially affective impacts that occur in mouse models of chronic pain.

Methods
We bilaterally injected inhibitory viral (hM4Di) or control (mCherry) into the vlPAG of GlyT2::Cre mice. After viral transduction, a prolonged inflammatory state was induced by injecting Complete Freunds Adjuvant (CFA; an inflammatory agent) or control (saline) in the left hindpaw. Following i.p injection of CNO (5mg/kg or vehicle), nociception testing was carried out using the von Frey, acetone, and hotplate tests. These tests were repeated for baseline testing, two days and one week after paw injection to assess short- and long-term changes. The animals were also observed in an open-field (locomotion), light-dark (anxiety-like behaviours) and nesting test (normal daily activity).

Results
To compare between groups, a one-way ANOVA followed by Bonferroni's multiple comparison test was used and if the data was non-parametric, Friedman ANOVA followed by Dunn's multiple comparison test was applied. The results suggest that in female and male mice, inhibition of glycine-PAG neurons did not relieve the increased mechanical and thermal nociception that develop two and seven days after inflammatory pain model induction (P>0.05, n= 8-10 animals). Preliminary data using automated tracking analysis of open field and light-dark tests also suggest that chemogenetic inhibition of glycine-PAG neurons had no effects on locomotion and anxiety-like behaviours (P>0.05, n= 8-10 animals).

Conclusion
Although inhibition of glycine-PAG neurons is anti-nociceptive during acute thermal pain tests, their inhibition cannot relieve nociception sensitivity or change locomotion and anxiety-like measures in a persistent inflammatory state. These results suggest persistent inflammatory pain is not modulated by glycine-PAG neurons and that the neuronal pathway of pain modulation in chronic inflammatory states is different from healthy states. Future studies will assess if chemogenetic inhibition of GlyT2vlPAG neurons can be therapeutic use on the neuropathic pain model.

Poster Abstracts

Poster Session 2: Thursday

THUR_60 Nutritional approaches in the treatment of Schizophrenia Spectrum Disorders: a Systematic Literature Review

Presenting Author: Calogero Longhitano

Calogero Longhitano - James Cook University, Queensland

Sabine Finlay - James Cook University, Queensland

Flavia Fayet-Moore - Nutritional Research Australia, NSW

Kylie Abbott - Nutritional Research Australia, NSW

Shaileigh Gordon - Queensland Health

Christopher Palmer - Harvard Medical School, MA, USA

Shebani Sethi - Stanford University School of Medicine, CA, USA

Zoltan Sarnyai – James Cook University, Queensland

Background
Schizophrenia spectrum disorders (SSD) are a cluster of severe, heterogeneous and multifactorial mental disorders, affecting 1% of the population. Environmental factors such as neurodevelopmental insults, psychosocial adversity, and substance use, interact with genetic susceptibility to produce widespread phenotypic variation. Dietary and metabolic approaches have demonstrated efficacy in a variety of related diseases, including autism spectrum disorder, brain trauma, Alzheimer's disease, sleep disorders, brain tumours, pain, and multiple sclerosis. While emerging data supporting dietary interventions for mental health are promising, questions remain unanswered. To our knowledge, no systematic review of the evidence for nutritional intervention in the treatment of SSD exists.

Methods
A systematic review of the available evidence in people with SSD was conducted according to PRISMA guidelines. PubMed, CINAHL, Embase, Web of Science, and Cochrane CENTRAL were searched from January 1970 to March 2021. Studies that investigated nutritional approaches in individuals of any age diagnosed with schizophrenia or related disorders (schizophreniform, schizoaffective disorder or delusional disorder), using any internationally recognised diagnostic criteria, e.g., DSM-IV, DSM-V, ICD10, and that reported on psychiatric or metabolic outcomes, were included. For studies that met the inclusion criteria, Risk of bias was assessed using the Cochrane Risk-of-Bias tool.

Results
Thirty-nine studies were identified, design ranging from case studies to randomised controlled trials. Studies can be grouped into those introducing single elements, groups of elements and whole diet approaches. Supplementation with oral NAC, ALA, vitamin C, gluten-free diet, tryptophan-deficient and ketogenic diet may offer some benefit, specifically in cognition and function, although further, well controlled studies are needed. Additionally, the results of this review suggest adjunctive treatment with fatty acids, gluten-free diet, or ketogenic diet, may confer some benefit in relation to metabolic parameters as well as measures of psychiatric symptom severity.

Conclusion
The results of this review support preliminary evidence on the efficacy of several nutritional intervention approaches, although due to the low-moderate quality of most trials included, further high-quality research into the use of nutritional therapy is warranted. Supplementation with n-3 fatty acids and the use of therapeutic ketogenic diets for SSD appear strongest in efficacy. The result also shows that greater attention to cognitive and functional outcome measures in trials of nutritional interventions in severe psychiatric disorders, is also warranted.

Poster Abstracts

Poster Session 2: Thursday

THUR_10 Genetic overlap between psychiatric disorders and migraine

Presenting Author: Charlotte Bainomugisa

Charlotte Bainomugisa - Queensland University of Technology, Center for Genomics and Personalized health

Dale Nyholt - Queensland University of Technology, Center for Genomics and Personalized health

Lyn Griffith - Queensland University of Technology, Center for Genomics and Personalized health

Divya Mehta - Queensland University of Technology, Center for Genomics and Personalized health

Background
Epidemiological studies show that migraine often co-occurs with various psychiatric disorders. Co-morbidity with psychiatric disorders may alter the prognosis of migraine and complicate its diagnosis, treatment and treatment adherence; thus increasing likelihood of remission and affecting the quality of life. Studies suggest that the relationship between migraine and its comorbidities may be uni-directional, bi-directional or there may be common shared aetiological factors that explain co-occurrence. The mechanisms underlying these co-morbidities are not fully understood, however there is increasing evidence of a strong genetic component. The shared aetiology between migraine and psychiatric disorders has been partly attributed to overlapping genetic effects.

Methods
We used large Genome-Wide Association Studies (GWAS) summary statistics to estimate genetic overlap at SNP and gene-level, and identify enriched pathways of overlapping genes between migraine (n = 873341) and 11 psychiatric disorders (n = 9907 - 807553). We estimated global and local genetic correlation using Linkage Disequilibrium Score Regression (LDSC) and Local Analysis of [co]Variant Association (LAVA) respectively. We identified local and genome-wide shared loci using Genome-wide association studies - pairwise (GWAS-pw) and Genome-Wide Analysis Meta-Analysis (GWAMA) respectively. We assessed for causal relationships using Mendelian Randomization to assess for causal relationships and identified shared novel genes and enriched pathways.

Results
Migraine showed a significant genetic correlation with Post-Traumatic Stress Disorder (PTSD), Major Depressive Disorder (MDD) and schizophrenia (SCZ). We identified significant locus-specific genetic overlap at locus p13 at (Chr3) for MIG/SCZ (p < 2.21 x 10-5). Locus 11p11.2 (chr11) indicated association with increased risk of migraine (P = 5.73 x 10-9) and reduced risk of SCZ (P = 1.10 x 10-9). There was a uni-directional causal association between migraine (outcome) and each of MDD and SCZ. Novel SNPs across SLC9B1, ARID5B, PAX5, HTT, CACNB2 and SLC7A6 genes were identified. The overlapping genes were enriched in ion channel and neuronal-related pathways.

Conclusion
Findings show evidence of shared genetic factors and biological pathways between migraine and psychiatric disorders. These support the role of genetically controlled biological pathways involving the neurological system, particularly HPA axis and processes such as inflammation which have previously been suggested to play a role in migraine-psychiatric comorbidities. The common genes and pathways between migraine and more than one psychiatric disorder indicate the spectral nature of psychiatric traits. The shared biomarkers (SNPs, loci and genes) can be used as basis for experimental validation as potential therapeutic targets and for improvement of current treatment of migraine-psychiatric comorbidities.

Poster Abstracts

Poster Session 3: Friday

FRI_12 The ability of cues to precipitate relapse to alcohol-seeking changes across abstinence.

Presenting Author: Christina J Perry

Christina J Perry - Macquarie University

Michelle H Shen - Macquarie University

Kate E O'Sullivan - Macquarie University

Andrew J Lawrence - The Florey Institute of Neuroscience and Mental Health

Jennifer L Cornish - Macquarie University

Background
Incubation of craving is the time dependent increase in craving elicited by drug-associated cues. This is modelled in rodents by measuring changes to cue-elicited drug-seeking across abstinence. We have confirmed that occurs where alcohol is the initial drug reinforcer. However, as with most research in this area, our study did not test incubation in the absence of the cue. Hence, the psychological mechanism underlying increased relapse is uncertain. Experiment 1 tested whether incubation involves an increase in incentive salience of the discrete cue, while Experiment 2 tested changes to the discriminative properties of alcohol-associated cues.

Methods
1: Rats were trained to lever-press for alcohol, delivered with a light cue: the conditioned stimulus (CS). Responding was extinguished by withholding both alcohol and CS. Rats underwent 29 days of abstinence, and alcohol-seeking was tested on day (D) 1 or D29 either with or without the CS.

2: We used a discriminative protocol where the presence of distinct discriminative stimuli (DS+/-) signalled availability/absence of alcohol, and lever presses were paired with distinct conditioned stimuli (CS+/-). Daily alternating DS+/CS+ and DS-/CS- sessions continued until responding was high during DS+/CS+ only. Alcohol-seeking was tested under each condition on D1 and D29.

Results
Experiment 1 showed that rats performed more lever presses in the presence of the alcohol-associated cue on D1. Responding overall was higher on D29, but there was no difference between cued and no-cued conditions. In Experiment 2, where there was no separate extinction phase, there was a significant difference between DS+/CS+ and DS-/CS- on D1 of abstinence. As with Experiment 1, overall response was higher on D29 compared to D1, but there was no longer a difference between the two cue conditions.

Conclusion
These results show that there is alcohol-seeking is prone to a robust time-dependent increase in relapse propensity. Although this is similar to the “incubation” effect described in for psychostimulants, it does not appear to be due specifically to increases in incentive salience of the cue. Rather, there is a net increase in motivation to seek alcohol that overshadows the ability to distinguish between conditions that signal alcohol availability versus those that signal its absence. Ongoing studies are investigating the neural mechanism behind this change. Overall, this has implications regarding the conditions that precipitate relapse in alcohol-use disorder.

Poster Abstracts

Poster Session 1: Wednesday

WED_20 Altered task-induced functional decoupling of the frontocingulate cortex in depression

Presenting Author: Christine Leonards

Christine Leonards - Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia

Ben Harrison - Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia

Alec Jamieson - Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia

James Agathos - Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia

Trevor Steward - Melbourne School of Psychological Sciences, The University of Melbourne, Parkville, Victoria, Australia

Christopher Davey - Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia

Background
Activity suppression of the frontocingulate cortex during externally directed attentional tasks reflects progressive disengagement of self-related mental processes. This suppression effect is an adaptive feature of brain function which represents cognitive flexibility and facilitates goal-directed behaviour. People with depression consistently show abnormal activity and functional connectivity of the frontocingulate cortex. However, the exact nature of these dysfunctional neural patterns during task-related suppression and what this represents in depression remains unknown. The aim of this study was to investigate task-related functional connectivity (i.e., decoupling and coupling) of brain regions with the frontocingulate cortex during task performance in people with depression.

Methods
Eighty-one 15- to 25-year-olds (51 females; M = 19.8, SD = 2.7) who met criteria for major depressive disorder (MDD) and 94 matched healthy controls (52 females; M = 20.1, SD = 2.8) were scanned while completing a functional magnetic resonance imaging (fMRI) emotional face-matching task which has previously shown to elicit robust frontocingulate suppression. Included MDD participants were part of a randomised clinical trial that compared the efficacy of 12-weeks cognitive behavioural therapy (CBT) with either fluoxetine (a selective serotonin reuptake inhibitor; SSRI) or placebo and consented to undergo optional baseline neuroimaging prior to the commencement of treatment.

Results
To identify brain regions functionally decoupled and coupled with the frontocingulate cortex during task performance, we conducted a psychophysiological (PPI) analysis on fMRI data. We found the groups showed differential patterns of functional connectivity during cognitive task performance. Specifically, the MDD group, compared to controls, showed significantly less decoupling of the frontocingulate cortex with task-dependent (i.e., face processing) and cognitive control regions as well as increased coupling with regions implicated in interoceptive and affective processes during the task condition.

Conclusion
These results demonstrate altered connectivity of the frontocingulate cortex with regions involved in cognitive and affective functions during task performance in people with depression. This neural inflexibility may reflect difficulty switching cognitive resources away from self-related and introspective processes to attend to the task at hand. These findings advance our understanding of the neural mechanisms underpinning maladaptive cognitive and affective processes commonly associated with depression. Our findings also have important clinical utility as they provide a novel way for identifying individuals with potentially more entrenched difficult-to-treat depression.

Poster Abstracts

Poster Session 3: Friday

FRI_67 Protocol: Structural brain networks implicated in co-occurring PTSD and alcohol use disorder

Presenting Author: Ellen E Towers

Ellen E Towers - Edith Collins Centre, University of Sydney

Kirsten Morley - Edith Collins Centre, University of Sydney

Warren Logge - Drug Health Services, Royal Prince Alfred

Paul Haber - Drug Health Services, Royal Prince Alfred Hospital

Katherine Mills - Matilda Centre, University of Sydney

Scott Mackey - ENIGMA ADDICTION, University of Vermont

Hugh Garavan - ENIGMA ADDICTION, University of Vermont

Rajendra Morey - PGC-PTSD, Duke University"

Background
Comorbid PTSD and alcohol use disorder (AUD) is highly prevalent and characterised by complex clinical presentations. Because of this the treatment process is complicated, whereby patient attrition and failure to respond is commonplace. Due to this complex clinical presentation, those with comorbid PTSD and AUD are routinely excluded from research leading to limited understanding of the comorbidity. Comparing the structural abnormalities that are common to PTSD and AUD, as well as what is unique to the comorbidity will offer a better understanding of the pathophysiology and may offer insight into what neurobiology driving the high prevalence.

Methods
Clinical and imaging data were collected from 3992 participants, globally. This sample comprised of four groups: PTSD only, AUD only, comorbid PTSD & AUD and healthy controls (HC), collected through a collaboration between PGC-PTSD (ENIGMA) and ENGIMA Addiction working groups. To be included a formal diagnosis using standardised instruments was required, and aged > 18 years. Those with concurrent axis 1 diagnoses (excluding depression, anxiety) were excluded. T1-weighted structural magnetic resonance imaging (sMRI) were processed using the FreeSurfer pipeline using the Desikan-Killiany atlas. ENIGMA imaging quality control protocols were applied to scans to ensure consistency (https://enigma.ini.usc.edu/protocols/imaging-protocols/).

Results
We will conduct structural covariance analysis using cortical morphological measures (cortical thickness (CT) & surface area (SA)) as well as subcortical volume. We will build groupwise structural Pearson correlation matrices of the 2278 pairs of cortical regions and 91 pairs of subcortical regions. The null hypothesis is that there are no differences between the pairs of regions across the groups. We will compare the connectivity strength between the cortical regions with morphological reductions to the connectivity strength of sets of randomly chosen cortical (or subcortical) regions to establish that the structural interconnectedness is occurring more strongly than chance.

Conclusion
This will be the first study to investigate the neurobiology underpinning comorbid PTSD and AUD. We hypothesise comparisons of PTSD vs HC, and AUD vs HC will reveal similar structural covariance networks. We also hypothesise that the comparison of comorbid vs HC will reveal more significant morphological changes in these same networks. We also expect that the comorbid group and AUD-only group will also show similar reductions in regions associated with alcohol-related structural insult that will not be present in the PTSD-only group.

Poster Abstracts

Poster session 1: Wednesday

WED_62 NMDA receptor antagonist-induced disruptions to oscillatory and aperiodic neural activity

Presenting Author: Elysia Sokolenko

Elysia Sokolenko - School of Biomedicine, University of Adelaide, Australia

Matthew Hudson - Central Clinical School, Monash University, Australia

Nigel Rogasch - Hopwood Centre for Neurobiology, Lifelong Health Theme, South Australian Health and Medical Research Institute (SAHMRI), Australia

Nigel Jones - Central Clinical School, Monash University, Australia

Mitchell Goldsworthy - Behaviour-Brain-Body Research Centre, Justice and Society, University of South Australia, Australia

Background
Schizophrenia is associated with impairments in cognition and gamma oscillatory activity. These same phenotypes can be induced in rodents with the administration of NMDAr antagonists. Here we aimed to identify whether NMDAr antagonists also alter the aperiodic component of neural activity.

Methods
C57/Bl6 mice were implanted with local field potential (LFP) recording electrodes in the medial prefrontal cortex (mPFC) and dorsal hippocampus (dHPC). Awake mice were administered vehicle or MK-801 (1 mg/kg) prior to recording LFPs at rest. The aperiodic component of neural activity was modelled using the FOOOF module in Python.

Results
MK-801 increased ongoing gamma power in the mPFC and dHPC. The aperiodic exponent was lower in both regions with MK-801 compared to vehicle, reflecting a flatter slope of the LFP power spectrum. The R2 of the model fit was significantly lower with MK-801 treatment compared to the vehicle. This was supported by a higher error of the model fit.

Conclusion
We conclude that NMDAr antagonists alter both aperiodic and periodic neural activity. MK-801 treatment decreased slope, which is thought to reflect altered excitation/inhibition balance. We note that FOOOF may be limited in its capacity to model data where excitation/inhibition balance is dramatically altered. Further analysis with pre-existing data (planned for completion prior to conference attendance) will explore whether the changes in aperiodic neural activity can be mechanistically linked with working memory impairment. Additionally, adjusting the modelling to better capture the spectra with NMDAr antagonists will be explored.

