Biological Psychiatry
AUSTRALIA

2024

Proceedings of the Biological Psychiatry Australia Scientific Meeting 2024

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Welcome

The 14th Biological Psychiatry Australia Scientific Meeting

3rd – 5th November 2024

Dear Friends and Colleagues,

On behalf of the Local Organising Committee, we warmly welcome you to the 14th Annual Biological Psychiatry Australia 2024 (BPA 2024) Scientific Meeting. This year we are back in Sydney, and we are excited to meet at the Mercure Sydney in the heart of the CBD. 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.

LOC Co-Chairs: Dr Christina Perry and Dr Natalie Matosin

Local Organising Committee: Christina Perry, Natalie Matosin, Brandon Richards, Tertia Purves-Tyson (President) **,** Leigh Walker (Treasurer), Shrujna Patel, Rose Chesworth, Warren Logge, Emiliana Tonini, Katrina Edmond, Mirim Shin, Gezelle Dali, Laisa De Siqueira Umpierrez, Muskan Khetan.

Stay connected with our Twitter accounts: @biolpsychaust @BPA_ECRN

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

All online material can be found at https://whova.com/xems/view/app_branding/biolo_202410/

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 Gadigal people of the Eora Nation and pay our respects to the 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	Samara Walpole	University of Wollongong
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 Sydney

ECRN Committee

Chair	Samara Walpole	NSW	University of Wollongong
Deputy Chair	Warda Syeda	VIC	University of Melbourne
Secretary	Cassandra Wannan	VIC	University of Melbourne/Orygen
Treasurer	Helen Clunas	NSW	University of Wollongong
Social Media	Juliana Lys de Sousa Alves Neri	NSW	University of Wollongong
	Xavier Maddern	VIC	University of Melbourne/Florey Institute of Neuroscience and Mental Health
Awards subcommittee	Sylvia Lin	VIC	University of Melbourne
	Eveline Mu	VIC	Monash University
	Trevor Steward	VIC	University of Melbourne
	Isobel Williams	NSW	University of New South Wales

Webinar subcommittee	Sevil Ince	VIC	University of Melbourne
	Emiliana Tonini	NSW	University of Sydney
	Elizabeth Haris	NSW	University of New South Wales
Mentoring subcommittee	Bruna Panizzutti	VIC	Deakin University
	Shrujna Patel	NSW	University of Sydney

Society Profile

Scientific Review Committee: Chair: Kelly Clemens

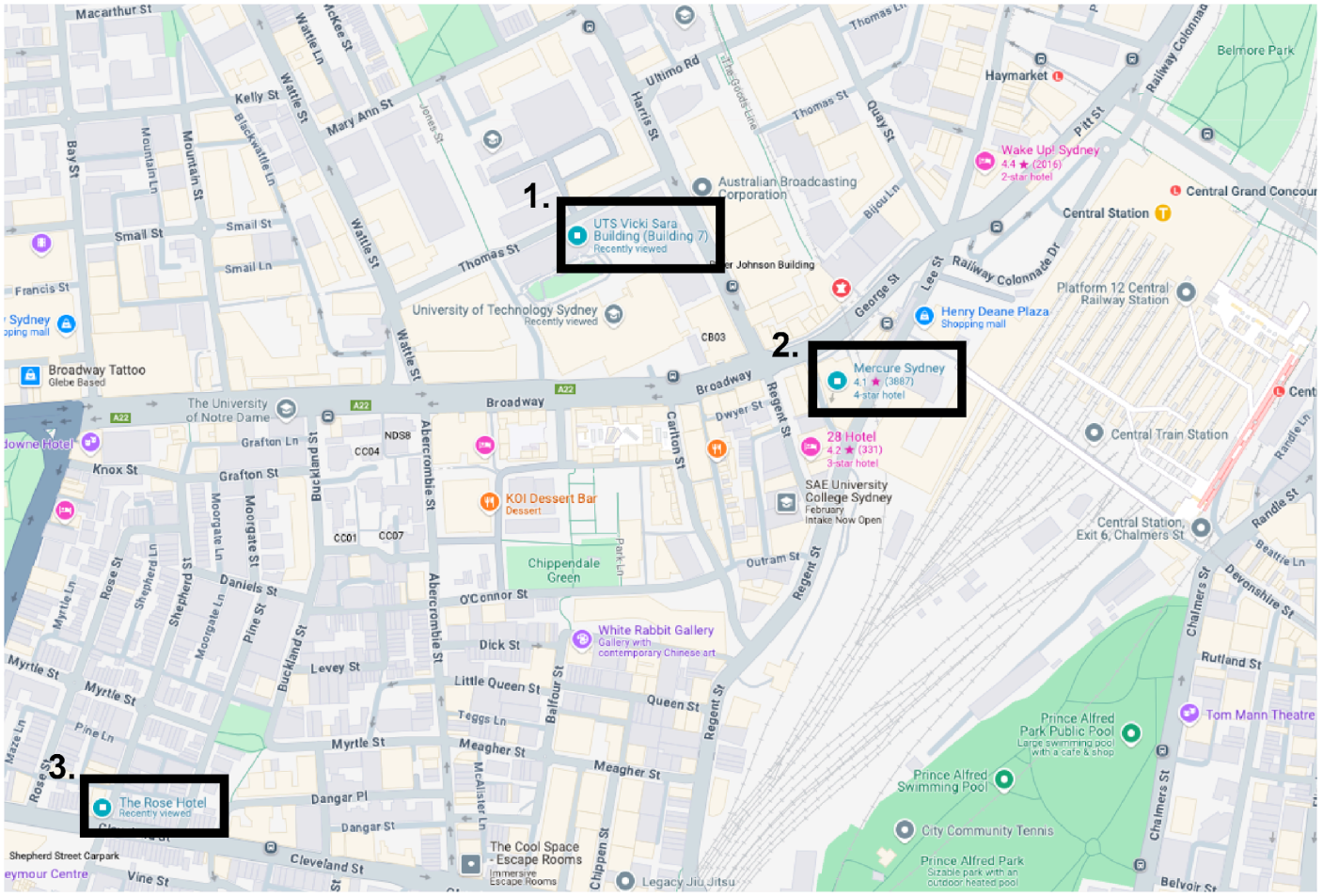
Robyn Brown, Thomas Burne, Erin Campbell, Rose Chesworth, Jennifer Cornish, Brian Dean, Chao Deng, Eske Derks, Darryl Eyles, Claire Foldi, Andrew Gibbons, Alex Guerin, Tony Hannan, Lauren Harms, Emily Jaehne, Matthew Kang, Tim Karl, Muskan Khetan, Christine Leonards, Luke Ney, Stevan Nikolin, Christina Perry, Alice Petty, Tertia Purves-Tyson, Yann Quide, Thibault Renoir, Zoltan Sarnyai, Elysia Sokolenko, Luba Sominsky, Trang Truong, Adam Walker, Nathan Wellington.

Annual Award Presentations

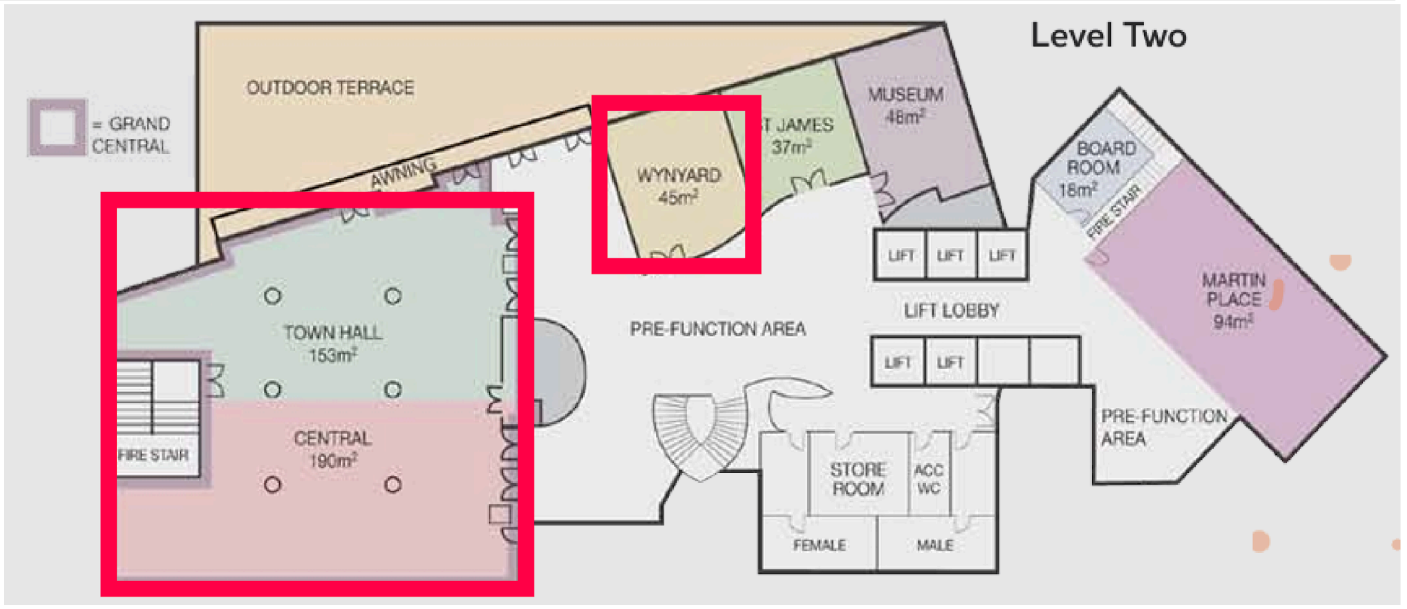
	Isaac Schweitzer Lecture		**Aubrey Lewis Award**
2010	-	2010	Mark Bellgrove
2011	-	2011	Melissa Green
2012	-	2012	Andrea Gogos
2013	Michael Berk	2013	Michael Breakspear
2014	Paul Fitzgerald	2014	Adam Guastella
2015	John McGrath	2015	Irina Voineagu
2016	Cyndi Shannon Weickert	2016	Andrew Zalesky
2017	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
2024	Colleen Loo	2024	Melissa Sharpe

Venue Information

1.	Sunday 3rd Addiction Neuroscience Australia	UTS	Vicki Sara Building (Building 7), Level 2 Green Theatre – 67 Thomas St, Ultimo
2.	Monday 4th – 5th	Mercure Sydney	818-820 George Street, Sydney NSW 2000
3.	Monday 4th Social Event	The Rose Hotel	52-54 Cleveland Street, Chippendale NSW 2008



Mercure Sydney



Program at a Glance

Sunday, 3 Nov	
University of Technology Sydney - Green Theatre, Vicki Sara Building (Building 7), 67 Thomas St, Ultimo	
11:00am – 4:30pm	Addiction Neuroscience Australia (ANA) Satellite Meeting
4:30pm – 5:00pm	Registration
5:00pm – 6:00pm	**OPENING EVENT/TALK – Professor Maree Toombs**
6:00pm – 10:00pm	Informal networking
Monday, 4 Nov	
Mercure Sydney, 818-820 George Street, Sydney NSW 2000	
8:30am – 9:00am	Registration
9:00am – 9:30am	Opening ceremony
9:30am – 10:30am	**12th Isaac Schweitzer Lecture – Professor Colleen Loo** Translational research in new treatments for severe depression
10:30am – 11:00am	Morning tea
11:00am – 11:30am	Mentoring and morning tea
11:30am – 12:30pm	**SYMPOSIUM 1** Decoding the Female Brain: Exploring Women's Health in Psychiatry
12:30pm – 1:30pm	**Kinoxis Data Blitz: 8 talks**
1:30pm – 2:30pm	Lunch
2:30pm – 3:30pm	**Poster session (including Data Blitz presenters)**
3:30pm – 4:30pm	**SYMPOSIUM 2** Therapeutic innovations for psychiatric disorders
4:30pm – 5:00pm	Afternoon tea
5:00pm – 6:00pm	**Highest Ranked Abstracts (20 min talks)**
The Rose Hotel, 52-54 Cleveland Street, Chippendale NSW 2008	
7:00pm - late	Dinner/social event
Tuesday, 5 Nov	
Mercure Sydney, 818-820 George Street, Sydney NSW 2000	
8:30am – 9:00am	Registration
9:00am – 10:00am	**15th Aubrey Lewis Award Lecture – Dr Melissa Sharpe** Distinct dopamine circuits encode unique neural signatures for learning
10:00am – 11:00am	**BPA ECR Plenaries**
	Mr Xavier Maddern Sex differences in the role of the neuropeptide cocaine- and amphetamine- related transcript in binge drinking
	Dr Sidhant Chopra Linking synapses, cells, and systems to understand the neurobiology of psychosis
11:00am – 11:30am	Morning tea
11:30am – 12:30pm	**SYMPOSIUM 3** New targets for alcohol use disorder treatment
12:30pm – 1:30pm	**Data Blitz 2: 8 talks**
1:30pm – 2:30pm	Lunch and poster viewing
2:30pm – 3:30pm	**Poster session (including Data Blitz presenters)**
3:30pm – 4:30pm	**SYMPOSIUM 4** Exploring the biology underlying physical comorbidities of neuropsychiatric disorders using genomics
4:30pm – 5:00pm	Afternoon tea

5:00pm – 6:00pm	**SYMPOSIUM 5** Icy Insights: Facilitating Dialogue to Advance the Treatment of Methamphetamine Use Disorder in Australia
6:00pm – 6:30pm	AGM, Prizes, Discussion, and Close

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 Grand Central 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
- Please arrive 15 minutes before your scheduled session. 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
- **Posters will be displayed <u>on the day of your presentation only.</u> You can put your poster up when you arrive in the morning, and please remove it at the end of the day.**
    - If you are allocated poster numbers 1 – 40, please place your posters in the Wynyard Room.
    - If you are allocated poster numbers 41 – 60, please place your posters in the Grand Central Room.
- We will provide pins and other material to help display your poster, just come ready to present!

Sponsors

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Scientific Program

Sunday, 3 November 2024

All events on Sunday 3 November will be held at University of Technology Sydney – Level 2, Green Theatre, Vicki Sara Building (Building 7), 67 Thomas St, Ultimo

Addiction Neuroscience Australia (ANA) Satellite Meeting
11:00 AM – 4:30 PM

Registration desk open
4:30 PM – 5:00 PM

Opening Event

Talk by Prof Maree Toombs
5:00 PM – 6:00 PM
Chair: Dr Tertia Purves-Tyson

Informal networking
6:00 PM – 10:00 PM

Monday, 4 November 2024

All events on Monday, 4 November and Tuesday, 5 November will be held at Mercure Sydney, 818-820 George Street, Sydney NSW 2000

Registration desk open
8:30 AM – 9:00 AM

Opening Ceremony
9:00 AM – 9:30 AM
Chair: Dr Tertia Purves-Tyson

12th Isaac Schweitzer Lecture
9:30 AM – 10:30 AM
Chair: Dr Tertia Purves-Tyson

Prof Colleen Loo
Translational research in new treatments for severe depression

Morning Tea
10:30 AM – 11:30 AM

Mentoring Program
11:00 AM – 11:30 AM

Symposium 1
11:30 AM – 12:30 PM

Decoding the Female Brain: Exploring Women's Health in Psychiatry
Chair/Discussant: Dr Leigh Walker (Florey Institute) and Dr Robyn Brown (University of Melbourne)
Speakers: Xavier Maddern (Florey Institute), Prof Bronwyn Graham (UNSW), A/Prof Rachel Hill (Monash), and Dr Eveline Mu (Monash)

Kinoxis Data Blitz
12:30 PM – 1:30 PM
Chair: Katrina Edmond

12:30 PM **Jordan Clarke**
Patient-derived microglia-containing organoids for investigating neuroanatomical phenotypes in schizophrenia

12:37 PM **Martine Skumlien**
The association between acute and non-acute cannabis exposure and the neural correlates of reward anticipation

12:44 PM **Ken Walder**
Mitochondrial function in stem cell models from participants with bipolar disorder and healthy controls

12:51 PM **Eva Guerrero-Hreins**
A novel fMRI investigation into the role of the BNST in stress and food cue reactivity

12:58 PM **Elizabeth Kleeman**
Paternal SARS-CoV-2 Infection Increases Anxiety in Offspring and Changes Sperm Small Noncoding RNA Profiles

1:05 PM **Brandon Richards**
Efferent connectivity and neurochemical phenotype of topographically distinct lateral hypothalamus and zona incerta RXFP3+ cells

1:12 PM **Danli Peng**
Sex-Dependent and Dynamic Brain Structure Changes Due to influenza A virus induced maternal immune activation: Insights from Longitudinal Mouse MRI

1:19 PM **Laura Kimble**
Test-retest reliability of the Dynamic Strategy Shifting Task in male and female mice

Lunch
1:30 PM – 2:30 PM

Poster Session 1 (including Data Blitz presenters)
2:30 PM – 3:30 PM
P_01a to P_40a in Wynyard Room
P_41a to P_60a in Grand Central Room

P_01a **Cassandra Ma**
Distinct contribution of cortico-striatal mechanisms to elucidate a pathway for conditioned punishment

P_02a **Rinjani Soengkoeng**
Investigating changes in immune signalling following prenatal opioid exposure

P_03a **Diane Webster**
A Roadmap for Prader Willi Syndrome Research in Australia

P_04a **Katrina Edmond**
Characterising the neuropeptide landscape of the postmortem human orbitofrontal cortex in health and psychopathology

P_05a **Kaixin Huang**
Identifying risk genes of susceptibility to activity-based anorexia in a corticostriatal pathway

P_06a **Elizabeth Kleeman**
Paternal SARS-CoV-2 Infection Increases Anxiety in Offspring and Changes Sperm Small Noncoding RNA Profiles

P_07a **Jamila Iqbal**
Personalised treatment of schizophrenia using patient-derived olfactory neuronal stem cells through a systems-based multi-omics analysis

P_08a **Tamim Ahsan**
Using spatially resolved single-nucleus multi-omics to understand how stress contributes to psychiatric disorders

P_09a **Kyle Hewitt**
Clozapine's Impact on Microglial Exosomes: A Potential Pathway to Cognitive Dysfunction in Schizophrenia

P_10a **Martine Skumlien**
The association between acute and non-acute cannabis exposure and the neural correlates of reward anticipation

P_11a **Nathan Wellington**
Novel BDNF haplotype linked to proBDNF down-regulation in PTSD – A study in predictive biosignatures.

P_12a **Nigel Jones**
Recording single neuron activity during working memory touchscreen testing, and the effects of pharmacological interventions.

P_13a **Lei Zhu**
Exosomes derived from microglia exposed to oxidized low-density lipoprotein impair healthspan, learning, and memory in Caenorhabditis elegans

P_14a **Yoshito Saito**
Alterations in Superficial White Matter and Their Association with Cognitive Function in Recent-Onset Psychosis: A Fixel-Based Analysis Study

P_15a **Eva Guerrero-Hreins**
A novel fMRI investigation into the role of the BNST in stress and food cue reactivity

P_16a **Hannah Machet**
Decision-making in electric barrier-induced voluntary abstinence

P_17a **Carlton Pavy**
Neurosteroid Replacement Therapy Using Tiagabine and Zuranolone Restores Cerebellar Neurodevelopment and Reduces Hyperactive Behaviour Following Preterm Birth

P_18a **Elizabeth Haris**
Structural covariance, regional topology, and volumetric aspects of amygdala subnuclei in posttraumatic stress disorder using ultra-high field imaging

P_19a **Jack Siddle**
Variations in density of high probability dopamine release sites negatively correlates with measures of cognitive flexibility.

P_20a **Danli Peng**
Sex-Dependent and Dynamic Brain Structure Changes Due to influenza A virus induced maternal immune activation: Insights from Longitudinal Mouse MRI

P_21a **Yan Li**
Glutamatergic dysfunction in dorsal striatum underlies compulsive eating in an animal model of binge eating

P_22a **Bart Cooley**
Fibroblast growth factor 21 reduces consumption and seeking

P_23a **Isobel Williams**
Reversing the effects of prenatal opioid exposure: the efficacy of sodium butyrate in an animal model

P_24a **Eleni Karanicolas**
How Prior Experience Shapes Adaptation to Changing Reversal Learning Environments in Mice

P_25a **Ken Walder**
Mitochondrial function in stem cell models from participants with bipolar disorder and healthy controls

P_26a **Olivia Gilmore McKimm**
Interactions of methamphetamine and psilocybin on cognitive flexibility using a novel social reversal learning task in female rats.

P_27a **Weijie Yi**
The effect of risperidone and voluntary exercise intervention on lipid metabolism in juvenile female rats: underlying mechanisms

P_28a **Zoltan Sarnyai**
The North Queensland Dietary Intervention Trial (NQDIT): A Randomized Controlled Clinical Trial investigating the effects of ketogenic metabolic therapy on psychiatric and metabolic outcomes in community patients with schizophrenia and bipolar disorder

P_29a **Kristiane Yacou**
The effect of N-acetylcysteine (NAC) on Neurometabolites and Cognitive Function in Alcohol Use Disorder

P_30a **Laura Kimble**
Test-retest reliability of the Dynamic Strategy Shifting Task in male and female mice

P_31a **Utsav Gyawali**
Orexin signaling in ventral tegmental area as a common mediator of sleep and drug seeking during acute cocaine abstinence

P_32a **Xinyuan Zhang**
Exploring the Role of Ketamine in a Central Insulin Resistance Model of Depression

P_33a **Heather Macpherson**
Unpredictable Circadian Rhythm Disruption in Wistar Rats: Striatal and Behavioural Changes Reflecting Bipolar Disorder Pathophysiology

P_34a **Sophie Welch**
Investigating transitions between Goal-Directed, Habitual and Compulsive Behaviour

P_35a **Jordan Clarke**
Patient-derived microglia-containing organoids for investigating neuroanatomical phenotypes in schizophrenia

P_36a **Gerardo Mendez-Victoriano**
Cell Death TNFRSF transcripts expressed by Immune cells are Increased in the Midbrains of Schizophrenia and Bipolar Disorder with High-Inflammation

P_37a **Christiana Milleniaputri Suhartono**
Neurobehavioral determinants of diet-induced obesity

P_38a **Naomi May**
Quercetin and chlorogenic acid: power duo for neuroprotection?

P_39a **Daniel Russell**
Genetic Variants Associated with Schizophrenia Lead to Allele-Specific Expression Through Epigenetic Regulation

P_40a **Brandon Richards**

Efferent connectivity and neurochemical phenotype of topographically distinct lateral hypothalamus and zona incerta RXFP3+ cells

P_41a **Emma Hilsley**
The antipsychotic actions of chronically-administered intranasal clozapine

P_42a **Sevil Ince**
Subcortical modulation of the fronto-insular and cingulate functioning during negative emotional processing in mood and anxiety disorders

P_43a **Amber Curry**
Expression of hippocampal cortisol receptors and FKBP5 in psychiatric disorder patients with trauma histories

P_44a **Layla Neuhaus**
NF-κB pathway gene expression is elevated in the midbrain of people with high-inflammation schizophrenia

P_45a **Ellen Towers**
Mega-analysis of structural covariance in co-occurring post-traumatic stress disorder and alcohol use disorder: common and distinct patterns of alterations

P_46a **Kevin Hou**
The heterogenous default mode network in major depressive disorder: A systematic review of diffusion tensor imaging

P_47a **Renee Papaluca**
Differential striatal gene expression profiles underlying the propensity for depression-like behaviour in a mouse model of vertical sleeve gastrectomy

P_48a **Rossana Rosa Porto**
Could heat therapy be utilised as a novel treatment for Alzheimer's disease? Insights from a pilot study in mice.

P_49a **Wenxin Zhang**
What striatal cells control social reward? Investigating the effects of chemogenetic Gq-coupled activation of neurons or astrocytes in the nucleus accumbens in a social operant task in female rats.

P_50a **Erin McLemon**
Chronic morphine induces persistent place preference and dose-dependently changes in faecal short chain fatty acid concentrations in mice

P_51a **Tong En Lim**
Effects of psychological trauma exposure in childhood or adulthood on brain morphology and function in chronic pain: a systematic review

P_52a **Caitlin Fenech**
Uncovering the role of glycinergic neurons in the periaqueductal grey

P_53a **Magdalene de Rozario**
Relationship between electroencephalography-based mismatch negativity and antipsychotic treatment response in young people at clinical high risk for psychosis

P_54a **Julianna Lys de Sousa Alves Neri**
Nutritional psychiatry: An in-vitro exploration of Antioxidant and Neuroprotective Benefits of colorful fruits.

P_55a **Alexander Athanasopoulos**
Characterising the pharmacology of social motivation in female rats, using the social operant conditioning task.

P_56a **Marta Rapado-Castro**
CAN N-ACETYL ASPARTATE BE A USEFUL BIOMARKER FOR COGNITIVE DEVELOPMENT IN EARLY ONSET PSYCHOSIS BY SEX?

P_57a **Maral Jkorkozian**
The Impact of Gestational Timing of a Prenatal Immune Insult on Behavioural Patterns of Adolescent Male and Female Offspring

P_58a **Nicola Acevedo**
Multimodal characterization of deep brain stimulation for obsessive compulsive disorder

P_59a **Elizabeth Virakorn**
Do not fear - fluoxetine enhances the extinction of fear in stressed adolescent rats.

P_60a **Tylah Doolan**
Is activity of hypothalamic oxytocin neurons necessary or sufficient to reduce methamphetamine addiction behaviours?

Symposium 2
3:30 PM – 4:30 PM

Therapeutic innovations for psychiatric disorders
Chair/Discussant: Bruna Panizzutti (Deakin) and Alex Cristino (Griffith)
Speakers: Prof Murray Cairns (Newcastle), Dr Jiayue-Clara Jiang (UQ), Dr Bruna Panizzutti (Deakin), A/Prof Dan Siskind (UQ)

Afternoon Tea
4:30 PM – 5:00 PM

Highest Ranked Abstracts
5:00 PM – 6:00 PM
Chair: Dr Natalie Matosin

5:00 PM **Joanna Yau**
Circuit- and -state-dependent opponent processing of fear

5:20 PM **Morgan Bucknor**
Influence of maternal stress, high-fat diet and postnatal infection on maternal and offspring behaviour in C57BL/6 mice

5:40 PM **Morgan James**
A biological basis for binge eating as 'self-medication'

Dinner Social Event – The Rose Hotel
7:00 PM – 11:00 PM

Tuesday, 5 November 2024

Registration desk open
8:30 AM – 9:00 AM

15th Aubrey Lewis Award Lecture
9:00 AM – 10:00 AM
Chair: Dr Christina Perry

Dr Melissa Sharpe
Distinct dopamine circuits encode unique neural signatures for learning

BPA ECR Plenaries
10:00 AM - 11:00 AM
Chair: Dr Samara Walpole

10:00 AM **Mr Xavier Maddern**
Sex differences in the role of the neuropeptide cocaine- and amphetamine- related transcript in binge drinking

10:30 AM **Dr Sidhant Chopra**
Linking synapses, cell, and systems to understand the neurobiology of psychosis

Morning Tea
11:00 AM - 11:30 AM

Symposium 3
11:30 AM - 12:30 PM

New targets for Alcohol Use Disorder treatment
Chair/Discussant: Roberta Anversa (Florey Institute) and Christopher Dayas (Newcastle)
Speakers: Dr Erin Campbell (Newcastle), Dr Roberta Anversa (Florey Institute), Dr Zayra Millan (UNSW), and Dr Warren Logge (USyd)

Data Blitz 2
12:30 PM – 1:30 PM
Chair: Dr Warren Logge

12:30 PM **Alexa Samiotis**
Systematic Review of MRI Markers of Psychopathology following Traumatic Brain Injury: Transdiagnostic Insights

12:37 PM **Michelle Yuqing Xiao**
Effect of Glucagon-Like Peptide-1 Receptor Signaling in the dorsal Lateral Septum on Alcohol Intake and Relapse Drinking

12:44 PM **Roger Varela**
Bioenergetic Dysregulation in Peripheral Immune Cells: Links to Anhedonia and Fatigue in Young Adults with Depression

12:51 PM **Miriam Matamales**
Local modulation of the striatal network: a new perspective on the mechanisms of action of antipsychotics

12:58 PM **Sarah-Jane Leigh**
Unveiling vulnerabilities: Insights from fetal single-cell transcriptomics on prenatal opioid exposure and the innate immune system

1:05 PM **Alice Petty**
Upregulated inflammation-relevant gene pathways in the midbrain of the EDiPS model of hyperdopaminergia

1:12 PM **Alex Cristino**
Linking Non-Canonical snoRNA Function and Schizophrenia Using Patient-Derived Olfactory Neurosphere Cells

1:19 PM **Oak Hatzimanolis**
Dysregulated circular RNAs in schizophrenia patient-derived olfactory stem cells perform key roles in cell adhesion and migration

Lunch
1:30 PM – 2:30 PM

Poster Session (including Data Blitz Presenters)
2:30 PM – 3:30 PM
P_01a to P_40a in Wynyard Room
P_41a to P_60a in Grand Central Room

P_01b **Alexander Athanasopoulos**
Exploring behavioural interactions between methamphetamine and psilocybin in mouse models of methamphetamine sensitization and head twitch response.

P_02b **Abbey Livermore**
The Effects of Food Insecurity on Eating Behaviours

P_03b **Marta Rapado-Castro**
Neuronal integrity in adolescent psychosis over the first 5 years after the first episode: A longitudinal proton magnetic resonance spectroscopy study

P_04b **Marta Rapado-Castro**
Neuronal integrity and cognitive development in early onset psychosis: A five years follow-up study using proton magnetic resonance spectroscopy

P_05b **Alexia Samiotis**
Systematic Review of MRI Markers of Psychopathology following Traumatic Brain Injury: Transdiagnostic Insights

P_06b **Priscilla Costa**
Maternal immune activation and raloxifene effects on behaviour across adolescence in male and female offspring

P_07b **Grace Jin**
The hidden influence of response latencies in the TUNL task of working memory

P_08b **Daryl Eyles**
Vitamin D a potent differentiation agent for dopamine neurons

P_09b **Rose Chesworth**
A novel mouse model of acute neuroinflammation shows schizophrenia-like behavioural phenotypes

P_10b **Michelle Yuqing Xiao**
Effect of Glucagon-Like Peptide-1 Receptor Signaling in the dorsal Lateral Septum on Alcohol Intake and Relapse Drinking

P_11b **Samuel Brennan**
Genetic correlations between Bipolar Disorder and co-morbid conditions across a broad array of body systems

P_12b **Elise Rowe**
Hybrid: A Pilot Study of Integrated Virtual Reality, Neurofeedback, and Cognitive Behaviour Therapy for the Treatment of Auditory Verbal Hallucinations

P_13b **Suzy Alexander**
Behavioural Stratification in animal studies – why its important

P_14b **Felicia Reed**
Towards an understanding of the therapeutic effects of psilocybin: a focus on dopamine and reward

P_15b **Kaspar McCoy**
Is it spore than just serotonin? The effect of psilocybin on neurotransmitter release in a corticostriatal pathway

P_16b **Kyna Conn**
Insights into the neurochemical mechanisms of psilocybin-induced improvements in anorexia-like behaviour in female rats

P_17b **Bonnie Quigley**
Investigating the complex relationships between peripheral brain-derived neurotrophic factor (BDNF) and post-traumatic stress disorder (PTSD) diagnosis and symptom severity

P_18b **Roger Varela**
Bioenergetic Dysregulation in Peripheral Immune Cells: Links to Anhedonia and Fatigue in Young Adults with Depression

P_19b **Xiaoying Cui**
Developmental vitamin D deficiency increases DNA methylation in embryonic mesencephalon

P_20b **Miriam Matamales**
Local modulation of the striatal network: a new perspective on the mechanisms of action of antipsychotics

P_21b **Laura Kimble**
Reversal Learning in mice: Model-based versus model-free approaches and altering levels of probabilistic uncertainty

P_22b **Kiruthika Ganesan**
Exploring the novel dopaminergic projections from Ventral Tegmental Area to Ventral Hippocampus in Alzheimer's disease

P_23b **Sarah-Jane Leigh**
Paclitaxel therapy induces sickness behaviour and microbiome changes in mice

P_24b **Sarah-Jane Leigh**

Unveiling vulnerabilities: Insights from fetal single-cell transcriptomics on prenatal opioid exposure and the innate immune system

P_25b **Alexandre Guerin**
Hippocampally-mediated cognition and hippocampal subfield volume as a function of cannabis use and cannabis use disorder

P_26b **Laisa de Siqueira Umpierrez**
Is alcohol incubation of craving driven by discrete alcohol-associated cues?

P_27b **Arvie Rodriguez Abiero**
Positive experience shifts the circuit for encoding of fear memories away from the basolateral amygdala

P_28b **Eddie Wise**
Instrumental Learning Enhances the Intrinsic Excitability of Basolateral Amygdala Neurons

P_29b **Christa Dang**
MiNDful Mediation: Psychological distress mediates the relationship between neuroticism and neurofilament light

P_30b **Alice Petty**
Upregulated inflammation-relevant gene pathways in the midbrain of the EDiPS model of hyperdopaminergia

P_31b **Lauren Sams**
The Effects of Early Life Inflammation on Maternal Behaviour and Fear Expression in Infant Rats

P_32b **Leigh Walker**
Midbrain ghrelin receptor signalling regulates binge alcohol consumption in a sex specific manner

P_33b **Kathryn Baker**
Effects of social buffering on fear extinction in adolescent rats

P_34b **Gezelle Dali**
Comparable effects of topiramate and naltrexone on neurometabolite levels and cognition in individuals with alcohol use disorder

P_35b **Nitharsaa Ambalavanar**
To what extent can treatments improve aberrant reward processing in psychopathology? A systematic review and meta-analysis

P_36b **Elysia Sokolenko**
Meta-analysis and systematic review of invasive and non-invasive brain stimulation interventions for the treatment of anorexia nervosa

P_37b **Belinda Lay**
Cholinergic modulation of the prefrontal cortex in the formation and extinction of fear memories

P_38b **Masakazu Taira**
Using a translational task to understand how Lateral hypothalamus may regulate learning processed relevant to schizophrenia and addiction

P_39b **Samara Walpole**

Sex-Dependent mGluR7 Alterations in Schizophrenia: Insights from the Nucleus Accumbens

P_40b **Oak Hatzimanolis**
Dysregulated circular RNAs in schizophrenia patient-derived olfactory stem cells perform key roles in cell adhesion and migration

P_41b **Trang Truong**
Gene Regulatory Networks: An Avenue for Drug Repurposing in Bipolar Disorder

P_42b **Jodie Naim-Feil**
Probabilistic modelling: Exploring how longer-term fluctuations in relapse triggers can be harnessed to develop an early warning system of relapse

P_43b **Philip Jean-Richard-dit-Bressel**
Understanding persistent detrimental behaviour: External and predictive validity of a novel experimental paradigm

P_44b **Dhamidhu Eratne**
Three uncreased expressions in a proteomic pilot study in treatment-resistant schizophrenia: shedding light on the illness or clozapine?

P_45b **Karly Turner**
Understanding impulsive actions through dopamine transients

P_46b **Hayley North**
Inflammation, metabolic factors and sex differences in a clinical trial of raloxifene (estrogen receptor modulator) in people with schizophrenia

P_47b **Gavin Cooper**
Hypatia Health: Cognitive Modelling Made Easy

P_48b **Sheida Shadani**
PSILOCYBIN TREATMENT FOR EATING DISORDERS: A FOCUS ON PROSOCIAL EFFECTS

P_49b **Iveta Gavljak**
The Effect of Maternal Immune Activation and Estrogen Receptor Modulation on Microglial Characteristics in the Adult Female and Male Ventral Midbrain

P_50b **Xi Chen**
Olanzapine accelerates aging through impaired mitophagy via dysfunctional lysosomes and defective SNARE complexes

P_51b **Tsz Ho Timothy Wong**
The effect of raloxifene on anxiety and stress-related gene expression in the ventral hippocampus of rat offspring exposed to maternal immune activation

P_52b **Ruchi Jayasinghe**
The impact of transient adolescent food insecurity on metabolic, reward, and mood-related behaviour.

P_53b **Megan Man**
Polygenic Contributions to Cognitive Dysfunction in Schizophrenia and Bipolar Disorder

P_54b **Hongjuan You**
Neuronal Mitochondrial Dysfunction Induced by Herpes Simplex Virus Type 1 Infection via VDAC1 in Alzheimer's Disease

P_55b **Christian Chiha**
Establishing a causal relationship between inflammation and hyperdopaminergia in mammalian brain and behaviour

P_56b **Michelle Shen**
Dissociated activity and neurotransmitter release within basolateral amygdala during punishment and fear learning

P_57b **Nicola Acevedo**
A scoping review on serotonergic psychedelics for obsessive compulsive and body image disorders

P_58b **Helen Clunas**
Characterization of Terpene and Phenolic Compounds in Native Australian Plants: Antioxidant and Neuroprotective Effects

P_59b **Wendi Gao**
Adrenergic Modulation of Inputs to the Paraventricular Thalamus

P_60b **Simone Rehn**
Food brand logos and their association with dietary habits

P_61b **Wenjuan Sun**
4-(4-Hydroxyphenyl) Butyric Acid: A Promising Butyrate Derivative for Lifespan Extension and Ameliorating Aging-Related Phenotypes

Symposium 4
3:30 PM – 4:30 PM

Exploring the biology underlying physical comorbidities of neuropsychiatric disorders using genomics
Chair/Discussant: William Reay (UTas) and Janice Fullerton (NeuRA)
Speakers: Dr Dylan Kiltschewskij (Newcastle), Prof Gillian Blue (Westmead/USyd), Dr David Stacey (UniSA), and Dr William Reay (UTas)

Afternoon Tea
4:30 PM – 5:00 PM

Symposium 5
5:00 PM – 6:00 PM

Icy Insights: Facilitating Dialogue to Advance the Treatment of Methamphetamine Use Disorder in Australia
Chair/Discussant: Rhianne Scicluna (Kinoxis Therapeutics)
Speakers: A/Prof Rebecca McKetin (UNSW), Dr Krista Siefried (NCCRED/St Vincent's Hospital Sydney), A/Prof Gillinder Bedi (Orygen/UniMelb), and Dr Nick Everett (USyd/Kinoxis Therapeutics)

AGM, Prizes, Discussion, and Close
6:00 PM – 6:30 PM

Discussants

Dr Iain Perkes
A/Prof Jess Nithianantharajah

AGM, Prizes, and Wrap up

Dr Tertia Purves-Tyson, Dr Christina Perry, Dr Natalie Matosin

Conference close

6:30 PM

Invited Plenary Speakers

12th Isaac Schweitzer Plenary Lecture

Translational research in new treatments for severe depression

Prof Colleen Loo - Professor, Psychiatry, UNSW Medicine; Professor, Black Dog Institute; Professorial Fellow, The George Institute; NHMRC Leadership Fellow; Medical Director, Neurostimulation and Interventional Psychiatry, Ramsay Clinic Northside

Colleen Loo is a psychiatrist, Australian NHMRC Leadership Fellow and Professor of Psychiatry at UNSW in Sydney and the Black Dog Institute, Sydney; Australia. She is an internationally recognised clinical expert and researcher in the fields of electroconvulsive therapy, transcranial magnetic stimulation, transcranial direct current stimulation and ketamine, and led the first Australian RCTs of these interventions in depression.

She has published over 300 peer reviewed papers and has received competitive grant funding from the Australian NHMRC, MRFF and major overseas grant funding agencies.

Prof Loo is active in ECT, neurostimulation and novel treatments research, practice and policy, providing advice to Australian government health departments, the Royal Australian and New Zealand College of Psychiatrists, and several international guidelines. She was President of the International Society for ECT and Neurostimulation (ISEN) 2018-2020. She has served on the Editorial Boards of the two leading international brain stimulation journals: Journal of ECT, Brain Stimulation. She directs professional training courses in ECT, TMS, tDCS and ketamine.

Chair: Dr Tertia Purves-Tyson

15th Aubrey Lewis Plenary Award

Distinct dopamine circuits encode unique neural signatures for learning

Dr Melissa Sharpe – Department of Psychology, University of Sydney, Sydney, NSW 2006, Australia

Dr. Melissa Sharpe received her Ph.D. in Psychology in 2015 (UNSW). Dr. Sharpe conducted postdoctoral research training in the United States in a joint position at the National Institute on Drug Abuse (NIDA) and

Princeton University, which was supported by an NHMRC CJ Martin Biomedical Fellowship.

Dr. Sharpe began her lab in the Department of Psychology at UCLA in 2018 and shortly afterward the prestigious US National Science Foundation (NSF) CAREER Award fellowship. Dr. Sharpe recently moved her research group to the University of Sydney. The lab investigates the neural circuits involved in reinforcement learning using a modern suite of neuroscience techniques including optogenetics and fiber photometry of genetically encoded activity sensors (e.g., calcium, dopamine, serotonin). The lab is funded by the US National Institutes of Health, including the National Institute on Mental Health and National Institute on Drug Abuse.

Chair: Dr Christina Perry

Early Career Researcher Network Plenary Award

ECRN Speakers

Mr Xavier Maddern – The Florey Institute of Neuroscience and Mental Health

Sex differences in the role of the neuropeptide cocaine- and amphetamine-regulated transcript in binge drinking

Binge drinking is the most common form of alcohol misuse and is the strongest predictor of the future development of alcohol use disorder. Despite this, the neurobiological mechanisms underpinning binge drinking, and potential sex differences in these, remain poorly understood. The neuropeptide cocaine- and amphetamine-regulated transcript (CART) has previously been implicated in reward, stress and other alcohol-related behaviors, but has not yet been investigated in the context of binge drinking. Thus, we conducted a series of experiments to determine whether CART is involved in binge drinking, and if so, whether there are sex differences in this role.

Dr Sidhant Chopra – Orygen, Parkville, Victoria, Australia; Centre for Youth Mental Health, The University of Melbourne, Melbourne, Victoria, Australia

Linking synapses, cells and systems to unravel the neurobiology of psychosis

Evidence from post-mortem, genetic, and pre-clinical studies suggests that synapse loss is key to the pathophysiology of psychosis in some individuals. Advances in molecular imaging now allow *in vivo* quantification of synaptic density, enabling tests of the synaptic hypothesis in living brains. I will present data from the largest patient study using synaptic density imaging. By combining this data with *ex vivo* transcriptomic cell typing, and *in vivo* imaging of neurotransmitter systems, we unpack the cyto- and chemo-architectonic vulnerabilities underlying synaptic pathology. Finally, using these data to build network-based simulations, we track the spatiotemporal dynamics of this process, opening the door to strategies to prevent or curtail synaptic pathology.

Chair: Dr Samara Walpole

Symposia Abstracts

Symposium 1. Decoding the Female Brain: Exploring Women's Health in Psychiatry

Understanding the unique biological underpinnings of women is essential for advancing psychiatry. Historically, research has predominantly focused on male subjects, leading to significant gaps in our understanding of how sex-specific factors influence mental health. Women exhibit distinct patterns in the prevalence, and symptomatology of psychiatric disorders compared to men, as well as response to treatment. Yet, these nuances are often overlooked or generalised from male-focused research findings.

This symposium seeks to address this critical gap by exploring the importance of women's biology across several facets of neuropsychiatric disorders. We will feature 4 expert speaks and 2 discussants who share a common goal to improve women's health. PhD candidate Mr Maddern (Florey) will discuss sex differences in alcohol use; Prof. Graham (UNSW) will speak about the influence of pregnancy on anxiety; A/Prof. Hill (Monash University) will speak on female specific risk genes for psychiatric disorders; Dr Mu (HER Centre) will discuss menopausal depression in a clinical population of women and the potential for new treatments.

Our symposia is a celebration of diverse perspectives, embracing voices from varied backgrounds and scientific expertise. We originate from four institutes across two states, with majority female presenters, we include 3 ECRs (inc. 1 PhD student), and underrepresented individuals (inc. LGBTQIA+). Our values and this proposal align with the core of BPA, in the importance of diversity, equity and inclusion. This symposium aims to close the gender health gap in neuropsychiatric disorders and promote effective approaches to prevention, diagnosis, and treatment of psychiatric disorders in women.

Chairs and Discussants: Dr Leigh Walker (Florey Institute) and Dr Robyn Brown (The University of Melbourne)

Mr Xavier Maddern, Florey Institute of Neuroscience and Mental Health

Biography: Xavier is a final year PhD candidate at the Florey Institute of Neuroscience and Mental Health in the Addiction Neurobiology Lab, supervised by Dr. Leigh Walker, Dr. Erin Campbell and Prof.Andrew Lawrence. His work focuses on investigating sex differences in the underlying neurobiology of alcohol use and misuse behaviours using translationally relevant rodent models. To date, Xavier has published 5 first authored articles (3 original articles) and presented his research at national and international conferences (BPA, ANS, HNNA, IBNS, CINP). His contribution to the field has been recognised by several prestigious awards including the Harold Mitchell postgraduate fellowship (2023), an International Behavioural Neuroscience Society postgraduate travel award (2023), and a Florey Postgraduate Travel Award for Neuroscience (2022). He is also currently a member of the BPA ECRN committee as part of the media team.

Abstract: Binge drinking is the greatest predictor of the future development of alcohol use disorder. Previously, most studies investigating alcohol use and misuse have excluded female subjects, despite known sex differences in alcohols neurobiological effects. Here, we examined sex differences in neuronal activation throughout the brains of mice in response to 1) voluntary binge alcohol consumption, 2) the expectation of alcohol or 3) alcohol naïve controls. Following tests, we performed whole-brain Fos-protein immunohistochemistry, with quantification of Fos-protein nuclei across 46 brain regions. We found reduced Fos-protein expression in female, compared to male, alcohol naïve mice across several regions, including the ventral tegmental area. Binge drinking increased Fos-protein expression in numerous regions, including the Edinger Westphal nucleus, whilst decreased expression in the nucleus incertus and ventrolateral medulla in both sexes. Interestingly, there was a Sex x Treatment group interaction in the basolateral amygdala, with a sex-specific increase in Fos-protein expression in the female binge drinking compared to

the alcohol naïve group. Inter-regional correlations revealed both basal differences in correlation coefficients, and differential patterns of Fos expression following alcohol consumption. These data highlight sex differences in Fos-protein recruitment in discrete brain regions and differential patterns of Fos expression following alcohol intake between sexes. Further, we have identified the basolateral amygdala as a key region of importance. Future studies will examine sex differences in the functional involvement of the basolateral amygdala in binge drinking which will provide greater insights into the factors driving alcohol use in females.

Prof Bronwyn Graham, University of New South Wales

Biography: Professor Bronwyn Graham is a clinical psychologist and behavioural neuroscientist at UNSW. Bronwyn's research examines how female-unique factors, like fluctuating sex hormones and pregnancy, impact women's mental health. She employs a cross-species translational methodology, in which she first investigates the hormonal regulation of behaviour in non-human animals, and then tests the application of these findings in clinical populations. Bronwyn has held numerous fellowships, including an ARC DECRA, a UKbased MQ Fellowship, an American Australian Association Neurological Fellowship, and she has received continuous funding from the ARC since 2014. Bronwyn's awards include a Psychological Science 'rising star', a NSW Young Tall Poppy, and the Biological Psychiatry Australia Aubrey Lewis Award (2020). Bronwyn regularly appears in the media and she disseminates her findings to health professionals through collaborations with organisations including Anxiety UK and Black Dog Institute.

Abstract: Pregnancy causes widespread changes to the brain that support maternal behaviour, but also impact other functions, including threat-defensive systems. Given females have a twice greater lifetime risk for anxiety disorders than males, and most females experience pregnancy, understanding how the maternal brain regulates anxiety is theoretically and clinically important. In this talk, I will present a series of studies illustrating how pregnancy fundamentally changes the neurobiological mechanisms of fear extinction, which forms the basis of exposure therapy, the first-line treatment for anxiety disorders. In all experiments, nulliparous (virgin) and primiparous (one prior pregnancy) female rats received fear conditioning (noise CS paired with shock; CS-elicited fear increases) followed by extinction training (CS presented alone; CS-elicited fear decreases), and test for extinction retention (CS presented alone; CS-elicited fear reflects the consolidation or retrieval of extinction training). Across different experiments, we applied pharmacological inactivation of amygdala subregions (BLA and CeA), and systemic pharmacological manipulations (benzodiazepines, SSRIs, NMDA receptor antagonists) to compare the neurobiological mechanisms of fear extinction in primiparous and nulliparous rats. Results highlight that post-pregnancy, fear extinction is resistant to psychotropic augmentation, NMDAindependent, BLA-independent, and relapse-resistant, suggesting a shift to non-learning based mechanisms. Yet, post-extinction benzodiazepines disrupt extinction retention in primiparous rats, suggesting memory consolidation is involved – but that the mechanisms of memory formation must be different after pregnancy. In combination, these findings illustrate that current models of memory and fear extinction, which are predominantly based on males, must be expanded to adequately represent the female brain.

A/Prof Rachel Hill, Department of Psychiatry, Monash University

Biography: A/Prof. Hill leads a multi-disciplinary program that spans the translational continuum, combining advanced neuroscience techniques with molecular biology, human clinical genomics and clinical trials. Her program explores both genetic and environmental risk factors associated with schizophrenia to identify biological pathways to target for therapeutic application. Following this pipeline, her program, transitioned two compounds from pre-clinical research to phase 1 clinical trial for psychosis-related disorders, suggestive of highly translational research. A/Prof. Hill completed her PhD in 2007 in biochemistry at Monash University and began postdoctoral training in neuroscience at The Burnham

Institute, California, before accepting a NHMRC early career fellowship at the Mental Health Research Institute (now Florey Institute). In 2014, A/Prof. Hill became an independent group head at the Florey Institute for Neuroscience and Mental Health, and in 2016 was recruited to Monash University, Department of Psychiatry to head the Behavioural Neuroscience program and was appointed Associate Professor in 2021. Since completing her PhD she has held continuous NHMRC fellowships (early career and career development) and Project/Ideas grants (GNT2029668, GNT2000893 (CIA), GNT20001907, GNT1144887, GNT1044887 (CIA), GNT1044777, GNT1004129) as well as internationally funded clinical trial grants (Stanley Medical Research Foundation, Co-PI, Monash Health site coordinator) grant support totalling over $6 million. She currently holds the Alan and Kate Gibson Foundation fellowship. She has made significant contributions to the fields of neuroscience, and psychiatry as demonstrated by her high quality / high throughput publication record (>70 pubs, >2800 citations, h-index 30).

Abstract: Sex differences in age of onset, symptom presentation and course of illness of schizophrenia suggest sex-specific aetiologies should be explored. While sex hormones can undoubtedly modify both the onset and presentation of schizophrenia, sex chromosome genes are also likely to contribute to sex-specific presentations. We recently identified a missense mutation in an X chromosome gene called ARX in a female with schizophrenia. Previously identified ARX mutations cause sex-specific presentations with males showing severe phenotypes of intellectual disability and epilepsy, while females present with milder disorders such as 28 / 29 autism or schizophrenia. This led us to hypothesise that the ARX gene may be female-specific risk gene for psychiatric disorders. To further investigate the specific mutation that we identified we generated a mouse carrying this mutation called the ArxR264Q mouse. Here, we report female, but not male ArxR264Q mice show interesting social behaviours whereby they are more interested in both familiar and novel mice than WT littermates. World-first in vivo neural network activity data simultaneously time stamped to social behaviour demonstrate reduced gamma frequency power from the prefrontal cortex of ArxR264Q female mice specifically when interacting with other mice. Sex-specific cellular phenotypes were also uncovered with female ArxR264Q mice showing reduced but males showing increased density of GABAergic interneuron subtypes in the prefrontal cortex. Overall, the study uncovers striking sex-specific cellular, neural network and behavioural phenotypes caused by the ArxR264Q mutation that align with our hypothesis that the Arx gene may be a female specific risk gene but for disorders of social function.

Dr Eveline Mu, HER Centre Australia, Monash University

Biography: Dr Eveline Mu is a research fellow and manager at HER Centre Australia, Monash University. She completed her PhD in Neuroscience at Swinburne University of Technology in 2021, focusing on the underlying mechanisms of emotional processing in the autistic phenotype. Eveline is an interdisciplinary neuroscientist, bridging cognitive neuroscience and clinical psychiatric research. Her research primarily centres on women's mental health, encompassing premenstrual dysphoric disorder, the effects of hormonal contraception on mood, psychotropic use during pregnancy, menopause-related mental health, and complex trauma disorders. She is also particularly interested about identifying trauma biomarkers using techniques such as EEG and eye tracking. Currently, Eveline serves as the co-chair of the Monash University's School of Translational Medicine EMCR committee and is actively engaged in various other EMCR committees nationally, including the BPA EMCR committee. Her research efforts are supported by prestigious MRFF and philanthropic research funding grants, enabling her to advance critical studies in mental health and neuroscientific understanding.

Abstract: Depressive symptoms are common in women in their mid 40's to early 50's. Women in mid-life (45-54 years of age) have the highest rates of recurrent depression of all women and women with no previous history of depression in this age group, are between 2-4 times as likely to experience depression in the menopause transition compared with younger and older women. Related to the increased depression rates in middle-aged women, is the tragic statistic that the highest completed suicide rates in women in

Australia in 2021 are in women aged 45-49. Women in this important middle part of their lives face many challenges that have major psychological impacts. However, a critical factor in the development of depression for the first time or exacerbation of previous depression – is the impact of menopause. This important ‘tipping factor’ is often overlooked by clinicians and women experiencing depression, which leads to inadequate treatment and poor outcomes. In my discussion, I will delve into the ongoing debate surround menopausal depression, explore available data on the efficacy of menopause replacement therapy, and present preliminary findings regarding the potential benefits of bazedoxifene combined with conjugate estrogen in addressing menopausal depression.

Symposia Abstracts

Symposium 2 – Therapeutic innovations for psychiatric disorders

Despite mental health disorders ranking among the top causes of years lived with disability, progress in developing effective treatments has faced obstacles ranging from treatment efficacy and resistance to limited funding. This symposium addresses these challenges head-on, spotlighting four researchers\' pioneering efforts to revolutionise mental health treatment. This symposium will showcase innovative strategies poised to reshape the mental health treatment landscape. The Speakers will delve into groundbreaking research, uncovering precise therapeutic targets crucial for effective mental health interventions. Innovative approaches harnessing stem cells and genomic insights to repurpose existing medications were employed, offering new avenues for efficacious treatments. These research projects yielded insights into new strategies aimed at overcoming treatment resistance barriers, paving the way for improved patient outcomes and enhancing their quality of life. These researchers strive to bridge gaps in mental health treatment, driving forward a vision of comprehensive and effective treatments.

Chairs and Discussants: Bruna Panizzutti (Deakin University) and Alex Cristino (Griffith University)

Prof Murray Cairns, The University of Newcastle

Biography: Murray is an NHMRC Leadership Fellow at the University of Newcastle's College of Health, Medicine and Wellbeing. Murray is the head of the Precision Medicine Laboratory in the School of Biomedical Sciences and Pharmacy. Murray has used his expertise in bioinformatics to establish an internationally recognised laboratory specialising in complex trait genomics. Murray is a leader in genetically informed precision medicine and is developing transformative approaches to address the problem of heterogeneity in the treatment of complex disorders. Murray is collaborating with international colleagues and other research laboratories to drive the discovery of genetic variations associated with various psychiatric and neurological disorders. Murray has been awarded over $25 million in research grants, filed 24 patent applications, supervised more than 30 Research Higher Degree students and has over 200 career publications including highest-ranking journals such as Nature, Science, Cell, Nature Biotechnology, Nature Reviews Genetics, Nature Genetics, Nature Neuroscience, Nature Communications, Science Advances, Circulation, Molecular Psychiatry, American Journal of Psychiatry, American Journal of Human Genetics, Biological Psychiatry, Schizophrenia Bulletin, American Journal of Pathology, and Pharmacology Reviews. Collectively, these publications have attracted more than 26,000 citations and highlight a significant international reputation in psychiatric genetics, functional genomics and precision medicine.

Abstract: Psychiatric disorders are complex traits that arise from a heterogeneous mixture of genetic and environmental risk factors. While large scale epidemiological approaches, including genome-wide association studies, are fractionating and quantifying these influences at the population level, we ultimately need to look at how these manifest within the molecular fabric of individuals and use this information to specifically design therapeutic interventions. To address this challenge, characterised by extreme levels of heterogeneity, we have implemented an approach that exploits systems biology, chemoinformatics and pharmacology to aggregate genetic burden of complex traits into clinically actionable pathways. When applied to psychiatric conditions, such as schizophrenia and bipolar disorder, we identified several existing compounds that could be directed with more biological specificity to patients with higher levels of risk in these pathways. While some of these compounds have been tested in the clinic, or are under investigation for use in psychiatric disorders, many are approved for use in other conditions and have not been considered in the context of psychiatric treatment. This approach has the potential to provide a mechanism for precision intervention, particularly in difficult treatment resistant cases. To refine this model, we are

exploiting causal inference and transcriptomics to map the functional components of these pathways and investigate the influence of environmental exposures. We are also developing patient-specific organoid models of precision medicine that we can use to test the inter-individual effect of experimental therapeutics ahead of trials of genetically informed interventions in the clinic.

Dr Jiayue-Clara Jiang, The University of Queensland

Biography: Dr. Jiayue-Clara Jiang is a postdoctoral research fellow at the Institute for Molecular Bioscience, the University of Queensland. Clara's research focuses on using genomic and transcriptomic analysis to investigate the genetic basis of cardiovascular and psychiatric disorders, with a particular focus on female health, as well as using statistical genomic approaches to explore possible opportunities for drug repurposing. Clara graduated from the University of Queensland with Bachelor of Advanced Science (First Class Honours) in 2017, and was awarded the University Medal. Clara was awarded her PhD at the University of Queensland in 2021, where she utilised bioinformatic approaches and molecular experiments to decipher the genetic aetiology of breast cancer, specifically the regulatory role of transposons or 'jumping genes' in modulating the transcriptional landscape in the cancer state. Clara is also a UQ Wellness ambassador and an advocate for promoting equity, diversity and inclusion in academia.

Abstract: Drug repurposing represents a cost-effective approach to identifying new treatments for depression. Observational studies and randomised controlled trials have reported inconsistent findings on the anti-depressive effects of cholesterol-lowering statins, which are commonly used cardiovascular medications. In this study, we investigated this gap using genomic approaches, namely transcriptional signature matching and Mendelian randomisation (MR). Using the Connectivity Map database, we directly compared the gene expression signatures from human cell lines treated with statins and antidepressants. Compounds inducing highly similar gene expression responses to statins (indicated by an average connectivity score with statins > 90) were found to be enriched for antidepressants. Pathway enrichment analysis showed concordant impacts by the two drug classes on diverse biological and metabolic pathways, as well as various immune and inflammatory pathways. We performed MR to explore the association of genetically predicted HMGCR inhibition (the primary target of statins) with depression risk and related symptoms. MR analysis did not identify any significant associations between HMGCR inhibition and depression risk or symptoms after multiple testing correction, but identified extensive associations with changes in monocyte and platelet-related traits, both of which were previously linked to depression. Analysis of the off-target effects of statins indicates that statins could potentially modulate diverse immune phenomena via both on and off-target (via ITGAL inhibition) effects. Our findings suggest that statins induce antidepressant-like gene expression responses in human cell lines, and can potentially confer anti-depressive effects by modulating immune pathways. Our findings warrant further investigation on the effects of statins in alleviating depressive symptoms.

Dr Bruna Panizzutti, Deakin University

Biography: Dr Panizzutti is an early-career researcher, currently based at the School of Medicine, Deakin University, as a Research Fellow. Dr Panizzutti obtained a PhD in Psychiatry and Behavioural Sciences from Universidade Federal do Rio Grande do Sul, Brazil (March 2016). Panizzutti’s research is focused on understanding the underlying pathophysiology of mental disorders in a comprehensive range of systems, from cell and animal models to clinical trials. With 10 years of experience in the laboratory and expertise in a range of methodologies, Dr Panizzutti has made significant contributions to the basic knowledge behind mood disorders, collaborating on 37 publications with >730 citations and an h-index 15. Dr Panizzutti has received several internal grants (>$70,000) that have funded the initial steps of recruiting and generating iPSCs from people with bipolar disorder and healthy controls. She has extensive experience and knowledge of stem cells as a result of her time as interim manager of a facility dedicated to developing and

characterising stem cells from different sources. In the past 3 years, Dr Panizzutti has led the stem cell lab at Deakin University, managing 2 post-docs and 2 ROs across various projects.

Abstract: Bipolar disorder (BD) poses significant medical challenges, with complex treatments and inadequate patient responses underscoring the pressing need for new therapeutic approaches. Our study introduces an innovative drug discovery platform that harnesses an in vitro model system derived from adult stem cells of BD patients, offering a unique opportunity to delve into BD pathophysiology in cells that mirror individual genetic backgrounds. Moreover, the Gene Expression Signature (GES) platform overcomes the lack of defined molecular targets for BD therapeutics. Therefore, we aspire to identify potential drugs for BD repurposing through a multistep analysis, potentially revolutionising the field of psychiatry and drug development. Our preliminary in silico analysis has identified compounds with the potential to be repurposed to treat BD. These include drugs currently or previously used to treat depression and/or anxiety, but also novel candidates for repurposing, including diclofenac (anti-inflammatory), resveratrol (antioxidant) and nemonapride (dopamine receptor antagonist). These drugs have either preclinical or clinical published evidence for potential antidepressant and/or anxiolytic activity. In addition, gene set enrichment analysis (GSEA) highlighted dysregulated pathways in BD, implicating cell signalling, fatty acid metabolism, and ribosome/protein synthesis pathways. These findings underscore the potential of drug repurposing for BD treatment, validated by mechanistic pathway analyses aligning with established drug mechanisms. Further investigations encompassing pharmacoepidemiology, mendelian randomisation, and behavioural studies will refine drug 19 / 29 selection for subsequent clinical trials in BD patients. This study contributes valuable insights into BD pathophysiology and drug repurposing strategies, paving the way for tailored treatments and continued exploration of this complex psychiatric disorder.

Adjunct Professor Dan Siskind, The University of Queensland

Biography: Prof Siskind is trained as a psychiatrist in Australia and the United States. Graduating from medicine at the University of Queensland in 1998, Prof Siskind worked with Doctors Without Borders in Chechnya in 2000, sparking an interest in psychiatry. In 2002, Prof Siskind moved to Boston for a psychiatry residency at Boston University and completed a Master of Public Health at Harvard University. Returning to Brisbane in June 2008, Prof Siskind became a clinical academic psychiatrist at the Metro South Addiction and Mental Health Service and completed a Ph.D. in February 2014. Research interests include clozapine and treatment refractory schizophrenia, the physical health of people with severe and persistent mental illness, supported accommodation, assertive community treatment, and mental health services research. Awarded an NHMRC Investigator Grant as an Emerging Leadership Fellow (2021-2025) and holding an NHMRC Early Career Fellowship (2016-2019), Prof Siskind currently has a CIA MRFF RCRDUN grant for reducing cardiometabolic morbidity in people with schizophrenia. With over 200 peer-reviewed publications, including first authorships in top journals like Lancet, World Psychiatry, and Lancet Psychiatry, Prof Siskind is a named investigator on over $40 million in competitive research grants, with over $6 million as CIA.

Abstract: Dan Siskind's presentation will focus on cutting-edge research strategies aimed at managing treatment-resistant schizophrenia. The presentation will discuss novel approaches, including pharmacological and therapeutic interventions, informed by his deep understanding of the underlying mechanisms contributing to treatment resistance. Specifically, novel trial approaches, including adaptive platform trials in schizophrenia that will improve trial efficiencies and allow testing of more agents for augmentation for clozapine resistant schizophrenia. Promising agents include cannabidiol, pimavanserin, cariprazine and trimetazidine. He will also look at the role of GLP-1RAs for managing antipsychotic induced weight gain, and provide an overview of recent clinical trial evidence. His insights promise to advance our understanding and management of this complex psychiatric condition.

Symposia Abstracts

Symposium 3 - New targets for alcohol use disorder treatment

The health burden and socioeconomic impacts of alcohol misuse are astounding. Annually, 2.4 million deaths globally are attributed to alcohol use disorder (AUD). These deaths are largely preventable. However, attempts to develop effective medications for the treatment of alcohol use disorder over the last 20 years have been unsuccessful. Thus, there is urgent need for improved therapeutic strategies.

In this symposium we explore recent insights into novel targets for the treatment of AUD. Across preclinical animal models and in work involving rodent and human imaging, our speakers will present recent research focusing on serotonin2C receptor positiveallosteric modulators (Campbell), the HCN channel inhibitor ZD7288 (Anversa), fibroblast growth factor 21 (FGF21) (Millan), and Nacetyl cysteine (NAC) on alcohol cues (Logge).

Our symposium brings together a diverse team in terms of gender (60% female), career stage (80% early-mid-career researchers and 20% senior researchers), and ethnicity (including representation from Australasia, South America, Philippines). We have speakers from four different institutions (Florey Institute, University of Newcastle, UNSW and University of Sydney) across two States. Our discussant is an established leader in treatments for mental health disorders with experience spanning the preclinical field to clinical feasibility studies. Speakers represent a broad mix of research backgrounds including behavioural neuroscience, psychology, pharmacology and clinical addiction medicine. Importantly, our chair is a female ECR and member of the Florey Equity in Science Committee.

Our symposium aims to inspire discussion around preclinical and clinical research on novel neuropharmacotherapies for AUD and where the field sits regarding informed treatment strategies.

Chairs and Discussants: Dr Roberta Anversa (Florey Institute of Neuroscience and Mental Health) and Dr Christopher Dayas (The University of Newcastle)

Dr Erin Campbell, The University of Newcastle

Biography: Erin Campbell is a DECRA Research Fellow at The University of Newcastle where she leads projects focussed on dissecting the brain circuitry underlying reward-seeking behaviours including relapse to alcohol use. Erin has published 36 peer-reviewed journal articles and one book chapter. 64% of these are as first/senior author published in Q1 scientific journals including The Journal of Neuroscience (ranked first in the field of neuroscience for citations) and Neuron (impact factor 16). Erin publishes in the fields of preclinical behavioural neuroscience and neuropsychopharmacology, with her recent research on alcohol use disorder resulting in two clinical pilot studies. Erin has a field weighted citation impact of 1.5 (Scopus) and an H-index of 20 (Scholar). Erin's national/international standing is recognized by invitations to present at 2 national and 6 international conferences including the International Society of Addiction Medicine. Erin has also been awarded 2 prestigious international prizes including an International Society for Biomedical Research on Alcoholism Young investigator Award. Finally, Erin has secured over $1.4 million in competitive research funding including ARC, NHMRC, Brain & Behavior Research Foundation, University of Melbourne and philanthropic funding.

Abstract: Alcohol misuse is one of the leading causes of preventable death in Australia. Alcohol use disorder is a relapsing brain condition that persists for life. Even with treatment, up to 75% if individuals with alcohol use disorder return to drinking (relapse) after a period of recovery. Attempts to develop effective pharmacotherapy over the last 20 years have been unsuccessful. This is perhaps in part driven by the overarching strategy to 'forward translate' findings from animal models to the clinic to identify the

neurobiological substrates underlying relapse. Here we will present data where we used a 'reverse translational' approach, taking findings from successful studies in humans back into animal models. In humans, we found that the serotonin2C receptor was critical for alcohol craving. However, selective medications targeting this receptor often result in adverse effects. In this study, we tested emerging serotonin2C-based treatment (positive-allosteric modulators) that retain efficacy while minimising long-term off-target effects. We trained male and female mice to self-administer 10% alcohol for 15 days. We then exposed mice to voluntary abstinence induced by 1 / 29 an electric foot shock. Finally, we tested the effect of two serotonin2C receptor positive-allosteric modulators on relapse-like behaviour. We saw no significant effect of serotonin2C receptor positive-allosteric modulation on relapse-like behaviour. Future research will investigate the anatomical distribution of serotonin2C receptor involvement in relapse to alcohol use.

Dr Roberta Anversa, The Florey Institute of Neuroscience and Mental Health

Biography: Dr Roberta Anversa is a research fellow at the Florey Institute. Her work explores novel treatments for alcohol and nicotine misuse. She uses multiple cutting-edge approaches including genetic, neuropharmacological, viral and physiological tools to observe and manipulate brain circuits and investigate how they underlie complex behaviours. She completed her PhD in Neuroscience in November 2021 at the University of Melbourne. Roberta has led many research projects and has already secured two research grants (~200k) as sole CI despite her early career stage. Relative to opportunity, Roberta's research outputs have been notable. She has published 9 original research articles in the field of neuroscience and pharmacology (5 as first author), 2 book chapters, and has 4 manuscripts currently under revision in Q1 journals (including British Journal of Pharmacology and Neuropsychopharmacology). Moreover, Dr Anversa holds 2 patents for describing the pharmacological properties of 2 different organic compounds, showing her contribution to translational research. Roberta has a strong track record with science outreach and community engagement. She is a am a member of the Florey Institute's Equality in Science committee, where she is committed to assist in providing equality, inclusion, and diversity in the workplace. Some of her other volunteer roles include Mental Health PhD Program (MHPP) Event Coordinator, mentorship of 2 Florey PhD students, and mentor at the In2Science mentoring program at Melbourne Girl's College, where she mentored school students in STEM.

Abstract: Cholinergic neurons in the medial habenula (MHb) are implicated in the modulation of stress, aversion and drug addiction related behaviors such as excessive drug intake and withdrawal. These neurons densely express pacemaker hyperpolarization-activated cyclic nucleotide-gated cation channel 4 (HCN4) and activity of these channels might contribute to the expression of symptoms of alcohol withdrawal and/or relapse. This study aimed to investigate the involvement of HCN channels in driving alcohol intake in alcohol preferring iP rats. We examined the expression of HCN4 channels in MHb cholinergic cells with RNAScope in-situ hybridization in male and female rats. Functional characterization of this channel in cholinergic neurons was assessed by patchclamp recordings of brain slices with bath-applied ZD7288. Lastly, we examined in vivo the role of HCN channels in the alcoholdeprivation effect following voluntary drinking by micro-injecting ZD7288 in the brain. More than 94% of HCN4-positive cells in the ventral MHb were ChAT-positive and co-expressed vGlut1 and VGlut2. Consistent with these data, bath application of ZD7288 significantly reduced the firing frequency of MHb cholinergic neurons. Acute i.c.v injection of ZD7288 (3ug/5ul) significantly attenuated the alcohol deprivation effect following 14 days of abstinence with no effect on spontaneous locomotor activity. Our data suggest a role for HCN channels in the alcohol deprivation effect and our current studies are examining a potential role for the MHb and related circuitry underlying this behaviour.