Poster Abstracts

Poster session 1: Wednesday

WED_26 The Arx R264Q mouse model of a human mutation identified in a person with schizophrenia recapitulates disease-relevant behavioural and neural network oscillation phenotypes

Presenting Author: Emily Jaehne

Emily Jaehne - Department of Psychiatry, School of Clinical Sciences, Monash University
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Background
Our laboratory previously identified a novel mutation in the Aristaless-related homeobox (ARX – R264Q) gene in a female with schizophrenia. ARX is involved in GABAergic interneuron specification and differentiation, and is located on the X chromosome. Mutations in the ARX gene are known to cause seizures and intellectual disability in males, while females with ARX mutations have been diagnosed with ASD, anxiety disorders and schizophrenia. The aim of this project was to better understand the causative nature of the ARX R264Q mutation by developing a mouse model with the R264Q mutation inserted into its genome using CRISPR-Cas9 gene editing.

Methods
Task-induced neural network oscillations in the gamma frequency are impaired in people with schizophrenia and are regulated by GABAergic interneurons, therefore we hypothesised that Arx R264Q mutant mice will show altered behaviour relevant to schizophrenia and altered task-induced gamma oscillations. Behavioural characterisation of the Arx R264Q mouse model was conducted, including measures of anxiety, learning and memory, social interaction and recognition, as well as psychosis related behaviours of pre-pulse inhibition (PPI) and stimulant induced locomotor hyperactivity. Local field potential recordings from the prefrontal cortex and hippocampus at baseline and during behavioural activities were performed to assess task-induced neural network oscillations.

Results
Male but not female Arx R264Q mice show disrupted pre-pulse inhibition (PPI) compared to wild-type (WT) controls (N=13-23/sex/group, p<0.05). In contrast, female but not male Arx R264Q mice show increased baseline hyper-locomotor activity (p<0.05), and increased hyper-locomotor response to NMDA receptor antagonist, MK-801 (p<0.05). Female Arx R264Q mice also show reduced preference for a novel mouse over a familiar mouse in the 3-chamber social interaction task (p<0.05). While baseline gamma and theta oscillations were unchanged, Arx R264Q mice show reduced gamma power in the prefrontal cortex when interacting with the familiar and novel mouse compared to WT controls (p<0.05).

Conclusion
The Arx R264Q mutation disrupts gamma power in the prefrontal cortex induced by social interaction and causes a social memory impairment in female mice. Striking sex-specific behavioural phenotypes were also uncovered with males showing sensorimotor gating deficits and females showing hyperlocomotion. Ongoing local field potential recordings while the mice are performing PPI and locomotor tasks will shed further light on neural network dysfunction aligned with behavioural performance. This model represents a novel and highly translational approach to understand network dysfunction in schizophrenia. Further planned molecular and cellular analysis of the model may uncover novel precision medicine treatments targets for schizophrenia.

Poster Abstracts

Poster Session 1: Wednesday

WED_2 Long-term characterisation of relationship between change in depression severity and change in inflammatory markers following inflammation-stratified treatment with vortioxetine augmented with celecoxib or placebo

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Background
Major depressive disorder (MDD) is a highly prevalent condition with a substantial incidence of relapse or treatment resistance. A subset of patients shows evidence of low-grade inflammation, with these patients having a higher likelihood of more severe or difficult to treat courses of illness. Anti-inflammatory treatment of MDD has been investigated with mixed results, and no known studies have included assessments beyond cessation of the anti-inflammatory agent, meaning it remains unknown if any benefit from treatment persists. The objective of the present study was to investigate treatment outcomes up to 29 weeks post-cessation of celecoxib or placebo antidepressant augmentation.

Methods
The PREDDICT parallel-group, randomised, double-blind, placebo-controlled trial (University of Adelaide, Australia) ran from December 2017 to April 2020. Participants with MDD were stratified into normal range or elevated inflammation strata according to screening concentrations of high sensitivity C-reactive protein (hsCRP). Participants were randomised to treatment with vortioxetine and celecoxib or vortioxetine and placebo for six weeks, and vortioxetine alone for an additional 29 weeks (35 total weeks). Exploratory analyses were performed on Montgomery–Åsberg Depression Rating Scale (MADRS) scores and selected peripheral inflammatory markers across the entire study duration up to week 35.

Results
Participants retained at each observation were baseline N=119, week 2 N=115, week 4 N=103, week 6 N=104, week 8 N=98, week 22 N=81, and week 35 N=60. The elevated hsCRP, celecoxib-augmented group had a significantly greater reduction in MADRS score and greatest clinical improvement from baseline to the final visit than all others, despite no group or strata differences at preceding time points. Changes in hsCRP between baseline and week 35 and Tumour Necrosis Factor-α (TNF-α) concentrations between baseline and week 6 and baseline and week 35 were significantly associated with MADRS scores observed at week 6 and week 35.

Conclusion

The present analysis suggests a possible clinical benefit to celecoxib augmentation of vortioxetine in inflammation-associated MDD treatment, but further research is needed to confirm the finding and to ascertain the reason for delayed effect. Furthermore, the trial suggests that TNF-α may have a stronger relationship with MDD anti-inflammatory treatment outcomes than hsCRP and should be investigated further for potential predictive utility.

Poster Abstracts

Poster Session 3: Friday

FRI_30 Changes in addiction-like behaviour towards palatable food after vertical sleeve gastrectomy in mice

Presenting Author: Eva Guerrero-Hreins

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Background
Addictive eating, a serious maladaptive behaviour, is often present in people with obesity. It hinders weight-loss goals and can exacerbate co-morbid mental-health disorders such as depression and anxiety. Both addictive eating and mood-related disorders are characterised by striatal dysfunction. Bariatric surgery, the obesity treatment, alters appetite via changes in the gut-brain axis. Evidence suggests resulting neuroendocrine adaptations may impact reward-related eating and mental health. Thus, we aim to assess the effect of bariatric surgery on (i) addictive-like eating, (ii) depression-like and anxiety-like behaviour, and (iii) associated proteomic changes in the striatum using a mouse model of vertical sleeve gastrectomy (VSG).

Methods
C57/BL6 male and female mice (12-15/group) were fed high-fat/high-sugar diet for 10+ weeks before undergoing VSG or sham surgery. Addictive-like behaviour towards food was assessed using operant-self-administration chambers, including (i) motivation to obtain food; modelled using progressive ratio schedule, (ii) loss-of-control over food-seeking; modelled by lever pressing during reward unavailability; and (iii) cue-induced reinstatement of food-seeking. Depression-like and anxiety-like behaviour was assessed using a battery of mood-related behavioural tests (elevated plus maze, open field test, light dark box, tail suspension test, forced swim test, sucrose preference). Data-independent acquisition proteomic analysis of limbic brain areas was then performed.

Results
VSG mice displayed reduced motivation to work for a palatable food reward, decreased impulsive-like food-seeking behaviour and relapse-like behaviour compared to sham mice. VSG and sham mice did not differ in the acquisition of the instrumental task or extinction timecourse, preference or operant responding for the palatable food reward (Ensure®) suggesting learning and rewarding value of Ensure® was not impacted by VSG. Further, VSG mice showed increase anxiety-like behaviour after surgery compared to sham mice but no changes in depression-like behaviour. Proteomic analyses are ongoing and will provide insight into the possible neurochemical changes underlying these behavioural effects of VSG.

Conclusion

Collectively, these data suggest bariatric surgery results in an amelioration of addictive-like behaviour towards palatable food, that may be reflected by discrete gut-driven neurochemical changes pertaining to reward and feeding. There is however a known risk of increased mental health issues after bariatric surgery, particularly in a sub-set of vulnerable people. Understanding the various individual trajectories that predict and sustain surgery outcomes (psychological and physiological) can lead to better personalised treatment and patient-care for people with obesity.

Poster Abstracts

Poster Session 1: Wednesday

WED_53 Topiramate versus naltrexone for alcohol use disorder: The effect on neural activation during an anticipatory anxiety task

Presenting Author: Gezelle Dali

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Background
Research has demonstrated the potential utility of topiramate in reducing alcohol use and craving. Further, there is evidence that topiramate attenuates anxiety severity in patients with alcohol use disorder. The current study aimed to determine the effect of topiramate versus a commonly prescribed alcohol pharmacotherapy – naltrexone – on the BOLD response of treatment-seeking alcohol use disorder patients during an anticipatory anxiety task.

Methods
Participants were 42 patients with alcohol use disorder who were randomised to receive either topiramate (n = 19; titrated dose up to 200mg/day) or naltrexone (n = 23; 50mg/day) for 12-weeks as part of a broader randomised controlled trial. Following 6 weeks of treatment, participants underwent an fMRI protocol wherein they were administered an anticipatory anxiety task. The task presented a series of high-threat and low-threat stimuli followed by an unpleasant or pleasant image, respectively.

Results
Primary whole-brain analyses revealed no significant differences in BOLD activation between topiramate and naltrexone groups. Across both groups, patients were found to respond with greater activation in the middle frontal gyrus, precuneus, cingulate gyrus, inferior frontal gyrus and inferior parietal lobule during threat cues relative to safe cues. Secondary analyses are currently underway.

Conclusion
The current study is the first to examine and compare neural activation during anticipatory anxiety in treatment-seeking individuals on topiramate and naltrexone. This preliminary research contributes to our understanding of the therapeutic mechanisms of these alcohol pharmacotherapies.

Poster Abstracts

Poster Session 2: Thursday

THUR_28 Altered endocannabinoid mRNA expression in the aging human brain in major depressive disorder

Presenting Author: Helen Clunas

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Background
Aging causes gradual neuroanatomical and neurochemical changes affecting the endocannabinoid system (ECS), particularly CB1 and CB2 receptors. In aging, the anterior cingulate cortex (ACC) also undergoes structural and functional alterations that may impact cognitive and emotional processes. Additionally, ACC alterations in glutamatergic, GABAergic and inflammatory processes are associated with major depressive disorder (MDD). As the ECS modulates these functions, dysregulation in this region may occur in both aging and MDD. We aimed to determine if expression of genes in the ECS are altered in the ACC of individuals with MDD, and whether older individuals were more susceptible to these changes.

Methods
ACC samples from individuals with MDD (<65 yrs n=27, ≥65yrs n=12) and age-matched controls ((<65yrs n=17, ≥65yrs n=13) were obtained from the National Institutes of Health (NIH), USA. Total RNA was extracted, synthesised into cDNA and the mRNA expression of genes coding receptors (seven: CNR1, CNR2, PPARA, PPARBD, PPARG, GPR18, GPR55, GPR119, TRPV1, TRPV2 and TRPV4) as well as synthesizing (four: DAGLA, DAGLB, NAPEPLD, GDE1) and degrading (seven: ABHD12, ABHD4, ABHD6, FAAH, FAAH2, MGLL, NAAA) enzymes of the ECS were measured utilising Fluidigm techniques. Two-way ANOVA/ANCOVAs with Bonferroni correction were used to assess any effects between diagnosis and age.

Results
In this study, we found that CNR1 expression was lower in individuals with MDD compared to controls (-13%, p=0.026) and significantly lower in older individuals (65 yrs) with MDD compared to older controls (-39%, p<0.05). Similarly, NAAA expression (endocannabinoid degrading enzyme) was lower in MDD (-14%, p=0.021). Meanwhile TRPV4 expression was elevated in MDD compared to controls (+43%, p=0.002), whilst both TRPV1 and TRPV4 expression were higher in older individuals (+33%, p=0.017 and +55%, p=0.047 respectively). There were no significant differences in other genes measured.

Conclusion
This study has, for the first time, measured ECS gene expression in the ACC in MDD and its relation to aging. Genetic deletion of CNR1 in preclinical models led to early onset cognitive decline and age-related brain changes and our findings reveal lower CNR1 levels specifically in older individuals with depression which may contribute to cognitive symptoms. Altered gene expression in NAAA, TRPV1 and TRPV4 was also evident. Although protein level confirmation is required, these results underscore the potential involvement of the ECS in the pathophysiology of MDD and that older individuals may present with a different neuropathology.

Poster Abstracts

Poster Session 3: Friday

FRI_55 Effects of Childhood Maltreatment on Adult Mental Health Outcomes

Presenting Author: Jessica Ann May Adams

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Background
The recent Australian Child Maltreatment Study (ACMS, 2023) reported that 62.2% of Australians aged 16 years and over experienced one or more types of childhood maltreatment (CM). Exposure to maltreatment and trauma during childhood has long-term detrimental effects on mental health outcomes, cognition, and interpersonal relationships that continue into adulthood. Understanding how the interactions between genetics and psychosocial factors such as social support affects the mental health outcomes of those exposed to CM is vital to developing treatment and support plans.

Methods
This project utilised a unique longitudinal study design, following first-year university students over three distinct timepoints to track their mental health in relation to a range of risk factors such as daily stressors and protective factors such as social support. Demographic, psychosocial, and mental wellness data was collected via validated questionnaires, including measures of PTSD, anxiety, and depression symptoms (eg. PCL-5, DASS-21, etc.). Concurrent saliva samples were also collected at each timepoint, from which genome-wide genetic and epigenetic data was extracted and analysed at >650,000 SNP sites and >860,000 CpG sites respectively. Statistical analyses were conducted in PLINK and R.

Results
Cross-sectional data from 171 students identified that 88.7% of participants reported one or more types of CM. CM was strongly associated with increased PTSD and anxiety symptoms (p < 0.001). In a subset of participants with available genotype data, CM interacted with 71 SNPs to predict PTSD and anxiety symptom severity (p < 5e-5). These SNPs were located not only within genes previously implicated with PTSD and anxiety such as RORA and CNR1, but also in novel genes such as SorCS2 (previously associated with social memory formation and ADHD) and KCNS3 (previously associated with schizophrenia).

Conclusion
This research indicates that CM is highly prevalent in the university student population and is strongly associated with negative mental health outcomes in adulthood, such as PTSD and anxiety. Our initial findings suggest that genetic variation between individuals interacts with CM to directly increase psychopathology symptom severity. Understanding

the genetic architecture underlying these conditions and how this interacts with CM is vital for the treatment of these conditions in the large portion of the population exposed to CM.

Poster Abstracts

Poster Session 2: Thursday

THUR_57 Modelling the dynamic brain response to TMS inhibitory perturbations in alcohol dependence during early recovery: A TMS-EEG study

Presenting Author: Jodie Naim-Feil

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Background
Transcranial magnetic stimulation (TMS) is a non-invasive experimental tool capable of perturbing the brain while electroencephalography (EEG) simultaneously measures the response. While alterations in cortical inhibition (CI) is a key mechanism underlying alcohol dependence (ALD), it can be difficult to non-invasively probe CI. However, long-interval-cortical-inhibition (LICI), a paired-pulse inhibitory TMS paradigm, is emerging as a useful technique to index cortical inhibition. The current study draws on methods from perturbation theory to quantify global and local features of the LICI-elicited neural dynamics, providing an index of the emergent dynamic brain response and how it differs with ALD patients during early recovery.

Methods
Eleven ALD patients and 16 healthy controls (HC) were administered 75 single(SPP)/75 paired-pulse (LICI) stimuli to left prefrontal cortex. Temporal features of TMS-evoked-response (50-950ms) following each stimuli type (SPP or LICI) were quantified across 6 consecutive time-windows of 150ms segments, for five frequency bands (delta, theta, alpha, beta and gamma over 50-950ms), and across the time-frequency domain. For global features, Perturbative Integration Latency Index (PILI) values were derived for each participant, averaged across stimuli type and compared between groups. For local features, temporal measures were extracted across 8channels (Left:F1,F3,FC3,FC5; Right:F2,F4,FC4,FC6) and ratio outcomes for each electrode compared between groups.

Results
Both groups showed a suppressed response following LICI, however ALD patients presented with altered pattern of response at later time-blocks, with differences in decay rate following LICI. For spectral measures, differences were observed at lower frequencies in ALD group. Across time*frequency analysis, strong inhibitory effect in ALD group was observed during early windows at lower frequencies, with weaker effects observed in gamma across the entire trace. For local features, no clear evidence of inhibition was identified across ALD patients for any electrodes compared to HC who demonstrated a pattern of bilaterally inhibition at early windows followed by returning to baseline.

Conclusion

Dynamic responses to perturbations underlying CI were altered in ALD patients. For global features, altered temporal and spectral response to LICI were identified in ALD patients, with a slower return to baseline. For local features, the ALD group showed impaired inhibition, a stark comparison to the HC group which demonstrated bilateral inhibitory effects at early time-blocks before returning to baseline. Therefore, the trajectory of response following LICI in understanding ALD during early recovery is more complex than previously understood, and moreover, utilizing methods drawn from perturbation theory is a promising approach for indexing these dynamics.

Poster Abstracts

Poster Session 3: Friday

FRI_58 Investigating the role of dorsal striatum in compulsive exercise using the activity-based anorexia (ABA) rat model

Presenting Author: Kaixin Huang

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Background
Anorexia nervosa (AN) has the highest mortality rate of all psychiatric disorders. Excessive exercise has been reported in up to 80% of the patients with AN and also occurs in the majority of rats exposed to the activity-based anorexia (ABA) paradigm. Excessive exercise in AN and ABA is often called "compulsive" and may share similar underlying biological mechanisms with obsessive-compulsive disorder (OCD), including an overreliance on habits caused by disrupted activity in the dorsal striatum and its cortical inputs. However, how dorsal striatum or cortico-striatal circuit activity are involved in the development of compulsive exercise in remains unknown.

Methods
In order to determine how activity in the dorsal striatum is involved in the development of compulsive wheel running in ABA and compulsive operant responding, we used both constitutive and pathway-specific chemogenetic approaches, as well as operant-paired fibre photometry. Female Sprague-Dawley rats were exposed to ABA conditions, and after weight recovery, they underwent the outcome-specific devaluation task (ODT) that was adapted for home-cage operant devices. We also conducted a pilot study to assess changes in calcium (GCaMP) activity that correlated with instrumental learning, with fibres implanted in either medial (DMS) or lateral (DLS) sub-compartments of the dorsal striatum.