Dr Zayra Millan, University of New South Wales

Biography: Zayra Millan is a Lecturer at the School of Psychology, University of New South Wales. Her research program spans across neuropharmacology, cognitive models of decision-making, associative learning, as well as direct stimulation of brain circuits to curb alcohol drinking. As an index of her developing leadership in research, she has been successful in research funding nationally and internationally. She is a Chief Investigator on current NHMRC funding totalling >$6M (Synergy and Ideas) and previously has received international funding from the NARSAD Behavior and Brain Research Foundation. She is currently leading research projects focused on in vivo cellular imaging during motivational conflict and also on understanding the therapeutic potential of FGF21. Through international collaborations with researchers at Duke University, she has a pending patent (under review) that has emerged from this latter work. Zayra did her Combined Masters in Psychology (Clinical) and PhD at the University of New South Wales. During her clinical training she worked with individuals seeking treatment for alcohol drinking and studied brain circuits of relapse in animal models. She completed postdoctoral training at the University of California San Francisco, then at the Johns Hopkins University.

Abstract: Fibroblast growth factor 21 (FGF21) is a liver-derived peptide induced by metabolic stressors including starvation, protein deficiency and ethanol. While there has been significant interest in developing the therapeutic application of FGF21 for metabolic dysfunctions associated with diabetes and obesity, there is now emerging and increasing interest in its potential for the treatment of alcohol use disorders. Here we investigated the effects of an FGF21 analogue - PF-05231023, on measures of alcohol intake and preference, incentive properties of alcohol-associated cues, and on transient activity of individual cells in the nucleus accumbens. We used the intermittent access model to assess voluntary alcohol drinking in mice. Subsequently, a Pavlovian conditioning preparation where mice are trained to associate an auditory cue with either alcohol or sucrose to assess the effects of PF-05231023 on anticipatory behaviours (Experiment 2). Finally, a head-mounted microscope to image PF-05231023-induced changes in calcium activity in the nucleus accumbens (Acb) during alcohol drinking (Experiment 3). We found that PF-05231023 significantly attenuated voluntary alcohol intake in a dose-selective manner in males but not females. Conversely, it attenuated the frequency of alcohol cue-elicited approach in females but not males. Finally, we identified, quantified and mapped the transient activity profile of cells that encoded drinking bouts in the Acb prior to and following PF-05231023 treatment. Data analysis is ongoing. Our current studies are investigating the effects of diet on the potency of FGF21, and on the combined actions of FGF21 and GLP1.

Dr Warren Logge, University of Sydney

Biography: Dr Warren Logge is an early career Research fellow at the University of Sydney and heads the Acute Psychopharmacology and Psychophysiology Laboratory in Addiction Medicine and the Royal Prince Alfred Hospital. His research focuses on neurocognitive mechanisms underlying addictive disorders and evaluating neural and psychophysiological biomarkers of cue-elicited brain responses in addictive disorders, including assessment of treatment outcomes. He applies multimodal neuroimaging and psychophysiological approaches to investigate new treatments for alcohol use disorder implementing novel psychophysiological and neuroimaging paradigms in clinic and simulated bar environments. Warren has 28 publications—12 specific to neuroimaging and psychophysiological research in alcohol problems in the last 3 years—an H-index of 13, and over 800 citations. Warren is an emerging leader using neuroimaging and psychophysiological techniques to examine mechanisms and predictive biomarkers of addictive disorders which has been recognised with 4 invited international presentations, and an invited plenary at a national conference. He is an AI as neuroimaging expert for a multicentre, multidisciplinary Synergy grant investigating novel treatments for alcohol use disorder.

Abstract: N-acetyl cysteine (NAC) shows promise as a pharmacotherapy for alcohol use disorder (AUD). However, its effects on neural activation to alcohol cues and intrinsic functional connectivity remain unclear.

This study examines whether NAC can reduce i) alcohol cue-elicited brain activation, and ii) intrinsic functional connectivity, in comparison to a placebo in AUD patients. Twentythree individuals with moderate-severe AUD were administered either daily NAC (2400 mg/day, n = 9) or a placebo (n = 14) for a minimum of two weeks. Participants underwent functional magnetic resonance imaging (fMRI) before (T0) and after treatment (T1), which included resting-state and visual alcohol cue reactivity tasks. Activation differences between sessions, treatment, and sessionby-treatment interaction were assessed. Resting-state functional connectivity was assessed using 377 node ROI-to-ROI analyses to determine if NAC reduced intrinsic connectivity post-treatment. No significant differences were found in alcohol cue reactivity for brain activation or subjective craving between the NAC and placebo groups during treatment or across sessions, and there was no significant interaction effect. However, a significant treatment-by-time interaction was observed, showing reduced intrinsic connectivity after treatment (T1) in NAC-treated patients compared to placebo. This reduction was seen in the posterior cingulate node (9, left hemisphere) of the dorsal attentional network and its connections to salience, ventral-attentional, somatosensory, and visual-peripheral networks implicated in AUD. Our findings suggest that NAC may reduce intrinsic functional connectivity in patients with moderate-severe AUD after treatment, although it does not appear to affect alcohol cue-elicited brain activation, indicating a potential neurobiological effect of NAC in AUD.

Symposia Abstracts

Symposium 4 - Exploring the biology underlying physical comorbidities of neuropsychiatric disorders using genomics

Individuals with a neuropsychiatric disorder are at increased risk of also being diagnosed with diseases that primarily impact organs in the periphery, such as cardiometabolic disease. This greater burden of comorbidities has a clear negative impact on long term outcomes in psychiatry. Explanations for this increased prevalence of physical comorbidities in neuropsychiatric disorders include medication effects, lifestyle factors, and systematic barriers to accessing care. However, there is also compelling evidence for shared biology between mental health and disorders of the periphery. Genomics has emerged as an important tool to explore the biological and clinical implications of shared risk between neuropsychiatric disorders and physical comorbidities. Here, we will outline how genomics is being used to answer clinically important questions related to the biological overlap between neuropsychiatric disorders and peripheral diseases. Dr Dylan Kiltschewskij and Dr David Stacey will both describe how genetics can be integrated with epigenetics/RNA-sequencing to identify pathways that may underlie shared risk for schizophrenia with cardiometabolic and autoimmune diseases, respectively. Prof Gillian Blue will discuss how ultra-rare genetic variants causing congenital heart disease also have neurodevelopmental manifestations. Dr William Reay will present evidence for a genetic overlap between psychiatric disorders and acne, and the implications of this for retinoid pharmacotherapies. A/Prof Janice Fullerton, as discussant, will synthesise how these diverse genomic approaches are useful to study physical comorbidities in psychiatry. Diversity: Gender (3 male speakers, 2 female), geographic (three states represented), career stage (ECRs, MCRs, and senior researchers represented), and institution (5 different institutions)

Chairs and Discussants: Dr William Reay (University of Tasmania), and A/Prof Janice Fullerton (NeuRA)

Dr Dylan Kiltschewskij, University of Newcastle

Biography: Dr Dylan Kiltschewskij is a Post-doctoral Research Fellow within the Centre for Complex Disorders and Precision Medicine at the University of Newcastle. His doctoral research investigated the dynamics of post-transcriptional regulation in neuronal cells by integrating multiple unique RNA sequencing strategies. Dr Kiltschewskij has since transitioned to statistical (epi)genetics, applying bioinformatic and statistical analyses to psychiatric conditions. In particular, he has a strong interest in elucidating (epi)genetic contributions to individual-to-individual heterogeneity that can be leveraged for precision medicine. Dr Kiltschewskij is particularly interested in using (epi)genetic data to better understand the relationship between cardiometabolic traits and psychiatric illness to improve cardiometabolic health in this population.

Abstract: Individuals with a mental health condition experience a staggering 80% higher risk of premature death due to cardiovascular disease compared to the general population. These conditions are often intertwined with elevated rates of metabolic syndrome in this population, thought to originate from lifestyle factors, adverse effects of psychotropic medications and poorer access to medical care. We have recently uncovered multiple lines of (epi)genetic evidence indicating the presence of a novel biological relationship between mental health and cardiometabolic traits that could drastically improve our understanding of this comorbidity. Using public DNA methylation data, we have identified patterns of epigenetic heterogeneity in schizophrenia that affect genes associated with fatty acid metabolism in the blood and post-mortem brain. Furthermore, we observed correlated patterns of DNA methylation between schizophrenia and cardiometabolic traits including body mass index, fasting glucose, fasting insulin and type II diabetes,

suggesting the presence of shared epigenetic architecture. Similar patterns of epigenetic correlation were observed between these cardiometabolic traits and features of schizophrenia such as cognitive deficits, treatment resistance and symptom severity, as uncovered amongst 381 individuals from the Australian Schizophrenia Research Bank. Overall, these findings broadly support genetic correlation and causation between a panel of 50 circulating metabolic biomarkers, psychiatric conditions and human cortical anatomy, wherein we have identified strong evidence suggesting C-reactive protein, an inflammatory biomarker intertwined with metabolic signaling, impacts mental health and brain structure. Together, our findings provide evidence for shared (epi)genetic biology between cardiometabolic traits and mental health with potential significance for clinical management.

Prof Gillian Blue, Westmead Children's Hospital/USyd

Biography: Prof Gillian Blue is Head of Genetic Research at the Heart Centre for Children in Sydney. She is a Clinical Senior Lecturer at the Specialty of Genomic Medicine, The University of Sydney and a Visiting Scientist at the Victor Chang Cardiac Research Institute. She is a translational researcher with basic science, psychosocial and clinical research skills. Her primary research interest is understanding the genetic mechanisms underlying congenital heart disease using genomic technologies, as well as how congenital heart disease genetic risk influences observed comorbidities such as neurodevelopmental disorders. She has over 16 years' experience in clinical and research genetic counselling, including translation of research findings into patient care and clinical management. Gillian is also the Head of the Kids Heart BioBank, a key resource facilitating genetic research in congenital heart disease, including local and international collaborations.

Abstract: Neurodevelopmental disability (NDD) is recognised as one of the most common comorbidities in children with congenital heart disease (CHD) and is associated with altered brain structure and growth throughout the life course. This has important implications for subsequent mental health across the lifespan. Causes and contributors underpinning the CHD and NDD paradigm are not fully understood, and include innate patient factors, such as genetic and epigenetic factors, among others. Significant advances in genomic technologies over the last decade, have enabled rapid evaluation of genetic variants with a landmark study providing the first evidence of shared variants, genes and genetic pathways in both heart and brain development. Further, studies are suggestive of an additive effect in heart-expressing genes with increasing non-cardiac phenotypic complexity. Genes and genetic pathways repeatedly implicated in studies to date, include chromatin modifying and connectome genes, with both sets of genes exerting widereaching phenotypic effects, spanning multiple organ and biological systems. Most studies have focussed on the contributions of rare and de novo variants; however common variants are also implicated. Understanding genetic and biological mechanisms associated with NDD in CHD, is important in advancing the development of effective intervention strategies for those at risk.

Dr David Stacey, University of South Australia

Biography: Dr David Stacey is Research Fellow within the Australian Centre for Precision Health (ACPreH) at the University of South Australia (UniSA). Dr Stacey UniSA in March 2023 from the University of Cambridge, UK, where he was a Senior Research Associate leading the Integrative Genomics team within the Cardiovascular Epidemiology Unit. Dr Sacey is a functional geneticist interested in translating genetic discoveries into an improved biological understanding of disease, with a primary focus on psychiatric illness and cardiovascular disease. Dr Stacey initially trained as a wet lab scientist, but has since transitioned into bioinformatic and genetic epidemiological methods.

Abstract: Evidence suggests an increased burden of comorbid diagnoses of autoimmune disorders in individuals with schizophrenia (SCZ), although the precise nature of this association remains elusive. To identify shared genetic risk hat may account for this, we conducted a transcriptome-wide Mendelian

randomization study that tests the association between genetically regulated gene expression and liability to schizophrenia. This leveraged genetics integrated with mRNA expression from 29 datasets encompassing 11 unique immune cell types, all publicly available from the eQTL catalogue. These analyses highlighted 196 genes, including 67 located within the human leukocyte antigen (HLA) region. Enrichment analyses indicated an over-representation of immune-related genes, though this was driven primarily by the HLA genes. Stringent validation and replication steps retained 61 candidate genes spread across 38 independent loci. At 27 of these loci there was only a single candidate gene, suggesting these candidates are likely not confounded by horizontal pleiotropy. As an exemplar, we performed follow-up analyses focused on interferon regulatory transcription factor 3 (IRF3), which coordinates interferon responses to viral infections. We found evidence of shared genetic aetiology between schizophrenia and autoimmune diseases at the IRF3 locus, and a significant enrichment of IRF3 chromatin binding at schizophrenia risk loci. Together, our findings suggest the HLA region may be responsible for a wide range of immune perturbations not directly related to schizophrenia aetiology. They also provide support for IRF3 as a schizophrenia hub gene responsible for mediating the impact of viral infections on schizophrenia risk, and as a potential novel therapeutic target.

Dr William Reay, University of Tasmania

Biography: Dr William Reay is a research fellow in Statistical Genetics at the Menzies Institute for Medical Research at the University of Tasmania and currently holds a highly competitive NHMRC EL1 Investigator Fellowship (2024-2028). Dr Reay is motivated to use genomics and other forms of big data to better understand and treat complex human disorders. He seeks to work at the interface of discovery and translational research, with his work on genetics informed treatment selection already proceeding to current clinical trials. Through this work, Dr Reay works with many stakeholders including researchers, clinicians, and consumers across a variety of disease areas, with a particular interest in psychiatric, neurological, and cardiovascular phenotypes. Dr Reay has been a CI on almost 3 million AUD in competitive funding despite only being just over 2 years post-PhD and his work has already shown progress on the path to rapid translation. His scholarly work has been highly cited in a short time and he has led studies in some of the highest-impact journals in biomedical research including Circulation, Nature Reviews Genetics, The American Journal of Human Genetics, Nature Communications, and Science Advances.

Abstract: Acne vulgaris appears to exhibit increased prevalence amongst individuals with mental health conditions; however, much is still unknown about this relationship. Whilst psychosocial factors are likely to be involved, evidence for shared biology between these conditions is mounting, although the direction of causality remains difficult to disentangle. Genetic factors influence liability to acne and psychiatric phenotypes, facilitating estimates of shared risk and potential causal effects that are immune to reverse causality given the immutable nature of germline genetic variants. Here, we comprehensively explore shared genetic risk factors between acne and ten psychiatric disorders. Acne liability displays positive genetic correlation with risk for schizophrenia, bipolar disorder, depression, anorexia, and obsessive-compulsive disorder. Causal modelling using genetic risk variants as instrumental variables further suggested a bidirectional relationship between acne and schizophrenia liability, whereby schizophrenia genetic risk increases the odds of acne, and vice versa. Functional interrogation of shared genetic risk between acne and schizophrenia highlighted an important role of the major histocompatibility complex region, as well as signalling pathways including transforming growth-factor beta and retinoic acid receptor function. Given that retinoids are used as the primary pharmacotherapy in acne, and are implicated in the pathogenesis of schizophrenia, the influence of retinoid signalling on both disorders warrants further investigation. In summary, we present the largest genetic study of acne and psychiatric disorders to date. These data provide genetic support to increased rates of comorbid acne and schizophrenia diagnoses beyond what is directly attributable to psychosocial factors.

Symposia Abstracts

Symposium 5 - Icy Insights: Facilitating Dialogue to Advance the Treatment of Methamphetamine Use Disorder in Australia

Amidst Australia\'s methamphetamine crisis, there are no approved pharmacotherapies and limited clinical assessment models for testing new treatments. It\'s time to leverage Australia\'s clinical expertise to advance the treatment of Methamphetamine Use Disorder (MAUD). This symposium will illuminate the current MAUD landscape and discuss strategies for developing novel pharmacotherapies. Speakers will provide an epidemiological overview of MAUD, highlighting its prevalence and impact on Australian communities. We will review current interventions, from pharmacotherapy to non-pharmacotherapy approaches, and their roles in clinical practice and trials. The symposium will explore ways to enhance outcomes in MAUD trials by measuring biological markers and learning from past trials. We will discuss \"fast fail\" approaches in substance use disorder medication development and their relevance to MAUD challenges. Additionally, the symposium will spotlight KNX100, a clinical-stage therapeutic developed through an academic-industry collaboration as a transdiagnostic treatment for substance use disorders, including MAUD. The role of biological psychiatry in understanding MAUD will be highlighted, with discussions on promising biomarkers and imaging techniques to improve the translation and development of new therapies. By uniting experts from academia and industry, the symposium aims to foster meaningful dialogue and collaboration to address Australia\'s methamphetamine crisis. The symposium emphasises diversity, with male and female participants and a mix of senior, mid, and early-career researchers spanning academia and industry across various geographical locations and institutions. Rhianne Scicluna, who led and will chair the symposium, recently completed her PhD, demonstrating our commitment to supporting early-career researchers.

Chair and Discussant: Rhianne Scicluna (Kinoxis Therapeutics)

A/Prof Rebecca McKetin, National Drug and Alcohol Research Centre, UNSW

Biography: A/Prof Rebecca McKetin (BSc(Psychol)Hons, PhD) leads a program of research into stimulant use epidemiology and interventions at the National Drug and Alcohol Research Centre, UNSW. Rebecca's current aspiration is to develop and disseminate effective treatment and harm reduction options for people using methamphetamine. Her work includes developing and evaluating online psychological self-help tools, pharmacotherapy trials and evaluating community-based treatment options. She is passionate about improving the coverage of treatment and other health services for people who use methamphetamine, and she has also done much research to help understand the relationship between methamphetamine use and mental health outcomes. Rebecca has consulted to the United Nations; she is a former NSW/ACT Young Tall Poppy, a Senior Editor for Addiction, a member of the UNSW Academic Board, and a member of the Australian Institute of Policy and Science.

Abstract: Harms arising from methamphetamine use continue to grow globally, presenting major challenges to health services in many parts of the world. Sustained and comprehensive strategies are needed to reduce mortality and non-fatal harms (poor mental health, violence, injury, sexually transmitted infections and blood borne virus risk). No effective pharmacotherapies are available to help people reduce methamphetamine use. Psychosocial interventions can be effective, but impacts are modest and treatment coverage is low. Contingency management is currently the most effective treatment approach, but it has not been widely implemented. Generic approaches to address mental health and blood borne virus infection risk could be tailored to reduce harms associated with methamphetamine use. A substantial and sustained investment is needed to develop more effective interventions to reduce methamphetamine-related harms.

Dr Krista Siefried, NCCRED and St Vincent's Hospital Sydney

Biography: Krista is a clinician researcher at the National Centre for Clinical Research on Emerging Drugs (NCCRED) and St Vincent's Hospital Sydney. She is a Senior Lecturer at the National Drug and Alcohol Research Centre (NDARC) at the University of New South Wales. Krista leads a program of research and knowledge translation, to improve clinical outcomes for people living with chronic illness. She works towards understanding how therapeutic interventions can improve outcomes, particularly for people in marginalised communities.

Abstract: Methamphetamine use exists on a spectrum, and addressing harms associated with methamphetamines likewise requires consideration of this – from harm reduction through to treatment of methamphetamine use disorder, which can significantly impact individuals, families and communities. Interventions are required that address delays in treatment seeking and low treatment coverage amongst people who consume methamphetamines. This presentation will explore novel interventions under investigation in Australia. It will overview how these may support people in achieving their goals around methamphetamine consumption at different stages, including when exploring the impact of methamphetamines on their life through a smartphone application, the impact of methamphetamines on sleep, the importance of managing withdrawal from methamphetamines, and novel pharmacotherapies to achieve reduction in use or abstinence from methamphetamines.

A/Prof Gillinder Bedi, Orygen and University of Melbourne

Biography: A/Prof Gillinder Bedi is Head of Substance Use Research at Orygen and Principal Research Fellow (Addiction and Youth Mental Health) at the Centre for Youth Mental Health at the University of Melbourne. She is also a clinical psychologist at headspace, treating young people with substance use problems and comorbid mental illness. Her current research seeks to (a) understand substance use and substance use disorders (with a focus on young people), (b) develop new early interventions and treatments for problematic substance use in youth, and (c) safely leverage the potential therapeutic effects of substances that are also 'abused' (e.g., MDMA). Prior to her current research focus, she employed human laboratory methods to investigate cannabis and cocaine use disorder and to screen candidate medications for these indications.

Abstract: Human laboratory models – or experimental medicine studies – represent a translational bridge between preclinical research and clinical trials. This approach employs laboratory-based studies to model aspects of human substance use disorder in order to investigate underlying mechanisms and test candidate treatments. Screening candidate pharmacotherapies in such models can provide a rapid go/no-go signal prior to initiation of costly clinical trials. Two human laboratory models – of cannabis and cocaine use disorder – will be described, alongside a description of the different component processes of substance use disorder that can be modelled in the human laboratory. To date, human laboratory models of methamphetamine use disorder are relatively underdeveloped. Potential future uses of these approaches in the study of methamphetamine use disorder and candidate treatments will be described.

Dr Nick Everett, The University of Sydney and Kinoxis Therapeutics

Biography: Nick is a preclinical behavioural neuroscientist and psychopharmacologist at The Brain and Mind Centre, School of Psychology at The University of Sydney. Nick leads multiple research programs develop novel pharmacotherapies for currently untreatable psychiatric disorders, with a focus on translatable neurobiological mechanisms within substance use disorders and social behaviour. In his academic team funded by an NHMRC Investigator Grant, Nick is developing multiple clinically-viable strategies for targeting the peripheral and/or central oxytocin system for the treatment of methamphetamine use disorder. He is also Head of Behavioural Neuroscience at Kinoxis Therapeutics, a spin-out from USyd, in which he has led the preclinical pharmacodynamics program for the now clinical-stage small molecule KNX100 for substance use disorders, which has led to successful IND applications to the FDA, completed Phase-I safety trials, and significant funding from NIDA to develop KNX100 for the treatment of

methamphetamine and opioid use disorder (Phase-II trials soon to commence). Nick also leads a neurobiology and behaviour team in partnership with 7 / 29 Boehringer Ingelheim, to develop novel small molecule oxytocin receptor agonists for transdiagnostically improving social dysfunctions. Nick is also Head of Behavioural Pharmacology at Psylo where he leads the preclinical development of novel nonhallucinogenic 5HT2A agonists for the treatment of mood, cognitive, and substance use disorders. Nick supervises PhDs and postdocs spanning basic circuit neuroscience projects, through to translational drug discovery efforts, with an emphasis on methamphetamine use disorder.

Abstract: Despite rising rates of methamphetamine addiction globally, there are no approved pharmacotherapies. While psychosocial interventions are effective for some, they are inaccessible for many. Therefore, novel pharmacotherapies are urgently needed. KNX100 is a novel molecular entity discovered through a phenotypic screen for positive effects on social behaviour in rodents, with a novel undisclosed mechanism of action. KNX100 is orally bioavailable, with peripheral administration having a good plasma and brain half-life and resulting in a high brain free concentration. KNX100 has undergone safety, tolerability, and pharmacokinetic testing in Phase 1 clinical trial under an FDA IND for mitigation of opioid withdrawal symptoms. However, preclinical experiments in both rodents and non-human primates suggest KNX100 may also have utility as a novel therapeutic for stimulant use disorder. This talk will present the rationale for pursuing KNX100 for methamphetamine use disorder. The data to be presented comes primarily from experiments in rat models of methamphetamine intravenous self-administration, utilising models of motivated intake (progressive ratio, behavioural economics), relapse-like behaviour (drug-primed and cue-primed reinstatement), methamphetamine preference over social reward, and methamphetamine sensitisation. These data have translated to similar effects in non-human primate models of cocaine self-administration. Importantly, we will show that KNX100 is not inherently sedating, rewarding, reinforcing, or aversive. We will also present the plan for translation of KNX100's effects to Phase 2 clinical trials in patients with methamphetamine use disorder. KNX100 is the first novel chemical entity developed and tested clinically in Australia for this indication.

Highest Ranked Abstracts

Circuit- and -state-dependent opponent processing of fear

Presenting Author: Joanna Yau

Joanna Yau - UNSW

Amy Li - UNSW

Lauren Abdallah - UNSW

Leszek Lisowski - University of Sydney

Gavan McNally - UNSW

Chair: Dr Natalie Matosin

Background
The basolateral amygdala (BLA) enables learning about positive and negative emotional events via different long-range projections. BLA neurons projecting to the central amygdala (CeA) preferentially encode aversive events whereas those projecting to the nucleus accumbens (Acb) preferentially encode rewarding events. The presence and organisation of functionally opposing BLA circuits is suggestive of opponent processes of learning. Yet, despite compelling evidence for opponent processes at the behavioural level, evidence for opposition between BLA circuits during fear learning is sparse. Here, we test this possibility by studying the roles of the BLA-CeA and BLA-Acb pathways in fear learning.

Methods
First, we used retrograde tracing and single-molecule fluorescence in situ hybridisation to probe the anatomical and molecular organisation of BLA-CeA and BLA-Acb pathways in the rat brain. We then used two-colour fibre photometry to simultaneously record activity from the BLA-CeA and BLA-Acb pathways during fear conditioning in a neutral or rewarding context. Lastly, we used optogenetics to inhibit specific BLA output pathways at the time of the footshock US during both forms of fear learning.

Results
We found the BLA-CeA and BLA-Acb pathways to be mostly segregated but share similar genetic profiles. We showed BLA-CeA neurons to be strongly recruited during fear learning regardless of where learning occurred whereas BLA-Acb neurons were only recruited by footshock when fear was conditioned in a reward context but not in a neutral context. Furthermore, we show this robust recruitment of BLA-CeA pathway by the footshock functions to promote fear, whereas the selective state-dependent recruitment of BLA-Acb pathway by the footshock functions to inhibit fear.

Conclusions
We identified a fear opponent process in the brain. We show that an aversive event can recruit distinct populations of neurons in the rat basolateral amygdala. One population projects to the central amygdala to promote fear learning. A second population projects to the nucleus accumbens to oppose fear learning. These nucleus accumbens projecting neurons limit how much fear is learned and are candidates for therapeutic targeting to minimise the amount of fear learned after a traumatic experience.

Highest Ranked Abstracts

Influence of maternal stress, high-fat diet and postnatal infection on maternal and offspring behaviour in C57Bl/6 mice

Presenting Author: Morgan Bucknor

Morgan C Bucknor - Charles Perkins Centre, University of Sydney

Anand Gururajan - Centenary Institute of Cancer Medicine and Cell Biology

Russell C Dale - Kids Neuroscience Centre, The Children's Hospital at Westmead

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

Chair: Dr Natalie Matosin

Background
Prenatal and postnatal stress critically influence offspring health. Maternal exposures like psychosocial stress and poor diet activate the immune system during pregnancy, increasing the risk of neurodevelopmental disorders in offspring. While animal models have explored this association, they often focus on isolated or acute stressors. We established a comprehensive animal model incorporating chronic high-fat (HF) maternal diet, intermittent social instability stress (SIS), and acute postnatal infection to better understand the impact of these combined environmental risk factors on both maternal health during pregnancy and offspring health and behaviour.

Methods
48 female C57Bl/6 mice were allocated to one of four groups: HF+/SIS- (n=8), HF+/SIS+ (n=16), HF-/SIS- (n=8), and HF-/SIS+ (n=16). Diet exposure started at 6 weeks of age and continued throughout gestation. SIS stress involved cage changes twice weekly with unfamiliar mates for 6 weeks before pregnancy. After SIS and 8 weeks of diet, glucose tolerance and behavioural tests (open field, elevated plus maze, nest building) were conducted before breeding. Offspring (n=112) received either poly IC injection (10mg/kg) (HF+/PIC+) or saline vehicle control at weaning and behavioural tested at 12 weeks of age (elevated plus maze, marble burying, social preference).

Results
Prior to pregnancy, all HF+ females demonstrated rapid weight gain, elevated fasting blood glucose, and impaired glucose tolerance, regardless of SIS exposure. Anxiety-like behaviours were similar across maternal stress groups, but HF+/SIS+ females exhibited a more mixed anxiety profile. HF+/SIS+ females did not show reductions in plasma ACTH and corticosterone levels after SIS exposure and showed significant postpartum neglect, leading to fewer live offspring. Offspring behavioural testing revealed marked sex differences in social preference: HF+/PIC+ males exhibited deficits in social recognition and sociability, while HF+/PIC+ females did not.

Conclusions
These findings suggest that prolonged maternal HF diet consumption, coupled with previous exposure to SIS (HF+/SIS+), places a significant burden on the maternal stress response system, resulting in reduced parental investment and negative postpartum behaviour towards offspring. Male offspring born from these dams that receive an acute postnatal infection (HF+/PIC+) demonstrate social deficits that are evident during adulthood, while female offspring appear less vulnerable to these neurodevelopmental impacts. Evidently, maternal stress and acute postnatal infection differentially impact male and female health and behaviour into adulthood and highlights the complexity of the stress response and its effects on foetal development.

Highest Ranked Abstracts

A biological basis for binge eating as 'self-medication'

Presenting Author: Morgan James

Utsav Gyawali - Rutgers University

Abanoub Armanious - Rutgers University

Jacqueline Mehr - Rutgers University

Robyn Brown - University of Melbourne

Morgan James - Rutgers University

Chair: Dr Natalie Matosin

Background
It has been proposed that binge eating can serve as a form of ‘self-medication’ against dysphoric states in persons of higher weight. Despite this, the neurobiological system(s) underlying this phenomenon remain to be characterized. Here, using rats, we developed model of diet-induced obesity model that promotes a depression-like phenotype. We tested the hypothesis that binge eating would restore hedonic tone associated with higher weight, in part via recruitment of a hypothalamic-midbrain circuit. We further hypothesized that repeated recruitment of this circuit would promote the development of 'addiction-like' behaviors for food, thus creating a 'vicious cycle' of problematic eating.

Methods
Female Long Evans rats were maintained on a regular chow or high fat diet (HFD; 45% fat) for 8w; binge-like eating was then promoted via intermittent, restricted access to sweetened fat for 4w. Hedonic tone was measured using intracranial self-stimulation (n=6-7/group) and social preference (n=8/group) assays. Release of orexin, a hypothalamic peptide involved in reward, was measured in ventral tegmental area (VTA) using fiber photometry recordings of the OxLight1 sensor (n=5-6/group). ‘Food addiction’ was assessed by measuring punished (footshock) responding for sucrose pellets and cued reinstatement of food seeking (n=12-15/group).

Results
Compared to chow-fed controls, HFD rats had higher ICSS thresholds and lower social preference, indicating a depression-like phenotype in these rats. These reward deficits were associated with blunted orexin release in VTA in response to reward-predictive stimuli. Binge eating partially restored reward thresholds, social preference, as well as orexin release in VTA, pointing a 'selfmedicating' role for this type of eating. Binge eating promoted the development of several 'food addiction' behaviors, which were normalized by inhibition of the orexin-VTA circuit.

Conclusions
Our data indicate that binge eating can be 'self-medicating' against dysphoric states associated with higher weight. The negatively reinforcing properties of binge eating, however, contribute to the development of 'food addiction' behaviors, creating a 'vicious cycle' of problematic eating. The orexin-VTA circuit is a potential biological target for interventions designed to normalize mood and eating outcomes in individuals of higher weight. This represents a novel and important advance in efforts to understand the biological basis of 'emotional' binge eating.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_1/P_35a Patient-derived microglia-containing organoids for investigating neuroanatomical phenotypes in schizophrenia

Presenting Author: Jordan Clarke

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Chair: Katrina Edmond

Background
Induced pluripotent stem cell (iPSC)-derived cortical organoids offer invaluable opportunities for studying neuroanatomical alterations in neuropsychiatric disorders. However, current protocols have several key limitations, including restricted development of microglia, limited recapitulation of the laminar architecture and labour-intensive protocols. Here, we introduce an automated protocol for generating microglia-containing cortical organoids exhibiting laminar organisation. This system can be utilised to investigate microglia-mediated mechanisms, including excessive synaptic pruning, which have long been proposed to underlie cortical thickness alterations in schizophrenia.

Methods
Microglia-containing cortical organoids (MiCOs) were generated by seeding a suspension containing patient-derived iPSCs and matched hemopoietic progenitors (HPCs) or early microglia progenitors (eMPs) using a BioTek MultiFlo FX with AMX modules.Neural induction and forebrain patterning occurred alongside proliferation and early differentiation of HPCs or eMPs towards amicroglial fate. The AMX system performed high-precision media changes throughout the neural induction process. After 17-days, MiCOs were moved to shaking culture to enhance oxygenation, nutrient exchange and media composition supported further differentiation. At D35, MiCOs were transferred to spinning-bioreactors for long-term culturing and a new media composition to encourage organoid maturation.

Results
Automation of neural induction enhanced inter-organoid consistency and MiCO formation. Expression of proliferative (Ki67) and forebrain and neural progenitor markers (EMX1, PAX6 & NESTIN) by D20 indicated successful neural induction. At D40, both HPC and eMP integrated MiCOs expressed early neuronal and cortical differentiation markers (TUJ1, MAP2, SOX2, NFM, TBR1 & CTIP2), displayed rosette-like formations and were positive for astrocytes (GLAST) and microglia (IBA-1, PU.1, CD11b & TREM2). D80 MiCOs exhibited early organisation of layer-specific markers (Reelin, SATB2, CTIP2, TBR1), mature uniform expression of neuronal and astrocyte markers, and ramified morphology of microglia (IBA-1+).

Conclusions

Successfully recapitulating cortical development in vitro will facilitate studies into the neurodevelopmental basis of cortical phenotypes in schizophrenia, commonly observed through neuroimaging. In doing so, these patient-derived models enable direct links between in vitro models and in vivo disease states, making this platform valuable for translational research and the development of improved, personalised therapeutics.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_2/P_10a The association between acute and non-acute cannabis exposure and the neural correlates of reward anticipation

Presenting Author: Martine Skumlien

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Chair: Katrina Edmond

Background
Cannabis, and its main psychoactive compound THC, may alter the brain's reward system both acutely and over time. However, the effects of THC on neural reward processing remain unclear. Adolescents may respond differently to cannabis exposure compared with adults, but no previous fMRI study has examined the acute effects of cannabis in this age group. The aims of this study were to investigate the association between acute and non-acute cannabis exposure on the neural correlates of reward anticipation and whether this association differed in adults and adolescents. We also examined whether the acute effect of THC was modulated by CBD.

Methods
This study used data from the 'CannTeen' project. In the non-acute arm, we investigated reward anticipation in 62 adult (26-29 years) and 63 adolescent (16-17 years) cannabis users and age-matched controls, using the Monetary Incentive Delay task during fMRI. The acute study was a randomised, double-blind, crossover experiment in which 23 adults and 24 adolescents performed the same task after inhaling cannabis with 0.107 mg/kg THC or with THC plus 0.320 mg/kg CBD, or placebo cannabis. We investigated neural responses to reward anticipation with whole-brain and region of interest analyses in the ventral striatum, anterior cingulate cortex, and right insula.

Results
The non-acute study showed no differences between users and controls and no interaction with age-group, supported by Bayesian analyses. However, THC acutely reduced reward anticipation activity in the right (p=.005, d=0.49) and left (p=.003, d=0.50) ventral striatum and the right insula (p=.01, d=0.42). THC+CBD also reduced activity in the right ventral striatum (p=.01, d=0.41) and the right insula (p=.002, d=0.49) compared with placebo. The effects of active cannabis were the same in adolescents and adults and there were no differences between the THC and THC+CBD conditions, supported by Bayesian analyses. There were no significant effects in the whole-brain analyses.