Results
Suppression of the mPFC to DMS pathway prevented weight loss in ABA rats, although the mechanisms underlying this remain to be determined. Local DMS activation during ABA accelerated initial weight loss, without influencing feeding. Interestingly, both activation and inhibition of DMS during ABA shifted circadian activity and increased food anticipatory activity. Post-hoc observations suggest that running activity was lower in rats with DREADDs expressed exclusively in DMS compared to expression in both DMS and DLS. Moreover, calcium release during instrumental training differed between striatal sub-compartments, with peak DMS activity at reward cue and peak DLS activity at reward receipt.

Conclusion
These results are the first to demonstrate a role for the dorsal striatum in excessive exercise that develops during ABA. The attenuation of weight loss following mPFC-DS suppression is in line with our previous studies and is likely driven by a change in reward-based decision-making. Considering that both activation and inhibition of DMS activity had effects on wheel running in the same direction, further analyses are required to determine how these changes align with operant measures of compulsive responding. Our studies provide initial clues that will inform the development of novel treatments targeting excessive exercise in AN in the future.

Poster Abstracts

Poster Session 1: Wednesday

WED_56 Lower FKBP5 DNA methylation at key enhancer sites associated with older age and higher gene expression in psychiatric disorders.

Presenting Author: Katrina Z. Edmond

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Background
FKBP51, encoded by the gene FKBP5, is a stress responsive allosteric co-chaperone of the glucocorticoid receptor (GR) that limits GR activity. FKBP5 gene regulation is strongly influenced by several glucocorticoid response elements (GREs). The extent of this glucocorticoid-induced regulation is moderated by genotype, as well as DNA methylation (DNAm) within the GREs, however evidence remains largely from the periphery. Therefore, genetic as well as environmental factors can influence an individual's transcriptional FKBP5 responsivity to stress. Exploring how changes to DNAm at key GREs in the brain contribute to increased risk of psychopathology across life is thus, a key next step.

Methods
Our previous work indicates that the T allele of the FKBP5 rs1360780 SNP dose-dependently increases FKBP5 expression. We tested for effects of this genotype on FKBP5 gex and DNAm across age in a human postmortem cohort of dorsolateral prefrontal cortex (dlPFC) samples. To do this we determined the average percentage DNAm of CpGs across five FKBP5 genomic regions using a combination of bulk RNAseq, DNAm arrays and SNP genotyping, analysed using sm.ancova comparisons. Subjects included a lifetime cohort of non-psychiatric controls (n=340, prenatal-85yrs), in addition to subjects with schizophrenia (n=121, 17-96yrs), major depression (n=144, 14-75yrs) and bipolar disorder (n=63, 21-76yrs).

Results
Our results demonstrate that case-status, age and genotype intersect to modulate the levels of FKBP5 mRNA expression in the human dlPFC, and that this could be mediated by convergent epigenetic effects on functional upstream enhancers. Specifically, case-status and age both associate with lower DNAm within a proximal enhancer that contains a series of

GREs, and for which lower DNAm correlates with higher FKBP5 expression. Following FDR-correction across the diagnostic groups, the greatest changes were observed in the schizophrenia cohort, with six CpGs showing significant differences in DNAm across life-course aging trajectories compared to matched controls.

Conclusion

We present the largest and most comprehensive analysis to date examining FKBP5 DNA methylation in the human brain and its association with FKBP5 mRNA expression in the human dlPFC, across both the neurotypical life-course trajectory and in severe psychopathology. We show that case-status, age and genotype intersect to modulate the levels of FKBP5 in this brain area, and that this could be mediated by convergent epigenetic effects on functional upstream enhancers, particularly in schizophrenia subjects. These mechanisms can shed light on FKBP5 transcriptional modulation in the human brain which is critical for propelling FKBP5-targeting treatment development.

Poster Abstracts

Poster Session 1: Wednesday

WED_41 Drug repurposing to treat bipolar disorder using participant-derived neural progenitor cells

Presenting Author: Ken Walder

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Background
Management of bipolar disorder is difficult, with most newly diagnosed patients not responding to the first medication they are prescribed. Most will eventually take multiple different medications to manage their symptoms, which has implications for cost, drug-drug interactions and compliance. New treatment options are urgently required for bipolar disorder.

Methods
Blood samples were collected from participants with bipolar disorder (n=7) and healthy control subjects (n=6). Peripheral blood mononuclear cells were isolated and transformed with episomal vectors expressing a cocktail of transcription factors to produce induced pluripotent stem cells. The stem cells were then differentiated into neural progenitor cells. Genome wide gene expression was measured using next generation sequencing, and drug repurposing analyses were completed using Connectivity Map (BROAD Institute) and LINCS2.

Results

The analyses highlighted a number of drugs that may be suitable for repurposing as well as a number of drugs currently or previously used to treat depression and/or anxiety such as ritanserin, nortriptyline and trimetozine, supporting the utility of this approach. Novel candidates for repurposing included diclofenac (anti-inflammatory), resveratrol (antioxidant), pizotifen (migraine) and nemonapride (dopamine receptor antagonist). All of these drugs have either preclinical or clinical published evidence for potential antidepressant and/or anxiolytic activity.

Conclusion

We have identified a number of drugs that can potentially be repurposed to treat bipolar disorder. Further investigations including pharmacoepidemiology, mendelian randomisation and animal behavioural studies will be performed to determine which of these drugs are most suitable for progressing to clinical testing in participants with bipolar disorder.

Poster Abstracts

Poster Session 2: Thursday

THUR_45 Impact of posttraumatic stress symptoms severity on white matter integrity in chronic pain

Presenting Author: Khaizuran Kamarul

Khaizuran Kamarul - School of Psychology, UNSW

Zina Trost - Department of Physical Medicine and Rehabilitation, Virginia Commonwealth University

Sylvia M. Gustin - School of Psychology, UNSW; Centre for Pain IMPACT, NEURA

Yann Quidé - School of Psychology, UNSW; Centre for Pain IMPACT, NEURA

Background
Posttraumatic stress symptoms (PTSS) are commonly experienced in people suffering from chronic pain disorders who experienced, or not, a traumatic event, indicating that chronic pain can be considered an extremely stressful experience. Reduced fractional anisotropy (FA), an index of white matter integrity, in the uncinate fasciculus (UNC) and two cingulum bundles (CGC, CGH), has been reported in separate studies of people with chronic pain, and negatively associated with PTSS severity. However, the relationship between chronic pain, PTSS and FA remains unclear. This study aims to determine if PTSS moderate the impact of chronic pain on white matter integrity (FA).

Methods
Forty-four subjects with chronic pain (CP) and 20 healthy controls (HC) underwent a magnetic resonance imaging session that included 3D T1-weighted anatomical and diffusion weighted scans, and completed the Posttraumatic CheckList-Civilian version questionnaire (PCL-C). Diffusion images were processed according to standard ENIGMA pipeline, and average FA values were extracted from six regions-of-interest (left and right UNC, CGC, CGH). A series of multiple linear regressions determined the main effects of Group (CP vs HC), PTSS (PCL-C total score) and their interactions on FA from each ROI separately, accounting for age and sex. Moderation analyses were performed in case of significant interaction.

Results
The models for the left UNC [adjusted R2=0.149, F(5,58)=3.162, p=0.014] and right CGC [adjusted R2=0.168, F(5,58)=2.458, p=0.044] were significant but did not survive correction for multiple testing (UNC: pFDR=0.082; CGC: pFDR=0.131). Further exploration suggests that, in the context of a significant main effect of PTSS (p<0.001), the group-by-PTSS interaction was significantly associated with left UNC FA (p=0.003); however, the main effect of group was not significant (p=0.196). Moderation analysis indicated that increasing PTSS were significantly associated with reduced left UNC FA in HC (p<0.001), but not in CP (p=0.453). No other significant association was found for any other ROI.

Conclusion
Consistent with previous studies, increasing PTSS levels were associated with reduced FA of the left UNC, across both CP and HC participants. Exploratory analyses showed that this association was only evident in HC and not in people with CP, suggesting that different mechanisms may be at play in CP. These results require cautious interpretation as the model statistics did not survive correction for multiple testing. Limitations include the relatively small sample size, reducing the statistical power to detect significant effects, as well as the heterogeneity of chronic pain types included. Future larger studies of homogeneous CP disorders are warranted.

Poster Abstracts

Poster Session 2: Thursday

THUR_16 Exploring Cortical Plasticity Changes with TMS-EMG: Differential Effects of High-Definition trans-cranial Direct Current Stimulation (HD-tDCS) Perturbation in Patients with Schizophrenia receiving Clozapine or Other Antipsychotics, and Healthy Controls

Presenting Author: Kiran Bagali

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Background

Studies looking at Short Interval Intracortical Inhibition(SICI), Long Interval Intracortical Inhibition(LICI), Intracortical Facilitation(ICF), cortical silent period(CSP), and stimulus intensity to elicit 1mV motor potentials(SI1mV) in patients with schizophrenia have yielded largely mixed results, except for a well replicated finding on enhancement of CSP – GABAB-mediated cortical inhibition unique to clozapine. In contrast, few studies have examined the effects of antipsychotics on motor cortical plasticity, specifically, the changes in motor potentials following perturbation with neuromodulation techniques. We examined motor cortical plasticity changes following HD-tDCS in healthy participants, and patients with schizophrenia receiving clozapine or other antipsychotic medications.

Methods

Following written informed consent, we recruited patients with schizophrenia with persistent symptoms to participate in an ongoing clinical trial with neuromodulation therapy. Before starting the allocated treatment, they underwent a detailed clinical evaluation, and a Transcranial Magnetic Stimulation – Electromyography experiment to determine motor cortical plasticity. In this experiment, cortical reactivity measures (20 recordings each of SICI and SI1mV) were recorded before and after (T10m, T20m, T30m, T40m intervals) 20m of cathodal HD-tDCS over the left M1. Within-subject changes in SICI and SI1mV across all the time intervals between the three study groups were compared using linear mixed effects models.

Results

We recruited 22 healthy controls, 24 & 18 patients with schizophrenia receiving clozapine and other antipsychotics respectively. Groups did not differ on age/gender. Patients on clozapine had significantly higher mean SAPS (33.45 vs 21.88, p=.0004) and SANS (56.08 vs 35.22, p=.0005) scores compared to patients on other antipsychotics. Linear mixed effects model showed a significant group*time interaction (p=.0116) for SICI across groups, while controlling for age, gender, SAPS and SANS scores. The slope of change of SICI in patients with schizophrenia on clozapine was similar to healthy controls, while it was markedly reduced in patients with schizophrenia not on clozapine.

Conclusion

This is the first study to demonstrate an association between cortical plasticity changes and treatment of schizophrenia with clozapine. Albeit in a small sample, our study highlights that clozapine appears to induce cortical plasticity differently compared to other antipsychotics when perturbed with HD-tDCS. After HD-tDCS, the decrease in SICI was in a similar direction as that of healthy controls, which suggests that clozapine induces a unique form of plasticity correction, a phenomenon not seen in patients receiving other antipsychotics . This effect may not be essential for symptom improvement, and is present even after controlling for differences in symptom severity.

Poster Abstracts

Poster Session 2: Thursday

THUR_63 Distinct contribution of brain geometry and connectivity for whole-cortex communication

Presenting author: Lachlan Hamilton

Lachlan Hamilton - QIMR Berghofer Medical Research Institute, Australia and University of Queensland, Australia

James A Roberts - QIMR Berghofer Medical Research Institute, Australia and University of Queensland, Australia

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Luca Cocchi - QIMR Berghofer Medical Research Institute, Australia and University of Queensland, Australia

Background
The brain mechanisms that describe how neural signals propagate throughout the cortex are poorly defined. This knowledge is essential to understand altered patterns of neural communications in mental disorders and develop effective and targeted therapeutic interventions. Recent findings suggest that the decomposition of neural signals with cortical geometry alone (cortical eigenmodes) can be used to understand the emergence of macroscopic cortical dynamics.

Methods
We used novel methods to estimate cortical eigenmodes, allowing us to unpack the distinct contribution of cortical geometry and brain wiring (the connectome) in supporting cortical dynamics. We assessed how eigenmodes support and predict whole-cortex signal propagation using an empirical dataset of single-pulse transcranial magnetic stimulation (TMS) given to three cortical regions.

Results
Results show that eigenmodes can accurately capture how a local perturbation in neural activity evolves into a widespread cortical response. Furthermore, eigenmodes provide key insights into how perturbation size, location, timing, and intensity affect the spread of changes in local neural signals. We also showed that long-range brain connections are required to fully account for the observed changes in whole-cortex activity. We provide estimates for the contributions of geometric and long-range propagation, and the implications of their imbalance.

Conclusions
Our results advance knowledge of large-scale brain communication by highlighting the distinct contribution of brain geometry and anatomical connectivity in propagating neural signals across the cortex. These findings are important in understanding macroscopic changes in cortical activity that are observed across mental disorders, and in developing targeted neuromodulatory interventions to restore cortical communication.

Poster Abstracts

Poster Session 2: Thursday

THUR_48 Can pre-treatment MRI Biomarkers predict treatment outcomes in PTSD?

Presenting Author: Liza van Eijk

Liza van Eijk - James Cook University

Background
Post-traumatic stress disorder (PTSD) has a significant impact on patients, families, and society. However, less than half of patients receive the appropriate treatment or continue to engage in therapy (McDonald & van Rooij, 2019) and about 30-50% do not benefit sufficiently from treatment (Zhutovsky etal, 2019). This has resulted in the search for neural correlates to predict treatment outcomes up front. This systematic review aims to establish a consensus of the previous literature in relation to whether pre-treatment MRI biomarkers can assist with predicting patients' treatment response in PTSD.

Methods
In this PRISMA-systematic review we included human studies examining pre-treatment MRI measures related to treatment outcomes in adults with PTSD. Studies with the following were excluded: low quality (<3 Tesla), children, comorbidity (except depression and anxiety disorder), non-English literature and non-original articles. Screening and bias and quality assessment (the National Institutes of Health design-specific quality assessment tools) were conducted by two independent reviewers.

Results
After screening 793 articles (88 full-text), 19 were included: 4 randomised control trials, 4 observational, and 11 cross-sectional studies. Most studies (17/19) received a moderate quality rating and two a high-quality rating. Overall, it was found that pre-treatment MRI measures correlated with treatment outcomes, in particular measures obtained from regions related to cognitive control and emotion processing. However, some variation was found, depending on the type and length of treatment, and type of MRI measure used. More research is needed to identify correlates of these MRI markers, examine longitudinal changes, and consider PTSD subgroups.

Conclusions
Pre-treatment MRI markers correlated with treatment outcomes in adults with PTSD, which was found across different treatment types. These markers may provide guidance for clinicians in the near future by assisting with selecting the optimal treatment for PTSD patients and consequently reduce the burden to patients and society.

Poster Abstracts

Poster Session 1: Wednesday

WED_59 Clinical and neurophysiological effects of transcranial magnetic stimulation of the frontal pole in OCD

Presenting Author: Luca Cocchi

Luca Cocchi, QIMR Berghofer

Background
This clinical trial (2016-2023) assessed the efficacy of repetitive frontal pole transcranial magnetic stimulation (TMS) in reducing symptoms of obsessive-compulsive disorder (OCD) and brain activity within a frontostriatal brain network.

Methods
50 participants underwent baseline clinical assessments and neuroimaging. Active and sham interventions consisted of 20-weekday sessions of neuroimaging-guided continuous theta burst stimulation of the frontal pole while participants were in a state of rest. Neuroimaging and clinical assessments were conducted at the 4-week endpoint, with an additional clinical assessment at the secondary 24-week endpoint (46 participants, 23 active).

Results
Symptoms of OCD decreased in both active and sham groups, but there was no significant group-by-time interaction. Changes in symptoms of anxiety and depression were also similar between groups. Active and sham groups displayed similar changes in frontal pole activity and related frontostriatal connectivity.

Conclusions
Our neuroimaging-guided resting-state TMS intervention did not reduce OCD symptoms more than sham, nor did it differentially change the activity of a related frontostriatal system. These findings provide a solid basis to develop and evaluate different brain stimulation protocols and techniques.

Poster Abstracts

Poster Session 1: Wednesday

WED_44 Stress induction, fear conditioning, trauma film viewing, and intrusive memories: Relationship between salivary alpha amylase, endocannabinoids, and cortisol

Presenting Author: Luke Ney

Luke Ney - Queensland University of Technology

Background
The endogenous cannabinoid (ECB) system is a small molecule lipid signalling system that is involved in stress response activation and is associated with PTSD. Recently it was shown that ECBs are quantifiable in saliva, but it is unclear whether salivary ECBs are part of the sympathetic nervous system response to stress and whether they can be used to quantify stress and learning in experiments.

Methods
We conducted two experiments: an adapted trauma film paradigm, where participants completed a cold pressor test (or control) while watching a 10-minute trauma film, and a fear conditioning task, where participants were conditioned to anticipate an aversive outcome following an otherwise neutral cue. We collected saliva and hair samples during the experiments and tested them for ECBs as well as stress markers cortisol and salivary alpha amylase (sAA).

Results
As hypothesised, there were significant positive correlations between sAA and salivary ECBs, particularly 2-arachidonoyl glycerol (2-AG). 2-AG was also a reliable predictor of the vividness and distress of intrusive memories. However, there were no differences between the experimental and control groups on subjective measures of stress reactivity or intrusive memories.

Conclusions
This study provides further evidence for the role of ECBs in the sympathetic nervous system and as a potential predictor of intrusive memory valence following viewing of a violent film.