Conclusions
Our results suggest that cannabis suppresses the brain's anticipatory reward response to money acutely, but there are no differences between cannabis users and controls non-acutely. Furthermore, the adolescent reward circuitry does not appear to be more sensitive or more resilient to the effects of cannabis on reward anticipation.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_3/P_25a Mitochondrial function in stem cell models from participants with bipolar disorder and healthy controls

Presenting Author: Ken Walder

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Olivia M Dean - IMPACT Institute, Deakin University

Jee Hyun Kim - IMPACT Institute, Deakin University

Michael Berk - IMPACT Institute, Deakin University

Ken Walder - IMPACT Institute, Deakin University

Chair: Katrina Edmond

Background
The mitochondrial hypothesis of bipolar disorder (BD) suggests that the disorder is essentially one of energy dysregulation, with impaired ATP production in depression and elevated ATP production in mania. While there is some evidence to support the hypothesis of mitochondrial dysfunction in bipolar disorder, most of it is indirect. In this study we investigated mitochondrial function in cells derived from participants with BD and healthy controls (HC), including induced pluripotent stem cells (iPSCs), neural progenitor cells (NPCs) and cortical networks (co-cultures of mature neurons and astrocytes; CNs).

Methods
We collected blood samples from individuals with BD and HC (n=12 each group) and generated iPSCs using episomal vectors. We differentiated these into NPCs using dual SMAD inhibition, and finally into CNs using various small molecules. Cells were investigated under basal conditions or in response to lithium treatment. Flux bioanalysis was used to measure aspects of mitochondrial function including basal respiration, maximal respiration, ATP turnover and uncoupled respiration. Data were normalised using genomic DNA concentration and analysed using factorial ANOVAs.

Results
Under basal conditions, iPSCs were significantly higher than NPCs and for all measures of mitochondrial function CNs ($p<0.05$). Lithium increased parameters including basal respiration, ATP turnover and maximal respiration rate ($p<0.05$) but there was no difference in effect between the BD and HC cell lines. For uncoupled respiration, we found a disease x drug interaction whereby lithium increased it in the HC, but not the BD cell lines ($p<0.05$).

Conclusions
Lithium had a differential effect on uncoupled respiration in BD cells compared with HC cells. There were no significant differences in mitochondrial function under basal conditions between cells derived from participants with BD and those from HC. Further studies are underway to investigate mitochondrial function in the cells under the influence of various cellular stresses, such as metabolic stress (oligomycin), inflammation (lipopolysaccharide) and oxidative stress (hydrogen peroxide).

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_4/P_15a A novel fMRI investigation into the role of the BNST in stress and food cue reactivity

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Chair: Katrina Edmond

Background
Stress is a trigger for binge eating behaviours and can increase food intake by influencing brain responses to rewarding food cues. The bed nucleus of the stria terminalis (BNST), a central hub for stress and reward, has previously been associated with stressinduced drug seeking. However, the BNST's role in mediating stress-induced eating has not yet been examined in humans. Using ultra-high resolution 7-Tesla fMRI, we tested the effects of acute stress on BNST connectivity with cortico-striatal regions during food cue presentation in a healthy control population.

Methods
47 healthy adults completed a novel stress beverage task with an MRI-compatible gustometer. Pictures ('CUE') of rewarding (chocolate milk) or neutral (water) cues were presented and then delivered to participants during scanning. The beverage task was completed twice - under low or high-stress conditions. Dynamic causal modelling (DCM) was used to map effective connectivity between the BNST, and cortico-striatal regions engaged during CUE presentation: the nucleus accumbens (NAcc), the orbitofrontal cortex (OFC), and the anterior insula (aINS). Self-reported stress and beverage ratings were recorded.

Results
Whole-brain activation to a beverage 'CUE' significantly activated cortico-striatal regions including the frontal and temporal poles, OFC, insula, dorsal and ventral striatum, the para-hippocampal region, amygdala and the BNST. DCM revealed stress having an inhibitory influence on connectivity from the BNST to the NAcc, anterior insula and OFC during CUE presentation. During reward cue presentation, stress had inhibitory effect on BNST-to-anterior insula and OFC connectivity, as well as an excitatory influence from the anterior insula on BNST activity. Effective connectivity was not associated with individual chocolate milk pleasantness or self-reported stress ratings.

Conclusion
This is the first study in humans to demonstrate that the BNST modulates cortical activity during food anticipation after acute stress. We identified the BNST has an inhibitory influence on brain regions involved in goal-directed behaviour, suggesting stress-induced shifts in motivated behaviour are informed by bottom-up interoceptive information. Moreover, the anterior insula had an excitatory influence on the BNST during high-stress reward cue presentation, indicating cue reward valence informs BNST-mediated stress-coping mechanisms. These findings represent a

significant reconceptualization of the potential role of the BNST in disordered eating and has implications for future research on stress and food-related psychopathology.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_5/P_06a Paternal SARS-CoV-2 Infection Increases Anxiety in Offspring and Changes Sperm Small Noncoding RNA Profiles

Presenting Author: Elizabeth Kleeman

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Chair: Katrina Edmond

Background
Previous reports indicate that parental experiences, such as poor diet and stress, can have mutigenerational impacts on offspring health in mice and humans. We have also previously shown that paternal pre-conceptual exposure to viral-like and bacterial-like immune activation in mice can alter sperm small noncoding RNAs and reprogram offspring brain and behavioural phenotypes. Given that the SARS-CoV-2 virus, and the COVID-19 pandemic, represents a recent major environmental challenge faced by an unprecedented number of people worldwide, we investigated whether paternal SARS-CoV-2 infection has impacts on sperm small noncoding RNAs, and intergenerational (F1) and transgenerational (F2) effects on offspring phenotypes.

Methods
Using an established mouse-adapted SARS-CoV-2 (P21) preclinical model, we infected adult male mice with the P21 isolate (versus mock control infection) and bred them with naïve female mice four weeks later. We performed a range of behavioural assessments looking at anxiety, depression, and cognition in both the adult offspring and

grand-offspring. Furthermore, we isolated the sperm small noncoding RNAs for sequencing to see if there were any associated sperm epigenetic changes. Finally, we microinjected the sperm RNAs from both infected and mock-infected fathers into naïve zygotes to see if this recapitulated the F1 offspring phenotypes in the natural mating studies.

Results
Here we show that male and female offspring of SARS-CoV-2 infected fathers displayed increased anxiety-like behaviours in both the light-dark box and open field test. In contrast, there were no transgenerational behavioural changes observed in the F2 grandoffspring. An analysis of the sperm small noncoding RNA profiles from SARS-CoV-2 and control fathers revealed that 22 RNAs, including PIWI-interacting RNAs and microRNAs, were differentially regulated by SARS-CoV-2 infection. Microinjection of isolated RNA from the sperm of SARS-CoV-2 infected males into naïve zygotes partially recapitulates the behavioural phenotype of the naturally born F1 offspring.

Conclusion
Hence, this study provides the first evidence that paternal SARS-CoV-2 infection can have intergenerational epigenetic impacts on anxiety that are directly associated with changes in the paternal sperm small noncoding RNA content. Given the enormous impact of the COVID-19 pandemic, these findings may have serious public health implications and will inform further research in human males affected by SARS-CoV-2, and their offspring.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_6/P_40a Efferent connectivity and neurochemical phenotype of topographically distinct lateral hypothalamus and zona incerta RXFP3+ cells

Presenting Author: Brandon Richards

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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

Chair: Katrina Edmond

Background
The relaxin-3/RXFP3 neuropeptidergic system is a potential target for treating neuropsychiatric diseases, given its role in arousal, stress, and cognition. However, this system's function is not fully understood in preclinical rodent models, which is essential to determining its putative translational utility. We have shown that chemogenetically activating RXFP3-expressing (RXFP3+) cells in the lateral hypothalamus (LH) and zona incerta (ZI) during conditioned fear extinction produced escape-like jumping, but only in a subset of mice. Consequently, the current study aimed to determine if RXFP3+ LH/ZI cells are neurochemically and connectively diverse, which may explain the bimodal phenotype observed.

Methods
RNAscope fluorescent in situ hybridisation was performed to examine the co-expression of Rxfp3 mRNA with slc17a6 (vGlut2; a glutamatergic marker), GAD1 (a GABAergic marker), Th (tyrosine hydroxylase; a dopaminergic marker), Pvalb (parvalbumin), and SST (somatostatin) mRNA throughout the entire LH/ZI of RXFP3-Cre mice (n = 4). To determine if the efferent connectivity patterns of RXFP3+ cells differed based on their topographical location within the LH/ZI, a Cre-dependent anterograde viral tracer was injected at systematically varying areas across the LH/ZI in RXFP3-Cre mice (n = 16, n = 4/area).

Results
Most Rxfp3+ ZI cells were GAD1-expressing (M=77.1%, SEM=2.4%). Known GABAergic clusters of Th-expressing (77.0% ± 2.9%), SST-expressing (58.7% ± 2.2%), and Pvalb-expressing (67.8% ± 3.9%) cells expressed Rxfp3 and populated distinct ZI areas. In contrast, the LH comprised a heterogeneous Rxfp3-expressing population of intermingled GAD1-expressing (33.4% ± 2.4%) and slc17a6-expressing cells (39.3% ± 2.7%). Anterograde tracing of topographically distinct RXFP3+ LH/ZI cells revealed differences in projections to fear and defensive behaviour-implicated nuclei. Notably, the periaqueductal gray received the most input from medial ZI RXFP3+ cells, while the lateral habenula received substantial input from rostral LH RXFP3+ cells.

Conclusion
Collectively, these results indicate that RXFP3+ LH/ZI cells are a heterogeneous population where topographical location dictates neurochemical composition and efferent output. This suggests that chemogenetically activating particular subpopulations of RXFP3-expressing LH/ZI cells that differ in their neurochemistry and hodology may have generated escape-like jumping behaviour in some mice but not others, which we will interrogate in a future study. These findings add to what is known about the anatomical properties of the relaxin-3/RXFP3 system, which may aid in determining the translational utility of its targeting in neuropsychiatric disease.

Data Blitz Abstracts

Data Blitz Session 1

DB1_7/P_20a Sex-Dependent and Dynamic Brain Structure Changes Due to influenza A virus induced maternal immune activation: Insights from Longitudinal Mouse MRI

Presenting Author: Danli Peng

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Chair: Katrina Edmond

Background
Maternal immune activation (MIA), triggered by infections or inflammatory insults during pregnancy, significantly impacts brain development, maturation and behaviour of the offspring throughout life. Preclinical animal models of MIA provide valuable tools to explore factors affecting neurodevelopment under controlled environments. MIA-induced brain structural changes can be assessed using MRI. Unlike previous studies that used synthetic viral mimetics like poly(I:C), live influenza A virus (IAV) was utilized to induce MIA (IAV-MIA), providing a more ‘real-world’, clinically relevant model. A longitudinal study imaged at multiple time points allows examination of neurodevelopmental changes from early adolescence (5 weeks) to adulthood (14 weeks).

Methods
Pregnant mice at gestation day 12 were exposed to IAV to induce MIA. T2*-weighted MRI was performed at 5, 8, 11, and 14 weeks of age using a Bruker 9.4T MRI scanner with multiple gradient echoes at a resolution of 100x100x100 μm3. Regional brain volumes were measured using registration-based method to the Allen atlas. A linear mixed-effects model was applied to regional volume examining treatment, sex, and age interactions. Tensor-based morphometry (TBM) observed voxel-level morphological changes with cluster-based multiple comparison correction.

Prepulse Inhibition (PPI) was performed immediately after the scan at 14 weeks to assess sensorimotor gating, indexing cortical function.

Results

Brain structural trajectory changes were found to be highly significant in the CA1 area of hippocampus ($P<0.0003$) in the atlas-based analysis. TBM showed IAV-MIA-dependent age effects with greater sex-related deviations among males than females in various subregions of the cerebral cortex, hippocampal formation, brain stem, and cerebellum. We also observed significant disruptions in PPI in adult mice, which assemble an aspect of schizophrenia.

Conclusion

Our findings show that IAV-MIA significantly impacts the neurodevelopmental trajectory depending on age and sex, with widespread dynamic changes in brain structure across several regions. Furthermore, atlas-based segmentation combined with TBM provided a more detailed assessment of brain regions whose neurodevelopmental trajectories were disrupted in our IAV-MIA model. The permutational cluster-based multiple comparison correction used in this research enhanced statistical power and increased chances for detecting subtle anatomical changes. Our IAV-MIA model is a more clinically relevant and useful model to study aberrant neurodevelopment compared to synthetic viral mimetics like poly(I:C).

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_8/P_30a Test-retest reliability of the Dynamic Strategy Shifting Task in male and female mice

Presenting Author: Laura Kimble

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Chair: Katrina Edmond

Background
Cognitive flexibility is the ability to adapt to rapidly changing environments, which is often impaired in neuropsychiatric disorders including schizophrenia. Cognitive flexibility refers to measures of sustained attention, working memory, response inhibition and switching, and dysfunction in these domains is one of the biggest predictors of functional outcomes. We developed a Dynamic Strategy Shifting Task (DSST) using standard operant chambers to improve preclinical research on cognitive flexibility. One aspect of testing drugs involves within-animal Latin-square designs, which involves repeated testing. The aim of this project was to examine test-retest reliability and stability amongst male and female mice across multiple sessions.

Methods
The DSST was used to assess cognitive flexibility in which mice have to adapt to changing rules within a single session. The task incorporated strategy shifts between spatial rules including responding to fixed target lever locations or left/right visual cues, and nonspatial rules including central visual and auditory cues. To progress through each stage of the task, a minimum of 6 consecutive correct responses were required within-session. C57BL6/J mice (n=24; male=12, female=12) were exposed to the same set of DSST rules over five sessions on separate days. The main measure was the number of trials to criterion for each rule.

Results
Male and female mice made an average of 3 strategy shifts per 30 minute testing session (Range 2-7). There was no significant effect of repeated testing on the number of rules completed or the number of trials to criteria for each rule. There were also no significant effects of repeated testing on other measures, including average trial duration, premature and perseverative responses or session duration. Mice reliably adapted to changing rulesets, demonstrating appropriate shifts in attentional processes and response strategies on each session, which demonstrated high test-retest reliability for the DSST task in mice.

Conclusion
Current treatments including first- and second-generation antipsychotic medications have failed to address the cognitive deficits observed in patients with schizophrenia, and high failure rates of clinical trials have been linked to a lack of translational validity between human and rodent studies. Therefore, improving the translational and predictive validity of cognitive tasks such as the DSST to determine the neurological basis of cognitive flexibility is pertinent to the development of novel treatments. The DSST offers a promising approach for bridging this gap, potentially leading to improved therapeutic avenues including effective drug treatments and screening of novel drug targets in rodents.

Data Blitz Abstracts

Data Blitz Session 1 – Kinoxis Data Blitz

DB1_9/__ Biomarkers of Bipolar Disorder: Elevated Plasma Neurofilament Light Chain and Glial Fibrillary Acidic Protein Levels and Their Clinical Correlates

Presenting Author: Matthew Kang

Matthew JY Kang - Neuropsychiatry Centre, Royal Melbourne Hospital; Department of Psychiatry, University of Melbourne

Dhamidhu Eratne - Neuropsychiatry Centre, Royal Melbourne Hospital; Department of Psychiatry, University of Melbourne

Chair: Katrina Edmond

Background
Recent methodological developments allow us to measure small amounts of brain-specific proteins in the blood, including neurofilament light chain (NfL), a marker of axonal pathology, and glial fibrillary acidic protein (GFAP), a marker of astrocytic activation. Given the evidence of potential astroglial pathology and neuronal dysfunction in bipolar disorder, these markers may provide further insight into its pathophysiology. We investigated plasma NfL and GFAP levels in people with bipolar depression and compared them with unaffected individuals.

Methods
We analysed plasma NfL and GFAP levels in 120 people with bipolar depression and compared them with 96 healthy controls usingbootstrapped general linear models (GLM) adjusting for age, sex, and weight. We examined associations between these biomarkers and clinical variables, including mood symptom severity, past psychiatric history, and functioning, adjusting for multiple comparisons. For additional sensitivity analyses, predictors were evaluated using Bayesian model averaging (BMA).

Results
GFAP and NfL levels in plasma were elevated in people with bipolar depression compared to healthy controls after adjusting for age, sex and weight. The duration of illness was positively associated with NfL. The BMA analysis also identified duration of illness as a strong predictor of NfL (Posterior Inclusion Probability, PIP = 0.85). Age of onset was positively associated with GFAP. The BMA analysis similarly found age of onset to be a moderately strong predictor (PIP = 0.67).

Conclusion
This study found elevated levels of plasma NfL and GFAP in bipolar depression compared to unaffected individuals, with significant associations with the duration of illness and age at onset, suggesting a degree of neuronal injury and astrocytic dysfunction in bipolar depression. These biomarkers may reflect specific illness stages, including neuroprogression and the later onset of bipolar disorder.

Data Blitz Abstracts

Data Blitz Session 2

DB2_1/P_05b Systematic Review of MRI Markers of Psychopathology following Traumatic Brain Injury: Transdiagnostic Insights

Presenting Author: Alexia Samiotis

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Chair: Dr Warren Logge

Background
The neural underpinnings of psychopathology following moderate-severe traumatic brain injury (TBI) are not well understood. Previous reviews found limited evidence for consistent neural markers across categorically defined psychopathology. In contrast to prior reviews, our review adopts a comprehensive approach that extends beyond individual diagnostic categories to investigate how neural markers may be implicated in different forms of post-TBI psychopathology ("transdiagnostically"). The aim of this systematic review was to integrate MRI findings across a spectrum of psychopathologies in adults with closed-head moderate-severe TBI to identify whether neural markers show consistent patterns across psychopathology categories rather than focusing on single categorical classifications.

Methods
Eligible studies explored associations between MRI markers, defined as any alteration to brain macro- or micro-structure, or functioning, that was related to psychopathology in adults with closed-head moderate-severe TBI. We searched English literature from Embase, PsycINFO, and MEDLINE via Ovid SP on 2nd November 2023. Risk of bias was assessed using a modified version of the Joanna Brigg's Institute Critical Appraisal Tools. Findings from eligible studies were synthesised descriptively for each MRI technique (structural, diffusion, and functional) across diverse psychopathology categories. Common trends were identified by focusing on MRI findings that were consistent across at least two different psychopathology categories.

Results
The total number of records screened was 7776 articles and there were 20 articles that met eligibility criteria. Several MRI findings were consistently associated with multiple categories of psychopathology in adults following moderate-severe TBI, including structural changes in the hippocampus, frontal and temporal lobes, thalamus, longitudinal fasciculus, fornix, and altered substantia nigra-left angular gyrus connectivity. The hippocampus emerged as the most frequently implicated region in post-TBI psychopathology. Reduced hippocampal volume was consistently linked to increased severity of depressive, anxiety, psychotic and apathy symptoms, while altered hippocampal connectivity with limbic regions was implicated in increased depressive symptom severity.

Conclusion
Our review findings suggest preliminary evidence that relationships between post-TBI neural markers and psychopathology may not fit neatly into conventional diagnostic categories. Further MRI research with robust

methodologies, including larger sample sizes, appropriate comparators, rigorous statistics, and consistent TBI definitions, is necessary. Moving forward, future research should consider adopting transdiagnostic frameworks for classifying psychopathology. This approach could offer a more comprehensive understanding of how neural markers relate to the diverse manifestations of psychopathology following TBI.

Data Blitz Abstracts

Data Blitz Session 2

DB2_2/P_10b Effect of Glucagon-Like Peptide-1 Receptor Signaling in the dorsal Lateral Septum on Alcohol Intake and Relapse Drinking

Presenting Author: Michelle Yuqing Xiao

Yuqing Xiao – School of Psychology, UNSW

Zhi Yi Ong – School of Psychology, UNSW

Jo Ann Yap – School of Psychology, UNSW

Chair: Dr Warren Logge

Background
Alcohol Use Disorder (AUD) is a chronic relapsing disorder and one of the most significant public health issues globally. The gut peptide and neuropeptide glucagon-like peptide-1 (GLP-1) have recently shown promise as a novel treatment for AUD. Current evidence shows that GLP-1 suppresses alcohol intake and relapse, but the underlying neural mechanisms remain unclear. Given that dorsal lateral septum (dLS) highly expresses GLP-1 receptors and is implicated in reward processing, this study investigated whether GLP-1 reduces alcohol intake and relapse via dLS.

Methods
Male Long Evans rats were trained to consume 20% alcohol using the Intermittent Access 2-Bottle-Choice Drinking method. After 4 weeks, rats underwent operant oral alcohol self-administration. Once learnt, operant responses were extinguished and relapse to alcohol-seeking were assessed. During test days, rats received intra-dLS delivery of either GLP-1 analogue Exendin 4 (Ex4; 0.025 µg) or Vehicle (saline). The effects of dLS Ex4 on alcohol self-administration, reacquisition and alcohol priming-induced reinstatement of alcohol seeking were examined. Food and water intake were measured post-tests and compared between groups.

Results
Results show that intra-dLS Ex4 significantly reduced alcohol self-administration and reacquisition but did not affect prime-induced reinstatement. The Ex4 dose used had no effect on food or water intake, nor did it impact body weight.

Conclusion
These findings support the dLS as a key region in mediating the effects of GLP-1 receptor signalling on alcohol self-administration and reacquisition but suggest different contributing mechanisms in primed reinstatement of alcohol seeking.

Data Blitz Abstracts

Data Blitz Session 2

DB2_3/P_18b Bioenergetic Dysregulation in Peripheral Immune Cells: Links to Anhedonia and Fatigue in Young Adults with Depression

Presenting Author: Roger Varela

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

Kathryn R Cullen - Department of Psychiatry & Behavioral Sciences, University of Minnesota Medical School – MN, United States.

Brooke Morath - Department of Psychiatry & Behavioral Sciences, University of Minnesota Medical School – MN, United States.

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

Chair: Dr Warren Logge

Background
Depression often begins early in life and is linked to significant suffering, disability, and risk of suicide. A core feature of depression is reduced energy levels, impacting daily functioning. Fatigue and anhedonia may stem from deficits in cellular energy metabolism, particularly in immune cells (immunometabolism). The physiologic basis for this theory is an area of active research interest but has not yet been effectively demonstrated in humans. This study assesses the metabolic profile of peripheral immune cells, and its correlation with anhedonia and fatigue ratings, in young adults with and without depression.

Methods
This cross-sectional case-control study included 12 healthy controls and 14 subjects with moderate/severe depression, aged 18-24. Following informed consent, participants underwent clinical interviews. Psychiatric diagnosis was confirmed with the Mini- International Neuropsychiatric Interview (MINI), depression severity with the Montgomery-Åsberg Depression Rating Scale (MADRS), hedonic tone with the Snaith-Hamilton Pleasure Scale (SHAPS), and fatigue impact with the Fatigue Severity Scale (FSS). Whole blood samples were collected, and Peripheral Blood Mononuclear Cells (PBMCs) were isolated and frozen for bioenergetic profiling using the Seahorse T-Cell Metabolic Profiling Assay.

Results
Depressed patients had higher fatigue levels ($p<0.0001$) and decreased hedonic tone ($p=0.0239$) compared to controls. Basal ATP production rate in PBMC tissue was also decreased in depressed subjects ($p=0.0367$), which comprised reduced glycolytic ATP ($p=0.0231$) and mitochondrial ATP ($p=0.0545$) production. The percentage of ATP from glycolysis did not differ between groups ($p=0.3081$). Additionally, mitochondrial spare respiratory capacity was significantly lower in depressed patients ($p=0.0411$). Motivation scores on the FSS correlated with total ($p=0.0037$), glycolytic ($p=0.0078$), and mitochondrial ($p=0.0038$) ATP production rates, while general fatigue levels correlated with total ($p=0.0466$) and glycolytic ($p=0.0414$) ATP production rates.

Conclusions
These findings indicate that depressive symptoms are associated with decreased energy production in PBMCs of young adults. Seahorse analysis further revealed impaired peripheral mitochondrial function in depressed patients, leading to reduced ATP spare respiratory capacity. Interestingly, the metabolic balance between mitochondrial respiration and glycolysis did not vary between the groups, suggesting an unstressed mitochondrial state despite impaired functioning and no immunometabolic shift function. Importantly, the bioenergetic state of peripheral immune cells correlated with motivational and fatigue symptoms, highlighting its potential as a novel intervention target to restore health and prevent long-term impacts of metabolic stress.

Data Blitz Abstracts

Data Blitz Session 2

DB2_4/P_20b Local modulation of the striatal network: a new perspective on the mechanisms of action of antipsychotics

Presenting Author: Miriam Matamales

Chelsea Goulton - University of New South Wales, Sydney

Christopher Nolan - University of New South Wales, Sydney

Christopher Shen - University of New South Wales, Sydney

Jay Bertran-Gonzalez - University of New South Wales, Sydney

Miriam Matamales - University of New South Wales, Sydney

Chair: Dr Warren Logge

Background
Despite the widespread use of antipsychotics, there is still a lack of consensus about how these drugs exert their therapeutic action in the brain. Most antipsychotics display varying degrees of affinity for dopamine D2-type receptors. The distinctively highest density of D2-type receptors is found in the striatum, where it is expressed by a subset of striatal neurons (D2-neurons). It has been suggested that the therapeutic, long-lasting effects of antipsychotics involve neuroplasticity in the striatum, but how this is achieved is largely unknown. We hypothesised that this learning-related process depends on local neuromodulatory signals amongst striatal neurons.

Methods
In this study, we combined neuropharmacology, high-throughput confocal imaging, in vivo fibre photometry and behavioural tracking in transgenic mice, to study the neurobiological processes mediating antipsychotic action in the mammalian brain.

Results
We show that administration of an antipsychotic drug that binds to the D2-receptor halted nuclear function in neighbouring D1-neurons, thus preventing dopamine-dependent transcriptional plasticity. We found that this effect was not due to a reduction in dopamine levels in the striatum or to alterations of second messenger homeostasis in D1-neurons. We evaluated the primary role of this molecular cross-talk in instrumental learning by functionally manipulating D1- and D2-neurons during acquisition of an action-outcome (A?O) contingency. Genetic ablation of D1-neurons in the dorsomedial striatum disrupted original A?O learning, an effect that was mimicked by pharmacologically enhancing D2-SPN function during training.

Conclusions
Our results suggest that antipsychotics act by potentiating the extensive and dynamic D2- to D1-neuron transmodulation across the striatum, which influences striatal plasticity and behaviour. It is concluded that the indirect action of D2-receptor blockers on D1-neurons may account for their clinical antipsychotic effects. These findings are important to push forward a new branch of transformative drug discovery based on naturally occurring regulatory striatal network interactions.

Data Blitz Abstracts

Data Blitz Session 2 – Kinoxis Data Blitz

DB2_5/P_24b Unveiling vulnerabilities: Insights from fetal single-cell transcriptomics on prenatal opioid exposure and the innate immune system

Presenting Author: Sarah-Jane Leigh

Sarah-Jane Leigh – University of New South Wales

Kelly Clemens – University of New South Wales

Chair: Dr Warren Logge

Background
The opioid-abuse epidemic is associated with increased prevalence of opioid exposure during pregnancy. While current clinical care ensures infants survive acute opioid withdrawal there are no available therapies to address the long-term neurodevelopmental consequences. These affect 1 in 2 children exposed to prenatal opioids and include increased risk of attention deficit hyperactivity disorder, conduct disorder and mood disorders. It is hypothesised that the neuropathology is mediated by direct effects of opioids on the foetus and placenta. However, we do not know the relative expression of opioid-related genes in foetal organs, and whether these genes are enriched in specific cell types.

Methods
We explored a publicly-available single-cell transcriptomics atlas of healthy human foetal tissue collected in the first trimester (Cao et al., 2020 Science) using online analysis platform CELLxGENE. We examined the prevalence and identity of cells positive for opioid-related genes, using relevant gene ontologies, “g protein-coupled opioid signaling pathway” which represents the classical mechanism by which opioids exert their effects (mu, kappa and delta opioid receptors and related genes) and “opioid growth factor receptor activity” which is a less-well characterized pathway by which opioids can regulate tissue growth.

Results
We demonstrated the opioid-related genes are expressed across all 15 human foetal organs, with highest prevalence of cells expressing gene representing classical opioid signalling in the central nervous system. In contrast, cells expressing genes related to opioid growth factor activity were most common in the kidney and pancreas. In the brain, cells with the highest prevalence of these gene pathways were identified as neurons and microglia. We show for the first time that the cell type with highest prevalence of opioid-related genes in peripheral organs were myeloid cells, progenitor cells of the innate immune system.

Conclusions
In summary, cells expressing opioid-related genes are present throughout foetal organ tissues, which may explain why infants who are prenatally exposed to opioids present with a wide range of health conditions in early life. While genes representing classical opioid signalling are most represented in the foetal brain, we show that opioids may regulate tissue growth in peripheral organs during foetal development. We identify myeloid cells as particularly sensitive to prenatal opioid exposure, suggesting a role for the innate immune syndrome in the resulting syndrome.

Data Blitz Abstracts

Data Blitz Session 2

DB2_6/P_30b Upregulated inflammation-relevant gene pathways in the midbrain of the EDiPS model of hyperdopaminergia

Presenting Author: Alice Petty

Alice Petty - Neuroscience Research Australia

Debora Rothmond - Neuroscience Research Australia

Oliver Howes - Imperial College London

Darryl Eyles - Queensland Brain Institute

Cyndi Shannon-Weickert - Neuroscience Research Australia

Chair: Dr Warren Logge

Background
Hyperdopaminergia is robustly evident in the striatum in people with schizophrenia, and elevated dopaminergic activity is also found in dopaminergic cell bodies in the midbrain (the nigra). Post-mortem studies have also shown an increase in neuroinflammatory markers in the midbrain of patients with schizophrenia. Dopamine has been shown to modulate the immune environment in the brain, and we hypothesized that the increase in dopaminergic activity in the midbrain may contribute to the elevated neuroinflammatory profile seen in this region. To test this hypothesis, we used the Enhanced Dopamine in Prodromal Schizophrenia (EDiPS) model, which recapitulates aspects of nigro-striatal hyperdopaminergia.

Methods
The EDiPS construct results in increased levels of the rate-limiting enzymes in the dopamine synthesis pathway; tyrosine hydroxylase (TH) and GTP cyclohydrolase (GCH1). The AAV-packaged EDiPS construct (or control construct, without TH) was delivered directly into the substantia nigra pars compacta of juvenile male rats (n=6/group). Animals were recovered, and 9-10 weeks later, animals were euthanised and the brains extracted. Four animals from each group were taken for RNAseq analysis; tissue including the bilateral midbrain was dissected, RNA was extracted, and RNAseq conducted (up to 400M reads). Differentially expressed genes (DEGs) were determined using edgeR.

Results
The RNAseq analysis revealed that 147 genes were upregulated in the midbrain of EDiPS animals compared to controls (FDR: 0.14). None were downregulated. The top two differentially expressed genes (sorted by fold-change) were the immunoglobulin-M (IgM) light (Igkvl6, adjusted p=0.049) and heavy chains (Ighm, adjusted p=0.006). The next largest fold-change differences were seen for genes relevant to B-cell differentiation and function (Mzb1, Pou2af1, Cd79a; all p<0.012). A gene ontology (GO) pathway analysis of all DEGs indicated that “immune system processes” was the main upregulated pathway (p=3.52E-49).

Conclusion
These data suggest that elevated dopamine synthesis capacity results in local neuroinflammation, and this may be mediated by memory B cells which secrete and express the IgM antibody. There is currently no strong evidence from post-mortem tissue indicating that B cells are increased in patients with schizophrenia. However, using this preclinical model of the schizophrenia prodrome, our findings suggest that an increase in infiltrating immune cells may be a feature early in the disorder. Understanding this mechanism further may reveal that immune cell infiltration is an ideal target to improve treatments during the schizophrenia prodrome.

Data Blitz Abstracts

Data Blitz Session 2

DB2_7 Linking Non-Canonical snoRNA Function and Schziophrenia Using Patient-Derived Olfactory Neurosphere Cells

Presenting Author: Alex Cristino

Caio Damski - Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia.

Alex Cristino - Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia.

Chair: Dr Warren Logge

Background
Small nucleolar RNAs (snoRNAs) are well known for their role in guiding chemical modifications of ribosomal RNA. Recent evidence, however, indicates that snoRNAs can also modify other classes of RNA transcripts, influencing processes such as alternative splicing and translation. Despite these findings, the non-canonical functions of snoRNAs, especially in relation to neurodevelopment and psychiatric disorders like schizophrenia, remain underexplored. Our research using Olfactory Neurosphere (ONS) cells aims to bridge this knowledge gap and identify novel biomarkers and therapies for patients with schizophrenia.

Methods
We conducted high-throughput RNA sequencing on ONS cells from adult and adolescent patients with schizophrenia, as well as agematched controls, to profile the expression of long, small, and circular RNA transcripts. Bioinformatics analysis identified differentially expressed genes, which were then validated using RT-qPCR. Biotin pull-down assays were employed to identify snoRNA-gene interactions, and knockdown experiments were performed to investigate the effects of changes in gene expression. High-contrast live cell imaging was used to assess the impact of altered snoRNA expression on cellular phenotypes.

Results
Our findings revealed several snoRNAs, including SNORD101, SNORD127, SNORD12B, and SNORD26, that were consistently downregulated in schizophrenia. Functional analyses indicated that these snoRNAs play critical roles in schizophrenia-related pathways, particularly those involved in synaptic plasticity and neurodevelopment. These results offer significant insights into the etiology of schizophrenia.

Conclusion
This research not only expands our understanding of snoRNA biology but also opens new avenues for exploring their potential as biomarkers and therapeutic targets in schizophrenia and other neuro-developmental disorders. Further research is needed to fully understand their functional contributions and explore their therapeutic potential.

DB2_8/P_40b Dysregulated circular RNAs in schizophrenia patient-derived olfactory stem cells perform key roles in cell adhesion and migration

Presenting Author: Oak Hatzimanolis

Oak Hatzimanolis - Institute for Biomedicine and Glycomics

Dr Jamila Iqbal - Institute for Biomedicine and Glycomics

Daniel Russel - Institute for Biomedicine and Glycomics

Caio Damski - Institute for Biomedicine and Glycomics

Dr Alex Sykes - Institute for Biomedicine and Glycomics

Dr Alexandre Cristino - Institute for Biomedicine and Glycomics

Chair: Dr Warren Logge

Background
Circular RNAs (circRNAs) are non-coding RNAs with diverse biological functions, including miRNA sequestration, transcriptional regulation, and RNA-binding protein interactions. Recent studies have highlighted the relevance of circRNAs in psychiatric disorders, notably schizophrenia, which is characterised by several risk variants in non-coding regions. CircRNAs are emerging as critical players in the cause of neuropsychiatric disorders, and key regulators of neuron development and function, however causal links between genotype and phenotype remains poorly understood. One way to elucidate these mechanisms are patient-derived olfactory neuronal stem (ONS) cells, as they offer a robust primary cell model for studying neurological conditions such as schizophrenia.

Methods
We employed total RNA sequencing of ONS cells from adolescent and adult patients, alongside age-matched controls. The sequencing data was analysed computationally to identify circRNA expression profiles. Bioinformatics analysis was conducted to discriminate circRNA expression signatures between patients and controls. To assess the diagnostic value, we trained a support vector machine (SVM) classifier on these circRNA profiles. Differential expression of circRNAs was validated using RT-qPCR and Sanger sequencing. High-content imaging analysis was employed to evaluate various features of nucleus, mitochondria and endoplasmic reticulum, and live cell imaging was used to assess migration characteristics.

Results
Our support vector machine model achieved accuracies of 0.91 and 0.89, and precisions of 0.92 and 0.93 for adult and adolescent groups, respectively. We validated circRIMS1 and circHAS2, which were upregulated and downregulated in patient ONS cells. RIMS1 and HAS2 are essential in synaptic vesicle exocytosis and cell adhesion/migration, respectively. Expression of circRIMS1 and circHAS2 was strongly correlated with disease-associated phenotypic traits observed in a high-content ONS cell image analysis. Our integrated analysis revealed dysregulated circRNAs are associated to subcellular distribution of mitochondria, endoplasmic reticulum, and nucleus. Furthermore, live cell imaging linked dysregulated circRNAs to cell velocity and travel distance.