Poster Abstracts

Poster Session 1: Wednesday

WED_14 Effects of sex hormones and hormonal contraceptives in adolescent fear extinction

Presenting Author: Madison Brooke

Madison Brooke - School of Psychology, Faculty of Science, University of New South Wales

Bronwyn M Graham - School of Psychology, Faculty of Science, University of New South Wales

Background
The mechanisms of extinction and the ability to inhibit fear of a threatening cue are thought to underpin the development, maintenance, and treatment of anxiety disorders. Extinction learning is modelled in rodents via repeated exposure to a fear-conditioned cue in the absence of threat. Research in adult females has consistently demonstrated that fluctuating sex hormones across the estrous cycle predict extinction retention, and suppressing sex hormones via hormonal contraceptives (HCs) impairs extinction retention. Despite high usage during adolescence, no research has examined HC effects during this period.

Methods
Adolescent (i.e., 5 weeks old) females received fear conditioning (3 x white noise conditioned stimulus; CS, paired with 0.4mA footshock), extinction training (60 x CS presentations; no footshock), and an extinction retention test (15 x CS presentations; no footshock) across three days. Experiment 1 grouped rats according to estrous phase as determined by vaginal epithelial cells. Phase was classified as high sex hormones (i.e., metestrus, diestrus, and estrus) v low sex hormones (i.e., proestrus) at the time of extinction. Experiment 2 evaluated a novel model of HCs whilst examining its effects on extinction, compared to vehicle controls.

Results
Estrous phase at the time of extinction training had no effect on adolescents freezing rates during fear conditioning or extinction training. However, during retention, low sex hormone rats showed increased freezing compared to those with high sex hormones at the time of extinction. Experiment 2 data collection is underway and due to be completed in September.

Conclusions
In line with research on adult females, our research demonstrates that sex hormones during extinction training affect extinction retention in adolescent females; with high sex hormones during extinction predicting better extinction retention compared to low sex hormones. These results indicate that the suppression of sex hormones (via HCs) also impairs extinction retention in adolescents as it does in adults.

Poster Abstracts

Poster Session 1: Wednesday

WED_68 Mitochondrial function is increased in lithium-treated neural progenitor cells derived from participants with bipolar disorder

Presenting Author: Megan Ellis

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Sean McGee - Deakin University, IMPACT, The Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong, Australia

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Ken Walder - Deakin University, IMPACT, The Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong, Australia"

Background
Previous studies have shown mitochondrial dysfunction in people with bipolar disorder. This study investigated how mitochondrial function and energy production changes throughout the cell differentiation process from induced pluripotent stem cells (iPSCs) to neural progenitor cells (NPCs) and the effects of lithium on mitochondrial function in the cells.

Methods
Participants with bipolar disorder (n=4) and healthy control subjects (n=3) had blood samples collected. From these samples, peripheral blood mononuclear cells were isolated and reprogrammed using episomal vectors containing specific transcription factors to create iPSCs. These cells were then differentiated into NPCs . Both iPSCs and NPCs

were then treated with lithium chloride (1mM) or vehicle as control. A mitochondrial bioenergetic profile was measured using a Seahorse XF24 Flux Analyser in the iPSCs and throughout differentiation into NPCs.

Results

Results highlighted the effects of time and treatment on the bioenergetic profile. The iPSCs produced energy primarily through oxidative phosphorylation, and as they differentiate into NPCs, more energy production is generated through the glycolytic pathway. There was no significant difference in mitochondrial function between groups. However, lithium treatment appeared to affect mitochondrial function in both groups increasing basal respiration, maximal mitochondrial capacity, ATP turnover and spare respiratory capacity. Further exploratory analysis of NPCs indicates improved mitochondrial function after lithium treatment in cell lines from participants with bipolar disorder but not in control-derived lines.

Conclusions

Preliminary data suggests that mitochondrial function and bioenergetics are affected by lithium treatment, suggesting a potential therapeutical mechanism of action. Nonetheless, further analysis of more participant samples is required for more conclusive evidence. However, initial findings look promising towards pinpointing beneficial effects of lithium on mitochondrial function.

Poster Abstracts

Poster Session 2: Thursday

THUR_42 Afferent pathways of RXFP3+ zona incerta cells during threat responses in mice

Presenting Author: Michelle H Shen

Michelle H Shen - Macquarie University

Jennifer L Cornish - Macquarie University

Simon McMullan - Macquarie University

Jee Hyun Kim - Deakin University

Andrew J Lawrence - Florey Institute of Neuroscience and Mental Health

Bowen Dempsey - Macquarie University

Christina J Perry - Macquarie University

Background

Defensive responses to threatening stimuli are differentially expressed depending on the degree of perceived threat. Biased cognitive threat appraisals can result in maladaptive behaviour, including anxiety. We identified a population of neurons in the zona incerta (ZI) that express the relaxin-family peptide receptor 3 (RXFP3). During Pavlovian extinction, activating these neurons altered the typical fear response (freezing), to one indicative of an immediate threat (escape-like jumps). Given the widespread connectivity of the ZI, and the established role of the relaxin-3/RXFP3 system in arousal regulation, this project aimed to identify the inputs recruited in response to different degrees of threat intensity.

Methods

To simulate threat, C57BL/6J mice injected with the retrograde tracer CTb into the ZI were subjected to an auditory loom protocol. Here, crescendos of white noise with a peak intensity of either 70dB (low threat), or 90dB (high threat) were used to trigger freezing, or flight behaviour, respectively. Following perfusion, Fos immunohistochemistry was performed to assess brain-wide neuronal activation. Projecting regions recruited during the different conditions were identified via co-localisation of Fos and CTb. Separately, retrograde tracing using the glycoprotein-deleted EnvA-pseudotyped rabies (SADΔG[EnvA]) virus, was performed on RXFP3-Cre mice to identify the monosynaptic inputs specific to the RXFP3+ ZI population.

Results

Data collection from both experiments remain underway, however, preliminary findings validate the auditory loom paradigm as a behavioural model of innate fear, such that looming auditory stimuli reliably evokes distinct threat responses. Furthermore, successful implementation of the genetically restricted viral tracing methodology has revealed preliminary insights into the direct presynaptic inputs of the RXFP3+ ZI population. These include dense inter-connectivity within the ZI, as well as projections from the paraventricular nucleus of the hypothalamus, and other hypothalamic regions.

Conclusions

The results from these experiments will identify the unique ZI afferent pathways recruited during different threat severities, and discover if such projections to the ZI can potentially synapse with its RXFP3+ cells. These findings represent the first steps to disentangling the complex functional role of the RXFP3+ ZI population in modulating fear- and arousal-associated behaviours. Better knowledge regarding how these behaviours are regulated will provide important insights into how maladaptive threat appraisals are generated, and how hyperarousal may contribute to the augmented fear responses typical of anxiety disorders.

Poster Abstracts

Poster Session 3: Friday

FRI_49 A high-fat diet and psychosocial stress mouse model for maternal immune activation

Presenting Author: Morgan C. Bucknor

Morgan C. Bucknor - Charles Perkins Centre and School of Life and Environmental Sciences, The University of Sydney

Anand Gururajan - The Brain & Mind Centre, The University of Sydney

Russell C. Dale - Kids Neuroscience Centre, The Children's Hospital at Westmead, Faculty of Medicine and Health

Markus J Hofer - Charles Perkins Centre and School of Life and Environmental Sciences, The University of Sydney

Background
Maternal health during pregnancy plays a critical role in determining health outcomes in offspring. Persistent activation of the maternal immune system during pregnancy is commonly referred to as Maternal Immune Activation (MIA) and has been shown to pose a risk for the development of neurodevelopmental disorders. Animal models have been used to understand this association; however, many are limited to the investigation of an isolated maternal source of MIA in an acute context. Here, we established an animal model encompassing chronic poor maternal diet and social instability stress (SIS), to better understand how these risk factors impact disease in offspring.

Methods
48 female C57Bl/6 mice were randomly allocated to four maternal stress groups: high-fat diet exposure only (SIS-) (n=8), high-fat diet + SIS(+) (n=16), control-diet exposure only (SIS-) (n=8), control-diet + SIS(+) (n=16). High-fat or control-diet exposure began at 6 weeks of age and continued throughout gestation. For 6 weeks prior to pregnancy, SIS stress mice were exposed to a novel cage composition twice weekly, involving rotating an individual mouse to a new cage with unfamiliar cage mates. Following SIS and 8-weeks of dietary exposure, glucose tolerance and behaviour testing (open field/elevated plus maze/nest building) were measured prior to breeding.

Results
All female mice fed a high-fat diet demonstrated rapid weight gain compared to all control-diet mice. Fasting blood glucose was significantly elevated in high-fat diet (SIS-) females compared to control-diet (SIS-) females. High-fat diet (SIS-) females also exhibited a significantly higher AUC over the testing period compared to control-diet (SIS+/-) mice. Anxiety-like behaviour was not significantly different between stress groups via open field and nest building testing. However, high-fat diet (SIS+) mice travelled a greater total distance during elevated plus maze compared to control-diet (SIS-) mice and maternal care was highest in control-diet (SIS+) mice compared to high-fat (SIS+) mice.

Conclusions
Our preliminary findings suggest that high-fat diet exposure leads to significant weight gain and changes to glucose tolerance prior to pregnancy irrespective of SIS exposure. The high-fat diet (SIS-) group demonstrated increased total locomotor activity but no significant changes in nest building behaviours were observed between stress groups. However, SIS stress did alter maternal care. High-fat diet (SIS+) mice exhibited more maternal neglect while conversely, control-diet (SIS+) mice exhibited more maternal care as opposed to neglect to offspring. Evidently, both environmental sources of maternal stress affect subsequent maternal behaviours which may be an artifact of contrasting levels of basal inflammation.

Poster Abstracts

Poster Session 2: Thursday

THUR_34 The effect of anthocyanin rich plum on memory and inflammation in MCI

Presenting Author: Naomi May

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Katrina Weston-Green - Molecular Horizons and School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong, NSW, 2522, Australia

Background
Mild Cognitive Impairment (MCI) is a neurocognitive disorder which involves significant memory loss and recent evidence suggests that MCI is associated with elevated inflammation. Therefore, compounds that target inflammation and cognitive function are of interest as novel therapeutics for MCI. Anthocyanins are naturally occurring compounds which have been shown to reduce inflammation and improve cognition but their benefit in older adults with MCI is unknown. We hypothesised that daily consumption of anthocyanin-rich, Queen Garnet Plum (QGP), will improve memory and inflammation in older adults with MCI compared to controls (placebo), and that reduced inflammation be correlated with improved memory.

Methods
Forty-two participants diagnosed with MCI participated in a double-blind, randomised controlled trial (ACTRN12618001184268). Participants consumed 250mL of juice daily for 8-weeks while attending a Memory Group program. Via block randomisation, participants were assigned to either the treatment (QGP juice; 144.5mg anthocyanins) or placebo (apricot juice, control; no anthocyanins). Visual memory was assessed using the Complex Figures Test (CFT) test and short-term verbal memory was assessed using Rey Auditory Verbal Learning Test (RAVLT). Serum inflammatory marker TNF-□ was also measured before and after the nutritional intervention. SPSS was used to conduct 2x2 mixed model ANOVAs. Correlations were assessed using Pearson Correlations.

Results
There was a significant main effect of time on visual memory, p=.036, and a non-significant trend towards a time x treatment interaction, p=.063. Split by treatment group, QGP significantly improved (p=.004), while controls did not (p=.870). Short-term verbal memory scores showed a significant main effect of time, p=.021, but no effect of treatment.

There was a significant interaction for TNF-a, p=.028, showing no difference between groups at baseline (p=.785) but a significant difference at post-testing (p=.010), TNF-a decreased in QGP group and increased in controls. Improved short-term verbal memory scores were correlated with a decrease in TNF-a, r=-.434, p=.007. Daily intake of fruit-based anthocyanins for 8 weeks reduced TNF-a in older adults with MCI and some improvements in visual memory were observed.

Conclusions

This novel finding suggests that high anthocyanin nutritional interventions may be effective for improving memory and reducing inflammation in older adults with MCI.

Poster Abstracts

Poster Session 3: Friday

FRI_24 Reward related attentional bias and problematic alcohol use

Presenting Author: Poppy Watson

Poppy Watson - UNSW Sydney

Mike Le Pelley - UNSW Sydney

Background
A wealth of research has demonstrated that stimuli associated with reward (e.g., money, food etc) automatically gain attentional prioritisation. This attentional bias to motivationally salient, reward-signalling stimuli is argued to be closely related to substance-related attentional biases that are often shown by individuals with problematic drug and alcohol use. These attentional biases are argued to arise from reward learning processes whereby stimuli that signal drug or monetary reward acquire incentive salience and become motivational magnets that are difficult to ignore. However, the link between attentional bias for monetary reward and risky drug use has typically been studied in healthy participants.

Methods
Individuals accessing drug and alcohol services with a primary diagnosis of alcohol use disorder were recruited within the first four to six weeks of intake to participate in an intervention study. At the baseline session, participants completed various self-report measures (including the Alcohol Use Disorders Identification Test; AUDIT) in addition to a visual search task measuring automatic attentional bias to monetary reward. Following the two-week intervention, self-reported abstinence at 3-month follow up was primary outcome measure. All analyses and hypotheses were pre-registered.

Results
Fifty-nine participants completed the baseline session. Following exclusions, data from forty-nine participants were included in correlational and regression analyses. AUDIT scores correlated with attentional bias to signals of monetary reward, a relationship that cannot be explained by overall response time in the task or demographic variables. Analyses investigating the factors that predict abstinence at three-month follow up are ongoing.

Conclusions
Drug-related attentional bias has been argued to stem from general reward-related attentional biases that are also observed in the healthy population. However, to date research linking attentional biases for non-drug reward and problematic drug use has typically used healthy participants. Our work demonstrates that the magnitude of attentional bias for non-drug reward is associated with problematic alcohol use, in a treatment-seeking sample. Whether automatic attentional prioritisation of reward is a consequence of, or vulnerability factor for, problematic drug use remains to be seen.

Poster Abstracts

Poster Session 3: Friday

FRI_36 Goal-Directed Behaviour under Uncertainty in the NLGN3R451C/Y Mouse Model of Autism

Presenting Author: Riki Dingwall

Riki Dingwall - Florey Institute, University of Melbourne

Emma Burrows - Florey Institute

Tony Hannan - Florey Institute

Warda Syeda - Florey Institute

Robyn Brown - University of Melbourne

Background
Autism is a neurodevelopmental condition caused by the complex interplay between rare genetic changes and the environment. While the clinical landscape is variable, impairment across social and non-social cognition is frequently reported. Cognition impacts not only daily functioning but may compound key autism features such as restricted and repetitive behaviours. In the present study, we use mice carrying an autism-associated arginine-to-cysteine mutation (R451C) of the neuroligin-3 (Nlgn3) gene: a synaptic adhesion protein widely expressed throughout the brain. Our previous cognitive work with the Nlgn3R451C/Y mouse model has identified reduced latency to collect reward and a cautious but accurate response strategy.

Methods
Using serial probabilistic reversal learning (PRL), a touchscreen-based task assessing goal-directed decision-making under uncertainty, we initially trained mice to respond to one of two identical but spatially separated stimuli: one of which is rewarded and the other unrewarded (deterministic). After five consecutive correct responses, the reward contingencies were reversed and mice were required to flexibly alter their response. Reward probabilities were subsequently altered to increase uncertainty (probabilistic), from 100:0 to 80:20, 70:30, and 60:40.

Results
Unlike other studies with mice and the serial PRL task, using extensive iterative training and larger reward deliveries, we successfully trained mice to a high caliber (>45% of possible reversals and >65% accuracy at 80:20) of stable task performance. When the association between a particular response and reward delivery was deterministic, the Nlgn3R451C/Y mice were no different from wildtypes in their degree of accuracy or number of reversals. However, the introduction of uncertainty revealed an impairment in their reversal learning driven by a reduction in their win-stay response strategy.

Conclusions
Akin to real-world interactions, where most behaviours are less deterministically associated with their outcomes, the Nlgn3R451C/Y mutation in mice produces cognitive phenotypes under conditions of uncertainty comparable to those reported in humans with autism.

Poster Abstracts

Poster Session 3: Friday

FRI_18 Role of peripheral metabolic changes underlying anhedonia phenotype in rats

Presenting Author: Roger B Varela

Roger B Varela - Queensland Brain Institute, The University of Queensland, QLD - Australia

Heather Macpherson - Queensland Brain Institute, The University of Queensland, QLD - Australia

Tristan Houghton - Queensland Brain Institute, The University of Queensland, QLD - Australia

Susannah Tye - Queensland Brain Institute, The University of Queensland, QLD - Australia

Background
Anhedonia is a hallmark of major depression, which is often comorbid with significant metabolic disturbances. This study aims to investigate the relationship between peripheral metabolic changes and anhedonia-like behaviour in an animal model of treatment-resistant depression induced by adrenocorticotrophic hormone (ACTH), and the effects of the bupropion treatment.

Methods
Adult male Wistar rats were trained in a progressive-ratio/concurrent effort related choice (ERC) paradigm to assess effort and motivation. After reaching a stable baseline in the ERC paradigm, animals received daily injections of ACTH or saline (n=8 each) for 24 days. Lever pressing, number of rewards and maximum ratio were recorded pre-and post-treatment. Additionally, peripheral markers of glucose metabolism were assessed using commercial glucose uptake kit and metabolomics approaches.

Results
ACTH treatment reduced lever pressing and rewards in the ERC task, and bupropion treatment was not able to reverse the anhedonia phenotype. ACTH also induced glucose resistance in PBMCs impaired glucose metabolism, key metabolite differences observed were identified in pentose phosphate and nucleotides pathway.

Conclusions
Compared to the saline group, chronic ACTH treatment was able to induce an anhedonia-like phenotype in rats. Peripheral changes in insulin signalling and glucose metabolic deficits may have led to changes in dopaminergic signalling underlying the anhedonia phenotype induced by ACTH chronic treatment.

Poster Abstracts

Poster Session 2: Thursday

THUR_22 Investigating risk-taking behaviour across multiple mouse models relevant to schizophrenia

Presenting Author: Sandesh Panthi

Sandesh Panthi - Department of Psychiatry, School of Clinical Sciences, Monash University, Australia

Ariel Dunn - Department of Psychiatry, School of Clinical Sciences, Monash University, Australia

Emily Jaehne - Department of Psychiatry, School of Clinical Sciences, Monash University, Australia

Suresh Sundram - Department of Psychiatry, School of Clinical Sciences, Monash University, Australia

Rachel Hill - Department of Psychiatry, School of Clinical Sciences, Monash University, Australia

Background
The use of phenotypic traits to understand the biological basis of neuropsychiatric disorders will enable the discovery of targeted symptom-specific treatments. Risk-taking behaviour is one such recognized characteristic and clinical feature of neuropsychiatric disorders, including schizophrenia. Tendency to take risk (such as substance abuse, suicide), in those with schizophrenia is significantly higher than the general population, particularly in males. The aim of this study was to investigate the biological basis of risk-taking behaviour in two different genetic mouse models with relevance to schizophrenia. We hypothesised increased risk-taking behaviour in our models that may be more pronounced in male genetic mutants.

Methods
Two models were assessed that represent key but distinct biological pathways altered in schizophrenia. ArxR264Q mice carry a mutation identified in a person with schizophrenia. Arx regulates GABAergic cell development. Betacellulin (Btc) knockout mice were assessed because we found reduced BTC in post-mortem schizophrenia brain. BTC is an epidermal growth factor receptor ligand. Risk-taking behaviour was assessed using the elevated plus maze, which has two oppositely positioned open and closed arms. Increased time in the closed arms indicates increased anxiety. However, frequent visits to the open arm and nose pokes over the open edge (cliff bouts) indicates risk-taking behaviour.

Results
ArxR264Q mice of both sexes showed a significant increase in the number of cliff bouts compared to wild-type (WT) controls (N=13-23/group; p=0.009), with no significant differences in time spent or entries to the open arm compared to closed arm. BTC knockout (KO) females show reduced time spent, arm entries and cliff bouts in the open arm, while male BTC KO show increased open arm entries and cliff bouts compared to WT (N=10-13/group; p<0.05). Treatment of BTC KO with the antipsychotic, clozapine, increased time spent in open arm in female KO but remarkably, reduced bouts in open arm in male KO.

Conclusions
In summary, increased risk-taking behaviour was identified in two genetic mouse models with high relevance to the biology of schizophrenia. Interestingly, in the BTC model, risk-taking behaviour was male specific with females showing a more anxious phenotype. This may suggest that altered BTC and consequent epidermal growth factor receptor signalling may interact with sex steroid hormones or sex-linked genes to impact risk-taking behaviour. This research has significant implications in terms of understanding the biology of risk-taking behaviour in schizophrenia. Indeed, rescue of the risk-taking behaviour with clozapine suggests this antipsychotic may be particularly beneficial for this specific trait.

Poster Abstracts

Poster Session 3: Friday

FRI_40 Translating Habenula Dysfunction in Depression: A Systematic Review

Presenting Author: Sarah Cameron

Sarah Cameron - Molecular Horizons, School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong

Kelly Newell - Molecular Horizons, School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong,

Katrina Green - Molecular Horizons, School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong

Background
Poster The habenula is an epithalamic brain structure that acts as a neuroanatomical hub connecting the limbic forebrain to the major monoamine centres. The habenula is increasingly implicated in depression, with a surge in publications on this topic in the last 5 years. Baseline habenula activity is reported to be greater in female rodents, suggesting a greater vulnerability to habenula dysregulation in females, however, how this translates to depression is unclear. This systematic review aimed to analyse and evaluate how the preclinical advancements regarding the habenulas involvement in depression translate to the clinical field, with a particular focus on sex differences.

Methods
A systematic literature search was conducted following the PRISMA guidelines. The two search terms depress* and habenula* were applied across the electronic databases; Scopus, Web of Science and PubMed. Studies eligible for inclusion must have examined changes in the habenula in clinical cases of depression or preclinical models relevant to depression. Articles were excluded if they examined the habenula following the administration of an external treatment intervention. Clinical studies were excluded if they did not have a non-psychiatric control group or examined depression amongst other diagnoses, where depression was not an independent factor.

Results
Preclinical studies (n=57) reported changes in markers of habenula activity (n=16), neuronal firing (n=21) neurotransmission (n=12), neuroconnectivity (n=1), inflammation (n=2), gene expression (n=2) and circadian rhythm (n=2). Only 7 preclinical studies (12.2%) included both male and female animals. From these, 5 studies (71%) reported a significant difference between the sexes in at least one habenula measure taken. Clinical studies (n=18) reported changes in habenula functional connectivity (n=11), volume (n=5) and molecular markers (n=2). Clinical studies generally included male and female subjects (n=15), however, only 5 adequately examined sex as a biological variable.

Conclusions
Preclinical evidence suggests habenula hyperactivity is a primary driver for the development of depressive symptoms. The few studies that examined sex differences suggest females exhibit a greater degree of habenula excitation following stress. The molecular basis of these sex differences is unclear and warrants further investigation. Clinical evidence suggests the complexity of depression may go beyond the simplicity of an overactive habenula. Clinical studies support gross habenula abnormalities such as altered activation, connectivity, and volume and as a clinical feature of depression, with emerging evidence of blood-brain barrier dysfunction, however, progress is limited by the lack of detailed molecular analyses.

Poster Abstracts

Poster Session 1: Wednesday

WED_32 Deciphering Effects of Nucleus Accumbens Deep Brain Stimulation on Effort-Based Decision Making and Local Phasic Dopamine Efflux

Presenting Author: Sebastian McCullough

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Roger B. Varela - Queensland Brain Institute, The University of Queensland, Brisbane, QLD

Tristan Houghton - Queensland Brain Institute, The University of Queensland, Brisbane, QLD

Heather Macpherson - Queensland Brain Institute, The University of Queensland, Brisbane, QLD

Susannah Tye - Queensland Brain Institute, The University of Queensland, Brisbane, QLD

Background
The initiation and continual expression of motivated behaviours has been strongly implicated to be regulated by mesolimbic dopamine (DA) release within the nucleus accumbens (NAc). Deep brain stimulation (DBS) has shown efficacy in the treatment of refractory psychiatric disorders in which the expression of motivated behaviours is pathologically disrupted. However, the mode of action of DBS at the local target region and circuit level remains elusive.

Methods
Here we explored the effects of delivering 2 hours of 130Hz DBS to the NAc in male Wistar rats, measuring changes in effort-based decision making and local phasic DA neurotransmission. Animals (n=8) were trained on a concurrent fixed-ratio 5/chow feeding choice task (FR5/CONC), a DA-dependent behavioural paradigm that examines preferential bias between differently valued food sources based upon associated effort costs. Utilising fast scan cyclic voltammetry, we then investigated changes in ventral tegmental area stimulation-evoked phasic DA dynamics in surrounding stimulated tissue within the NAc in urethane anaesthetised animals (n=4 sham, 5 DBS).

Results
It was observed that within the FR5/CONC task, an acute session of bilateral stimulation prior to testing temporarily reduced the total food intake, while preserving relative preference between food sources. Likewise, while DA reuptake dynamics were unchanged, a reduction in DA release was observed in both sham and DBS-treated animals over time. However, this effect was significantly greater in the active DBS group.

Conclusions
These data show that NAc DBS temporarily reduces an animal's overall interest in food consumption, while preserving effort-based motivational bias. Attenuated phasic DA neurotransmission with active DBS may contribute to this behavioural effect.

Poster Abstracts

Poster Session 3: Friday

FRI_46 Genetic and psychosocial and drivers of mental health and well-being: a comparison of pre and duringCOVID university students

Presenting Author: Shruthi Malappurath Suresh

Shruthi Malappurath Suresh - School of biomedical sciences, QUT

Jessica Ann May Adams - School of biomedical sciences, QUT

Anita Sathyanarayanan - School of biomedical sciences, QUT

Charlotte Bainomugisa - School of biomedical sciences, QUT

Mackenzie Ashley Victor Rubens - School of biomedical sciences, QUT

Dagmar Bruenig - School of biomedical sciences, QUT

Patricia Obst - School of Psychology and Counselling, QUT

Ian Schochet - School of Psychology and Counselling, QUT

Divya Mehta - School of biomedical sciences, QUT

Background
The mental health of university students is a matter of public health concern. While previous genome-wide association studies have identified genetic drivers of depression, psychosocial factors such as university belonging and receiving social support have been established as protective of mental health. Conversely, daily hassles, a microstressor, is a risk factor. However, limited efforts have been made to elucidate the relationship of psychosocial factors and mental health outcomes, from a genetic perspective. The current study investigated the relationship between psychosocial factors and mental health outcomes from a genetic perspective, comparing preCOVID and duringCOVID university students

Methods
Psychological survey data was collected from 415 preCOVID and 433 duringCOVID university students. Additionally, saliva samples from a subset of university students were genotyped. To investigate the consistency of the relationship of university belonging with mental health outcomes across preCOVID and duringCOVID groups, regression analysis was conducted using SPSS v27. To investigate genetic drivers of the interaction effects of psychosocial factors including university belonging, receiving social support, trait resilience and daily hassles, a genome-wide gene-by-environment interaction study (GWGEIS) was performed using PLINK 1.9, with Bonferroni multiple testing corrections. The KEGG functional database was used for pathway analysis.

Results
University belonging was significantly higher among the duringCOVID students (p <0.05) and remained positively associated with mental being and negatively associated with depressive symptoms across pre and duringCOVID groups (p <0.05). The GWGEIS identified 28 SNPs that interacted with university belonging and 52 SNPs that interacted with receiving social support, mapped to genes including CNTNAP5 and PLCB1 to predict depressive symptoms. Interestingly, daily hassles interacted with multiple SNPs in GIMAP8 and HSD17B3, among other genes, to predict both depressive and anxiety symptoms. The pathways identified included intracellular transport pathways with calcium as cofactor.

Conclusions
University belonging emerged as a significant driver of mental health, among others, in conjunction with genetic variants. Among the genes identified, both CNTNAP5 and PLCB1 have been implicated in major depression. The genes mapped to plausible biological pathways provide novel insight into the interaction effects of psychosocial factors with genetic predisposition. The study provides evidence for university policy to cultivate psychologically supportive learning environments that foster belonging while supporting students in dealing with microstressors such as daily hassles. The implications of the findings extend to the general population as well and illuminates avenues for further research.

Poster Abstracts

Poster Session 3: Friday

FRI_43 Maternal immune activation and estrogen receptor modulation induce distinct changes in inflammatory-related gene expression in the substantia nigra of female and male offspring

Presenting Author: Sophie R Debs

Sophie R Debs - Preclinical NeuroPsychiatry Laboratory, Neuroscience Research Australia, Randwick, NSW 2031, Australia

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Tertia D. Purves-Tyson - Preclinical NeuroPsychiatry Laboratory, Neuroscience Research Australia, Randwick, NSW 2031, Australia

Background
Maternal immune activation (MIA) recapitulates aspects of schizophrenia pathophysiology in adult offspring, including dopamine dysregulation, behavioural abnormalities, cognitive impairment, and midbrain neuroinflammatory changes comparable to those observed in individuals with schizophrenia. The selective estrogen receptor modulator, raloxifene, improves cognition and symptom severity in women and men with schizophrenia possibly by modulating neuroinflammation. To test if raloxifene can alter inflammatory-related proteins in the substantia nigra (SN) of female and male adult rat offspring, we exposed pregnant dams to the viral mimetic polyinosinic:polycytidylic acid [Poly(I:C)] in utero and treated the offspring with raloxifene in adulthood.

Methods
MIA was induced in Wistar rat dams on gestational day 19 with high molecular weight Poly(I:C) via tail vein injection [4mg/kg, saline/poly(I:C) n=11/10]. Raloxifene (5mg/kg) was administered to offspring daily (cookies) from postnatal day (PND)58-84. The cohort consisted of four groups per sex, including: vehicle/placebo, vehicle/raloxifene, MIA/placebo, MIA/raloxifene (n=22-30 per group per sex). Half of these animals completed behavioural tests. Offspring were euthanised (PND83-84), SN was dissected, and protein (tissue lysate) prepared. Protein levels of 23 inflammatory-related cytokines and chemokines were then measured in the SN of female and male offspring using a multiplex immunoassay and analysed with two-way ANOVAs.

Results
Of 23 brain cytokines measured, 7 [interleukin (IL)-2, IL-5, IL-4, IL-10, IL-12p70, macrophage inflammatory protein-1 alpha (MIP-1α), interferon gamma (IFN-γ)], were significantly altered in female or male rat SN. Raloxifene reduced IL-4 in females ($p=0.042$) and IL-10 in males ($p=0.039$), but increased IL-2 in males ($p=0.023$). In females, IL-5 was reduced in MIA/placebo group relative to vehicle/placebo group ($p=0.037$), whereas in males, IL-12p70 and IFN-γ were reduced in MIA/placebo group relative to vehicle/placebo group ($p=0.038$; $p=0.012$, respectively). In males, MIP-1α was increased in vehicle/MIA group relative to vehicle/placebo group ($p=0.002$), and raloxifene ameliorated this effect in MIA animals ($p=0.04$).

Conclusions
We show novel, sex-specific alterations in SN cytokines following MIA and raloxifene. Our findings suggest that immunomodulatory effects of MIA and/or raloxifene in the SN are sex- and- pathway-specific. MIA reduced pro-inflammatory IL-12p70 and IFN-γ in males, but reduced anti-inflammatory IL-5 in females. Raloxifene reduced anti-inflammatory IL-4 and IL-10 in females and males, respectively, and pleiotropic IL-2 in males. In male MIA rats, raloxifene reduced immune cell chemoattractant MIP-1α, supporting an anti-inflammatory role for raloxifene in MIA-exposed males. These findings suggest that depending on the inflammatory milieu of the SN, and sex, raloxifene acts via either pro- or anti-inflammatory pathways.

Poster Abstracts

Poster Session 2: Thursday

THUR_54 Oxytocin effects on deficits in neonatal ultrasonic vocalizations in a model of prenatal valproic acid exposure

Presenting Author: Stela P Petkova

Stela P Petkova - University of Sydney, Brain and Mind Centre & School of Psychology

Michael T Bowen - University of Sydney, Brain and Mind Centre & School of Psychology

Background
Autism spectrum disorder (ASD) is a behaviourally defined neurodevelopmental disorder with primary diagnostic criteria of abnormal social communication and interaction and repetitive behaviours. Recently, there has been a focus on environmental risk factors for ASD diagnosis. One such environmental factor is prenatal exposure to the anti-epileptic and mood stabilizing medication valproic acid (VPA). Children born to mothers who used VPA during pregnancy are at ~2.5-fold higher risk for ASD diagnosis (Bromley et al, 2013, Christiansen et al, 2013).

Methods
Pregnant dams were injected with either VPA (600mg/kg) or saline on embryonic day 12.5 to model VPA exposure during early second trimester. Offspring were then tested in a battery assessing ASD-like behaviours. Of particular interest was early life social communication, or production of ultrasonic vocalizations (USV). Neonatal pup USVs were recorded and quantified on postnatal days (PND) 5,7,9, 11, and 13 during a 3-minute separation from the dam and littermates. In a subsequent experiment, we administered either oxytocin (20ng in 50uL) or saline (50uL) in PND9 pups to observe whether acute dosing with oxytocin would affect USV production.

Results
In saline-exposed pups, USV call rates showed the canonical inverted U-shape from PND5 to 13 with a peak at PND9 (223 ± 23.6 calls/3-min). However, in our VPA-exposed pups, we observed a flattening of this curve with only a moderate peak at PND9 (133 ± 13.3 calls/3-min). VPA-exposed pups produced significantly fewer calls on PNDs 7, 9, and 11 suggesting abnormal social communication in this early neonatal period. Based on previous literature, we expect acute oxytocin dosing will ameliorate this deficit, boosting USV production to saline-exposed levels; these studies are currently underway.

Conclusions
Preclinically, prenatal exposure to VPA shows high face validity as offspring show ASD-related phenotypes in anxiety, social, repetitive, and cognitive behavioural domains (Chaliha et al, 2020). Here, we show prenatal valproic acid exposure has a clear effect on offspring in an assessment of ultrasonic vocalisations, supporting the face and construct validity of the model in ASD-linked social communication deficits. Further, early-life social communication may be sensitive to oxytocin and oxytocinergic signaling and this model may provide a useful platform for assessing effects of oxytocin-targeting therapeutics on social communication deficits.

Poster Abstracts

Poster Session 2: Thursday

THUR_51 The Role of Developmental Timing of Adverse Childhood Experiences in Shaping Brain Structure: A Systematic Review

Presenting Author: Stephanie Hartanto

Stephanie Hartanto - University of Melbourne

Ebony Forlano - Swinburne University of Technology

Catherine Orr - Swinburne University of Technology

Sarah Whittle - University of Melbourne

Background
Adverse childhood experiences (ACEs) are reported to be associated with structural brain alterations. Many developmental neuroscience researchers have theorised that the timing of ACEs is important, given the likely presence of sensitive periods, during which the brain is most vulnerable to the effects of ACEs. In one model (i.e., the Life Cycle Model of Stress), sensitive periods were suggested to occur during periods of rapid brain development. This systematic review aimed to explore the role that the developmental timing of ACEs on brain structure and evaluate support for the Life Cycle Model of Stress.

Methods
Literature searches on MEDLINE (OVID), PsycINFO, Scopus, and Web of Science yielded 2,132 articles, with a total of 22 studies on brain structure included in the final review. Empirical findings for sensitive periods were synthesised to determine whether they align with those presented in the Life Cycle Model of Stress.