Conclusions
These findings collectively highlight the value of our primary human cell model in elucidating the diagnostic potential of circRNAs, providing new insights into their functional role in schizophrenia aetiology. The significant correlation between dysregulated circRNAs and disease-associated phenotypic traits underscores their potential as biomarkers for early diagnosis and targeted therapeutic strategies. Our research not only advances the understanding of circRNA involvement in schizophrenia but also emphasizes the importance of integrating multi-faceted analytical approaches to uncover the molecular mechanisms underlying neuropsychiatric disorders. Future research could further explore therapeutic interventions targeting circRNA pathways, offering promising avenues for personalized treatment strategies.

Poster Abstracts

Please note that Poster Abstracts are displayed in alphabetical order.

Poster Abstracts

Poster Session 2: Tuesday

P_02b The Effects of Food Insecurity on Eating Behaviours

Presenting Author: Abbey Livermore

Abbey Livermore - UNSW: Honours Student

Zhi Yi Ong - UNSW: Supervisor

Background
Food insecurity (FI) is defined as having inconsistent access to food of adequate quality and quantity to meet basic needs. FI effects 2.4 billion people globally and is dramatically increasing in Australia given the current cost-of-living crisis. Despite FI being characterised by having limited access to food, there is evidence suggesting that FI is positively associated with obesity. However, the mechanisms that underlie this relationship are unclear. This study examined the hypothesis that FI increases the risk of obesity through changes in eating behaviours.

Methods
To mimic FI, female adolescent rats received a variable amount of food at a random timepoint daily for 4 weeks. After this, they had free access to food. Food secure (FS) rats had ad libitum access to food throughout the experimental period. We tested their eating behaviours in response to internal (gastrointestinal signals) and external (food cues) signals: 1) We examined their sensitivity to gastrointestinal signals by measuring liquid diet intake in response to a satiation peptide cholecystokinin (CCK), 2) we examined cue-induced eating behaviours using an appetitive conditioning task.

Results
Results show that whilst both FI and FS animals decreased intake following high dose CCK, only FS animals reduced food intake with low dose CCK. This suggests that FI animals were insensitive to the satiating effect of CCK. When cue-induced eating behaviours were examined, FI animals acquired the appetitive conditioning task faster and showed greater appetitive responses to the food cue compared to FS animals, suggesting increased food-cue salience in FI animals.

Conclusion
This is the first study to show that FI causes sensitisation to food-cues in the environment and dampens satiation signals resulting in greater food intake. These mechanistic adaptations help elucidate the relationship between FI and obesity.

Poster Abstracts

Poster Session 2: Tuesday

P_01b Exploring behavioural interactions between methamphetamine and psilocybin in mouse models of methamphetamine sensitization and head twitch response.

Presenting Author: Alex Athanasopoulos

Alexander G. Athanasopoulos - School of Psychology, Brain and Mind Centre, The University of Sydney

Tylah J. Doolan - School of Psychology, Brain and Mind Centre, The University of Sydney

Nicholas A. Everett - School of Psychology, Brain and Mind Centre, The University of Sydney

Background
Psilocybin shows promise for the treatment of substance use disorders, although its interactions with methamphetamine are understudied. Importantly, methamphetamine-induced psychosis is prevalent in 37-43% of users and is an exclusion criterion for psilocybin clinical trials, which may be related to methamphetamine-induced changes to expression of psilocybin's primary neural target, the cortical 5HT2A receptor. These interactions need to be understood to inform safety and accessibility of psilocybin- assisted therapy. Therefore, our study addresses two questions: 1)Does withdrawal from chronic methamphetamine alter the potency of psilocybin for inducing hallucinogenic-like behaviour? 2)Does psilocybin administered throughout withdrawal alter the development of sensitization to methamphetamine?

Methods
112 male C57BL/6J mice were administered methamphetamine (2.5mg/kg, i.p.) or saline daily for 8 days, and were then withdrawn for 14 days. On withdrawal day 14, mice were challenged with methamphetamine. Throughout withdrawal, mice were allocated to receive saline or a dose of psilocybin (0.3, 1, 3 mg/kg), which were administered at different periods during withdrawal: acute (withdrawal day 1), protracted (withdrawal day 13), or a combination (withdrawal days 1 & 7). The head-twitch-response (HTR) to psilocybin was assessed using custom software. Locomotor activity was recorded following methamphetamine injection on days 1, 8, and challenge day 22.

Results
This experiment is underway, however based on the scarce but available literature we have several hypotheses. Firstly, we anticipate that chronic methamphetamine administration will alter the potency for inducing HTR (ED50) and efficacy (maximum HTR at any dose), and that this will interact with withdrawal stage. Similarly, we anticipate that psilocybin treatment in early, but not late withdrawal from methamphetamine will reduce the development of methamphetamine sensitization.

Conclusion
The present study may provide critical knowledge regarding the interactions between methamphetamine and psilocybin necessary to inform clinical trial design. The results from the head-twitch assay will provide insight into whether giving psilocybin to chronic methamphetamine users may exacerbate psychosis symptoms, which is significant for determining eligibility for psilocybin-assisted psychotherapy. Further, the methamphetamine locomotor sensitisation findings will identify the optimal timing and dosing to begin psilocybin treatment relative to last methamphetamine use, which would be impactful for understanding the mechanism, as well as the timing underlying psilocybin's therapeutic effects.

Poster Abstracts

Poster Session 1: Monday

P_55a Characterising the pharmacology of social motivation in female rats, using the social operant conditioning task.

Presenting Author: Alex Athanasopoulos

Alex Athanasopoulos - School of Psychology, Brain and Mind Centre, University of Sydney

Isabella Courtney - Brain and Mind Centre, University of Sydney

Tylah Doolan - School of Psychology, Brain and Mind Centre, University of Sydney

Nicholas Everett - School of Psychology, Brain and Mind Centre, University of Sydney

Background
Many psychiatric conditions are associated with deficits in social motivation, which can present barriers to engaging in psycho-social therapies and can worsen the condition due to isolation from protective social networks. There has been little progress made on the development of therapies to treat social anhedonia, due in part to the lack of animal models which model social motivation. Here we use the relatively novel operant model of social motivation in rats to characterise FDA-approved drugs and tool compounds which selectively agonise receptors which are hypothesised to modulate social motivation.

Methods
40 pair-housed female Sprague-Dawley rats underwent daily 1-hour social operant conditioning, and were counterbalanced to undergo pharmacological testing every 3-4 sessions. We investigated selective agonists of 5-HT1A receptors, which are biased towards post-synaptic receptors (NLX-101, approved for Rhett's syndrome), or agonise pre- and post-synaptic receptors (NLX-112, in Phase-2 trials for Parkinsonian dyskinesia). Due to its serotonin releasing and pro-social effects, we investigated MDMA, and methamphetamine as a stimulant control. We investigated a selective 5-HT1B agonist (CP 94253), which causes oxytocin- dependent social reward in other models, as well as oxytocin itself, and the 5HT2A agonist psilocybin acutely and 24-hours post dosing.

Results
We found surprising results, indicating that the majority of these compounds paradoxically reduce social operant self-administration. We hypothesise this is due to increases in social rewards, leading with rapid satiety, as rats do rapidly satiate in this task at baseline. Specifically, oxytocin, MDMA, and buspirone all acutely reduced social lever pressing. Clinical 5HT1A agonists NLX-101 and NLX-112 either had no impact on the behaviour, or subtly delayed satiety (NLX-112 at one dose). The 5HT1B agonist had no impact on social behaviour, nor did psilocybin at 24 hour post-dosing. Methamphetamine profoundly increased lever-pressing likely due to its stimulant effects.

Conclusion
This social operant model is fairly new to behavioural neuroscience and psychopharmacology. Here we present some of the first pharmacological investigations into modulation of volitional social reward in rats, and identify surprising but crucial insights, using human-validated (E.g. FDA approved) pharmacology, and novel exploratory pharmacology. This research is ongoing, and will further investigate oxytocinergic and serotonergic targets for promoting social rewards. We will also conduct neuorobiological experiments to characterise this satiety-promoting effect, to determine if it is due to promoting rewards, or an other currently unknown mechanism.

Poster Abstracts

Poster Session 2: Tuesday

P_25b Hippocampally-mediated cognition and 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

Lok-Kin Yeung - Columbia University Irving Medical Center

Adam Brickman - 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. Pattern separation – the cognitive capacity to discriminate between similar stimuli – appears to be mediated by distinct hippocampal subfields: cornu ammonis 3 (CA3) and dentate gyrus (DG). No research has assessed pattern separation and hippocampal subfield volume in relation to cannabis use or cannabis use disorder (CUD). This project aimed to assess pattern separation and CA3 and DG subfield volume in 1) people with near daily cannabis use compared to controls; and 2) people with no, mild, or moderate/severe CUD.

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 smoked cannabis ?4x/month with mild (n=19; 4F, 15M) or moderate/severe (n=23; 5F, 18M) CUD and people who smoked cannabis but did not have current CUD (n=20; 8F, 12M) were recruited. Two pattern separation tasks were administered: the Mnemonic Similarity Task (MST), and the Modified Benton Visual Retention Test (ModBent). Hippocampal subfield volumes were assessed based on T2-weighted MRI scans optimized for automated analyses using the Automatic Segmentation of Hippocampal Subfields package (UPenn). The analytic plan was preregistered (https://osf.io/c4rzh).

Results
There were no differences in CA3 or DG volumes between groups (Study 1: $F(1,38) = 1.924$, $p = 0.172$, $n2 = 0.048$; Study 2: $F(2,54) = 0.092$, $p = 0.912$, $n2 = 0.003$). There were no differences in MST or Modbent performance between groups (Study 1: $F(1,36) = 2.914$, $p = 0.096$, $n2 = 0.075$; Study 2: $F(2,45) = 0.454$, $p = 0.638$, $n2 = 0.020$), and no interactions between group, CA3 or DG volumes and cognition in Studies 1 or 2 ($ps > 0.05$).

Conclusion
Contrary to expectations, there were no differences in pattern separation as a function of cannabis use or CUD, and no association with hippocampal subfield volumes. Given previous associations between cannabis use and reduced hippocampal volume, further research using larger samples with more varied patterns of cannabis use is warranted.

Poster Abstracts

Poster Session 1: Monday

P_43a Expression of hippocampal cortisol receptors and FKBP5 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; School of Medical Sciences, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia

Dominic Kaul - School of Medical Sciences, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, 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; School of Medical Sciences, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia

Background
Dysfunction of the stress response is a major risk factor for psychopathology, yet, human evidence of this association is limited. Hippocampal cortisol receptors (NR3C1 and NR3C2) and their modulators (e.g. FKBP5) are key coordinators of this stress response. If and how the receptors and FKBP5 are altered by stress exposure in psychopathology in the human brain at spatial resolution is yet to be explored.

Methods
Human postmortem hippocampus tissue was acquired from individuals who lived with either schizophrenia or bipolar disorder, 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 spatially resolved gene expression. Hippocampal subregions were manually annotated with expression levels, and the distribution of the expression of cortisol receptors (e.g. glucocorticoid receptors, mineralocorticoid receptors) and FKBP5, was then compared between groups.

Results
FKBP5 expression in childhood stress had lower FKBP5 expression in the CA4 subregion compared to controls (-35%, PFDR=0.046) and no stress (- 53.2%, PFDR=9.150e-15). FKBP5 expression was lower in the polymorphic layer in childhood stress compared to controls (-19.7%, PFDR = 0.016) and no stress (-29.5%, PFDR=0.0034), with the distribution higher compared to control (6.26, PFDR=0.0034) and no stress (6.78, PFDR=0.0052). The distribution of FKBP5 expression in adulthood stress cases was higher compared to controls (+4.54%, PFDR=0.01242) and no stress (4.75%, PFDR=0.000573) in the molecular layer of the dentate gyrus. No changes in cortisol receptor expression was observed.

Conclusion
This data indicates that in the human hippocampus, prior exposure to severe stress associates with lasting changes in the expression of FKBP5 in psychiatric disorders. This may contribute to dysfunction of the stress response via alterations to cortisol receptor activity. Subregion specific changes in FKBP5 between the adulthood and childhood stress cases suggests that the mechanism of psychiatric disorder development and progression may be biologically distinct. This is an important preliminary study investigating stress-related psychopathology of the hippocampus at a spatial transcriptomic level and provides promising direction for future studies.

Poster Abstracts

Poster Session 2: Tuesday

P_27b Positive experience shifts the circuit for encoding of fear memories away from the basolateral amygdala

Presenting Author: Arvie Abiero

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Background
Prior experience changes the way we learn and conceptualize our world. Individuals with traumatic experiences in early life are more likely to develop an anxiety disorder, while individuals with positive experiences are less likely to succumb to this fate. The basolateral amygdala (BLA) is believed to be the brain's fear center, necessary for formation and storage of fear memories. Yet, we know less about how positive experience can be a variable that could change these processes. However, we have shown previously that GABAergic neurons in the lateral hypothalamus (LHGABA) become critical for formation of fear memories with recent positive experience.

Methods
This project establishes how recruitment of LHGABA neurons to encode fear memories after positive experience influences the role of BLA fear memory encoding. First, we examined the effect of optogenetic inhibition of BLA pyramidal neurons during formation of fear memory with or without positive experience. We concurrently tested the impact of optogenetic inhibition of LHGABA neurons in another group to ensure that any consequence of positive experiences on BLA encoding of fear would be accompanied by recruitment of LHGABA neurons. Next, we examined whether a more permanent neurotoxic lesion of BLA would show results consistent with our temporally-specific optogenetic approach.

Results
First, we showed that the BLA is necessary for development of the fear memory in rats without positive experience. That is, both optogenetic and lesion experiments showed that the BLA was required to form a fear memory in naïve rats, consistent with the literature. However, positive experience abolished the role of the BLA in fear memory encoding. This was the case in both our optogenetic and lesion approaches. We also successfully replicated the results found in our previous work that LHGABA neurons are recruited in encoding fear memories after experience with positive experience.

Conclusion
These results demonstrate that positive experience shifts the encoding of fear memories away from BLA and towards the LH. Given that one of the most replicable findings is that BLA lesions in rats prevents the formation and recall of fear memories, these data require a modification of existing models of fear processing. A shift in fear circuit to LH could underlie the protective effect of positive experience on future mental health and produce resilience. This work shows that prior experience can change the way we encode memories in the future and suggests a more fluid approach to conceptualising mnemonic processing.

Poster Abstracts

Poster Session 1: Monday

P_22a Fibroblast growth factor 21 reduces consumption and seeking

Presenting Author: Bart Cooley

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Willow Ash Heller – School of Psychology, UNSW Sydney, Australia

Alyssa Wenqian Lim - School of Psychology, UNSW Sydney, Australia

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Gavan McNally - School of Psychology, UNSW Sydney, Australia

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Background
Fibroblast growth factor 21 (FGF21) is a liver-derived hormone which reduces alcohol consumption in mice and non-human primates; however, the role of FGF21 in regulating other alcohol-related behaviours is poorly understood. Here we sought to test the effect of a long-acting analogue of FGF21, PF-05231023 on established intermittent home cage drinking in mice as well as on Pavlovian conditioned approach to alcohol cues and motivation for alcohol rewards. Additionally, we developed an instrumental choice model which allows for testing of FGF21 compounds on both continuous and discrete choice between alcohol and non-drug rewards.

Methods
In Experiment 1, the effects of PF-05231023 (1,3,10 mg/kg i.p.) were tested on alcohol consumption in C57BL/6J mice with a history of intermittent alcohol access using a within-subjects Latin-square design. In Experiment 2 we validated a within-subjects conditioned approach protocol and confirmed the conditioned reinforcing properties of 15% v/v alcohol and sucrose cues. We then assessed the effect of PF-05231023 (3-10mg/kg i.p.) treatment on 15% v/v alcohol and sucrose conditioned approach behaviours. In Experiment 3 we assessed PF-05231023 (3-10mg/kg i.p.) in combination with a glucagon-like peptide-1 agonist Exendin-4 (GLP-1, 2.4ug/kg i.p.) on progressive ratio responding for 15% v/v alcohol rewards. Finally, in Experiment 4 we validated a continuous and discrete choice model between alcohol and grain rewards.

Results
In Experiment 1, PF-05231023 reduced alcohol consumption and preference in a dose- and sex-specific manner. In Experiment 2, PF-05231023 impaired approach behaviours in a dose and outcome selective manner. Similarly, in Experiment 3, PF-05231023 reduced alcohol breakpoint in a dose-selective manner indicating reduced motivation for alcohol rewards. In Experiment 4 mice showed biased instrumental choice during a continuous choice extinction test, but dynamic choice across a continuous reinforcement test. Additionally, we found in a discrete setting animals choices outcome and latencies are related and are amendable to computational cognitive modelling used in human tasks

Conclusion
These findings show that FGF21-containing treatments can attenuate established alcohol drinking and seeking behaviours. Additionally, our choice procedure provides a promising translational model for testing FGF21 compounds.

P_37b Cholinergic modulation of the prefrontal cortex in the formation and extinction of fear memories

Presenting Author: Belinda Lay

Belinda P. P. Lay - UNSW Sydney

Vincent Laurent - UNSW Sydney

Background
The prefrontal cortex receives a dense cholinergic innervation from the basal forebrain, the horizontal limb of the diagonal band of Broca (HDB). Acetylcholine release in the medial prefrontal cortex (mPFC) is thought to have important regulatory control in fear. However, how this regulation occurs and its underlying mechanisms remains poorly understood. The present study sought to examine whether HDB projections to the mPFC regulates the formation, extinction and renewal of fear memories.

Methods
We used optogenetics in ChAT:cre transgenic rats to silence the HDB to infralimbic (IL) cortex cholinergic pathway or HDB to prelimbic (PL) cortex cholinergic pathway. Silencing took place either during Pavlovian fear conditioning or extinction.

Results
Silencing HDB projections to the IL cortex during fear extinction, but not fear acquisition, enhanced retrieval of the extinction memory and prevented renewal. By contrast, silencing HDB terminals in the PL cortex during either conditioning or extinction had no effect.

Conclusion
These findings suggest that the basal forebrain cholinergic projections to the IL cortex from the HDB plays a critical role in controlling the durability of fear memories. Additionally, this function is specific to the IL cortex.

P_17b Investigating the complex relationships between peripheral brain-derived neurotrophic factor (BDNF) and posttraumatic stress disorder (PTSD) diagnosis and symptom severity

Presenting Author: Bonnie Quigley

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Adem T Can - National PTSD Research Centre at the Thompson Institute, University of the Sunshine Coast

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Background
Post-traumatic stress disorder (PTSD) can develop following exposure to traumatic events leading to debilitating quality-of-life impacts. Among PTSD-related biomarkers, brain-derived neurotrophic factor (BDNF) has been at the forefront of investigation. BDNF is essential for learning and memory, making it of great interest in the development and symptomology of PTSD. However, investigations of peripheral BDNF in relation to PTSD have generated mixed results. Factors contributing to this variability include the co-presence of both pro-BDNF and mature BDNF (which have opposite biological effects) in circulation and significant differences in BDNF between serum and plasma (due to platelet contributions of BDNF).

Methods
BDNF levels were examined in a group of older adults with PTSD (n=24, Mean age=56.2±6.9, 15F) and without PTSD (n=24, Mean age=56.8±5.7, 16F), as well as in a larger PTSD-only cohort (n=43, Mean age=47.6±12.0, 27F). Both serum and plasma were tested using three distinct BDNF assays (targeting BDNF generally, only pro-BDNF and only mature BDNF). Differences in BDNF levels by PTSD diagnosis were determined by Mann Whitney U test and correlations between BDNF levels and symptom severity (from CAPS-5 and PCL-5 scores) were determined by Spearman's rank correlation.

Results
BDNF levels were found to be significantly higher in the older adult group with PTSD compared to the group without, but only when serum was measured using the general BDNF assay (z=-2.49, p=0.013). Within the larger PTSD cohort, a significant correlation between BDNF levels and symptom severity was detected, but only when mature BDNF was measured from serum (CAPS-5 - rs(43)=-0.435, p=0.004; PCL-5- rs(42)=-0.331, p=0.032). No

measurements of BDNF from plasma or pro-BDNF from serum were associated with PTSD diagnosis or symptom severity.

Conclusion

This evaluation of testing methods and targets for peripheral BDNF from both serum and plasma revealed that significant relationships between BDNF and both PTSD diagnosis and symptom severity can be detected, but only with specific testing strategies. It also revealed that overall higher levels of general BDNF in serum associated with a diagnosis of PTSD but that lower levels of mature BDNF in serum associated with more severe PTSD symptoms. These findings highlight the complex relationship between peripheral BDNF and PTSD and the importance of considering the testing strategy and form of BDNF measured when investigating this neurotrophin.

Poster Abstracts

Poster Session 1: Monday

P_52a Uncovering the role of glycinergic neurons in the periaqueductal grey

Presenting Author: Caitlin Fenech

Caitlin Fenech - Pain Management Research, Kolling Institute of Medical Research, 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
The debilitating condition of chronic pain is a significant health issue that affects 1 in 5 people globally 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. We have demonstrated that these neurons, marked by the glycine transporter GlyT2, can bidirectionally modulate acute nociception in mice, whereby chemogenetic inhibition is analgesic. In addition, activation of these neurons increased locomotor activity in both males and females.

Methods
We bilaterally injected inhibitory viral (hM4Di), excitatory (hM3Dq) or control (mCherry) into the vlPAG of GlyT2::Cre mice. After viral transduction, the animals were observed in a light-dark test to measure anxiety-like behaviours. In a separate cohort of animals, we induced a persistent inflammatory pain state via injection of Complete Freunds Adjuvant (CFA; an inflammatory agent) in the left hind paw. Following i.p injection of CNO (5mg/kg or vehicle), nociception testing was carried out using the von Frey, acetone, and hotplate tests. The animals were also observed in an open-field (locomotion) and light-dark (anxiety-like behaviours) test.

Results
Chemogenetic activation of GlyT2+ PAG neurons significantly increases the time in the light zone in the light-dark test in both males and females (paired t-test), suggesting that activation of these neurons is anxiolytic. For the persistent inflammatory pain animals, (i.e. CFA injected) chemogenetic modulation of GlyT2+ PAG does not alter the deficits in nociception and maintains the ability to modulate anxiety-like behaviours in the light-dark test in both males and females (unpaired t-test).

Conclusion
These results demonstrate that activation of GlyT2+ PAG neurons is both pro-nociceptive and anxiolytic, suggesting these neurons contribute to not only nociceptive signalling but also the wider affective pain experience.

Poster Abstracts

Poster Session 1: Monday

P_17a Neurosteroid Replacement Therapy Using Tiagabine and Zuranolone Restores Cerebellar Neurodevelopment and Reduces Hyperactive Behaviour Following Preterm Birth

Presenting Author: Carlton Pavy

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

Background
Preterm birth exposes the neonate to hypoxic-ischemic and excitotoxic insults which impair neurodevelopment and are magnified by the premature loss of placentally supplied, inhibitory neurosteroids. The cerebellum is a neuronally dense brain region which undergoes critical periods of development during late gestation, when preterm births frequently occur. We propose that neurosteroid replacement therapy using tiagabine and zuranolone will protect the cerebellum against preterm associated insults.

Methods
Guinea pig dams received c-section surgery preterm (gestational age (GA)64) or at term (GA70) with preterm pups administered tiagabine (2.5mg/kg/day), zuranolone (1mg/kg/day) or vehicle (15% ?-cyclodextrin) until term equivalent age (GA70). Behavioural testing was performed at corrected postnatal day 8 (PND8) and PND41 with tissue collection occurring at PND42. Neurodevelopmental markers (MBP, OLIG2 and NeuN) were assessed within the cerebellum by immunohistochemistry whilst GABAergic and glutamatergic pathway expression was quantified using high throughput RT-PCR.

Results
Zuranolone and to a lesser extent, tiagabine were able to protect against hyperactive behaviour at PND8 in males whilst in females, a less marked hyperactive phenotype was present with neither treatment impacting behaviour further. Both treatments improved MBP staining whilst tiagabine was found to restore oligodendrocyte maturation in females only. GABAergic and glutamatergic pathway expression was found to be restored by both treatments in females.

Conclusion
Overall, this study demonstrates the neuroprotective attributes of neurosteroid replacement therapy using tiagabine and zuranolone, thereby demonstrating their potential to mitigate long-term neurodevelopmental impairments. Furthermore, the sexually dimorphic effects observed suggest future investigations may show increased benefit by using sex-specific treatment regimes.

Poster Abstracts

Poster Session 1: Monday

P_01a Distinct contribution of cortico-striatal mechanisms to elucidate a pathway for conditioned punishment

Presenting Author: Cassandra Ma

Cassandra Ma – School of Psychology, University of New South Wales

Laura Bradfield – Centre for Neuroscience and Regenerative Medicine, University of Technology Sydney

Gavan McNally – School of Psychology, University of New South Wales

Simon Killcross – School of Psychology, University of New South Wales

Background
Aversive events in our environment shape our behaviours and how we respond to them. Instrumental behaviours are punished when an action results in an aversive event. Yet there are instances where behaviours appear inappropriately sensitive to potential threats. The neural underpinnings of these inappropriate behaviours are poorly understood. The brain regions of the cortico-striatal pathway, including the prelimbic (PL) and infralimbic (IL) cortices, and the nucleus accumbens core (AcbC) and shell (AcbSh), have been implicated in motivated behaviours in response to fear and rewarding outcomes respectively, but not in choice behaviours dependent on punishment contingencies.

Methods
In a conditioned punishment task, we trained rats to press two levers for pellets. Their responding suppressed on one lever when it also earned a conditioned stimulus (CS+) that was paired with a footshock, whilst responding continued on the other lever that earned a neutral conditioned stimulus (CS-) that did not elicit a footshock. Following conditioned punishment and fear learning, animals were micro-infused with the GABA agonist, muscimol, or saline (counterbalanced) into either the PL, IL AcbC or AcbSh prior to an expression test.

Results
Here, we show that regions of the cortico-striatal pathway are implicated in punishment and fear expression in different ways. Inhibiting the IL or PL increased responding on the punished, whilst inhibiting the AcbC or AcbSh decreased responding on the unpunished lever. Suppressed responding to both levers during the CS+ was abolished following inhibition of the PL and AcbSh, but not the IL and AcbC.

Conclusion
These results suggest there is an effect of cued punishment expression that is distinct from non-cued punishment and fear expression to the target cue, that is mediated by cortico-striatal circuitry. We then proposed to determine whether the neurons that are activated following learning the punishment and fear contingency in the PL and IL are also those that project to the AcbC and AcbSh respectively by double-labelling the neurons with a retrograde tracer and c-Fos. This will inform future experiments targeting specific pathways that may be implicated in conditioned punishment.

Poster Abstracts

Poster Session 2: Tuesday

P_29b MiNDful Mediation: Psychological distress mediates the relationship between neuroticism and neurofilament light

Presenting Author: Christa Dang

Christa Dang – National Ageing Research Institute, The University of Melbourne

Dhamidhu Eratne – Neuropsychiatry Centre, The Royal Melbourne Hospital; Department of Psychiatry, The University of Melbourne

Dennis Velakoulis – Neuropsychiatry, Royal Melbourne Hospital; Melbourne Neuropsychiatry Centre & Department of Psychiatry, University of Melbourne

Background
Personality traits such as neuroticism and symptoms of depression, anxiety and stress have been associated with biomarkers of Alzheimer's disease and neurodegeneration, and increased risk of poor mental health and dementia. The aim of this study was to examine relationships between mood symptomology and personality factors with blood-based biomarkers of neuronal injury, neuroinflammation, and Alzheimer's disease.

Methods
Control participants from the Markers in Neuropsychiatric Disorders (MiND) Study were included in analyses examining relationships between blood-based biomarkers (neurofilament light (NfL), glial fibrillary acidic protein (GFAP) and p-tau217) and 1) DASS-21 scores and 2) Big 5 personality traits (Mini-IPIP). Covariates were age, sex, and weight.

Results
Participants with higher neuroticism scores tended to have higher levels of NfL and p-tau217. Greater levels of total psychological distress were associated with higher levels of NfL and GFAP. Psychological distress mediated the relationship between neuroticism and NfL.

Conclusion
Neuroticism is associated with increased susceptibility to psychological distress and poor mental health, which is associated with higher levels of NfL. Given the utility of NfL as an early diagnostic marker for dementia, the mediating effect of psychological distress presents an opportunity for future research to examine mental health interventions for reducing dementia risk.

Poster Abstracts

Poster Session 1: Monday

P_37a Neurobehavioral determinants of diet-induced obesity

Presenting Author: Christiana Milleniaputri Suhartono

Christina Milleniaputri Suhartono – Department of Biochemistry and Pharmacology, University of Melbourne

Diana Sketriene – Department of Biochemistry and Pharmacology, University of Melbourne

Yan Li – Department of Biochemistry and Pharmacology, University of Melbourne

Nimshitha Pavathuparambil Abdul Manaph – Department of Biochemistry and Pharmacology, University of Melbourne

Priya Sumithran – Department of Surgery, School of Translational Medicine, Monash University

Bianca Jupp – Department of Neuroscience, School of Translational Medicine, Monash University

Robyn M. Brown – Department of Biochemistry and Pharmacology, University of Melbourne

Background
Factors that enable some individuals to maintain control over their eating habits, while others engage in maladaptive eating behaviour and develop obesity, remain largely unknown. Behavioural attributes (traits) reflecting shared genetic and/or biological aetiologies likely interact with a person's environment to drive overeating and, consequently, diet-induced obesity. Yet determining whether these attributes pre-date obesity or emerge as a consequence of extended high-fat/high-sugar food consumption in people with obesity is not a question easily answered in humans. This study utilised an established rat model of diet-induced obesity to determine, for the first time, specific neurobehavioral markers predictive of vulnerability to obesity.

Methods
Outbred Sprague Dawley rats (n = 35) were allowed free access to a high-fat/high-sugar diet (52% kcal fat) for 10-weeks then separated by weight gain into obesity-prone and obesity-resistant subgroups. Multidimensional behavioural profiling was performed prior to the diet period to examine predisposing risk traits (novelty seeking, anxiety, sign/goal tracking, attribution to incentive salience, cognitive inflexibility, impulsivity). Structural magnetic resonance imaging (MRI) and fluorodeoxyglucose positron emission tomography (FDG-PET) were conducted pre- and post- diet to examine structural and functional neuroimaging correlates of diet-induced obesity, and to determine the mechanistic trajectory towards the state of obesity.

Results
The future tendency to develop diet-induced obesity was found to correlate with the reversal learning parameter ? ($p = 0.0409$), which plays a central role in cognitive flexibility. MRI and PET scan analyses are still ongoing. It is hypothesised that, as brain plasticity mechanisms are tightly linked to learning, functional connectivity between the prefrontal cortex (PFC) and posterior dorsomedial striatum (pDMS) may be related to these findings.

Conclusion
Outcomes from this study can provide valuable insight into the neurobehavioral underpinnings of pathological overeating and diet-induced obesity, and allow early identification of at-risk individuals.

Poster Abstracts

Poster Session 1: Monday

P_39a Genetic Variants Associated with Schizophrenia Lead to Allele-Specific Expression Through Epigenetic Regulation

Presenting Author: Daniel Russell

Daniel J. Russell – Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia

Jamila Iqbal – Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia

Alexandre S. Cristino – Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia

Background
Schizophrenia is a complex mental disorder with a significant genetic component. Recent genome-wide association studies (GWAS) on schizophrenia have revealed most single nucleotide polymorphisms (SNPs) associated with this condition are in non-protein coding regions, suggesting that variation to gene regulation has a greater effect on this disorder than genetic variation to proteins themselves.

Methods
To uncover the potential epigenetic mechanisms of these associated genes, we developed a computational pipeline that integrated Illumina whole genome sequencing and RNA sequencing as well as Oxford Nanopore Technology DNA sequencing data from human olfactory neurosphere-derived stem cells from an adolescent cohort to investigate allele-specific expression and allele-specific DNA methylation in schizophrenia patients.

Results
We identified 150 allele-specific differentially methylated loci at schizophrenia-associated SNPs, including several cases due to imprinting or haplotype-specific regulation affecting genetic penetrance of heterozygous genotypes. One notable case involves SNP rs29553636 A>G, located inside a CpG island adjacent to a transcription start site within the MYO15A gene. Expression quantitative trait locus (eQTL) analysis of this SNP reveals lower MYO15A expression in the GG genotype compared to AA and AG in our samples and the Genotype-Tissue Expression (GTEx) project cerebellum data. Notably this variant creates an additional CG motif, resulting in an extra methylation site and consequent gene downregulation.

Conclusion
These insights into allele-specific expression and DNA methylation help further our understanding of schizophrenia's genetic architecture, which may pave the way for future investigations into targeted therapies and personalised treatment approaches.

Poster Abstracts

Poster Session 2: Tuesday

P_08b Vitamin D a potent differentiation agent for dopamine neurons

Presenting Author: Darryl Eyles

Darryl W Eyles - Queensland Brain Institute and Queensland Centre for Mental Health Research

Renata Pertile - Queensland Brain Institute

Vanshika Raman - Queensland Brain Institute

Xiaoying Cui - Queensland Brain Instituteand Queensland Centre for Mental Health Research

Background
Maternal Vitamin D deficiency is an epidemiologically-validated risk factor for schizophrenia. My group has provided multiple pieces of evidence to show how the absence of this hormone delays the maturation of dopaminergic neurons in vitamin D deficient embryos. To understand the basic mechanisms driving this relationship, we have previously studied the effects of vitamin D on cultured neuroblastomas/FACS sorted embryonic dopamine neurons/ mesencephalic explants/midbrain tissue. However, to date we have not established the long-term effects of vitamin D directly in cultured primary dopamine neurons.

Methods
We obtained ventral mesencephalon (Embryonic day 14-16) from (GFP tagged Dopamine transporter (DAT),cre mice. We dispersed this tissue and cultured cells in neurobasal plus media containing B27 and charcoal stripped sera (to exclude endogenous vitamin D) for 15 days. 1,25dihyroxy vitamin D (20nm) was added at DIV3 and refreshed every 4-5 days. Sholl analysis was used to establish neuronal branching and neurite length. Dopamine release was assessed using 2photon imaging after loading cells with a fluorescent dopamine ligand (FFN200) and monitoring FFN200 release after amphetamine perfusion. Synapse protein intensity was assessed by immunohistochemistry.

Results
We show culturing DAT+ primary neurons in the presence of vitamin D increases neurite outgrowth, and the number of neurite branches. We also show a redistribution of (Synaptophysin 1) as a measure of general synaptic density to more distil neurites. We also show staining intensity of presynaptic proteins associated with neurotransmitter release i.e. Rim 1 and 2 are decreased. Finally, by visually establishing dopamine uptake in DAT+ neurons we show these neurons release more dopamine in response to amphetamine when cultured with vitamin D.

Conclusion
Here we provide further evidence that vitamin D is an important differentiation agent for developing dopamine neurons. For the 1st time we show in cultured DAT+ mesencephalic dopamine neurons, that chronic exposure to the active vitamin D hormone changes neurite and synaptic architecture and increases the neurons functional capacity to release dopamine. Vitamin D is therefore well positioned to affect the early innervation of dopaminergic targets in the striatum. Such a mechanism may be operating in vitamin D deficient human embryos that later develop abnormal dopamine function potentially underlying the risk relationship between vitamin D deficiency and schizophrenia.

P_28b Instrumental Learning Enhances the Intrinsic Excitability of Basolateral Amygdala Neurons

Presenting Author: Eddie Wise

Eddie T Wise – Macquarie University

Philip Jean-Richard-dit-Bressel – University of New South Wales

Joanna O-Y Yau – University of New South Wales

Gavan P McNally – University of New South Wales

John M Power – University of New South Wales

Background
The basolateral amygdala (BLA) is a structure that is critical for forming Pavlovian (stimulus-outcome) and instrumental (action-outcome) emotional associations. Previous studies have established that Pavlovian fear conditioning increases the intrinsic excitability of BLA projection neurons. Learning-associated increases in excitability are hypothesised to facilitate the induction of synaptic plasticity and integration of neurons into functional learning circuits. Here we examined whether instrumental emotional association learning produces similar changes in excitability.

Methods
Male and Female Long Evans rats (2-4 months) were split into 3 behavioural groups; fear conditioned, punished, and reward. All groups were food deprived and trained to make lever press responses for food reward on a VI30 schedule across seven daily sessions. On day 8, punished rats received response-contingent footshocks, fear conditioned rats received response-independent footshocks, and reward rats received no shock. After training, brains were extracted, coronal brain slices prepared, and whole-cell patch-clamp recordings were made from BLA projection neurons. Intrinsic excitability was measured as the number of action potentials (APs) evoked by a series of depolarising current injections.

Results
Reward learning increased the intrinsic excitability of BLA projection neurons compared to naive controls. Pavlovian fear conditioning arrested reward-associated increases in excitability, reverting the BLA neurons to a naive state. Fear conditioning increased the current underlying the post-burst afterhyperpolarisation (IAHP) and decreased the AP half-width. Punishment training maintained reward-associated excitability and excitability was correlated with performance on the punishment task. Punishment was associated with an increased AHP and reduced spike half-width.

Conclusion
These results show instrumental learning induces cellular changes akin to those observed with Pavlovian conditioning. Specifically, reward training increased the excitability of BLA projection neurons. While Pavlovian fear conditioning arrested reward-associated excitability increases, excitability was maintained in punished subjects. While instrumental learning broadly increased BLA excitability, and shock exposure (instrumental and Pavlovian) had a common action on the AP waveform and the IAHP. Understanding the neurobiology of instrumental emotional association learning may provide insight into and assist with the development of therapies directed at psychiatric disorders associated with instrumental learning deficits, such as major depressive disorder or conduct disorder.

Poster Abstracts

Poster Session 1: Monday

P_24a How Prior Experience Shapes Adaptation to Changing Reversal Learning Environments in Mice

Presenting Author: Eleni Karanicolas

Ms Eleni Karanicolas - Queensland Brain Institute

Ms Suzy Alexander - Queensland Brain Institute and Queensland Centre for Mental Health Research

Dr James Kesby - Queensland Brain Institute and Queensland Centre for Mental Health Research

Background
The pathophysiological mechanisms of cognitive symptoms in schizophrenia are poorly understood. The dopamine hypothesis suggests a link between increased presynaptic dopaminergic function in the associative striatum and schizophrenia symptoms. We have shown differing prior experience can shape how mice make decisions, however, it is unknown how this affects their abilities to integrate changes in environmental feedback. This project aims to determine how past exposure to differing environments impacts the rate at which mice respond to changes in environmental feedback, as well as understanding how prior experience and adaptability is associated with dopamine neurochemistry.

Methods
Mice were trained to perform reversal learning using different protocols; block (trial-based reversals), consecutive correct responses (CCR) (response-based reversals) and mixed (alternating between the two). All mice were then tested on both protocols. To assess how changes in the reversal learning environments (reward contingencies for target:nontarget choices) altered behaviour, we are testing mice at each contingency for 6 days. At each contingency mice will be administered saline, amphetamine and MK801 (counterbalanced) to see how dopaminergic and glutamatergic systems affect performance. Brains will be collected to analyse dopamine and metabolites levels in corticostriatal regions to relate to behaviour.

Results
Overall, mice performed best on the protocol they had prior experience in. However, mixed-trained mice performed optimally in both. Compared to the other groups, mice exposed to the block protocol were most likely to win-stay (select the same choice after a reward), least likely to lose-shift (select the alternative after a loss) and made the most perseverative errors (number of errors made in the first 6 trials after a reversal). Mixed-trained mice therefore appear to be more equipped to handle differing reversal learning environments, indicating greater cognitive flexibility. Ongoing experiments will determine psychostimulant effects and associated dopamine neurochemistry.

Conclusions

Exposing mice to differing reversal learning protocols effects the strategies they use and their ability to perform in multiple dynamic environments. Understanding how prior experience impacts adaptation to change in outcome feedback in the reversal learning environments will allow us to optimise preclinical reversal learning studies. Furthermore, understanding how experience, psychostimulants and neurochemistry underly reversal learning will help to identify novel mechanisms underlying impaired cognition in disorders such as schizophrenia.

Poster Abstracts

Poster Session 2: Tuesday

P_12b Hybrid: A Pilot Study of Integrated Virtual Reality, Neurofeedback, and Cognitive Behaviour Therapy for the Treatment of Auditory Verbal Hallucinations

Presenting Author: Elise Rowe

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Background
Current treatments for schizophrenia and other psychotic disorders have limited efficacy, with high rates of non-response to ‘gold standard’ treatments. New approaches are therefore urgently required. To address this, we have developed a new treatment approach for auditory verbal hallucinations (AVH), a major symptom of psychotic disorders. This treatment (‘Hybrid’) integrates psychological therapy (cognitive-behaviour therapy for psychosis,

CBTp), technology (virtual reality, VR) and neuroscience (EEGbased neurofeedback). Hybrid takes a ‘symptom capture’ approach where participants are progressively exposed to symptom triggers in a controlled VR environment while receiving CBT for psychosis (CBTp) in-vivo and down regulating neural activity using neurofeedback.

Methods

Hybrid will recruit 10 first episode psychosis (FEP) patients who are currently experiencing AVH. Participants will receive the intervention package weekly over 12 sessions. In each session, they are progressively exposed to increasing levels of symptom triggers. The aims of the current pilot study are to: investigate the feasibility, acceptability, safety and usability of Hybrid treatment (primary aim); explore Hybrid’s engagement of treatment targets (secondary aims). The treatment targets are self-directed modulation of high-beta neurophysiological activity (neural target) and progressing upwards through a VR-based symptom-eliciting exposure hierarchy (psychological target).

Results

As of June 2024, Hybrid has begun recruitment activities. No participants have been recruited yet; however, we anticipate results of the pilot study to be available towards the end of 2024.

Conclusion

The Hybrid study is piloting a novel approach which has the potential to address the shortcomings of current treatments for psychotic symptoms. If there is favourable evidence for the acceptability, feasibility, safety and usability of Hybrid, the study team will move on to efficacy trials.

Poster Abstracts

Poster Session 1: Monday

P_59a Do not fear - fluoxetine enhances the extinction of fear in stressed adolescent rats.

Presenting Author: Elizabeth Virakorn

Elizabeth A. Virakorn - UNSW

Dr. Kathryn D. Baker - La Trobe University

Prof. Rick Richardson - UNSW

Background
Anxiety is the most common mental disorder in adolescence. Individuals who develop anxiety early in life have more severe symptoms than those who develop anxiety in adulthood. Human, and rodent, adolescents are impaired at regulating their fear, especially when they have been exposed to high levels of stress-related hormones. Selective serotonin reuptake inhibitors (SSRIs) are the first line of pharmacotherapy for the treatment of anxiety and has been shown to improve extinction retention in non-stressed and stress-exposed adult rodents. Whether the extinction-enhancing effects of SSRIs extends to younger animals is unknown.

Methods
In this study, we investigated whether fluoxetine (an SSRI) enhances extinction retention in non-stressed and stress-exposed adult and adolescent rats. Animals received either ethanol vehicle (2.5%) or corticosterone treatment in their drinking water for either one (adolescent) or three weeks (adults). At the end of the treatment period, animals were handled, given three pairings of a white noise and shock (conditioning), two weeks of fluoxetine in their drinking water, extinction training (white noise repeatedly presented alone), and an extinction retention test.

Results
We replicated past studies showing that fluoxetine enhances extinction retention in stress-exposed and non-stressed adult rats. Additionally, our research shows that the negative effects of stress on fear extinction in adolescence can be “reversed” by fluoxetine treatment. Specifically, we found that non-stressed adolescent rats given one day of extinction training have high levels of fear at test and that chronic stress exposure exacerbates this fear. However, stressed animals given one day of extinction and also exposed to fluoxetine (a serotonin reuptake inhibitor) do not exhibit this stress-induced impairment in fear extinction.

Conclusion
Our findings add to the vast body of evidence that adolescence is a stress-sensitive window in development, and, importantly, suggest that exposure to fluoxetine can reduce the stress-induced impairments in fear extinction in adolescent rats.

Poster Abstracts

Poster Session 1: Monday

P_18a Structural covariance, regional topology, and volumetric aspects of amygdala subnuclei in posttraumatic stress disorder using ultra-high field imaging

Presenting Author: Elizabeth Haris

Elizabeth Haris - The University of New South Wales

Trevor Steward - The University of Melbourne

Kim Felmingham - The University of Melbourne

Christopher Davey - The University of Melbourne

Ben Harrison - The University of Melbourne

Richard Bryant - The University of New South Wales

Mayuresh Korgaonkar - The University of Sydney

Background
The amygdala is a small, yet key subcortical brain structure involved in the stress response and implicated in various psychopathology. Previous efforts to map amygdala subnuclei connectivity have been hindered due to technological limitations. In this study, we used ultra-high field imaging to investigate the covariance profiles of amygdala subnuclei to better understand their contribution to trauma-related psychopathology and posttraumatic stress disorder (PTSD).

Methods
Participants included 59 non-trauma-exposed controls (NEC), 78 trauma-exposed controls (TEC), and 73 individuals with PTSD who completed T1-weighted MP2RAGE anatomical scans using a 7T MRI scanner. FreeSurfer was used to parcellate 105 brain regions including nine bilateral amygdala subnuclei. Pearson's r correlations were computed for each subnuclei and all other brain regions, corrected for age, sex, education, and total brain volume. Gray matter volumes, a graph measure of topological connectivity (nodal degree), and subnuclei-brain region covariances were compared between groups.

Results
Results demonstrated between-group volumetric differences for bilateral lateral nuclei, and higher nodal degree for TEC (vs NEC) for the right paralaminar nucleus. Group differences also demonstrated greater PTSD (vs NEC) structural covariances for left cortical and central nuclei, and lower TEC (vs NEC) covariances for left lateral, basal, and cortical nuclei, left anterior-amygdaloid-area, right cortico-amygdaloid transition, and bilateral paralaminar nuclei.

Conclusion
These results are the first to reveal important differences in amygdala subnuclei and their covariance profiles along the trauma spectrum using ultra-high field imaging. They highlight the need for further exploration of amygdala subnuclei to understand the nuances in the neural circuitry of PTSD.

Poster Abstracts

Poster Session 1: Monday

P_45a Mega-analysis of structural covariance in co-occurring post-traumatic stress disorder and alcohol use disorder: common and distinct patterns of alterations

Presenting Author: Ellen Towers

Ellen E Towers - Edith Collins Centre for Translational Research in Alcohol, Drugs and Toxicology, Royal Prince Alfred Hospital, Sydney Local Health District, NSW, Australia // Specialty of Addiction Medicine, Central Clinical School, Faculty of Medicine and Health, University of Sydney, NSW, Australia.

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Hugh P Garavan - Department of Psychiatry, University of Vermont, Burlington, Vermont, USA

Rajendra A Morey - Duke University, Durham, North Carolina, USA.

Background
Despite the high prevalence of comorbid post-traumatic stress disorder (PTSD) and alcohol use disorder (AUD) in the population there is limited understanding of the underlying neurobiology. We thus aimed to examine the structural morphology across PTSD, AUD, PTSD&AUD, and controls. We hypothesized that focal structural abnormalities present in either disorder (PTSD or AUD) would manifest in an accumulative fashion in comorbid PTSD&AUD, but cortico-cortical connectivity would reveal a distinct pattern unique to those with the comorbidity.

Methods
Structural images across 23 sites for individuals with PTSD&AUD (n = 69), PTSD (n = 207), AUD (n = 207) and controls (n = 207) were analyzed. Cortical thickness and subcortical volume were compared independently for each region (Desikan-Killiany atlas) across all four groups using a generalized linear model with an interaction effect. Structural connectivity between pairs of cortical regions was quantified with structural covariance (SC) analysis.

Results
Compared to controls, all groups (PTSD, AUD and PTSD&AUD) exhibited thinning in a common set of regions. The AUD group predominantly showed cortical thinning and reduced subcortical volume, while the PTSD&AUD and PTSD groups displayed a heterogenous pattern of cortical thickening and thinning and increased subcortical volume. SC analysis revealed unique patterns of reduced connectivity across all groups compared to controls. This primarily involved intra-temporal connections in AUD, inter-lobule connections in PTSD, and frontal-parietal connections in PTSD&AUD, while both PTSD and PTSD&AUD groups revealed a similar pattern of increased connectivity in parietal regions.

Conclusion
Our findings suggest that focal structural abnormalities are similarly aligned between PTSD and PTSD&AUD cohorts

while the widespread cortical thinning in AUD was not apparent in the PTSD&AUD cohort. There was a similar configuration of connections with increased SC in PTSD and PTSD&AUD, suggesting this is driven by PTSD. However, each cohort revealed a distinct pattern of weaker cortico-cortical connectivity.

Poster Abstracts

Poster Session 2: Tuesday

P_36b Meta-analysis and systematic review of invasive and non-invasive brain stimulation interventions for the treatment of anorexia nervosa

Presenting Author: Elysia Sokolenko

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

Jiexi Cow - School of Psychology, The University of Adelaide, SA, Australia

Katie Koch - School of Psychology, The University of Adelaide, SA, Australia

Elaine Fox - School of Psychology, The University of Adelaide, SA, Australia

Background
Currently available interventions for anorexia nervosa (AN), including psycho- and pharmacotherapies, are insufficient. This is concerning given the chronic nature of AN and the associated high risk of mortality One promising treatment for AN is the repurpose of repetitive transcranial magnetic stimulation (rTMS), a form of non-invasive brain stimulation used in the treatment of major depressive disorder. The aim of this study is to comprehensively assess the evidence of rTMS compared to other methods of invasive and non-invasive brain stimulation interventions for the recovery of core symptoms and associated features of AN.

Methods
We will include all human studies testing any form of invasive or non-invasive brain stimulation compared to baseline, sham, or standard of care for people currently diagnosed with or with a historic diagnosis of anorexia nervosa. Studies including participants of any age will be included. The primary outcome of interest will be core symptoms/weight-restoration. A literature search of studies was performed using PubMed, Embase, PsychINFO, and Web of Science. Risk of bias will be assessed using the appropriate Cochrane Risk of Bias Tools given the relevant study design. This study was registered on PROSPERO.

Results
Nine hundred and seven studies have been identified for title and abstract screening for inclusion. At data extraction, the following features will be assessed: demographics of sample, brain stimulation intervention protocols, main outcome, and additional outcomes. The main outcome will be a change in core symptoms, operationalised through self-report measures, interviewer assessments, weight, or a combination of these. Additional outcomes will include cognitive assessment.

Conclusion
Abstract and title screening will be complete by the end of August 2024. Full text screening and extraction will be complete by the end of September 2024. This will allow sufficient time to prepare a presentation of the key findings of this work. This will inform the design of future studies assessing brain stimulation interventions for the treatment of core and associated features, namely cognitive impairment, of anorexia nervosa.

Poster Abstracts

Poster Session 1: Monday

P_41a The antipsychotic actions of chronically-administered intranasal clozapine

Presenting Author: Emma Hilsley

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

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Harendra S Parekh - Senior Lecturer, School of Pharmacy

Dan J Siskind - Stream Lead - Queensland Centre for Mental Health Research, Prof of Psychiatry – Faculty of Medicine, UQ, Psychiatrist - Princess Alexandra Hospital, Metro South Hospital and Health Service, Qld

Preeti Pandey - Research Officer & Honorary Research Fellow, School of Pharmacy

Masood Ali - Research Officer, School of Pharmacy

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

Background
Schizophrenia presents as a devastating disorder. Clozapine (Cloz) stands out as the most effective agent for treatment-resistant schizophrenia. However, it is hampered by adverse peripheral side effects including agranulocytosis, diabetes, myocarditis, massive weight gain and gastrointestinal issues. A novel intranasal (IN) delivery system utilizing Sol-Gel technology shows promise in bypassing the periphery to minimise side effects. Although we have shown IN Cloz induces a robust acute antipsychotic effect by suppressing conditioned avoidance response however as tolerance develops with chronic Cloz we do not know the antipsychotic potential of long-term IN Cloz.

Methods
Adult male Sprague-Daley rats (n=48) are being chronically dosed for 8 weeks under the following conditions: IN vehicle (n=12), IN Cloz (n=12), Oral vehicle (n=12), and Oral Cloz (n=12). IN and Oral Cloz doses were matched based on baseline conditioned avoidance. Clozapine's ability to ameliorate both apomorphine impairments in prepulse inhibition (PPI) and amphetamine-induced hyperlocomotion were chosen to examine long-term antipsychotic actions on alternate weeks. PPI: baseline data was collected before daily dosing. Apomorphine (0.5mg/kg) was then injected 15 mins later and PPI reassessed. Amphetamine locomotion (2mg/kg) was assessed in an open field 15 mins after their daily Cloz/vehicle dose.

Results
Testing is ongoing. During the initial week of Clozapine exposure, the hyperlocomotion induced by amphetamine was noticeably reduced by both IN and oral administration of Clozapine. However, this reduction was only statistically significant in the animals that received the intranasal dosage (P= 0.013). The PPI impairments induced by Apomorphine were clearly evident in IN vehicle (22.3%, P=0.05) and oral vehicle (32.4%, P=0.0006) treated animals. IN Cloz significantly attenuated this impairment (18.2%,P=0.38) consistent with antipsychotic action. However Oral Cloz appeared to enhance Apomorphine's effects (41.3%, P=0.01).

Conclusion
Our study is ongoing, however our initial data indicates that IN Cloz is showing promising potential as a long term antipsychotic. Therefore, this novel route of administration may have the capacity to reduce the debilitating, and in

some cases, life-threatening side effects associated with the use of Cloz as it bypasses the periphery. This research acts as a preclinical necessity prior to clinical tolerability testing and eventual clinical trials. The hope is that in the future, IN Cloz administration in patients may drastically reduce the debilitating side-effect profile in patients, leading to much more wide-spread use of this gold-standard APD.

Poster Abstracts

Poster Session 1: Monday

P_50a Chronic morphine induces persistent place preference and dose-dependently changes in faecal short chain fatty acid concentrations in mice

Presenting Author: Erin McLemon

Erin McLemon – Western Sydney University

Nhan Ho Trong **-** Western Sydney University

Sonyia Juarez - Western Sydney University

Anandwardhan Hardikar - Western Sydney University

Tim Karl - Western Sydney University

Rose Chesworth - Western Sydney University

Background
The gut microbiome has been linked to opioid use disorder in both clinical and preclinical research. Research to-date has focused on opioid-induced changes to gut microbe composition and diversity, but functional effects of gut metabolites, and its relation to opioid-induced behaviours, remains largely unknown. Here we assessed the effects of chronic morphine administration on behaviour and gut metabolites, including short-chain fatty acids (SCFAs) in female mice.

Methods
Female C57BL/6J mice were conditioned to associate saline, 5 mg/kg or 10 mg/kg morphine with a distinct environment for 10 sessions over 18 days, using a conditioned place preference apparatus. Preference for a morphine-paired environment was assessed throughout drug administration. Faecal samples were collected prior to morphine administration, periodically throughout morphine administration and after the final morphine treatment. Gut metabolites were quantified using liquid chromatography mass spectrometry (LC-MS).

Results
Mice showed a persistent preference for 5 mg/kg morphine, an aversion for 10 mg/kg morphine and no preference for saline. Mice administered 5 and 10 mg/kg morphine developed locomotor sensitisation. Chronic administration of 10 mg/kg morphine reduces faecal concentration of acetic acid and kynurenine while 5 and 10 mg/kg morphine increase faecal concentration of propionic acid compared to saline ($n>10$/group; $p<0.05$).

Conclusion
The present study analysed gut metabolites to establish an alternative measurement of gut dysbiosis following opioid use, focusing on the functional effects of changes to the gut microbiome. Here we showed that chronic morphine changes several gut metabolites in female mice. Considering morphine-induced gut dysbiosis and SCFA dysregulation has been shown to increase drug-seeking behaviour in rodents, our data suggest that treating gut metabolite dysfunction, through the administration of short-chain fatty acids (SCFAs), which are known epigenetic regulators of gene expression, could be a promising approach for managing opioid use disorder.

P_14b Towards an understanding of the therapeutic effects of psilocybin: a focus on dopamine and reward

Presenting Author: Felicia Reed

Felicia Reed - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Kaspar McCoy - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Aashian Ibnat - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

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Alex Horner - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Alex Reichenbach - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Claire Foldi - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Background
Psilocybin is in clinical trials for a range of mental health conditions marked by alterations in mood, reward and cognition. Strikingly, symptomatic relief can occur after a single dosing session, pointing toward long-lasting neuroplastic changes as a core mechanism. Research to date has primarily focused on the serotonin (5-HT) system, despite the fact psilocybin is known to interact with other neuromodulatory systems, including the midbrain dopamine (DA) system. Therefore, the aim of this study was to understand the impact of psilocybin on acute and sustained responses to food reward, and the contribution of ventral striatal (VS) DA signalling.

Methods
We first evaluated the contribution of D1-receptor (D1R) antagonist SCH23390 (0.01mg/kg, i.p) or D2-receptor (D2R) antagonist Raclopride (0.5mg/kg, i.p) on the psilocybin-evoked head twitch response (HTR; 1.5mg/kg, i.p). We then performed fiber photometry recordings from the VS of mice expressing either a DA sensor (AAV-hSyn-GRABDA2m) or calcium indicator (AAV-hSyn-jGCaMP7f) and recorded repeated exposures to palatable food to understand the effect of psilocybin on reward-evoked DA release and neuronal responses, respectively. The role of D1R or D2R on food-evoked neuronal responses under psilocybin were evaluated with systemic pre-treatment of SCH23390 or Raclopride. Adult female C57Bl6/J mice were used for all experiments.

Results
As expected, psilocybin administration induced a significant HTR ($p<0.01$; n=5/group), however, pre-treatment with either Raclopride (0.5mg/kg, i.p) or SCH23390 (0.01mg/kg, i.p) 30 min prior to psilocybin significantly attenuated this acute behavioural readout of psychedelic activity (both p's<0.001; n=5/group), without impacting locomotor activity or other natural behaviours. Psilocybin also significantly increased VS DA responses to palatable food (n = 8/group; $p<0.01$), but did not significantly increase VS neuronal activity to the same stimulus. Pre-treatment with Raclopride or SCH23390 significantly reduced neuronal activity in a psilocybin-independent manner. There were no sustained effects of psilocybin on VS function 24h after administration.

Conclusion
These findings suggest both D1R and D2R signalling are necessary for the acute "subjective" effects of psilocybin in a manner independent of motoric action. While psilocybin acutely increased VS DA release in response to rewarding (food) stimuli, the absence of effects on VS calcium activity suggests that actions through D1 and D2 receptor mechanisms may occur outside of the ventral striatum. These results highlight a novel mechanism through which psilocybin may exert its therapeutic action. Ongoing studies aim to determine the interacting roles of 5-HT and DA signalling and in the encoding of reward under psilocybin.

Poster Abstracts

Poster Session 2: Tuesday

P_47b Hypatia Health: Cognitive Modelling Made Easy

Presenting author: Gavin Cooper

Gavin Cooper - Royal Holloway, University of London

Dr Catia Oliveira - University of York

Dr Alexandra Pike - University of York

Dr Lei Zhang - University of Birmingham

Dr Joseph Barnby - Royal Holloway, University of London

Background
Applying cognitive modelling to behavioural data can add important information about the underlying processes that lead to this behaviour. Cognitive modelling has significantly impacted research into aspects of cognition such as reinforcement learning, decision-making, memory and more. Additionally, there is a growing movement towards personalised treatment in psychiatry. Understanding and measuring change for the underlying computational mechanisms is a promising direction for achieving this personalisation. There are significant barriers to applying cognitive modelling to psychiatry as researchers cannot be experts in all fields.

Methods
Hypatia Health is designed to make the application of cognitive modelling to your domain as seamless as possible. We offer robust and rigorous mathematical and statistical models, all within an easy-to-use interface. You can interact with the models, receiving visual feedback as you manipulate model parameters. You can also plan your studies, adjusting the trials per participant and the participants per group, and then simulate participant responses to ensure your studies are appropriately specified.

Results
When you have your simulation results, you can feed them back into our estimation module, allowing you to assess whether the known model parameters are recoverable. Additionally, when you have run your cognitive task, you can bring your empirical data back to Hypatia Health and have the confidence that your cognitive modelling analysis is being performed with the most up-to-date cutting-edge developments and open cognitive science practices.

Conclusions
Hypatia Health is designed to be used by researchers and clinicians for experimental/intervention design and data analysis and to track cognitive change over time. We plan to integrate with experiment design platforms to reduce friction between a project's planning and implementation stages. We are instantiating a gold standard for model simulation and estimation, ensuring that code and model variation are removed from analysis bottlenecks, making it easier for experimentalists and clinicians to focus on their research theory, questions and outcomes.

Poster Abstracts

Poster Session 1: Monday

P_36a Cell Death TNFRSF transcripts expressed by Immune cells are Increased in the Midbrains of Schizophrenia and Bipolar Disorder with High-Inflammation

Presenting Author: Gerardo Mendez-Victoriano

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Background
Proinflammatory molecules promote the activation of Tumor Necrosis Factor Receptor Superfamily (TNFRSF) cell death pathways. We have found increased expression of proinflammatory molecules and decreased dopamine transcripts in the midbrains of people with schizophrenia and bipolar disorder (BD). However, it is not known if transcripts of the TNFRSF cell death pathway are altered in the midbrains of psychotic patients with high-inflammation. Herein, we aimed to evaluate the mRNA levels of cell death-associated TNFRSF markers in the midbrains of people with schizophrenia and bipolar disorder with high inflammation compared to healthy controls.

Methods
Normalized mRNA levels of five TNFRSF receptors (TNFR1/2, DR4, FAS and TWEAKR), and ten downstream markers (APAF1, BAX, BID, BCL2, MCL1, P53, caspases 1,3,8 and 9) were measured and compared via RT-qPCR from human post-mortem midbrains of 61 healthy controls, 63 schizophrenia, and 33 BD cases. Sub-cell clustering for TNFRSF receptors TNFR1/2, and FAS was analyzed from a previously sorted snRNA-seq database.

Results
TNFR1 and FAS were incrementally expressed in high-inflammation schizophrenia astrocytes. The mRNA levels of all five TNFRSF receptors (all $p<0.01$) and GFAP ($p<0.05$) were significantly increased in high-inflammation schizophrenia and BD compared to low inflammation controls. mRNA levels of pro-cell death downstream markers (P53 and caspases 1/8) were significantly higher in high inflammation schizophrenia, while mRNA levels of pro-cell survival downstream markers were increased in high-inflammation BD (BCL2 and MCL1) and schizophrenia (MCL1) compared to low-inflammation controls (all $p<0.05$). mRNA expression of all five TNFRSF receptors had positive correlations with their downstream markers (all $p<0.05$) and with GFAP mRNA (all $p<0.001$).

Conclusions
Our results suggest a transcriptional immune cell-based activation of TNFRSF cell death pathways in the midbrains of psychotic disorder patients, and show that individuals with these disorders who fall into a high inflammatory subgroup may be at greatest risk of midbrain dopamine-related degeneration.

Poster Abstracts

Poster Session 2: Tuesday

P_34b Comparable effects of topiramate and naltrexone on neurometabolite levels and cognition in individuals with alcohol use disorder

Presenting Author: Gezelle Dali

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Kirsten C. Morley - a. Specialty of Addiction Medicine, Sydney Medical School, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia b. Edith Collins Centre for Translational Research (Alcohol, Drugs & Toxicology), Royal Prince Alfred Hospital, Sydney Local Health District, Sydney, NSW, Australia

Background
The current study sought to examine neurometabolite concentrations following administration of either topiramate or naltrexone in individuals with alcohol use disorder. Further, this study compared the effect of treatment and neurometabolite levels on measures of cognition to clarify whether subjective cognitive complaints associated with topiramate translate to impaired executive functioning.

Methods
Participants were 45 patients with AUD who were randomised to receive either topiramate (titrated dose up to 200mg/day) or naltrexone (50mg/day) for 12-weeks as part of a broader randomised controlled trial. Following 6-weeks of treatment, participants underwent magnetic resonance spectroscopy to determine concentrations of GABA, glutamate, glutathione and N-acetylaspartate (NAA) in the anterior cingulate cortex. Participants also completed the Stroop task and Trail Making Test (TMT) to assess executive functioning.

Results
Multiple linear regression analyses revealed no significant predictive effect of treatment on GABA, glutamate, glutathione and NAA levels, controlling for age, antidepressant use, severity of dependence and recent alcohol consumption. There were also no effects of neurometabolite levels nor difference between the treatment groups on Stroop and TMT performance.

Conclusions
The current results suggest that topiramate and naltrexone may enact similar effects on neurometabolite levels, which may be underpinned by significant reductions in alcohol consumption at the time of scanning. Furthermore, subjective reports of topiramate-induced cognitive impairment do not appear to correspond to impaired performance on

executive functioning tests. These findings have important clinical implications for the use of topiramate in the treatment of alcohol use disorder.

Poster Abstracts

Poster Session 2: Tuesday

P_07b The hidden influence of response latencies in the TUNL task of working memory

Presenting Author: Grace Jin

Grace Jin - Monash University

Leah Liu - University of Melbourne

Louise Inger - University of Melbourne

Chitra Vinnakota - Monash University

Matthew Hudson - Monash University

Rachel Hill - Monash University

Nigel Jones - Monash University

Background
The Trial-Unique Nonmatch to Location (TUNL) task is a touchscreen-based assessment of spatial working memory (WM) in rodents. When combined with investigative techniques such as electrophysiology or optogenetics, as well as pharmacological interventions, insights into the cellular and network mechanisms underpinning WM processing can be elucidated. However, nuances in mouse behaviour observed during the task can impact the interpretation of results if not considered. Here, we characterised the variation in TUNL response latencies across a variety of conditions, with respect to successful execution of the task.

Methods
We trained male C57BL/J mice (n = 18) on a 5-window TUNL protocol until training accuracy reached >80% success. Mice were either connected to an electrophysiological tether or left untethered in the testing chamber. In total, we included 3662 trials in the analysis. Distributions of response latencies for the Sample and Choice phases of the task were calculated, and compared for correct and incorrect trials across the different conditions.

Results
Both Sample and Choice response latencies were significantly faster in trials showing correct responses compared to incorrect responses ($U<0.0001$). The variances of latencies exhibited exponential curves, with curves shifting towards increased latencies for incorrect responses. All conditions exhibited responses greater than 10 seconds which did not fit the exponential curve. In tethered sessions the proportion of these responses was strikingly lower for correct responses compared to incorrect responses (Sample: 3.2% vs 13.2%; Choice: 16.6% vs 39.1%), while these differences were modest in untethered sessions (Sample: 1.7% vs 6.9%; Choice: 1.9 vs 7.4%).

Conclusions
We conclude that response latency is an important factor to consider when interpreting data from the TUNL task regarding WM, especially while also performing tethered measurements. Perhaps up to 40% of trials (i.e. >10 second response latency) should be excluded from analyses, since data from such trials are unlikely to reflect WM ability. These discrepancies are particularly important while introducing procedures that would affect cognition such as pharmacological treatments and optogenetic stimulation.

Poster Abstracts

Poster Session 1: Monday

P_16a Decision-making in electric barrier-induced voluntary abstinence

Presenting Author: Hannah Machet

Hannah Machet - University of New South Wales

Bart Cooley - University of New South Wales

Zayra Millan - University of New South Wales

Gavan McNally - University of New South Wales

Background
In alcohol use disorder, individuals consistently choose alcohol consumption over alcohol-free activities, with abstinence being linked to recognition of the adverse consequences of these choices. There has been a significant effort to incorporate choice into rodent models of alcohol-seeking and abstinence to understand the mechanisms of these choices. Here we report experiments assessing the nature of choice in an electric barrier-induced voluntary abstinence model of alcohol-seeking.

Methods
We trained mice to seek and consume alcohol, then we induced voluntary abstinence by introducing an electric barrier. Next, mice received intermittent exposure to alcohol in their home cages before further assessment of voluntary abstinence with the electric barrier. Crucially, across the experiment, we used behavioural microstructure analyses to identify individual choices to approach or abstain from alcohol and we submitted these choices to formal cognitive modelling to deconstruct choice into its latent cognitive mechanisms.

Results
Introduction of an electric barrier induced voluntary abstinence in most mice, with high levels of individual variability. Subsequent intermittent exposure to alcohol before re-testing had no effect on decisions to approach alcohol but promoted faster decisions to abstain. This suggests mice became more efficient in abstaining from alcohol. Formal cognitive modelling supported this, showing increased accumulation rates for decisions to abstain from alcohol after intermittent exposure, demonstrating a stronger evidence base for abstaining and aligning with faster abstinence responses.

Conclusions
These findings identify a specific decision-making process driving voluntary abstinence and they provide a potential mechanism for the efficacy of approach bias modification tasks used to promote abstinence in human drinkers.

Poster Abstracts

Poster Session 1: Monday

P_33a Unpredictable Circadian Rhythm Disruption in Wistar Rats: Striatal and Behavioural Changes Reflecting Bipolar Disorder Pathophysiology

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Background

Circadian disruption is a common feature of bipolar disorder (BD) and is associated with increased vulnerability to inflammatory, stress, and metabolic disturbances. Therefore, investigating the mechanisms by which circadian disruption interacts with these critical components of BD pathophysiology could assist in the development of a translational model of the disease. We developed a novel unpredictable circadian disruption (UCD) protocol to characterise the impact of diurnal rhythm perturbation and/or stress hormone exposure on locomotor behaviour and its association with metabolic, inflammatory, stress, and circadian markers in the nucleus accumbens (NAc).

Methods

Forty-eight Wistar rats (24 male; 24 female) were exposed to combinations of UCD/non-UCD and corticosterone (200µg/ml in drinking water)/vehicle for five weeks. UCD consisted of unpredictable exposure to light and sound (65-80dB). Weight was measured regularly, and locomotor activity was quantified through nine sessions of the open field test over the final fortnight of UCD/non-UCD. RT-PCR was used to measure NAc gene expression of inflammatory (TNFA, IL1B, AMPK, NFKB, and MAPK), metabolic (INSR and PEPCK), stress (NR3C1), and circadian (MTNR1A, MTNR1B, and CLOCK) markers. NAc concentrations of acetylcholine, GABA, dopamine, serotonin, and central carbon metabolites were quantified using LC-MS/MS.

Results

UCD animals demonstrated increases in time in centre (p=0.0094), central crossing frequency (p=0.0203), and rearing (p=0.0489) on day one of testing; and decreases in distance travelled (p=0.0149) and rearing (p<0.0001) on day nine. Increased NAc concentration of acetylcholine (p=0.0315), and expression of IL1B (p=0.0004), TNFA (p=0.0049), INSR (p=0.0131), PEPCK (p=0.0355), NR3C1 (p=0.0172), and MTNR1B (p=0.0445) were seen in UCD animals. Male UCD animals gained significantly more weight (p=0.0028) than controls, while UCD females gained significantly less weight (p=0.0246). Guanosine diphosphate (p=0.0472), NADP phosphate (p=0.0352), succinate (p=0.0310), NAD (p=0.0101), glycerol-3-phosphate (p=0.0211), and uridine monophosphate (p=0.0509) were significantly reduced in UCD animals.