Results
There were two main findings: (1) Among studies that conceptualised timing as duration of exposure or age of onset, longer duration of exposure and/or earlier age of onset tended to be associated with larger ventricles, and smaller intracranial, cerebral, cerebellar, grey and white matter volumes; (2) among studies that investigated ACEs exposure across various developmental timepoints (e.g., exposure during childhood versus adolescence), we found little consistency in findings, with no clear pattern of sensitive periods for different brain regions. Sensitive periods suggested by study findings did not necessarily align with those presented in the Life Cycle Model of Stress.

Conclusions
Methodological factors may have contributed to inconsistent findings, including heterogeneous conceptualisations of ACEs, varying statistical approaches to test sensitive periods, and sample characteristics (e.g., adult versus paediatric samples). Studies also differed in the age range of ACEs exposure that they explored, limiting conclusions about certain ages (e.g., early childhood) that some studies did not capture. Further studies are needed to investigate the factors that might have contributed to inconsistencies in findings. A mega-analysis combining all data across all existing studies may also be beneficial to advance our understanding regarding sensitive periods for the effects of ACEs on the brain.

Poster Abstracts

Poster Session 1: Wednesday

WED_8 Parent Emotion Socialization is Associated with Neural Correlates of Emotion Regulation in Early Adolescents

Presenting Author: Sylvia Lin

Sylvia Lin - The University of Melbourne

Elena Pozzi - The University of Melbourne

Christiane Kehoe - The University of Melbourne

Sarah Whittle1 - The University of Melbourne

Background
Early adolescence is a developmental period marked by significant biological and social-emotional changes, and is also a time of heightened vulnerability to emotion regulation difficulties. During this period, neural networks supporting emotion regulation undergo dynamic alterations, rendering early adolescents particularly sensitive to environmental influences. Parent emotion socialization behaviors play a critical role in shaping the healthy development of emotion regulation; however, the impact of such behaviors on the neural correlates of emotion regulation is not well understood. In this study, we aimed to examine the association between parent emotion socialization and neural activity during emotion regulation tasks in early adolescents.

Methods
Participants were 47 female adolescents aged between 10 to 12 years. Adolescents reported on their parents' emotion socialization behaviors and performed two fMRI tasks: an affect labeling task (implicit emotion regulation) and a cognitive reappraisal task (explicit emotion regulation). We performed both hypothesis-driven region of interest (prefrontal cortex [PFC], amygdala) analyses, in addition to exploratory whole-brain analyses, to investigate associations between supportive and unsupportive parent emotion socialization behaviors and adolescent brain function during emotion regulation.

Results
Supportive parent emotion socialization behaviors were associated with greater activation in the dorsomedial and ventromedial PFC (dmPFC, vmPFC) and dorsal anterior cingulate cortex (dACC) during implicit emotion regulation (affect label vs shape label). Unsupportive emotion socialization behaviors were associated with less activation in the dmPFC, vmPFC, and right hippocampus during implicit emotion regulation. Parent emotion socialization was not associated with neural activation during explicit emotion regulation (cognitive reappraisal vs passive viewing of negative pictures).

Conclusions
Findings from this study suggest that both higher levels of supportive emotion socialization (e.g., validating children's emotions) and lower levels of unsupportive emotion socialization (e.g., dismissing and punishing emotions) may influence emotion regulation-related brain function in early adolescents. Associations with brain function during implicit but not explicit emotion regulation may indicate that neural infrastructure underlying explicit emotion regulation typically develops throughout adolescence. As such, early adolescents may vary in their ability to employ cognitive reappraisal, which may explain why we did not observe any significant association between parent emotion socialization and neural activity during explicit emotion regulation.

Poster Abstracts

Poster Session 1: Wednesday

WED_65 Understanding the role of dynorphin in the therapeutic effects of KNX100, a novel clinical stage molecule in development for the treatment of opioid withdrawal.

Presenting Author: Theresa Salthouse

Theresa Salthouse - University of Sydney

Nicholas Everett - University of Sydney

Gabriella Guy - University of Sydney

Bianca Wilson - University of Sydney

Michael Bowen - University of Sydney

Background
Opioid deaths in Australia are rising, with a key factor driving this being opioid withdrawal syndrome. KNX100 is a novel molecule in Phase-I clinical trials for treatment of opioid withdrawal, based on findings in rats and mice that KNX100 reduces negative affective symptoms of withdrawal. Therapeutic effects of KNX100 involve the nucleus accumbens shell (NAcSh), a key region for negative reinforcement, and RNAseq analysis of NAcSh genes identified that the dynorphin-kappa opioid system may be involved in KNX100's inhibition of opioid withdrawal. Here we test the hypothesis that KNX100 inhibits withdrawal-induced dynorphin signalling in the NAcSh at the protein level.

Methods
Mice underwent 9 days of escalating oxycodone doses to induce dependence, or saline for control groups. Mice were treated with either KNX100 (11mg/kg, i.p) or saline, 15-minutes before naloxone-precipitated withdrawal (10mg/kg, i.p). This produced four experimental groups: withdrawal + vehicle, withdrawal + KNX100, no withdrawal + vehicle and no withdrawal + KNX100. 90 minutes after KNX100 treatment, mice were euthanised for brain tissue collection. Brains were sliced and immunohistochemical staining was performed against anti-dyn A and anti-pdyn antibodies to assess expression levels of dynorphin and its precursor peptide prodynorphin within the NAcSh (sections between bregma points +1.33 and +1.69mm).

Results
Data will be reported for optical density of pDyn and Dyn-A protein expression in the NAcSh, between the four treatment groups.

Conclusions
Based on evidence that withdrawal is associated with heightened NAcSh dynorphin activity, driving increased KOR activity and negative affect (Koob, G., et al., Lancet Psychiatry 2016), we hypothesise that withdrawal mice will exhibit higher dynorphin expression levels compared with controls. Based on RNAseq data, we expect a reduction in NAcSh dynorphin levels in KNX100-treated withdrawal compared to vehicle treated withdrawal groups. This finding would be impactful for substance use disorders beyond opioid withdrawal, as the National Institute on Drug Abuse's top-10 hitlist for addiction therapies has emphasised the need for therapies targeting the dynorphin/kappa system.

Poster Abstracts

Poster Session 3: Friday

FRI_52 Mode-based morphometry: a new approach to mapping human neuroanatomy

Presenting Author: Trang Cao

Trang Cao - Monash University

James C. Pang - Monash University

Ashlea Segal - Monash University

Yu-Chi Chen - Monash University

Kevin M. Aquino - University of Sydney

Michael Breakspear - University of Newcastle

Alex Fornito - Monash University

Background
Classical magnetic resonance imaging (MRI) approaches to mapping anatomical brain changes in clinical disorders rely on statistical inferences at individual voxels, vertices, or region-of-interest and thus are confined to a specific spatial scale, obscuring underlying patterns expressed over multiple scales. We introduce a new method for characterizing neuroanatomical effects using the fundamental, resonant modes—eigenmodes—of brain anatomy. Recent work (Pang et al. 2023) has shown that such modes can be used to gain new insights into diverse aspects of brain activity. We term the method mode-based morphometry (MBM) and demonstrate its utility in mapping group differences in cortical thickness(CT).

Methods
The eigenmodes represent an orthogonal basis set of spatial patterns, that can be used to obtain a multi-scale characterization of diverse brain maps. We leverage this property to model CT differences between two groups as linear combinations of eigenmodes, which allows us to identify characteristic spatial scales of neuroanatomical variation through the resulting beta coefficient spectrum. To validate the approach, we develop a model with a known ground truth to study the resulting CT maps using a classical vertex-based analysis and our mode-based morphometry (MBM) approach. We also compare the two approaches using empirical data with multiple sites.

Results
Using simulated and empirical data, we find that the accuracy and consistency of our new MBM approach is either comparable or superior to classical vertex-based morphometry for capturing differences in CT maps between two experimental groups. MBM models neuroanatomical variations as resulting from the differential involvement of distinct fundamental modes of cortical shape, offering insights into generative processes and the spatial scales at which those variations are most salient.

Conclusions
MBM offers a robust, accurate, and informative new method for characterizing empirical maps of neuroanatomical variability that can be used in studying psychiatry.

Poster Abstracts

Poster Session 3: Friday

FRI_6 Oxytocin as a treatment for methamphetamine addiction - why is it not translating?

Presenting Author: Tylah Doolan

Tylah Doolan - University of Sydney

Joel Raymond - University of Sydney

Rhianne Scicluna - University of Sydney

Erin Lynch - University of Sydney

Morgan James - Rutgers University

Michael Bowen - University of Sydney

Nicholas Everett - University of Sydney

Background
Methamphetamine use disorder (MUD) is increasingly prevalent. There is an urgent need to develop novel therapies, as current psychosocial interventions are inaccessible, and no approved MUD pharmacotherapies exist. The neuropeptide oxytocin (OT) has therapeutic potential due to its interactions with addiction neurobiology and compelling preclinical findings, however, clinical trials using intranasal (IN) OT have disappointed. We suggest this is due to low OT doses, and inadequacy of the IN route for overcoming OT's poor physiochemical properties. Furthermore, it is unknown whether IN OT is efficacious in preclinical MUD models.

Methods
Female and male rats acquired intravenous METH self-administration (0.1 mg/kg/infusion, fixed ratio-1; 6h/day, 4 days), then an intermittent access schedule (12 cycles of 5 mins availability, 25 mins unavailability; 6 days) to mimic human patterns of bingeing. Rats were then trained on a behavioural economics procedure to assess motivation for METH, and IP and IN OT (0.01–3 mg/kg) was administered 30 minutes prior to METH sessions. Rats then underwent 14 days of forced abstinence, then received IN OT (0 or 3 mg/kg) prior to cue-induced reinstatement.

Results
In both sexes, IP OT significantly reduced METH intake at 0.3–3 mg/kg, yet IN OT had no effect at any dose. Similarly, 3 mg/kg IN OT did not alter cue-induced reinstatement, yet IP OT reduced reinstatement in prior research.

Conclusions
Overall, the MUD-suppressing effects of IP OT are not recapitulated by IN OT, suggesting that IN OT may not be suitable for treating MUD clinically. Furthermore, IP OT doses which produce plasma OT levels similar to what is achieved in humans did not reduce METH intake, suggesting higher doses may be needed clinically. These findings motivate the development of novel approaches for stimulating the oxytocin system.

Poster Abstracts

Poster Session 1: Wednesday

WED_47 Genetic influences on circulating retinol: implications for mental health

Presenting Author: William Reay

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Laura Greco - School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia

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Background
Retinol (Vitamin A) is a fat-soluble vitamin that plays an essential role throughout the human lifespan. In particular, retinol metabolites (e.g., retinoic acid) exert control over critical neurological processes like neuronal differentiation and are implicated in the aetiology mental health conditions. Genetics is known to impact the concentration of retinol available serum to be delivered around the body; however, these genetic factors remain poorly characterised. Increasing our understanding of genetic variants that associated with circulating retinol can also allow us to study its causal relationship with psychiatric relevant phenotypes.

Methods
We performed the largest genome-wide association study (GWAS) of circulating retinol to date in up to 22,274 participants .Genetic proxies of circulating retinol were then used to estimate causal relationships with almost 20,000 clinical phenotypes via a phenome-wide Mendelian randomisation study. Mendelian randomisation leverages the random inheritance of genetic variants to estimate causal relationships provided certain statistical assumptions are met. Signature mapping was also used to genetically predict pharmacological agents that may impact the concentration of circulating retinol

Results
We identified several novel regions of the genome associated with circulating retinol. Multi-omic interrogation of of these association signals revealed evidence that genetic effects on serum retinol are partially mediated via impacting hepatic transport proteins, as well as through processes such as lipid biology and glycaemic signalling. High-throughput genetic prediction of relationships with > 20,000 clinical phenotypes revealed evidence that retinol influences adult cortical structure and functional connectivity, including regions implicated in mental health conditions. Signature mapping suggested that drugs relevant to psychiatry like valproic acid (HDAC inhibitor) may impact circulating retinol abundance.

Conclusions

This work provides a comprehensive evaluation of the genetics of circulating retinol, as well as revealing traits which should be prioritised for further clinical investigation with respect to retinol related therapies or nutritional intervention. These data supports that circulating retinol has an effect on the brain in adults and that drugs used in psychiatry may alter retinol concentration in serum.

Poster Abstracts

Poster Session 3: Friday

FRI_64 Baicalin enhanced neuroprotection and mitochondrial function in a human neuronal cell model

Presenting Author: Zoe SJ Liu

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Background
Baicalin is a flavone glycoside derived from flowering plants belonging to the Scutellaria genus. Previous studies have reported baicalin's anti-inflammatory and neuroprotective properties in rodent models, indicating the potential of baicalin in neuropsychiatric disorders where these processes are implicated. However, it is unknown whether these effects can be reproduced in a human neuronal cell model.

Methods
We treated NT2-N cells (human neuronal-like cell model) with three different doses of baicalin (0.1, 1 and 5□M) or vehicle control (DMSO) for 24 hours. To determine the transcriptional effects of baicalin on NT2-N cells, RNA extraction, genome-wide mRNA expression profiles and gene set enrichment analysis (GSEA) were utilised. We also performed

neurite outgrowth assays and mitochondrial flux bioanalysis (Seahorse) in NT2-N cells treated with baicalin or vehicle control.

Results
We found in NT2-N cells that baicalin positively affected neurite outgrowth and transcriptionally up-regulated genes in the tricarboxylic acid cycle and the glycolysis pathway. Similarly, flux bioanalysis showed increased oxygen consumption rate in baicalin-treated NT2-N cells, an indicator of enhanced mitochondrial function.

Conclusions
Our findings have confirmed the mitochondria enhancing effects of baicalin in human neuronal-like cells, suggesting potential therapeutic application of baicalin in human neuropsychiatric disorders where these processes are operative.

Late-Breaking Abstracts

Poster Session 1: Wednesday

WED_83 Modelling and treating impairments caused by prenatal methamphetamine exposure in rats

Presenting Author: Abigail Marcus

Abigail Marcus - UNSW, Sydney

Prof. Simon Killcross - UNSW, Sydney

Dr. Kelly Clemens - UNSW, Sydney

Background
Methamphetamine is the second-most widely abused illicit drug worldwide. Of particular concern is use amongst pregnant women, which may impact as many as 5% of pregnancies. Methamphetamine is a known neurotoxin and readily crosses the placenta, yet the acute and long-term effects for children exposed in-utero are poorly understood. Here we will use an animal model of prenatal methamphetamine exposure (PME) to assess various physical and cognitive measures across early development through to adulthood. This research will inform the development of future behavioural and pharmacological supports for children exposed to methamphetamine in-utero.

Methods
Pregnant Sprague-Dawley rats were treated with methamphetamine (5 mg/kg/day; delivery via osmotic minipump) from gestational day 10 to postnatal day (PD) 21 (i.e., weaning). Offspring were assessed in the neonatal period (PD3-21) for impairments in physical development milestones and reflex tests. These offspring were then tested on behavioral and cognitive measures in the juvenile period (PD25-34), such as the open field test (OFT), as well as novel object recognition (NOR) and novel place recognition (NPR). Finally, offspring were tested in adulthood (P70+) on latent inhibition and response conflict tasks.

Results
Across gestation, pregnant rats given methamphetamine gained less weight relative to controls ($p=.001$). For offspring, in the neonatal period, PME delayed incisor eruption ($p=.002$) and ventral fur development ($p=.042$). In the juvenile period, PME decreased time spent in the inner quadrant for males ($p=.022$), which is a measure of increased anxiety. Also in the juvenile period, PME increased total exploration during NPR for females ($p=.050$), and reduced total exploration during NOR across both sexes ($p=.039$). In adulthood, however, PME did not impair performance in latent inhibition or response conflict tasks.

Conclusion
PME caused impairments in early development and during infancy. However, we did not find evidence of behavioural deficits in adulthood. This is surprising, suggesting that long-term deficits caused by PME are subtle and specific. Our results during neonatal and juvenile periods may be indicative of dopaminergic and serotonergic dysfunction, as perhaps suggested by findings of increased anxiety and dysregulated locomotor activity. In future studies, we will thus employ measures with increased sensitivity to aberrant neurotransmitter signalling. We will also explore this hypothesis in relation to pharmaceutical treatments and brain mechanisms that may drive some of the impairments caused by PME.

Late-Breaking Abstracts

Poster Session 2: Thursday

THUR_78 The effect of intergenerational stress exposure on peripheral BDNF levels in adult rats

Presenting Author: Aqsa Shahid

Aqsa Shahid - University of New South Wales

Kathryn Baker - La Trobe University, University of New South Wales

Rick Richardson - University of New South Wales

Background
Growing research demonstrates that the effects of stress can be transmitted across generations. That is, an individual's behaviour and physiology is not only impacted by their lived experiences, but also by their parent's, especially their mother's, past stressful experiences. Transmission of such effects across generations can make offspring more vulnerable to psychopathology risk. Brain-derived neurotrophic factor (BDNF) is an important biomarker in modulating stress-related psychopathology. This may be through the impacts of BDNF on both stress reactivity and fear regulation. In the current study we investigated whether rearing history (i.e., past stress exposure) impacts peripheral BDNF levels in adult rats.

Methods
Male Sprague Dawley rats were divided into three rearing conditions: (1) direct exposure to early-life stress (e.g., maternal separation as pups), (2) reared by a mother that had been separated from her previous litter (e.g., intergenerational or indirect stress exposure), and (3) standard-reared. Taking into account the two-hit stress hypothesis, half of the animals from each rearing condition were exposed to acute restraint stress in adulthood. Serum samples were collected 7 days after the acute stressor and analysed for BDNF concentrations using an enzyme-linked immunosorbent assay.