Conclusions

UCD animals demonstrated behavioural changes consistent with manic-like (increased locomotor activity) then depressive-like behaviours (decreased locomotor activity) at three and five weeks of treatment, respectively. Significant increases in inflammatory, stress, and circadian markers were seen in UCD animals. Weight gain over five weeks was significantly affected by UCD. Significant increases in NAc PEPCK and INSR and decreases in NAc central carbon metabolites observed in UCD animals demonstrates critical impacts on striatal glucose metabolism. Together, these data suggest that UCD affects systems relevant to BD, and sheds light on the complex interplay between circadian disruption, striatal immunometabolic signalling and locomotor behaviour.

P_58b Characterization of Terpene and Phenolic Compounds in Native Australian Plants: Antioxidant and Neuroprotective Effects

Presenting Author: Helen Clunas

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Background

Phenol-rich plants, including the Queen Garnet plum (QGP) [1–4], possess antioxidant and anti-inflammatory properties that may mitigate oxidative stress and inflammation linked to mental and neurodegenerative disorders [5–8]. However, not all plants exhibit these effects suggesting that some compounds, or combination thereof, offer superior neuroprotection. Native Australian plants are hypothesised to have unique pharmacological potential due to their evolutionary isolation [9] but the potential therapeutic properties for brain health are not well understood. This study examined the antioxidant and neuroprotective effects of two native Australian peppers in vitro and correlated these results to their phenolic and terpene profile.

Methods

Samples of both leaf and fruit from Tasmannia lanceolata (Mountain Pepper, MP) and Tasmannia stipitata (Dorrigo Pepper, DP) were analysed for their antioxidant and neuroprotective capacities in preventing and treating induced oxidative stress (H2O2 and 6-OHDA) in vitro using SH-SY5Y cells. The phenolic content, oxygen and nitrogen radical scavenging, and metal chelating capacities were determined using colourimetric assays. Mass spectrometry was employed to identify the specific terpene and phenolic species of each sample. One-way ANOVAs and Dunnett's tests determined significant differences between plant samples and a positive control (QGP, known to have high phenolic levels and antioxidant capacity).

Results

In vitro, DP both prevented and reversed H2O2-induced stress in SH-SY5Y cells ($p<0.05$ and $p<0.001$), while MP ($p<0.001$) and QGP ($p<0.001$) were able to reverse 6-OHDA-induced stress. MP and DP exhibited higher total phenolic levels ($p<0.001$), and higher oxygen and nitrogen radical scavenging capacity than QGP ($p<0.01$). MP had a higher Cu2+ chelating capacity ($p<0.001$) and DP had a higher Fe2+ chelating capacity ($p<0.001$) than the QGP. The highest phenolic and terpene species for MP and DP were apigenin, catechin, and ?-pinene, which differed from the isopulegol and orientin in QGP.

Conclusions

This study demonstrates that the native Australian peppers, Tasmannia lanceolata (Mountain pepper) and Tasmannia stipitate (Dorrigo pepper), exhibit significant antioxidant and neuroprotective effects in vitro, resulting in higher cell viability than treatment with QGP. Apigenin, catechin and ?-pinene possess neuroprotective effects [10]. Therefore, the unique phenolic and terpene profiles of MP and DP may contribute to their superior neuroprotective capacities. These novel findings highlight the therapeutic potential of native Australian plants for brain health, warranting further investigation.

Poster Abstracts

Poster Session 1: Monday

P_05a Identifying risk genes of susceptibility to activity-based anorexia in a corticostriatal pathway

Presenting Author: Kaixin Huang

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Background
Anorexia nervosa (AN) is a complex psychiatric disorder with psychosocial, metabolic, neurobiological and genetic causes. The first genome-wide significant locus was recently identified in AN, however, it remains unclear how these genes give rise to anorectic pathologies. Activity-based anorexia (ABA) is a biobehavioural rodent model recapitulating key phenotypes of AN, with which we have previously shown that suppressing neural activity in the medial prefrontal cortex (mPFC)-nucleus accumbens shell (AcbSh) circuit could prevent pathological weight loss. Here, we used the translating ribosome affinity purification (TRAP) technique within this neural pathway to identify risk genes associated with susceptibility to pathological weight loss.

Methods
We used a dual viral approach in which retrogradely-transporting Cre was injected into AcbSh coincident with a Cre-dependent TRAP construct (AAV-FLEX-EGFPL10a) into mPFC to selectively isolate RNA from this neural pathway. Female Sprague-Dawley rats (n=12) were exposed to ABA conditions, which consisted of time-limited access to food paired with unlimited access to running wheels, until they lost >20% body weight (Susceptible) or for a maximum of 10 days (Resistant). Following body weight recovery, EGFP-tagged polysomes were extracted via immunoprecipitation with antibody-labelled Dynabeads and RNA extracted. Gene-set enrichment and gene ontology analyses were used to identify differentially regulated genes (DRG).

Results
We identified 1424 DRGs between Resistant and Susceptible groups, including five risk genes previously reported as associated with AN. These included ERLEC1, MYL6, ZC3H10, IKZF4, which were downregulated, and SMARCC2, which was upregulated. Gene set enrichment analysis (GSEA) showed that the DRGs were involved in pathways associated with metabolic functions and neurodegenerative diseases, including Parkinson's, Alzheimer's and Huntington's disease. Our conservative gene ontology (GO) analysis considered both gene expression level and variability across samples. Here, we identified 24 downregulated and 2 upregulated genes, with downregulated genes associated with postsynaptic, cytoskeletal and axonal functions whereas upregulated genes were related to metabolism.

Conclusions
This study revealed transcriptional changes in a specific neural circuit related to vulnerability to pathological weight loss that were not influenced by current calorie deficit, because rats exposed to ABA conditions were weight recovered at sample collection. That multiple dysregulated genes identified in individuals with AN were also significantly altered in ABA rats highlights the utility of this model for examining the causal role these genes play in anorectic behaviour. Moreover, the intriguing set of downregulated genes associated with postsynaptic function represent novel molecular targets through which overactive cortical circuits could be suppressed to prevent pathological weight loss.

Poster Abstracts

Poster Session 1: Monday

P_23a REVERSING THE EFFECTS OF PRENATAL OPIOID EXPOSURE: THE EFFICACY OF SODIUM BUTYRATE IN AN ANIMAL MODEL

Presenting Author: Isobel Williams

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Sarah J Baracz - School of Psychology, Faculty of Science, University of New South Wales

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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 incidence of children born with prenatal opioid exposure (POE). POE has negative long-term impacts on brain, behaviour and cognition. The mechanisms underlying these symptoms are poorly understood, but have been linked to alterations in myelination and inflammation. Here we test the efficacy of short-chain fatty acid sodium butyrate (NaB) to reverse POE-related deficits.

Methods
Pregnant rat dams were treated with the opioid methadone (9/mg/kg/day) and NaB (3% in drinking water) across the perinatal period. Brain tissue from offspring was collected at post-natal day 21 for analysis inflammation and myelination, and remaining offspring were assessed for changes adult cognition and behaviour.

Results
Prenatal methadone exposure impacted expression of genes regulating the myelination process. POE pups showed decreased expression of SOX10 and MYRF, essential regulators of oligodendrocyte differentiation. However, NaB partially normalised this, as perinatal treatment with NaB reversed the decrease MYRF expression associated with methadone exposure. NaB exposure also mediated the pups' immune profile, resulting in increased expression of anti-inflammatory cytokine IL10 and macrophage marker CD68. Additionally in adulthood methadone-induced deficits in working memory (TUNL-task) and attentional processing (5-CSRTT) were somewhat reversed by perinatal NaB treatment.

Conclusions
These results highlight a link between altered myelination and cognition in an animal model of POE. Furthermore, they suggest NaB as a possible treatment for these changes, potentially through mediation of myelination and immune function. Together this indicates NaB as a treatment that could significantly improve outcomes for POE children.

Poster Abstracts

Poster Session 1: Monday

P_19a Variations in density of high probability dopamine release sites negatively correlates with measures of cognitive flexibility.

Presenting Author: Jack Siddle

Jack Siddle – QBI, UQ

Background
The cognitive symptoms of schizophrenia are currently untreatable and may be driven by alterations in striatal function. Reversal learning assess cognitive flexibility by assessing how a subject reacts to a reversal in stimuli reward. Previous experiments trained mice using three differing protocols based on when said reversal occurs; Block - reversal after a set number of trials, Correct Consecutive Response (CCR) – reversal after 6-8 consecutive correct responses, and mixed methods – alternating Block and CCR training. We aimed to understand if different protocols cause alterations in synaptic density within the striatum and if variations lead to different behavioural phenotypes.

Methods
Brain slices from 76 behaviourally-phenotyped mice were stained to quantify high-probability dopaminergic release sites (Tyrosine Hydroxylase [TH], Bassoon [BSN]) and cortical glutamatergic synapses (Vesicular Glutamate Transporter 1 [VGLUT1], Post Synaptic Density Protein 95 [PSD-95]). Twenty-one z-stack images over 2µm were taken at 100x magnification, deconvolved and reconstructed using IMARIS. Glutamatergic synapses were identified as PSD95 spots within 100nm of a VGLUT surface, and high probability dopaminergic release sites when a BSN spot was on/within a TH surface. Glutamatergic synapses and dopaminergic release sites density values were compared with prior behavioural outcomes.

Results
There were no group differences in synaptic density, indicating exposure to different reversal learning protocols did not impact striatal architecture. However, using linear regression analyses, dopaminergic release sites were negatively correlated with lose-shift use (shifting choice after a loss) at contingencies (target:nontarget reward probability) with higher misleading feedback (60:20 and 70:30). Behavioural data after drug administration (MK801, Amphetamine) was examined next, and showed that dopaminergic release sites were negatively correlated with win-stay (continuing choice after a win) and this was more pronounced following amphetamine administration.

Conclusions
This work demonstrates that exposure to different reversal learning protocols (Block, CCR, and Mixed) do not alter synaptic architecture within the dorsal striatum. However, the density of dopaminergic release sites is associated with changes in cognitive flexibility when subjects are tested in environments with high misleading feedback. Additionally, baseline levels of synaptic/release sites can alter the response to drugs that push these synaptic systems beyond physiological levels. Ultimately, our findings suggest that changes in dopaminergic synaptic densities could contribute to cognitive deficits and drug sensitivity in those with schizophrenia.

Poster Abstracts

Poster Session 1: Monday

P_07a Personalised treatment of schizophrenia using patient-derived olfactory neuronal stem cells through a systems-based multi-omics analysis

Presenting Author: Jamila Iqbal

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Background
Schizophrenia is a complex polygenic disorder with several hundred genetic variants contributing to disease risk, most of which are located in regulatory non-coding regions of the genome. These genetic variants impact the regulation of gene networks and biological pathways that control fundamental cellular processes and subcellular organisation, extending beyond synapses and neurotransmitters. Our goal is to develop a systems-based multi-omics approach using patient-derived olfactory neuronal stem cells (ONS cells) to identify optimal therapeutic interventions for schizophrenia patients.

Methods
We generated multi-omics data from 57 samples of ONS cells (30 schizophrenia patients and 27 healthy controls), including adult and early-onset cases. The data includes high-content cell imaging, whole genome sequencing, transcriptome profiling (long, small and circular RNAs), and proteome analysis. Our systems-based approach integrates genome-wide association studies (GWAS), Connectivity Map drug-induced expression signatures (CMap), ONS expression profiles, bioinformatics predictions of binding motif sequences, and correlation analyses. This comprehensive integration aims to identify disease-associated gene networks and cell traits, enabling the selection of FDA-approved drugs that can potentially reverse the dysfunctional cell traits and gene signatures observed in individual patients.

Results
Our results show that schizophrenia patient-derived ONS cells have significant differences in several cell traits related to subcellular organisation and cell motion. Notable changes include differences in cell area and shape, mitochondria and endoplasmic reticulum morphology, and cell motility, specifically in travel distance and speed. We identify gene networks associated with cell adhesion and migration that show significant correlation with genes previously identified in GWAS and CMap. These findings suggest potential markers for ranking optimal drug response for each patient, aiming to restore dysregulated traits observed in our patient-derived ONS cells.

Conclusions
We propose an agnostic, data-driven approach to identify dysfunctional genes signatures and cell traits associated with schizophrenia, and to rank FDA-approved drug signatures capable restoring healthy cellular and molecular profiles. Our systems-based drug discovery pipeline provides new insights into the mechanisms of FDA-approved drugs and assists clinicians in selecting optimal treatments based on individual responses of patient-derived stem cells.

Poster Abstracts

Poster Session 2: Tuesday

P_42b Probabilistic modelling: Exploring how longer-term fluctuations in relapse triggers can be harnessed to develop an early warning system of relapse

Presenting Author: Jodie Naim-Feil

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Background

Alcohol dependence is a devastating and chronically relapsing disorder. While triggers for relapse such as craving, stress and drugexposure are well-documented, there is limited research into how these triggers fluctuate over the addiction process. Advances in neural-engineering produced mathematical tools capable of indexing these longer-term patterns. However, these techniques have not yet been applied to psychiatric conditions. This presentation will provide examples of the probabilistic model in epilepsy and discuss the application of this advanced methodology in addiction. By mapping these long-term dynamics, we could uncover personalized biomarkers of relapse, potentially leading to an early warning system of relapse risk.

Methods

Two examples of applying this methodology in epilepsy research. Study 1: Both heart rate (continuously monitored via a wearable device) and self-report seizures monitored over 6-months. Long-term patterns were extracted (using wavelet transform) and applied to a probabilistic framework. Cortisol/DHEAS samples were collected at estimated high-risk times from the seizure forecast. Study 2: Self-report seizures documented over a 12-month period. Long-term cyclic patterns extracted and applied to a probabilistic model to forecast periods of seizure likelihood. The diagnostic yield was compared for those who were monitored during estimated ‘high-risk’ (n = 305) relative to those in baseline (n = 3586).

Results

Study 1: From the 300 saliva samples were collected from 15 participants, the cortisol/DHEAS ratio model (linear mixed effects model) revealed significant associations with seizure risk (0.28, 95% CI [0.05, 0.51], p=0.019). Study 2: Test of Proportions and Risk- Ratios (RR) indexed differences in proportions and likelihood of capturing outcome measures during monitoring. During monitoring, those monitored during high-risk were significantly more likely to have an abnormal vEEG report (190/305:62% vs 1790/3586:50% (%change=12%), RR=1.25, 95% CI[1.137:1.370], p<0.001) and present with a confirmed seizure (56/305:18% vs 424/3586:11% (%change=7%), RR=1.63, 95% CI[1.265:2.101], p<0.001).

Conclusions

Both studies applied a probabilistic framework, with Study 1 showing the interplay between stress hormones (cortisol/DHEAS), cycles of heart-rate, and seizure likelihood. Study 2 demonstrates the clinical translation of the probabilistic framework, with the diagnostic yield of monitoring improved when timed according to seizure likelihood. Application of this robust methodology within the field of addiction has potential to uncover long-term biomarkers of relapse, which could form the basis of early warning system of relapse risk. This could transform personalized clinical management and enable the introduction of ‘protective’ intervention strategies prior to relapse, with potential to disrupt the cycle of dependence.

Poster Abstracts

Poster Session 1: Monday

P_54a Nutritional psychiatry: An in-vitro exploration of Antioxidant and Neuroprotective Benefits of colorful fruits.

Presenting Author: Julianna Lys de Sousa Alves Neri

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

Background
Nutritional therapeutics are a promising new avenue for mitigating against oxidative stress in the brain and may be relevant to neuropsychiatric disorders. Evidence suggests that bioactive compounds, such as phenolics and betalains (which provide red, yellow, and purple colors in fruits), can reduce oxidative damage1-6. This suggests a need for exploration into novel plant-based phenolic and betalain sources with potential antioxidant benefits. The aim of this study was to investigate the neuroprotective effects of key fruit extracts, and correlate these to their phenolic, betalain, and antioxidant capacity.

Methods
The efficacy of Dragon fruit (DF), Apricot (AP), Queen Garnet Plum (QGP) and green apple (GA) extracts (10, 25, 50, 100 ?g/mL) in preventing oxidative stress- (H_2O_2) induced loss in viability of SH-SY5Y neuroblastoma-like cells was examined (in-vitro). The phenolic and betalain concentrations, as well as Oxygen Radical Absorbance Capacity (ORAC) were also determined. Statistical differences between the extracts compared to a positive control (QGP) were examined using ANOVA and Tukey post hoc analyses. Spearman's correlations investigated relationships between parameters. PCR examining mRNA expression of antioxidant enzymes and inflammation are ongoing.

Results
Pre-treatment with DF completely prevented the loss in cell viability during H_2O_2-induced oxidative stress, restoring healthy control-like levels (p 0.05 vs healthy control). There were significant increases in cell viability following pre-treatment with phenolic-rich QGP, GA and AP; however, these did not reach healthy control-like levels ($p < 0.001$ vs H_2O_2, $p < 0.05$ vs healthy control). Interestingly, DF contained the highest ORAC and a strong correlation ($r_s = 0.804$, $p < 0.01$) was observed between the ability to prevent H_2O_2-induced oxidative stress and ORAC. DF was also the only extract to contain betalains.

Conclusions
These findings demonstrate a novel neuroprotective effect of DF that may be attributed to its oxygen free-radical scavenging capacity and betalain concentration. QGP, GA and AP had some neuroprotective effects and were high in phenolics; however, this was insufficient to prevent H_2O_2 damage. These results are promising for future nutritional psychiatric research into the therapeutic potential of fruit-derived compounds in combating oxidative stress-related damage in psychiatric disorders. Mechanistic studies are required and are currently being conducted.

Poster Abstracts

Poster Session 2: Tuesday

P_33b Effects of social buffering on fear extinction in adolescent rats

Presenting Author: Kathryn Baker

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Jia Ni Teo - School of Psychology, UNSW Sydney, NSW

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Kathryn Baker - Department of Psychology, Counselling and Therapy, La Trobe University, Melbourne, VIC

Background
Across social species, the presence of another individual can reduce stress reactions to adverse stimuli, a phenomenon known as social buffering. We investigated whether social buffering influences the expression and extinction of learned fear in adolescence, a developmental period of diminished fear inhibition and increased social interaction.

Methods
Male and female adolescent rats were fear conditioned and then given extinction training either in the presence of a same-age, same-sex rat or alone. Animals were then tested alone for extinction retention.

Results
In two experiments in males, the presence of a conspecific robustly reduced conditioned fear responses during extinction training. Interestingly, a persistent social buffering effect was observed when the extinction and conditioning contexts had prominent differences in features, but not when these contexts were relatively similar. In females, the presence of a conspecific reduced conditioned fear expression and increased exploratory behaviour during extinction when animals were in high or low ovarian hormone stages of the estrous cycle. However, social presence at extinction training did not enhance subsequent extinction retention or reduce renewal of extinguished fear when females were tested alone.

Conclusions
These findings suggest that social buffering robustly dampens fear responses during adolescence when a peer is present; however, there are limited long-term effects of social buffering on extinguished fear when the peer is absent. These studies highlight the importance of further work identifying how peers help individuals cope with exposure to feared stimuli, with studies examining the neurotransmitter systems underpinning social buffering in progress.

Poster Abstracts

Poster Session 1: Monday

P_04a Characterising the neuropeptide landscape of the postmortem human orbitofrontal cortex in health and psychopathology

Presenting Author: Katrina Edmond

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Background
Neuropeptides are a diverse class (>100 members) of endogenous neurotransmitters. They are understood to be strongly influenced by psychological stress, specifically glucocorticoids like cortisol, with evidence of (mal)adaptation across several phenotypes of psychiatric illness. While it is hypothesised that changes in their expression contribute to an altered balance of inhibitory and excitatory signalling in the brain, the mechanistic details - including the relevant spatial context - of these changes are yet to be fully understood. To move forward, the field of psychiatry requires a high-resolution understanding of how stress manifests at the molecular level across the postmortem human brain.

Methods
Using genome-wide transcriptomic data from >800,000 individual postmortem nuclei, we used bioinformatics to understand the effects stress exposure has on the cell type-specific expression patterns of neuropeptides in the human orbitofrontal cortex (n=101). Further, using spatial transcriptomic data from the same subjects, we were able to visualise the spatial context of these changes. Finally, we are working to adapt a multimodal approach to tissue analysis by Vicari et al (Nature Biotechnology, 2023) which combines histology, mass spectrometry and spatial transcriptomics to give a holistic overview of mRNA, proteins, lipids and metabolites within a single tissue sample, to also detect neuropeptides.
Results
Preliminary analysis of the snRNAseq data showed that compared to controls, individuals exposed to early life stress have differentially expressed levels of somatostatin and proenkephalin, with the most pronounced changes seen in excitatory and inhibitory neurons. Using spatial transcriptomics, we found that somatostatin expression appeared consistent throughout the grey matter of the orbitofrontal cortex, which was distinct from somatostatin positive inhibitory neurons that were predominantly located within the deeper layers of the cortex. We also investigated several

neuropeptide-related synaptic receptors, three of which (synaptoporin, secretagogin and HTR2C (serotonin)) showed cell type specific changes in early life stress compared to controls.

Conclusions

In line with previous evidence, we show that exposure to severe stress, particularly early in life, associates with an altered landscape of neuropeptide expression in the human orbitofrontal cortex. Further, we show that the spatial context over which said changes occur are peptide specific, and therefore, likely unique to disorder phenotype. Given the importance of neuropeptides as facilitators of neuronal transmission, and therefore, upstream regulators of gene and protein expression, understanding these changes moves us closer to developing a system of biological classification for psychopathology. Specifically, identifying treatment options which directly target the underlying molecular changes at a patient-specific level.

Poster Abstracts

Poster Session 2: Tuesday

P_22b Exploring the novel dopaminergic projections from Ventral Tegmental Area to Ventral Hippocampus in Alzheimer's disease

Presenting Author: Kiruthika Ganesan

Kiruthika Ganesan - The University of Sydney

Masakazu Taira - The University of Sydney

Melissa Sharpe - The University of Sydney

Background
It is well known that people with Alzheimer's disease (AD) exhibit severe hippocampal atrophy and impaired cognitive functions. This is often a consequence of reduction in learning capacity, that involves an understanding of how events are related in time and space, formally regarded as associative learning. The role of dorsal hippocampus in associative learning has been well characterized, with studies reporting a deregulation of ventral tegmental area dopaminergic (VTADA) inputs to dorsal hippocampus (dHP) in early stages of AD patients. However, the role of ventral hippocampus (vHP) in such forms of learning remain largely unknown.

Methods
To establish a novel projection from VTADA neurons to vHP, we performed retrograde tracing by injecting Cholera toxin subunit B (CtB) into vHP and imaging VTA stained for tyrosine hydroxylase (TH). We then took advantage of fibre photometry, to precisely record dopamine release during associative learning. We captured dopamine signals in vHP as rats learnt simple associations between neutral cue (e.g., tone) and food reward through early, middle, and late stages of cue-reward learning. We repeated the same with another neutral cue (e.g., light) and mild foot shock, to clarify the role of this region in differentially valanced associative learning.

Results
We found a dense projection from VTADA neurons to vHP. Further, dopamine release adjacent to these terminals reflected associative learning. Specifically, a neural signal developed to the reward cue across learning sessions, revealing an interesting temporal dynamic, which does not reflect a quintessential dopamine prediction error (i.e., phasic increase in dopamine at cue onset). Instead, we saw a slow increase and then decrease in dopamine activity across the cue, which seemed to reflect the same temporal dynamic of dopamine release seen to reward consumption at cue offset. Interestingly, we saw a similar response of dopamine in vHP during cue-shock learning.

Conclusions
These results are one of the first to confirm that VTADA neurons directly project to vHP. We hypothesize that VTADA neurons do not reflect a typical dopamine teaching signal, rather, reflects a 'stimulus-stimulus' association. This highlights the importance of vHP dopamine in associative learning and dissociates this circuit from canonical dopamine circuits (e.g., nucleus accumbens). Moreover, these results are consistent with an idea that depleted input from VTADA neurons to hippocampus in patients with Alzheimer's disease could lead to deficits in learning and other neuropsychiatric symptoms. Next, we will perform these studies in a rodent model of Alzheimer's disease.

Poster Abstracts

Poster Session 1: Monday

P_29a The effect of N-acetylcysteine (NAC) on Neurometabolites and Cognitive Function in Alcohol Use Disorder

Presenting Author: Kristiane Yacou

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Paul S. Haber - Specialty of Addiction Medicine, Sydney Medical School, Faculty of Medicine and Health, University of Sydney, Edith Collins Centre for Translational Research (Alcohol, Drugs & Toxicology), Royal Prince Alfred Hospital

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Background
Preclinical studies have demonstrated that n-acetylcysteine stabilises levels of glutamate and glutathione and reduces alcohol- seeking behaviours and thus may have potential for the management of alcohol use disorder. In this study, we aimed to examine brain metabolites and cognitive functioning following treatment with n-acetylcysteine or placebo in individuals with alcohol use disorder enrolled in a randomised placebo-controlled trial (Morley et al., 2023).

Methods
Twenty-three participants with moderate to severe alcohol use disorder (DSM-5) were randomised to receive 2400 mg/day of n-acetylcysteine or placebo. At baseline and follow-up (average 19 days post-baseline), participants underwent magnetic resonance spectroscopy (1H-MRS) to assess levels of glutamate, glutathione and total n-acetylaspartate in the anterior cingulate cortex and completed the Stroop Colour and Word Test and the Trail Making Test.

Results
There were no significant differences between the n-acetylcysteine or placebo groups in neurometabolite concentrations (GSH/Cr: p = 0.75, CI; -0.12 – 0.09, tNAAG/Cr: p = 0.797, CI; - 0.10 – 0.13, Glu/Cr: p = 0.60, CI; -0.19 – 0.32), or cognitive scores (Stroop: p = 0.57, CI; - 306.93 – 172.78, TMT: p = 0.166, CI; -6.62 – 36.77).

Conclusions

These results indicate that n-acetylcysteine did not alter brain neurometabolite levels or show improvements in certain domains of cognitive functioning, specifically resistance to distractor interference and set-shifting ability, in individuals with alcohol use disorder.

Poster Abstracts

Poster Session 1: Monday

P_09a Clozapine's Impact on Microglial Exosomes: A Potential Pathway to Cognitive Dysfunction in Schizophrenia

Presenting Author: Kyle Hewitt

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Nathan Nagaratnam - School of Medical, Indigenous and Health Sciences, University of Wollongong, Wollongong, Australia

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Xu-Feng Huang - School of Medical, Indigenous and Health Sciences, University of Wollongong, Wollongong, Australia

Background
Schizophrenia is a complex neuropsychiatric disorder marked by cognitive impairments and psychotic episodes. Clozapine, a highly effective atypical antipsychotic drug, is commonly used for drug-resistant schizophrenia. However, its impact on cognition and brain structure remains under investigation, with evidence suggesting negative effects on cognitive performance and brain volume. Changes in the immune system are linked to variations in cognitive functioning in schizophrenia. Microglia, the brain's primary immune cells, are associated with decreased cognitive performance when dysfunctional. Microglial exosomes, integral to neuroinflammation and cellular communication, could provide insight into the neurobiological mechanisms underpinning the cognitive effects of clozapine treatment.

Methods
Human microglial clone 3 cell line (HMC3) microglial cells were treated with varying clozapine concentrations for 24 hours. Phenotypic changes, including cell eccentricity, ramifications, inflammatory markers (IL-1?, IL-6, and TNF-?), migration, and proliferation, were assessed using the live-cell analysis system Incucyte and qPCR assays. Exosomes were isolated from microglial supernatants via ultracentrifugation and characterized by nanoparticle tracking analysis (NTA), confocal microscopy, and western blot for CD9, CD63, and CD81. The human neuronal model SH-SY5Y and primary murine cortical neurons were treated with clozapine-induced microglial exosomes for 72 hours. Neurite outgrowth was quantified using Incucyte.

Results
Clozapine treatment resulted in increased microglial eccentricity, decreased process length, decreased proliferation, impaired migration ability, decreased levels of IL-1? and IL-6, and increased TNF-?. NTA, confocal, and western blot analysis confirmed the successful isolation of exosomes (~150nm in diameter) positive for CD9, CD63, and CD81. Exosomes derived from clozapine treated microglia significantly reduced neurite outgrowth in SHSY-5Y cells and primary murine cortical neurons. (Ongoing analyses of neuron BDNF expression, synaptic marker expression, and cognitive function in C. elegans are in progress).

Conclusions
Clozapine-induced changes in microglial phenotype and exosome composition contribute to reduced neurite outgrowth. These findings highlight the potential role of microglial exosomes in mediating the neurobiological mechanisms of clozapine's impact on cognition and pave the way for future research in in vivo models.

Poster Abstracts

Poster Session 2: Tuesday

P_16b Insights into the neurochemical mechanisms of psilocybin-induced improvements in anorexia-like behaviour in female rats

Presenting Author: Kyna Conn

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Background

Psilocybin is being explored as a novel therapeutic for anorexia nervosa (AN), and is proposed to act by alleviating cognitive inflexibility, a hallmark characteristic observed across a range of neuropsychiatric disorders. Accordingly, we have shown that a single clinically relevant dose of psilocybin (1.5mg/kg) attenuates the development of pathological weight loss in the activity-based anorexia (ABA) rat model. We then aimed to determine the serotonergic and dopaminergic mechanisms that could underlie this improvement in body weight maintenance and to further explore psilocybin's effects on cognitive flexibility in rodents using two different types of reversal learning paradigms.

Methods

Psilocybin effects on cognitive flexibility were assessed using a between-sessions reversal learning task where rats were trained on FED3 devices to poke into one of two ports to obtain a reward. Effects of psilocybin in combination with selective serotonin receptor (5-HTR) antagonism on reversal learning was examined 18h after administration. Additionally, alterations in 5-HTR mRNA expression caused by psilocybin in the prefrontal cortex using RNAscope were measured. We then used fibre photometry to measure dopamine (DA) release in the nucleus accumbens of psilocybin-treated rats while they performed a within-session probabilistic reversal learning task, where probabilistic contingencies of 80:20 were utilised.

Results

For the between-sessions RL task, the action of psilocybin via 5-HTR subtypes was antagonised with pre-administration of MDL100907 (selective 5-HT2A; n=18) or WAY100635 (selective 5-HT1A; n=26). Psilocybin enhanced cognitive flexibility by improving response accuracy ($p=.03$), which was negated with antagonism of 5HT1A ($p=.001$), but not 5HT2A receptors. In the infralimbic cortex, psilocybin transiently increased 5-HT1A transcription ($p=.02$) with the most prominent alterations observed in cortical layer V ($p<.0001$). Psilocybin also caused increased DA release during positive reinforcement in the within-session RL task and exaggerated the decent of DA in the absence of expected reward.

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 cortical 5-HT2A receptor subtype, due to its necessity for the acute "hallucinogenic" effects, these results suggest its actions at the cortical 5-HT1AR and subcortical dopamine may be more relevant for therapeutic outcomes related to cognitive flexibility and food reward valuation. Future studies will

examine the functional consequences of psilocybin, and the indirect effects on the dopaminergic and cholinergic subcortical systems thought to be involved in generation of anorectic behaviours using in vivo fiber photometry.

Poster Abstracts

Poster Session 2: Tuesday

P_26b Is alcohol incubation of craving driven by discrete alcohol-associated cues?

Presenting Author: Laisa de Siqueira Umpierrez

Laisa de Siqueira Umpierrez - Macquarie University

Mia Lavee - Macquarie University

Rhys Vorillas - Macquarie University

Alexander Kilby - Macquarie University

Jennifer Cornish - Macquarie University

Christina Perry - Macquarie University

Background
Alcohol use disorder (AUD) is characterised by high relapse rates and intense craving. Craving can be triggered by cues associated with alcohol, and notably this cue-elicited craving tends to become stronger the longer a person stays abstinent, a phenomenon known as “incubation of craving”. Our lab has replicated this phenomenon in an animal model, however the specific role of cues in relapse behaviour during abstinence has not been thoroughly explored. This study aimed to determine whether alcohol-associated cues are necessary for relapse-like behaviour and whether the increase in alcohol-seeking after abstinence was dependent on the presence of alcohol-associated cues.

Methods
Male and female Long Evans rats were trained to lever press for alcohol, paired with a discrete cue which was presented as alcohol was delivered. The alcohol-seeking behaviour was then extinguished by removing both alcohol and the discrete cue. Rats were tested either in the presence of the cue (reinstatement group) or not (extinction group), and these tests were conducted either immediately following extinction (no-abstinence group), or after 28 days of home-cage withdrawal (abstinence group).

Results
Both male and female rats exhibited increased alcohol-seeking behaviour after 28 days, regardless of the presence of cues. Furthermore, planned multiple comparisons showed that the difference between extinction and reinstatement was only significant in the abstinence group.

Conclusions
This study demonstrates that incubation of craving is not solely dependent on cues. However, the results indicate that cue-induced relapse is more pronounced after a period of abstinence. Finally, we saw no sex differences, which suggests that incubation of craving is not sex-dependent. In conclusion, alcohol-associated cues increase the likelihood of relapse-like behaviour after a period of abstinence.

Poster Abstracts

Poster Session 2: Tuesday

P_21b Reversal Learning in mice: Model-based versus model-free approaches and altering levels of probabilistic uncertainty

Presenting Author: Laura Kimble

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Suzy Alexander - Queensland Brain Institute, University of Queensland , Brisbane, QLD; Queensland Centre for Mental Health Research, Brisbane, QLD, Australia

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Background
The ability to adapt to rapidly changing environments is a crucial component of cognitive flexibility, which is impaired in several neuropsychiatric disorders, including schizophrenia. Reversal learning tasks (RLT), which require individuals to learn a stimulus-outcome association and then dynamically reverse that association, have been established as tests of cognitive flexibility. While rodents are commonly used in RLT, extensive training regimes may promote strategies that hinder its translational capacity. To better understand neural and behavioural mechanisms underlying cognitive flexibility, we developed a novel RLT in mice, emphasising mixed model-based and model-free learning (akin to humans).

Methods
We implemented a probabilistic RLT training regimen to generate three groups; performance-based (n=10), time-based (n=10), and mixed (n=20). Performance-based mice were trained using a protocol in which reversals occur after 6-8 consecutive correct responses (CCR). For time-based mice, reversals occurred after 26-36 trials regardless of performance. Mixed mice were trained using a combination of both. In this study, the predictability of rewarding outcomes was changed within-session to observe how different groups navigate contingencies, and to see whether the protocol these contingencies are presented on affects behavioural phenotypes.

Results
This study showed for the first time that navigating changing contingencies is dependent on the PRL protocol they are presented on. On a CCR protocol, the level of positive feedback from the non- target lever was inversely associated with performance. Specifically, mice exhibit challenges in navigating contingencies on the CCR protocol when faced with increasing amounts of misleading positive feedback on the incorrect target lever. This pattern was not observed for the Block protocol. Rather, the overall reward difference between the two levers, or the discriminability, was associated with performance.

Conclusions
We found for the first time that altering levels of probabilistic uncertainty validated the fundamental strategies mice employ to navigate probabilistic reversal learning in each protocol. Consequently, this study offers a nuanced understanding of how environmental variables, when intersected with prior learning experiences, can shape decision-making and behavioural phenotypes. Moreover, it suggests that different protocols may be more sensitive to distinct cognitive approaches, and potentially complex problems in neuropsychiatric disorders.