Results
Adult male offspring of a previously stressed mother, that is, animals exposed to intergenerational stress, had significantly lower levels of peripheral serum BDNF levels relative to maternally separated and standard reared animals. Further, animals exposed to acute stress in adulthood also showed significantly lower levels of serum BDNF relative to non-acutely stressed animals, regardless of rearing condition.

Conclusion
These findings suggest that the effects of a mother's stress history can be transmitted intergenerationally and impact her offspring's physiology. It is possible that a mother's experiences of stress result in potential epigenetic changes or alterations to the intrauterine environment that subsequently impact the developing fetus. Lower levels of BDNF in offspring of stressed mothers may contribute to impairments in emotion regulation and subsequently increase psychopathology risk.

Late-Breaking Abstracts

Poster Session 2: Thursday

THUR_75 Effect of cannabidiol on neurotransmitter and neuroimmune signalling pathways in a maternal immune (Poly I:C) model of schizophrenia: potential antipsychotic mechanisms

Presenting Author: Courtney Crawford

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Background
Schizophrenia is a heterogeneous and debilitating disease affecting approximately 1% of the population worldwide. Current antipsychotic drug efficacy is varied with frequent reporting of negative side effects. Treatment options have largely remained unchanged for decades and novel therapeutics are required. Cannabidiol (CBD) is an anti-inflammatory compound that has recently been investigated as an antipsychotic drug, with varied efficacy reported in clinical trials. Understanding the mechanisms by which CBD exerts its antipsychotic effects could assist in identifying populations of individuals that are likely to respond to this treatment.

Methods
Pregnant dams were treated with Poly I:C (POLY) or saline (control; CONT) on gestational day 15. Male and female offspring were administered either vehicle (VEH) or CBD (10mg/kg/day) twice daily for 3 weeks from post-natal day 56. Brain tissue was obtained post treatment and regions of interest micro-punctured then stored at -80oC. Quantitative polymerase chain reaction (qRT-PCR) was used to examine inflammatory markers, dopaminergic, serotonergic, and glutamatergic receptor mRNA expression changes in male and female poly I:C and CBD-treated rats in the ACC and NAc.

Results
In the NAc, poly I:C exposure decreased Tnf-α gene expression, whereas CBD restored to control-like levels ($p=0.031$). CBD also increased glutamatergic Grin2a ($p=0.07$) and serotonin 5-Ht2a ($p=0.042$) receptor gene expression in males (POLY +VEH vs POLY +CBD), with no effect on dopamine D1 or D2 receptors or interleukin-6 (IL6) gene expression. In the ACC, CBD decreased Grin1 ($p=0.025$) Grin2a ($p=0.025$) and 5-Ht2a ($p=0.047$) mRNA expression independent of prenatal infection or sex (vs VEH).

Conclusion
CBD restored Tnf-α gene expression and increased glutamatergic and serotonergic receptor gene expression in the NAc in a sex-specific manner, but did not alter dopamine receptors (i.e., traditional antipsychotic drug target). On the other hand, CBD decreased glutamatergic and serotonergic receptors in the ACC regardless of model or sex. The results suggest a different mechanism of action of CBD compared to existing antipsychotic drugs; however, further research is required to understand the functional implications of these changes.

Late-Breaking Abstracts

Poster Session 1: Wednesday

WED_80 Clinically predictive modulation of cognitive deficits in a mouse working memory touchscreen task

Presenting Author: Daisy L Spark

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Christopher J Langmead - Drug Discovery Biology, Neuroscience and Mental Health Therapeutic Program Area, Neuromedicines Discovery Centre, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia; Phrenix Therapeutics, Parkville, Victoria, Australia

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Background
Cognitive deficits in individuals with schizophrenia present a significant barrier to maintaining interpersonal relationships, employment, and independent living. Moderate to severe impairments have been found in cognitive domains including working memory, attention, learning and executive function. Despite the clear impact on functional outcomes, there are currently no approved treatments for cognitive impairments associated with schizophrenia (CIAS). Extensive efforts to develop pro-cognitive medicines, both for CIAS and other neuropsychiatric disorders, have repeatedly led to clinical trials that do not reflect the efficacy predicted in preclinical models.

Methods
The rodent touchscreen platform has begun to bridge the gap between preclinical and clinical assessments of cognitive function. However, there has been little pharmacological validation of whether these tests are stringent enough to be clinically predictive. Here, we use an NMDA receptor antagonist mouse model (acute low-dose administration) that we have validated for cognitive deficits in working memory performance on the trial-unique delayed nonmatch-to-location touchscreen task. We then measured the effect of 1) current standard of care (aripiprazole, olanzapine), 2) failed investigational new drugs (IND) for CIAS (atomoxetine, encenicline), and 3) current IND for schizophrenia (xanomeline) on working memory deficits.

Results
For the first time, we demonstrate that compounds which do not improve cognition in schizophrenia also have no effect on cognitive measures in our preclinical model. Conversely, we show that xanomeline ameliorates working memory impairments in our model, consistent with emerging data from clinical trials indicating pro-cognitive effects.

Conclusion
These results provide critical insight into the predictive validity of our preclinical assay and cognitive deficit model, and have significant implications for informing future development of pro-cognitive medicines.

Late-Breaking Abstracts

Poster Session 3: Friday

FRI_ 76 Investigating the antioxidant potential of medicinal mushrooms and their effect on oxidative stress

Presenting Author: Ella Parkes

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Julianna De Sousa Alves Neri - Molecular Horizons and School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong, NSW, 2522, Australia.

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Background
Oxidative stress is a factor that aids in the progression of neurodegenerative diseases. Antioxidants can alleviate oxidative stress and may be of interest as potential novel therapeutics for neurodegenerative pathologies. In recent years, the antioxidant capacity and potential efficacy of medicinal mushrooms to combat oxidative stress has garnered research interest. Mushrooms can be a source of phenols, which are plant-derived compounds with antioxidant properties; however, further research is required to understand the relationship between phenolic content and antioxidant properties of medicinal mushrooms, and their potential to protect against oxidative stress in the brain.

Methods
In this study, five common medicinal mushroom extracts (chaga, reishi, lion's mane, turkey tail and cordyceps) were analysed, together with the Queen Garnet plum (QGP), a high phenolic content and antioxidant comparator. Colourimetric assays were used to determine the phenolic content (total phenolics, flavonoids and anthocyanins), antioxidant capacity (nitrogen and oxygen radical scavenging capacity), and metal chelating capacity of the samples. Additionally, SH-SY5Y cells were pre-treated with the extracts then exposed to H2O2 (an oxidative stressor) and an MTT assay was used to measure preventative effects of the mushrooms against oxidative stress on cell viability.

Results
Chaga mushroom had significantly higher total phenolic, flavonoid and oxygen scavenging capacity (p > 0.001 vs QGP). QPG was the only extract that contained anthocyanins, while the cordyceps mushroom had significantly higher Fe2+ chelating capacity compared to other samples (p 0,05), chaga (+38.3%, p > 0.05), cordyceps (+29.43%, p > 0.01) and QGP (+66.2%, p > 0.001) prevented the oxidative stress-induced reduction in SY-SY5Y cell viability (vs H2O2). Cell viability was significantly positively correlated with Cu2+ chelation and oxygen scavenging. Both antioxidant properties were significantly positively correlated with phenolic content of mushrooms.

Conclusion
The results of this study suggest that the cordyceps, chaga and reishi mushrooms as well as the queen garnet plum can help prevent the effects of oxidative stress in neuron-like neuroblastoma cells. Data suggests a relationship between the antioxidant and metal chelating capacity of the samples and their phenolic content. Overall, this study highlights the link between the neuroprotective abilities of the medicinal mushrooms and their phenolic content, presenting them as promising candidates for further investigation into the potential of these extracts to reduce oxidative stress in the brain.

Late-Breaking Abstracts

Poster Session 1: Wednesday

WED_74 Reversing the effect of prenatal opioid exposure: the efficacy of sodium butyrate in animal models

Presenting Author: Isobel A R Williams

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Meredith C Ward - School of Women's and Children's Health, Faculty of Medicine, University of New South Wales; (4) Department of Newborn Care, Royal Hospital for Women, Randwick, NSW, Australia

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Kelly J Clemens - School of Psychology, Faculty of Science, University of New South Wales

Background
The global opioid epidemic has dramatically increased the number of children with prenatal opioid exposure (POE). POE has negative long-term impacts on children's behaviour and cognition, increasing risk of mental illness. The underlying effects of POE are poorly understood, but are linked to a range of central nervous and enteric system issues such as neuroinflammation, impaired white matter development and gut dysbiosis. Sodium butyrate (NaB) is a short-chain fatty acid that is anti-inflammatory, pro-myelinating and enhances the gut microbiome. This study aimed to assess whether NaB could reverse the gut, brain and behavioral deficits associated with POE.

Methods
Pregnant rat dams were treated with methadone (9/mg/kg/day) and NaB (3% in drinking water), from gestational day ten until postnatal day 17. Their offspring were assessed for changes in physical development, behaviour and cognition during juvenile development (open field test, novel object/place recognition) and into adulthood (five choice serial reaction time task - 5CSRTT, trial unique non-matching to location – TUNL-task). Fresh and fixed brain tissue were collected for analysis of inflammation and myelination. Fecal samples were collected from dams and pups at four timepoints and processed using 16S ribosomal sequencing for gut bacteria diversity and abundance.

Results
Across juvenile development methadone accelerated eye opening and weight gain, and increased anxiety in the open-field test. In adulthood, methadone-induced deficits in impulsivity and attentional processing (5-CSRTT), and working and spatial memory (TUNL-task) were reversed in rats that had received prenatal NaB. Treatment with NaB also reversed a decrease in myelination associated with prenatal methadone exposure. NaB promoted gut health – it reversed methadone-induced reductions in alpha diversity in dams. In pups methadone increased bacteria linked to obesity and inflammation, an effect ameliorated with concurrent NaB treatment, which additionally reduced bacteria associated with neuroinflammation and microbiome inflammation.

Conclusion
Perinatal exposure to methadone led to persistent impairments, from early development into adulthood, particularly impacting attentional processing, and working and spatial memory. Notably, this was associated impaired myelination in pups, as well as altered gut microbiome composition both in dams and their offspring. Treatment with NaB across the perinatal period reversed the majority of methadone-induced cognitive and behavioral deficits, increased myelination and reversed methadone-induced gut dysbiosis. Together these results highlight the link between cognition, myelination and gut composition in animal models of POE. Furthermore, it indicates that treatment with NaB could significantly improve outcomes of children born with POE.

Late-Breaking Abstracts

Poster Session 3: Friday

FRI_82 Investigating the relationship between inflammation, angiogenesis, the blood brain barrier and neurogenesis in schizophrenia

Presenting Author: Jessica Sarah Lim

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Hayley F North - Neuroscience Research Australia, Sydney, NSW Australia; Discipline of Psychiatry and Mental Health, Faculty of Medicine and Health, University of New South Wales, NSW Australia

Christin Weissleder - Neuroscience Research Australia, Sydney, NSW Australia Mechanism and therapy for genetic brain diseases, Institut Imagine, Paris, France

Cynthia Shannon Weickert - Neuroscience Research Australia, Sydney, NSW Australia; Discipline of Psychiatry and Mental Health, Faculty of Medicine and Health, University of New South Wales, NSW Australia; Department of Neuroscience and Physiology, Upstate Medical University, Syracuse, NY USA

Background
Microvasculature dysfunction within the human brain can inhibit neurogenesis and can be caused by alterations to the blood brain barrier (BBB) and angiogenesis (the growth of new blood vessels). The subependymal zone (SEZ) retains the capacity for neurogenesis throughout life, and neurogenic capacity appears blunted in schizophrenia, particularly in a subgroup of schizophrenia cases with elevated inflammation. In the SEZ, the complex vasculature provides a healthy microenvironment to support neurogenesis, however inflammation can alter the BBB and angiogenesis. Therefore, further research is needed to delineate the relationship between inflammation and microvasculature in the SEZ in schizophrenia.

Methods
In order to address the heterogeneity of schizophrenia, we have identified a high-inflammation schizophrenia (HI-SCZ) subgroup and low-inflammation schizophrenia (LI-SCZ) subgroup. To determine any abnormal microvasculature changes across schizophrenia and control groups, a fluidigm qPCR was conducted for BBB genes (CLDN5, OCLN, ZO-1 and PECAM1) and angiogenesis genes (VEGFA, ANGPT1, ANGPT2, TEK and VEGFR1). Statistical analysis was conducted based upon diagnosis (control and schizophrenia) and clustered diagnosis (HI-SCZ and LI-SCZ) to determine any significant changes in mRNA gene expression.

Results
Statistical analysis of BBB genes demonstrated that PECAM1 was significantly upregulated in HI-SCZ compared to controls. CLDN5 was also significantly upregulated in the HI-SCZ subgroup compared to controls and LI-SCZ, suggesting that a high inflammatory state in the SEZ is disrupting BBB function. Abnormalities within angiogenesis were also observed, as VEGFA was significantly upregulated in HI-SCZ compared to controls, and ANGPT1 and ANGPT2 significantly downregulated in HI-SCZ compared to controls. This suggests that angiogenesis is increased within the SEZ, furthermore, upregulated VEGFA may also be contributing to increased BBB permeability and dysfunction.

Conclusion
My findings in HI-SCZ demonstrate that on an mRNA level, increased PECAM-1 may increase leukocyte trafficking across the BBB, whereas increased CLDN5 (a BBB tight junction protein) may be a compensatory mechanism to reduce BBB permeability. Additionally, increased VEGFA (promoter of blood vessel growth) but decreased ANGPT1 (remodels blood vessels) and ANGPT2 (induces vascular regression) within HI-SCZ suggests the SEZ is increasing angiogenesis. These findings reveal that alterations in the BBB and angiogenesis may differentially affect schizophrenia patients depending on inflammatory level. The results suggest more severe vascular dysfunction within the SEZ in HI-SCZ which may relate to reduced neurogenesis.

Late-Breaking Abstracts

Poster Session 3: Friday

FRI_79 Systematic review of effects of flavonoids on adiponectin: Implications for inflammation and brain function

Presenting Author: Julianna Lys de Sousa Alves Neri

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Background
Obesity is associated with chronic low-grade inflammation. Although the pathophysiology is not completely understood, studies suggest that reduced levels of adiponectin in obesity may contribute to inflammation in the brain, potentially exacerbating declined brain function (eg mood and cognition). Flavonoids are dietary bioactive compounds that exhibit antioxidant and anti-inflammatory properties. Emerging evidence suggests that flavonoids may increase adiponectin, which is of interest for research into novel therapies to improve inflammation in obesity. Unfortunately, there is currently limited understanding of the link between effects of key flavonoids on adiponectin in relation to inflammation in obesity.

Methods
With the use of the PRISMA statement and the Rayyan tool, we performed a systematic literature review to evaluate the effects of specific flavonoids on adiponectin and inflammation in obesity. The literature search was conducted by two researchers independently using the databases PubMed, ScienceDirect, Scopus, Web of Science, and MEDLINE to search all studies that report the effects of flavonoids on adiponectin levels. The protocol for this systematic review was registered on PROSPERO (CRD42023425413).

Results
Preclinical studies (n=27), using a model of hypertrophied adipocytes (n=10) and rodents obesity-induced models (n=17), demonstrated an up-regulation of adiponectin (n=24) and down-regulation of IL-6 (n=15), TNF-α (n=18), ROS (n=5), IL-1β (n=5), IL-10 and NF-kB (n=3), IL-8, IL-17, IL-13, IL-2 and IL-7 (n=1) after treatment with different concentrations of flavonoid. Studies reported changes in plasma adiponectin (n=5), TNF-α (n=4), IL-6 (n=2) and IL-10 (n=1) in clinical trials (n=6) after supplementation with dietary flavonoid. One cross sectional study reported that habitual intake of flavonoid was associated with higher adiponectin plasma levels. Brain function was not reported.

Conclusion
Clinical and preclinical evidence suggests that flavonoids may increase adiponectin levels and decrease inflammatory biomarkers. Obesity-related peripheral inflammation can affect central nervous system physiology, generating neuroinflammation; however, further research investigating the role of adiponectin in mood and cognition in obesity, and response to flavonoid supplementation, is required.

Late-Breaking Abstracts

Poster Session 2: Thursday

THUR_72 Perinatal Sertraline Exposure Induces Changes in Glutamatergic Receptor Gene Expression in Male but Not Female Adolescent Offspring

Presenting Author: Justine Kissane

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Samara Brown - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

Justine Kissane - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

Noor Jarbou - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

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Elise Kulen - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

Lucas Mushahwar - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

Kelly A Newell - Molecular Horizons and School of Medical, Indigenous and Health Sciences, University of Wollongong

Background
The selective serotonin reuptake inhibitor (SSRI), sertraline, is the frontline pharmacotherapy for the treatment of depression and anxiety during pregnancy. SSRIs, including sertraline, readily cross the placenta, raising questions about the potential consequences of in utero exposure. Our group previously showed that perinatal exposure to the SSRI, fluoxetine, induces changes to glutamatergic markers in the adolescent brain. However, it is unclear if this also occurs following perinatal exposure to sertraline. Utilising a rodent model, this study aimed to examine the effects of perinatal sertraline exposure on gene expression of glutamatergic receptors in the brains of male and female adolescent offspring.

Methods
Wistar-Kyoto (WKY) rats (model relevant to depression) were treated with sertraline (10 mg/kg; WKY-SERT; n=8) or vehicle (66% propylene glycerol; WKY-VEH n=8) twice daily from gestational day 0 (GD0) to postnatal day 14 (PN14). Wistar (WIS; healthy control) rats were treated with vehicle (n=6). Offspring underwent behavioural tests followed by euthanasia at adolescence (PN42). Quantitative polymerase chain reaction (qPCR) was used to quantify mRNA expression of the following glutamate receptors/subunits in the prefrontal cortex (PFC) and ventral hippocampus (vHPC) of both female and male offspring (n=5-7/group): NMDA (Grin1, Grin2a, Grin2b); AMPA (Gria1, Gria2); Grm5. ANOVAs and Pearson's/Spearman's correlations were employed.

Results
Sertraline exposed WKY male offspring showed significantly increased Grin2a, Grin2b and Grm5 mRNA in the vHPC compared to WKY-VEH offspring (+27-35%; p<0.05). There were positive correlations between time spent in the closed arms of the elevated plus maze (EPM) and Grin1 (r=0.597), Grin2b (r=0.463) and Gria1 (r=0.502) mRNA in the male vHPC (p<0.05). There were negative correlations between time spent in the open arms of the EPM and Grin1 (r=-0.531) and Grin2a (r=-0.046) in the male vHPC (p<0.05). No effects of sertraline exposure were found in the male PFC or in the PFC or vHPC in female offspring.

Conclusions

This study has for the first time, shown that perinatal sertraline exposure, in a rodent model of relevance to depression, induces sex-specific and brain region-specific effects on gene expression of glutamate receptors. Further studies are needed to determine whether these changes are reflected at the protein level. Ultimately, antidepressant medications such as sertraline, play a critical role in minimising risk associated with untreated maternal depression and associated disorders. Further studies are needed to fully characterise the potential risks and benefits of perinatal SSRI exposure and minimise any unwanted effects.

Late-Breaking Abstracts

Poster Session 3: Friday

FRI_70 White blood cell proportions predict remission of psychosis risk in Ultra High Risk individuals

Presenting Author: Lauren Barker

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Patrick D McGorry - Orygen, The National Centre of Excellence in Youth Mental Health, The University of Melbourne, Parkville, Victoria, Australia; Centre for Youth Mental Health, The University of Melbourne, Parkville, Victoria, Australia

Background
The development of full psychosis is generally preceded by a prolonged prodromal period in which individuals may experience attenuated psychotic symptoms or impaired functioning, known as the 'Ultra High Risk' (UHR) period. The Staged Treatment in Early Psychosis (STEP) clinical trial aimed to evaluate the effectiveness of a sequential intervention strategy in the prevention of psychosis in UHR youth. It used a clinical staging model of sequential intervention, with the first two stages comprising different forms of psychosocial therapies. We used a systems genomics approach to identify potential leading biomarkers of remission of UHR status after psychosocial therapy.

Methods
A subset of STEP trial participants provided samples that were used to generate genotypes, DNA methylation and gene expression profiles. Samples were provided at trial baseline and at 6 months, after completion of the psychosocial therapy stages. We estimated white blood cell (WBC) proportions using DNA methylation samples and validated them against a subset of participants with WBC differential results from a pathology service. We used logistic regression to identify associations between baseline WBC proportions and remission status after 6 months. Differential gene expression and methylation-wide association analyses were also carried out, both at baseline and at 6 months.

Results
DNA-methylation derived WBC proportions were available for 30 remitters and 61 non-remitters at trial baseline. Lymphocytes were significantly decreased in remitters compared to non-remitters, and remained so after adjusting for potential clinical confounders. Within the lymphocyte cell-category, natural killer and CD4+ T-cells were nominally associated with remission status, however did not survive multiple testing correction. After adjustment for cell-type proportions, there were no significantly differentially-expressed genes or differentially-methylated sites between remitters or non-remitters at either baseline or 6-months.

Conclusions
Altered WBC profiles have previously been reported in schizophrenia and psychotic disorders, including first-episode psychosis. We show that WBC proportions may also have potential as a biomarker for treatment responsiveness within UHR patients. These results, if replicated, may have use in further stratifying risk of transition to psychosis in patients presenting with symptoms indicative of UHR, as well as in guiding treatment choice. Finally, we believe these results should encourage future psychiatric clinical trials to collect WBC differential information, due to it being cost-effective, easily obtained and highly informative. (ANZCTR Registration Number: NCT02751632).

Late-Breaking Abstracts

Poster Session 2: Thursday

THUR_69 Investigating the neural correlates of stress-induced binge eating in binge prone versus binge resistant female mice.

Presenting Author: Mia J O'Shea

Mia J O'Shea - Department of Biochemistry and Pharmacology, University of Melbourne, Parkville, Australia

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Priya Sumithran - Department of Surgery, Central Clinical School, Monash University, Victoria, Australia
Suheng He - Department of Biochemistry and Pharmacology, University of Melbourne, Parkville, Australia

Background
It is well established that stress and negative affect (e.g., sadness, anger) trigger overeating. This form of maladaptive eating behaviour, commonly referred to as “emotional eating”, is particularly common in women, and is associated with binge eating and higher risk of obesity. The neural mechanisms that underpin this form of dysregulated eating are yet to be elucidated but likely implicate neuronal substrates involved in both stress and reward. This study aimed to identify brain regions and specific neuronal phenotypes associated with the propensity for stress-induced binge eating in females using a translationally relevant mouse model.

Methods
Female Corticotropin Releasing Hormone (CRH)-IRES-Cre x tdTomato reporter mice were separated into stress-binge prone and resistant sub groups groups based on the extent of binge eating observed in an intermittent access protocol involving exposure to a mild, psychological stressor. Immunohistochemical analyses of coronal brain sections were then performed in order to assess levels of the neuronal activity marker Fos and the neuropeptide oxytocin. Use of the CRH reporter mice in combination with immunolabelling for Fos and oxytocin allowed the identification of differences in recruitment of specific regions between behavioural groups and the neurochemical phenotype of these cells.

Results
Binge prone mice displayed significantly higher binge eating of a palatable food reward compared to both binge resistant mice and a control group consisting of mice that consumed the same food in the absence of prior stress exposure. Quantification of immunohistochemical data is ongoing and will provide insight into the neural correlates which potentially underlie the differential behavioural response to both the food reward and the “emotional” stressor in our stress binge paradigm. Quantification of double and triple labelling of oxytocin and CRH positive cells will reveal whether there is a potential role for these neuropeptides stress induced binge eating.

Conclusions
Ultimately, individual variation in binge eating displayed by our stress-exposed female mice recapitulates the natural individual differences characteristic of the human, female binge eating continuum. Hence using this model to investigate discrepancies in the recruitment and activation of different regions between prone and resistant groups may facilitate our understanding of the precise neural mechanisms driving this behaviour.

Late-Breaking Abstracts

Poster Session 1: Wednesday

WED_71 The Effects of Psilocybin on Social Behaviour in Mice

Presenting Author: Sheida Shadani

Sheida Shadani*, Zane B Andrews, Claire J. Foldi - Monash University, Department of Physiology, 26 Innovation Walk, Clayton VIC 3800, Monash Biomedicine Discovery Institute, Metabolism Diabetes and Obesity (MDO) Program

Background
Social behaviour shapes the structure and stability of societal networks and relationships. Deficits in social behaviour are core features of numerous mental disorders, including anxiety and depression. Recent studies in humans have demonstrated that psychedelics like LSD and psilocybin, can induce prosocial behaviour. Repeated administration of LSD in mice enhanced social behaviour by increasing the interaction time with a novel conspecific in the direct social interaction test and 3-chamber test. These prosocial effects are attributed to serotonin-2A receptors in the prefrontal cortex. Nevertheless, the impact of a single dose of psychedelics, especially psilocybin, on acute and sub-acute sociability remains unexplored.

Methods
To determine the time course of effects of a single dose of psilocybin (1.5 mg/kg) on social behaviour, we employed the widely used 3-chamber social preference paradigm. Adult male and female group-housed C57BL/6J mice received psilocybin (n=8 male, n=8 female) or saline (n=8 male, n=8 female), with testing conducted 4h, 24h and 7 days following administration. Behaviour was analysed over three 10-minute trial periods to investigate baseline activity (habituation), sociability and preference for social novelty. We further segmented the analysis into two parts: the first half of the trial assessed social exploration and the second half social choice.

Results
In male mice, psilocybin administration 24h prior to the test did not alter locomotor activity ($p = 0.1306$) or social preference indices (p Sociability Index $= 0.9859$, p Social Novelty Index $= 0.1473$). However, it increased the frequency of interaction with a familiar conspecific ($p = 0.0441$), which was driven by behaviour during the exploratory phase ($p = 0.0076$) rather than the social choice phase ($p = 0.1173$). Psilocybin-treated mice spent significantly more time exploring both familiar and novel mice ($p = 0.0422$) in the social choice trial. No significant effects of psilocybin were seen on sociability in female mice at the same time point after administration.

Conclusions
Together these data highlight the importance of using both sexes in preclinical research models and suggest that a single dose of psilocybin promotes prosocial behaviour in male but not female mice, particularly related to the exploration of a familiar conspecific mouse. To better understand what drives these changes, we are currently analysing ethologically relevant behaviours and assessing the acute effects of psilocybin on aspects of social behaviour in the more naturalistic setting of the home cage. Future studies will examine whether neuronal activity in the prefrontal cortex is altered by psilocybin during social interaction events using GCaMP fiber photometry.

Late-Breaking Abstracts

Poster Session 3: Friday

FRE_73 Molecular evidence for glial pathology in Schizophrenia and Bipolar Disorder Midbrains

Presenting Author: Suhaana Shaik

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Gerardo Mendez-Victoriano - Discipline of Psychiatry and Mental Health, Faculty of Medicine, University of New South Wales, Sydney, Australia; Schizophrenia Research Laboratory, Neuroscience Research Australia, Randwick, New South Wales, Australia.

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Cyndi S. Weickert - Discipline of Psychiatry and Mental Health, Faculty of Medicine, University of New South Wales, Sydney, Australia; Schizophrenia Research Laboratory, Neuroscience Research Australia, Randwick, New South Wales, Australia; Department of Neuroscience & Physiology, Upstate Medical University, Syracuse, New York, USA.

Background
Schizophrenia and Bipolar disorder are heterogenous diseases with unknown aetiology, yet both include dopamine dysregulation and psychosis. Two inflammation subgroups of each disorder have been identified, one having normative level of cytokines and the other increased levels. Increased astrocyte markers are detected in cortical and midbrain regions of SCZ and BPD, mainly in the high inflammation subgroups. Despite this, the extent to which gliosis occurs in the midbrain in SCZ compared to BPD is uncertain. To address this, we investigated mRNA expression levels of astrocyte (GFAP) and microglia (Iba-1) markers in high and low inflammatory subgroups of post-mortem human midbrains.

Methods
Midbrains from 33 CTRL, 35 SCZ and 33 BPD cases were taken from the SMRI array cohort as microglia and astrocytes are key resident immune-responsive cells. Analysis on RT-PCR fluidigm data was conducted to examine if there were diagnostic or inflammation subgroup differences in mRNA expression levels. In-situ hybridisation was used to localise in which region (substantia nigra, ventral tegmental area, cerebral peduncles) GFAP mRNA was most expressed.

Results
We found a significant increase in GFAP expression in the high-level inflammation bipolar group compared to controls ($p=0.028$). Iba-1 mRNA levels were increased in high-inflammation schizophrenia and decreased in high-inflammation bipolar compared to controls ($p=0.0003$). GFAP mRNA levels did not significantly correlate with Iba-1 mRNA in our human midbrain cohort. By in-situ, we found that GFAP mRNA was highest in the ventral tegmental area compared to the substantia nigra and cerebral peduncle. In contrast to the RT-PCR findings, GFAP mRNA levels did not significantly differ by diagnosis or inflammation in any midbrain subregion by in-situ in our preliminary analysis.

Conclusions
We confirm that GFAP mRNA can be elevated in the midbrain of those with psychotic illness and inflammation. Our earlier study detected this in the schizophrenia midbrain. However, in this study we find elevated GFAP in bipolar disorder. The opposing change in Iba-1 mRNA in schizophrenia compared to bipolar midbrains suggest that microglial pathology in the midbrain may be distinct across these two diagnoses. Future studies should distinguish between subtypes of astrocytes and microglia under different inflammatory conditions to gain more insight into the subtypes that are most pathological in the midbrain of people with psychosis-related disorders.

Late-Breaking Abstracts

Poster Session 2: Thursday

THUR_81 Early life inflammation accelerates the development of emotion regulation in infant rats

Presenting Author: Tayla B McCutcheon

Tayla B McCutcheon - UNSW, Sydney

Sara Simenson-Braun - UNSW, Sydney

Rick Richardson - UNSW, Sydney

Background
Exposure to inflammation early in life is a well-documented risk factor for neuropsychiatric disorders like depression, bipolar, and schizophrenia. However, it is unclear what the mechanisms behind this life-long risk are. One possibility is that stress exposure alters the developmental trajectory of neural systems, including those involved in emotion regulation, instigating long-lasting vulnerability to psychopathology. Previous research from our lab found exposure to a postnatal psychosocial stressor led to accelerated maturation of fear regulation during infancy. We investigated whether postnatal exposure to an inflammatory stressor would have a similar effect.

Methods
Male and female Sprague-Dawley rats were either undisturbed (Standard Reared; SR) or injected with lipopolysaccharide on postnatal day (P)3 and P5 (Early life inflammation; ELI). On P17, rats were trained to associate an auditory conditioned stimulus (CS) with foot shock in context A, had their fear of the CS extinguished the following day in context B, and then were tested for either extinction retention (in context B) or renewal (in context A) on the third day.

Results
There were no group differences in mean CS-elicited freezing across conditioning and extinction trials. In line with previous findings, SR infants had similarly low levels of CS-elicited freezing at test in both contexts. However, infants exposed to ELI had increased levels of CS-elicited freezing in context A compared to context B at test. In other words, the ELI infants exhibited a precocious emergence of context-mediated relapse of extinguished fear, similar to infants exposed to other types of stress in previous studies. Our results showed no interaction of sex in mean CS-elicited freezing.

Conclusions
We found that infant rats, of both sexes, exposed to an inflammatory stressor exhibited renewal of extinguished fear during test whereas SR infants did not. This suggests that early-life inflammation accelerated infant emotion regulation development. Similar findings in previous studies with other types of stressors (e.g., psychosocial) suggest similar or shared underlying mechanisms for adverse long-term effects. Future research should examine neural correlates of these behavioural findings to further elucidate mechanisms. According to the stress acceleration hypothesis, deviations from normative developmental trajectories can lead to long-lasting changes, potentially contributing to heightened psychopathology risk in adults who experienced early life stress.

Late-Breaking Abstracts

Poster Session 3: Friday

FRI_77 Comparing the effects of topiramate versus naltrexone in neural alcohol cue reactivity and intrinsic functional connectivity in alcohol use disorder

Presenting Author: Warren Logge

Warren Logge - Edith Collins Centre (Translational Research in Alcohol Drugs and Toxicology), Sydney Local Health DIstrict, Royal Prince Alfred Hospital

Paul Haber - Edith Collins Centre (Translational Research in Alcohol Drugs and Toxicology), Sydney Local Health DIstrict, Royal Prince Alfred Hospital

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Background
Topiramate has been shown to effect fMRI indices, including alcohol cue reactivity, in alcohol use disorder, but potential varying effects compared to comparator treatment naltrexone levels has not comprehensively been examined. This study investigated whether topiramate attenuates craving and alcohol cue-elicited brain activation, and intrinsic functional connectivity more than naltrexone in alcohol use disorder treatment seekers, and the relationship between this response and clinical outcomes.

Methods
Forty-seven participants with alcohol use disorder received daily topiramate (titrating the dose up to 200 mg/day n = 21) or naltrexone (50 mg/day, n = 26) for at least 6 weeks. We examined fMRI alcohol cue-elicited neural activation during a visual alcohol cue reactivity task, and intrinsic functional connectivity during resting-state 120 minutes following treatment administration. Associations with activation patterns and percentage of heavy drinking days (% HDD) associations were assessed.

Results
Both treatment groups reported fewer post-scan % HDD, but no subjective craving group differences were found. Overall, participants showed Increased alcohol cue-elicited activation in regions two clusters spanning prefrontal regions implicated in cue reactivity, chiefly frontal regions (i.e., frontal and precentral gyri, anterior cingulate cortex). There were no differences in alcohol cue reactivity between treatment groups. There were no differences seen in intrinsic functional connectivity between the treatment groups.

Conclusions
There were no treatment differences seen for subjective craving, or for fMRI brain activity indices alcohol cue reactivity or intrinsic functional connectivity, evidenced between topiramate- and naltrexone-treated patients with alcohol use disorder. Overall, patients demonstrated some alcohol cue-reactivity in regions that can be attributed to the regulation of cue-elicited responses, but again not specific to treatment. Taken together, these results suggest topiramate is comparable to naltrexone regarding modulation of cue-elicited and intrinsic functional connectivity brain patterns in individuals with alcohol use disorder.

List of BPA Annual Scientific Meetings

2010	Society Launch at the Royal Society of Victoria, Melbourne
2011	1st meeting at the Melbourne Cricket Ground, Melbourne
2012	2nd meeting at the Melbourne Brain Centre, Melbourne
2013	3rd meeting at the Queensland Brain Institute, Brisbane
2014	4th meeting at the Monash Alfred Psychiatry Research Centre, Melbourne
2015	5th meeting at the Coogee Bay Hotel, Sydney
2016	6th meeting at Noahs on the Beach, Newcastle
2017	7th meeting at the Novotel, Wollongong
2018	8th meeting at the South Australian Medical Research Institute, Adelaide
2019	9th meeting at the Florey Institute, Melbourne
2020	10th meeting hosted by Neuroscience Research Australia, Sydney (Whova)
2021	11th meeting hosted by the Queensland Brain Institute, Brisbane (Whova)
2022	12th meeting at Newcastle City Hall, Newcastle
2023	13th meeting at Pullman Palm Cove Sea Temple Resort & Spa, Cairns, Queensland

BPA 2024 will be held in Sydney, NSW

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