Poster Abstracts

Poster Session 1: Monday

P_44a NF-κB pathway gene expression is elevated in the midbrain of people with high-inflammation schizophrenia

Presenting Author: Layla Neuhaus

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Background
Approximately 40% of people with schizophrenia exhibit elevated peripheral and central inflammation indicated by elevated proinflammatory cytokines. The reasons for higher levels of inflammation in schizophrenia compared to controls are unknown. Increases in transcriptional pathways (NF-?B) induce these cytokines and can be activated by various cell surface receptors, but no change in these upstream activators in the NF-?B pathway has been reported in the schizophrenia midbrain. Since midbrain dopaminergic neurons are dysfunctional in schizophrenia and sensitive to pro-inflammatory cytokine signalling, it is important to determine which NF-?B pathway is altered in high vs. low inflammation schizophrenia to control inflammation.

Methods
Age-matched midbrain tissue from two post-mortem cohorts (NSW Brain Tissue Resource Centre and Stanley Medical Research Institute) including healthy controls (n = 62) and people with schizophrenia (n = 62) was analysed using high-throughput qPCR (Fluidigm; Ramaciotti Centre for Genomics) for 17 major transcripts in the NF-?B pathway (CD40, IL1R1, LTBR, TLR4, TNFR1, TNFR2, CHUK, IKBKB, MAP3K14, NFKB1, NFKB2, REL, RELA, HIVEP2, NFKBIA, NFKBIB, NFKBIE). Each case has been previously classified as either low- or high-inflammation based on cytokine and SERPINA3 mRNA levels using recursive two-step clustering. NF-?B pathway mRNA expression was analysed by both diagnosis and inflammatory subtype.

Results
On a diagnosis-level, we found significantly increased mRNA expression levels in schizophrenia midbrain for four pathway activating receptors (CD40, IL1R1, TNFR1, TNFR2), one inducing kinase (MAP3K14), three NF-?B subunits (NFKB1, NFKB2, RELA), and one inhibitor (NFKBIA) (all $P < 0.05$). Analysis based on inflammatory subtype confirmed significant changes in the high inflammation subtype of schizophrenia, and also revealed that mRNA for another cell surface receptor, LTBR, was significantly upregulated in schizophrenia (all $P < 0.05$). Only one transcript, IL1R1, was increased in the low-inflammation schizophrenia group compared to low-inflammation controls.

Conclusions
NF-?B activity in the midbrain is upregulated in high-inflammation schizophrenia cases, consistent with its role in cytokine regulation. The elevation in four cell surface receptors suggests multiple upstream drivers could converge to activate NF-?B activity. Elevated IL1R1 mRNA levels in low inflammation schizophrenia suggest patients may be more

susceptible to inflammatory stimuli or primed to overreact. These findings indicate NF-?B is a causal pathway for midbrain inflammation in a subset of schizophrenia patients, contributing to the dopamine neuron pathophysiology in this region.

Poster Abstracts

Poster Session 2: Tuesday

P_32b Midbrain ghrelin receptor signalling regulates binge alcohol consumption in a sex specific manner

Presenting Author: Leigh Walker

Amy Pearl - Florey Institute of Neuroscience and Mental Health

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William Giardino - Stanford University

Andrew Lawrence - Florey Institute of Neuroscience and Mental Health

Leigh Walker - Florey Institute of Neuroscience and Mental Health

Background
Rates of risky drinking are continuing to rise, particularly in women, yet sex as a biological variable has been largely ignored. An emerging yet understudied potential component of this circuitry is the central projecting Edinger Westphal (EWcp), which is made up of two prominent, but distinct cell populations expressing either an array of neuropeptides (including cocaine and amphetamine regulated transcript; CART) or vGlut2 (glutamatergic). Interestingly these cells also express receptors for feeding related hormones (including the ghrelin receptor -GHSR).

Methods
Here, we use a combination of approaches including genetic, molecular biology, behavioural testing, and electrophysiology to understand how the EWcp contributes to alcohol consumption in female versus male mice and whether ghrelin receptor signalling is involved.

Results
Inhibition of EWcp CART cells reduced binge drinking in female, but not male mice. Further, inhibiting EWcp CART cells prevented ghrelin-induced drinking, and viral-mediated GHSR knockdown in the EWcp reduced binge drinking specifically in female mice. RNAscope revealed GHSR expression across peptidergic (CART) and glutamatergic EWcp populations, with neurons from females more sensitive to bath application of ghrelin than male mice. Targeted knockdown of GHSR from distinct EWcp populations revealed GHSR signalling on peptidergic, but not glutamatergic cells mediate binge drinking in female mice. Finally, both a GHSR inverse agonist and antagonist delivered intra-EWcp reduced binge drinking in female mice.

Conclusions
These findings suggest the EWcp is a region mediating excessive alcohol bingeing through GHSR actions on peptidergic cells (CART-expressing) in female mice and expand our understanding of the neural mechanism(s) underpinning how the ghrelin system mediates alcohol consumption.

Poster Abstracts

Poster Session 1: Monday

P_53a Relationship between electroencephalography-based mismatch negativity and antipsychotic treatment response in young people at clinical high risk for psychosis

Presenting Author: Magdalene de Rozario

Magdalene de Rozario - Orygen & The University of Melbourne

Elise Rowe - Orygen & The University of Melbourne

Moritz Haaf - University Medical Centre Hamburg-Eppendorf

Julia Adams - Orygen & The University of Melbourne

Ilvana Dzafic - Orygen & The University of Melbourne

Andrew Thompson - Orygen & The University of Melbourne

Gregor Leicht - University Medical Centre Hamburg-Eppendorf

Stephen J. Wood - Orygen, The University of Melbourne & The University of Birmingham

Background
Some evidence suggests that antipsychotic medications can treat symptoms and prevent psychosis in some individuals at clinical high risk for psychosis (CHR-P). However, up to 75% of these individuals do not develop psychotic disorders and may not benefit from these medications. Hence, it's crucial to tailor antipsychotic prescriptions in this cohort based on individual prognostic markers. Reduced mismatch negativity (MMN) is associated with glutamatergic NMDAR hypofunction – a well-documented abnormality in psychotic disorders. Because first-line antipsychotics have minimal impact on the neurotransmission of glutamate, we hypothesize that CHR-P individuals with reduced baseline MMN amplitude might respond less to antipsychotic medications.

Methods
This study examines the relationship between MMN response and treatment outcomes in participants from the North American Prodrome Longitudinal Study (NAPLS-3) who were prescribed antipsychotic medications. Participants engaged in a Roving, and an Oddball MMN paradigm at their baseline assessment. In these paradigms, participants were required to ignore auditory stimuli while simultaneously performing either a tactile or visual oddball task. Average electroencephalographic waveforms and peak MMN amplitudes were quantified at Fz and Cz electrodes. These results were then correlated against symptomatic outcomes, as measured by The Scale of Prodromal Symptoms (SOPS) at baseline and relevant follow-ups.

Results
Preliminary analyses with a subsample of all available data indicated that baseline Oddball MMN measures did not correlate with symptomatic changes after 8-weeks of antipsychotic treatment. Baseline Roving MMN measures did not predict 12-month outcomes, such as the remission of CHR-P status, nor transition to a psychotic disorder in CHR-P individuals prescribed antipsychotics. The analyses will be repeated in the full sample as the preprocessing of all available data is completed. Further analyses to examine the relationship between baseline Oddball MMN and 12-month outcomes, as well as between Roving MMN and 8-week outcomes are also planned.

Conclusions
This research aims to understand the utility of electroencephalography (EEG) assessments for predicting treatment outcomes as early into a patient's treatment as possible. This hopes to spare patients a trial-and-error approach to treatment, and reduce delays in prescribing effective treatments to patients experiencing CHR-P syndrome or psychotic disorders. Given the costs and burdens associated with psychosis, this research also hopes to enhance patient welfare and bring a considerable economy to governments, healthcare systems, and society.

Poster Abstracts

Poster Session 2: Tuesday

P_38b Using a translational task to understand how Lateral hypothalamus may regulate learning processed relevant to schizophrenia and addiction

Presenting Author: Masakazu Taira

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Samuel J. Millard - Department of Psychology, University of California, Los Angeles, California, USA

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Background
Our study showed that GABAergic neurons in the lateral hypothalamus (LHGABA) differently regulate learning about reward cues depending on the relative distance of the cue to a reward. This led to the hypothesis that LHGABA neurons bias behaviours toward cues closest to reward. This has relevant to addiction and schizophrenia as they are characterised by changes in the balance of learning about cues. To investigate this in rats, we adapted the “Daw two-step task” used extensively in healthy human and clinical populations. This task allows us to measure behavioural controls as dependent on cues that have different distance to reward.

Methods
A trial began with one of two distal cues that are further form reward (A or B; e.g., click or white noise) followed by two levers (left or right). After pressing one of the two levers, the rats received one of two proximal cues that are closest to reward (C or D; e.g., tone or siren). The distal cues inform the transition from lever to the proximal cue (e.g. the left lever mostly predicts presentation of C after A, but the left lever predicts presentation of D after B). In turn, the proximal cues inform the fluctuating reward probabilities (high/low).

Results
As rats experienced more trials, they became better at making the choice to “find” the most rewarding proximal cue throughout the session and using the transitional structure of the task, achieving high proportions of correct trials (~90%). We analysed how rats adapted their choices depending on the outcome of the last trial (i.e., whether the trial was rewarded) and the transitional structure dictated by distal and proximal cues. Using logistic regression model, we were able to dissociate the influence of distal and proximal cues on behaviour in the task, suggesting they are computationally distinct processes.

Conclusions
Overall, these results demonstrate that rats are able to perform complex translational tasks used in humans. Our results show that use of the distal and proximal cues are behaviourally dissociable from both a computational and temporal standpoint. This will allow us to combine our task with optogenetic approaches to parse the contribution of different neural circuits, including LHGABA neurons, in differential weighting of distal and proximal cues over learning and behaviour. This will produce work that is directly translational to clinical findings, helping us to reveal neural circuits that balance learning about distal and proximal predictors in addiction and schizophrenia.

Poster Abstracts

Poster Session 1: Monday

P_38a Quercetin and chlorogenic acid: power duo for neuroprotection?

Presenting Author: Naomi May

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Background
Oxidative stress contributes to neurodegeneration and is associated with increased risk of neurodegenerative disease. Plant foods high in phytochemicals, including phenolic compounds, are of interest as novel treatments for these conditions due to the ability of these compounds to reduce free radicals in the brain. Several plant foods that are high in phenolics have demonstrated antioxidant and neuroprotective abilities however the species of phenolic compounds that could be driving these benefits are unclear.

Methods
The concentration of 23 phenolic species in plant foods (Queen Garnet plum (Prunus salicina), black pepper (Piper nigrum), clove (Syzygium aromaticum), elderberry (Sambucus nigra), lemon balm (Melissa officinalis) and sage (Salvia officinalis)) and the ability of these samples to prevent H2O2-induced oxidative stress in SH-SY5Y cells was determined. Spearman's correlations were conducted to examine the relationship between phenolic species and cell viability after oxidative stress.

Results
The plum samples had the highest concentration of the phenolics measured, followed by elderberry and clove. Pre-treatment with plum, elderberry and clove also prevented oxidative stress-induced reduction in cell viability (all $p < 0.01$ compared to H2O2 treatment group). However, only the plum was able to maintain healthy control-like levels ($p = 0.700$ vs healthy untreated controls). Both the total concentration of phenolics measured and quercetin 3-glucoside concentration had a significant positive correlation with cell viability in the prevention paradigm ($rs = 0.620$, $p = 0.032$ and $rs = 0.797$, $p = 0.002$, respectively).

Conclusions

Plum, elderberry and clove prevented cell death from oxidative damage in neuron-like cells. These samples were also high in total phenolics and more specifically, contained quercetin derivatives as a major component. Only the plum was able to completely prevent oxidative damage and maintain healthy control-like levels and this sample also contained chlorogenic acid as a major component. Previous research has shown a benefit of quercetin and chlorogenic acid for inflammation and oxidative stress, suggesting that the combined antioxidant and anti-inflammatory effects of these species could be a multipronged approach that's worthy of future research for prevention of neurodegenerative diseases.

Poster Abstracts

Poster Session 1: Monday

P_11a Novel BDNF haplotype linked to proBDNF down-regulation in PTSD – A study in predictive biosignatures.

Presenting Author: Nathan Wellington

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Anna V. Kuballa - School of Health, UniSC, Sippy Downs, QLD Australia

Background
Brain-derived neurotrophic factor (BDNF) plays a crucial role in regulating neuronal development, synaptic plasticity, and survival in both the central and peripheral nervous systems, and is essential for normal brain function. In PTSD, BDNF disruption influences stress responses and neuroplasticity in critical brain regions like the hippocampus and prefrontal cortex, impacting disorder onset, severity, and treatment outcomes. Its involvement in fear extinction and memory consolidation is central to PTSD symptom development, with dysregulation potentially hindering traumatic memory extinction. Genetic variants in the BDNF gene contribute to PTSD susceptibility, yet their differentiation to other disorders poses challenges in neuropsychiatric research.

Methods
In this study, we sequenced six BDNF DNA regions associated with neuropsychiatric disorders and measured BDNF protein levels in 35 clinically evaluated PTSD and non-PTSD participants. Genomic DNA extracted from whole blood was used for PCR amplification of target regions via Sanger sequencing by Macrogen (Seoul, Korea). BDNF protein quantification was achieved via enzyme-linked immunosorbent assay (ELISA), separately measuring pro and mature BDNF. Data was exported, cross-referenced with RSID numbers and global frequencies from dbSNP in NCBI, and prepared for further analysis in RStudio using Hardy-Weinberg analysis, binomial GLM, linkage disequilibrium, and graphical analysis.

Results
We identified SNPs at 62 locations across the BDNF gene, with nine variants deviating significantly from Hardy-Weinberg equilibrium (p 0.97) and were identified as potential biosignatures. Among PTSD participants, the three SNPs were collectively present in 61% compared to 17% in non-PTSD participants. Carriers of the triple SNP haplotype SCV00424443 showed a notable decrease in proBDNF protein levels (p=0.023) compared to those with fewer SNPs. While individually these variants did not affect BDNF quantification, together they significantly down-regulated proBDNF in the PTSD cohort.

Conclusion
These findings suggest that the identified triple SNP haplotype may down-regulate BDNF expression, potentially influencing PTSD susceptibility and enabling haplotype-specific diagnostic differentiation. These variants exert unique regulatory functions at specific domains, affecting BDNF transcription and translation. The study showed a significant association between the 3SNP haplotype (rs6265, rs2049045, rs11030099), proBDNF down-regulation, and PTSD. We proposed that this synergistic interaction of the three variants forms a heritable haplotype that predisposes to PTSD, influenced by genetic and environmental factors. This research supports precision medicine in neuropsychiatric disorders, aiming to personalise therapies using genetic biomarkers for enhanced clinical outcomes.

Poster Abstracts

Poster Session 1: Monday

P_12a Recording single neuron activity during working memory touchscreen testing, and the effects of pharmacological interventions.

Presenting Author: Nigel Jones

Nigel C Jones - Department of Neuroscience, School of Translational Medicine, Monash University

Leah Liu - Department of Neuroscience, School of Translational Medicine, Monash University

Louise Inger - Department of Neuroscience, School of Translational Medicine, Monash University

Grace Jin - Department of Neuroscience, School of Translational Medicine, Monash University

Matthew R Hudson - Department of Neuroscience, School of Translational Medicine, Monash University

Background
The Trial-Unique Non-match to Location task is a translational task of spatial working memory. When performed in touchscreen testing chambers, the test can be conducted in conjunction with synchronised electrophysiological recordings. The goals of this project were to validate the impact of pharmacological agents known to disrupt working memory in humans, and to identify associated neural firing patterns.

Methods
Male C57Bl/6 mice (n=24) were trained to criterion on the TUNL task, and were implanted with 4 x 25um stainless steel electrodes twisted together in tetrode assemblies to record single and multi-unit activity in the prefrontal cortex and dorsal hippocampus. After recovery, mice were connected to electrophysiological cables, then injected with MK801 (0.03 – 1mg/kg ip), ketamine (3-10mg/kg ip), scopolamine (0.03 – 1mg/kg ip nicotine (0.03 – 1mg/kg ip), or saline, and placed into the chamber. Working memory performance was as % correct responses, neural activity was synchronised to the different phases of the task, and related to behavioural performance.

Results
MK801 dose-dependently impaired accuracy on the task ($p<0.0001$) and increased the number of correction trials performed by the mice ($p<0.0001$). Over the course of the experiment, ketamine did not impact WM performance – however, sub-analysis of the first 12 trials revealed a significant impairment in the higher doses of ketamine, compared to vehicle ($p<0.005$). Scopolamine dose-dependently impaired performance ($p<0.0001$), but nicotine was without effect. Electrophysiological recordings identified multi-unit activity throughout recordings, and single units reflecting the properties of wide-spiking excitatory cells, and fast-spiking inhibitory interneurons were identified.

Conclusion
We have successfully optimised recording of single- and multi-unit neuronal activity during touchscreen testing. The impairment of working memory observed with MK-801, ketamine and scopolamine reflect the observations from human literature studying these interventions, suggesting that task performance is influenced by similar neurotransmitter systems across species. Characterisation of neuronal firing patterns during TUNL testing will uncover the neural basis of working memory, and open up avenues to understand the mechanisms of why this cognitive construct is so frequently impaired in disease.

Poster Abstracts

Poster Session 1: Morning

P_26a Interactions of methamphetamine and psilocybin on cognitive flexibility using a novel social reversal learning task in female rats.

Presenting Author: Olivia Gilmore McKimm

Olivia Gilmore McKimm - School of Psychology, Brain and Mind Centre, University of Sydney

Alex Athanasopoulos - School of Psychology, Brain and Mind Centre, University of Sydney

Tylah Doolan - School of Psychology, Brain and Mind Centre, University of Sydney

Nicholas Everett - School of Psychology, Brain and Mind Centre, University of Sydney

Background
Methamphetamine use causes cognitive impairments which may maintain addiction and drive relapse. This is hypothesised to occur via methamphetamine-induced changes to the prefrontal cortex. The 5-HT2A agonist and psychedelic psilocybin improves cognitive flexibility in humans and rats, which is hypothesised to be via promoting neuroplasticity in the prefrontal cortex. Methamphetamine use alters expression of the 5-HT2A receptor in the prefrontal cortex. This project investigates if methamphetamine exposure alters psilocybin's effects on cognitive flexibility in rats using a reversal learning task. The study also examines whether the type of reward (food vs. social) influences methamphetamine-induced cognitive deficits and psilocybin's pro-cognitive effects.

Methods
104 female Sprague-Dawley rats were trained to self-administer either sucrose pellets (Exp 1, n=32) or 30-s of access to a social partner (Exp 1, n=32; Exp 2, n=40), under fixed ratio-1/2/3 schedules of reinforcement in daily 1-hour sessions, until stable at >80% accuracy (active / total presses). Rats in experiment 1 underwent a day of binge saline or methamphetamine dosing (4x2 mg/kg s.c.), and then 2 days later underwent a reversal learning test. Rats in experiment 2 received higher methamphetamine dosage (4x5 mg/kg), and saline or psilocybin (1.5 mg/kg i.p.) 18-hours prior to the reversal learning test.

Results
This study is ongoing, however below is a subjective description of the results of experiment 1. 25 of 32 rats acquired social self-administration, and 15 of 25 successfully achieved an arbitrary performance criterion of 75% after reversal of the reward contingency. 31 of 32 rats acquired sucrose self-administration, and 25 of 31 achieved an arbitrary performance criterion of 80% after reversal. Methamphetamine exposure (2x4 mg/kg) did not overtly impact reversal learning for either reward type. Sub behaviour analyses of methamphetamine's effects are underway, including quantification of perseverative and regressive errors. Experiment 2 (psilocybin intervention and higher methamphetamine dose) is underway.

Conclusion
We have demonstrated that operant reversal learning procedures typically used for food rewards can be used with social rewards, providing a novel model for understanding social cognitive flexibility. A binge dose of methamphetamine did not impact reversal learning for social or sucrose rewards, however, experiment 2 is underway using higher methamphetamine dosing, and investigating the effects of psilocybin on reversal learning in saline- vs. methamphetamine-exposed rats. This will determine whether the methamphetamine-induced changes alter the beneficial effects of psilocybin on cognitive flexibility, which has relevance to ongoing clinical trials of psilocybin for methamphetamine addiction.

Poster Abstracts

Poster Session 2: Tuesday

P_43b Understanding persistent detrimental behaviour: External and predictive validity of a novel experimental paradigm

Presenting Author: Philip Jean-Richard-dit-Bressel

Philip Jean-Richard-dit-Bressel - School of Psychology, UNSW Sydney

Background
Behaviour that persists despite its negative consequences ("punishment insensitivity") is a hallmark of various psychiatric conditions, including addictions (eg. substance-related, gambling), conduct disorders, and compulsive disorders. Despite its transdiagnostic relevance, traditional protocols for studying punishment insensitivity fail to track psychological root causes for behavioural differences, limiting insight into causes and potential interventions. Moreover, these protocols lack proven indicators of external and predictive validity.

Methods
We developed a "Planets & Pirates" task based on a well-controlled protocol used to understand mechanisms of punishment insensitivity in rodents. In this task, participants could make two responses (R1, R2) for point rewards across 3-min game blocks. However, R1 also led to a cue (CS+) that predicts "attack" (substantial point loss), whereas R2 only led to a neutral cue (CS-). Task-related valuations and inferences were surveyed after each block, and task structure was revealed to participants before the final block. Four experiments examining the influence of punishment delay/probability, generality of findings, and test-retest reliability were conducted.

Results
Across experiments, avoidance of detrimental R1 was bimodally distributed, with data-driven clustering reliably identifying 3 behavioural phenotypes: "Sensitive" individuals that acquired adaptive avoidance through experience, "Unaware" individuals that only avoided when given explicit information, and "Compulsive" individuals that were unresponsive to either experience or information. These profiles were underpinned by specific deficits in Action-Punisher learning and cognitive-behavioural integration, not differences in CS learning, motivations, behavioural control, or self-reported traits. Low probability punishment (even if severe) drove individuals to be "compulsive". Findings were replicated in an international sample, and behavioural phenotypes were found to be stable across a 6-month interval.

Conclusion
Trait-like tendencies to persist in detrimental behaviour is common in the general population. Using a task that isolates causes for this, we show poor Action-Punisher awareness is a common obstacle to beneficial behaviour change. Accordingly, providing accurate information drastically improved choices in the majority, though not all, punishment insensitive individuals. A critical barrier to information-driven behaviour change was if punishment was infrequent (albeit severe). Reduced cognitive-behavioural integration in Compulsives highlights a new obstacle and intervention target for promoting beneficial choices.

Poster Abstracts

Poster Session 1: Monday

P_47a Differential striatal gene expression profiles underlying the propensity for depression-like behaviour in a mouse model of vertical sleeve gastrectomy

Presenting Author: Renee Anne Papaluca

Renee Anne Papaluca - University of Melbourne, School of Biomedical Sciences, Department of Biochemistry and Pharmacology + Florey Institute of Neuroscience and Mental Health

Eva Guerrero-Hreins - University of Melbourne, School of Biomedical Sciences, Department of Biochemistry and Pharmacology + Florey Institute of Neuroscience and Mental Health

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Priya Sumithran - Monash University, School of Translational Medicine, Department of Surgery

Robyn Brown - University of Melbourne, School of Biomedical Sciences, Department of Biochemistry and Pharmacology

Background
Bariatric surgery is the most effective long-term treatment for obesity, leading to reduced appetite and improved glycaemic control through significant changes to the gut-brain axis. However, a small patient subset experiences increased rates of adverse mental health outcomes, such as depression and anxiety, post-surgery. While emerging longitudinal studies begin to explore this association, research on how gut-brain axis alterations mechanistically contribute to these adverse mental health outcomes is limited. Therefore, the aim of this study was to investigate individual differences in the effect of bariatric surgery on depressive-like behaviour using a mouse model of vertical sleeve gastrectomy (VSG).

Methods
Male and female C57BL/6 (n=57) mice were fed a high-fat, high-sugar diet (45%kcal fat; 11 weeks) before undergoing VSG or sham surgery. Before and after surgery, mice were tested for depression-like and anxiety-like behaviour. RNA was extracted from tissue punches of the dorsal striatum, a brain region associated with depression, and subjected to next-generation bulk RNA-sequencing. Analysis of this data is currently ongoing.

Results
Compared to sham surgery mice, VSG resulted in significant and sustained weight loss, accompanied by reduced food intake. VSG mice also showed a trend for higher immobility times in the forced swim test and decreased preference for sucrose solution, suggestive of depressive-like behaviour. Results from analysis of RNA-sequencing of the dorsal striatum are pending.

Conclusion
Outcomes from this study will provide valuable insight into the neurobiological underpinnings of adverse mental health outcomes following bariatric surgery, potentially informing future clinical directions.

Poster Abstracts

Poster Session 1: Monday

P_02a Investigating changes in immune signalling following prenatal opioid exposure

Presenting Author: Rinjani Soengkoeng

Rinjani Soengkoeng - School of Psychology, University of New South Wales

Arshman Sahid - School of Psychology, University of New South Wales

Abigail Marcus - School of Psychology, University of New South Wales

Dr Adam Walker - Neuroscience Research Australia

Conjoint Professor JuLee Oei - School of Women's & Children's Health, University of New South Wales

Dr Meredith Ward - School of Women's & Children's Health, University of New South Wales

Associate Professor Kelly Clemens – School of Psychology, University of New South Wales

Background
Prenatal opioid exposure (POE) impairs foetal brain development. Maternal treatments with synthetic opioids (methadone, buprenorphine) prolong infant exposure, and have unknown long-term consequences. Preclinical research links POE with white matter alterations and brain inflammation, however, it is unclear how these responses are activated, and how they differ across brain regions and opioids. Using an animal POE model, we investigated immune gene expression in regions controlling opioid-impaired functions: hippocampus (non-verbal memory) and prefrontal cortex (executive functioning). Both methadone and buprenorphine were predicted to increase inflammatory gene expression. A smaller increase was expected for buprenorphine, which is associated with improved maternal-neonatal outcomes.

Methods
Pregnant Sprague-Dawley rats were continuously exposed to methadone (9mg/kg/day), buprenorphine (1 mg/kg/day) or saline using mini-osmotic pumps from early gestation until pup weaning. Pup brains were collected a week post-weaning, avoiding acute drug effects on neural physiology. Immune gene expression in the prefrontal cortex and dorsal hippocampus was measured with reverse transcription quantitative PCR. We assessed an array of pro-inflammatory cytokines (TNF?, IL-6, IL-1?) and an anti-inflammatory cytokine (IL-10). Changes in JAK-STAT and MAPK cascade signalling were probed by assessing relevant intracellular and membrane-bound signalling mediators: TLR4, the p65 NF-?B subunit, STAT3, MAPK3, MAPK14, IL-6r.

Results
We found several gene expression differences across both the prefrontal cortex and dorsal hippocampus indicating disruption to immune functioning. POE strongly downregulated IL-6 expression in both regions, with a non-significant trend towards methadone exposure producing stronger downregulation in the dorsal hippocampus. In this region POE also upregulated expression of proinflammatory TNF?, without differences between opioid groups. There was no group change in anti-inflammatory IL-10 expression in either region. In the prefrontal cortex, expression of MAPK3 – which is activated by IL-6 – was down-regulated, as was expression of the IL-6 receptor in exposed males.

Conclusion
POE induces a complex pattern of cytokine and signalling mediator expression in the prefrontal cortex and dorsal hippocampus of juvenile rats, revealing lasting neuro-immune impacts of methadone and buprenorphine. Downregulated IL-6 expression – required for neurodevelopment and normal immune responses – provides a possible mechanism for opioid-induced neural and cognitive disruptions. POE may reduce MAPK cascade activation in the prefrontal cortex through IL-6 suppression, impacting cell development regulation, while elevated dorsal hippocampus TNF? Levels suggest heightened risk of apoptosis and tissue damage. Through improved understanding of the lingering consequences of synthetic opioids, safer treatments for opioid-affected infants can be developed.

Poster Abstracts

Poster Session 2: Tuesday

P_09b A novel mouse model of acute neuroinflammation shows schizophrenia-like behavioural phenotypes

Presenting Author: Rose Chesworth

Rose Chesworth – School of Medicine, Western Sydney University

Maxine Lindaur – School of Medicine, Western Sydney University

Tim Karl – School of Medicine, Western Sydney University

Background
Neuroinflammation is evident in approximately 50% of individuals with schizophrenia, with increased pro-inflammatory cytokines found in brain and blood. Despite this, the contribution of neuroinflammation to schizophrenia pathophysiology and symptoms is unclear. It is hypothesised that neuroinflammation can lead to disruption of midbrain dopamine neurotransmission, contributing to psychosis and negative symptoms in schizophrenia. To assess this hypothesis, here we validated a novel mouse model of acute neuroinflammation in adulthood, to determine if elevated pro-inflammatory signalling contributes to schizophrenia-relevant behavioural phenotypes.

Methods
We administered 2x lipopolysaccharide (LPS, 0.83 mg/kg, N=12/group), 16 hr apart to adult male and female C57BL/6J mice, to induce an acute neuroinflammatory response. Behavioural responses were assessed across the following 3 days. We evaluated behavioural responses to acute dexamphetamine (5 mg/kg) in the open field and prepulse inhibition tests, to assess behaviours relevant to positive symptoms and sensorimotor gating impairment in schizophrenia. We also evaluated social behaviours following 2xLPS, modelling negative symptoms. ELISAs were performed to determine neuroinflammatory signatures following acute neuroinflammation.

Results
Male LPS-treated mice were more sensitive to the increase in locomotion caused by dexamphetamine than vehicle-treated controls, mimicking the increased sensitivity to psychomimetic agents observed in individuals with schizophrenia. Prepulse inhibition was reduced in female LPS-treated mice, similar to what is seen in schizophrenia; however, LPS did not exacerbate dexamphetamine-induced disruption of PPI in female mice. There was no reduction in social behaviours following LPS treatment in male mice. Analysis of pro-inflammatory cytokines (tumor necrosis factor alpha, interleukin 1 beta) in schizophrenia-relevant brain regions (e.g. striatum, midbrain) is ongoing and will be presented at the conference.

Conclusion
Our data suggest that acute neuroinflammation via 2x LPS can recapitulate schizophrenia-relevant behaviours which rely on dopaminergic signalling (e.g. dexamphetamine-induced locomotion, PPI deficits), supporting a link between neuroinflammation and schizophrenia symptoms. Thus, we provide a novel model for testing new therapeutics which can normalise neuroinflammation-induced dopaminergic dysfunction, to better treat schizophrenia pathology rather than merely mitigating symptoms.

Poster Abstracts

Poster Session 1: Monday

P_48a Could heat therapy be utilised as a novel treatment for Alzheimer's disease? Insights from a pilot study in mice.

Presenting Author: Rossana Rosa Porto

Rossana Rosa Porto - Western Sydney University

Benjamin Smits - Western Sydney University

Orla Solier - Western Sydney University

Erin McLemon - Western Sydney University

Rose Chesworth - Western Sydney University

Tim Karl - Western Sydney University

Background
Pharmacological treatments for Alzheimer's disease (AD) have severe side effects without pronounced beneficial impact on disease progression. Heat treatment (HT) induces heat shock proteins of 70 kDa (HSP70) and has therapeutic properties in chronic diseases such as cardiovascular disease, obesity and depression. Most importantly, there is an inverse correlation between sauna frequency and risk of AD and dementia. HT has no significant side effects, thus, could be easily implemented into clinical settings. We aimed to develop a HT protocol for mice, that is safe, affordable and translatable to humans, to be applied in future studies in mouse models of AD.

Methods
Male C57BL/6 mice (5 months) were subcutaneously implanted with a tag to monitor their body temperature. We first performed an acute session, at 40.8±0.2°C for 20 or 30 minutes, or 42±0.2°C for 20 minutes, using a fan-forced incubator. We evaluated behaviour and temperature every minute during HT. Body weight and health parameters were recorded before, immediately after, and every 30 minutes thereafter, until tissue was collected 4 h after HT. The protocol that caused significant elevations on HSP70 was repeated 2 times a week for 4 weeks (chronic protocol). Tissue was collected 72 h after last session.

Results
When incubator temperature was increased to 42±0.2°C, HSP70 levels was detectable in the hippocampus, prefrontal cortex, brain regions relevant to AD. Exploration behaviour was decreased in HT animals, while immobility time was increased when compared to control mice. They also recovered dehydration levels 90 minutes faster than controls after HT (no water access with increased activity during HT causes a reduction in body weight). Chronic HT increased basal levels of HSP70 in the hippocampus and prefrontal cortex, with faster recovery of body temperature after HT when compared to controls (handling increases body temperature in control mice).

Conclusion
We developed a new sauna-like protocol that can easily be translated to clinical trials, an effective low-cost therapy with no severe side effects. That is a refinement from the current literature, which uses higher temperature/ duration, or put animals under anaesthesia, which can cause inhibition of compensatory thermogenic responses and negatively influence cognition. Our animals did not show any health related issues, while increasing levels of HSP70 in tissues relevant to AD. It therefore confirms the efficacy of this protocol, which will now be applied in AD transgenic mice models aiming to use HT to prevent or rescue disease progression.

Poster Abstracts

Poster Session 2: Tuesday

P_39b Sex-Dependent mGluR7 Alterations in Schizophrenia: Insights from the Nucleus Accumbens

Presenting Author: Samara Walpole

Samara Walpole - University of Wollongong, Wollongong, New South Wales, Australia

Jeremy Lum - University of Wollongong, Wollongong, New South Wales, Australia

Rose Chesworth Vieyra - Western Sydney University, Campbelltown, New South Wales, Australia

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Cynthia Shannon Weickert - Neuroscience Research Australia, Randwick, New South Wales, Australia

Kelly A. Newell - University of Wollongong, Wollongong, New South Wales, Australia

Background
Group III metabotropic glutamate receptors (mGluRs) (mGluR4, 7 and 8) are increasingly relevant to the pathophysiology and treatment of schizophrenia. These presynaptic receptors regulate neurotransmitter release in various brain regions, including the nucleus accumbens (NAc), a key area for reward learning and motivated behaviour that is altered in schizophrenia. Group III mGluRs can regulate the activity of medium spiny neurons within the NAc, through tight control of glutamate, GABA and dopamine release. Their involvement with both glutamatergic and dopaminergic systems makes them promising targets for novel antipsychotic drugs. However, their expression levels in the NAc in schizophrenia remains largely unknown.

Methods
To investigate group III mGluR mRNA and protein levels in the nucleus accumbens (NAc), frozen postmortem NAc tissue from 30 individuals who had schizophrenia and 30 matched controls was obtained from the NSW Brain Tissue Resource Centre, Sydney. Gene expression of the individual group III mGluRs, GRM4, GRM7 and GRM8 was measured via qRT-PCR. Protein expression of mGluR4 and mGluR7 was assessed via western blot. We used t-tests or ANCOVAs to uncover differences between schizophrenia and control cases. Exploratory subgroup analyses were performed to examine the impact of sex and suicide on glutamate receptor levels.

Results
Gene and protein expression of the group III mGluRs in the NAc was not different between schizophrenia and control subjects (all $p>0.05$). However, subgroup analyses, revealed that females with schizophrenia had increased mGluR7 protein (+33%, $p=0.014$) and a trend increase mGluR4 protein (+36%, $p=0.067$) compared to female controls. In contrast, males with schizophrenia showed decreased mGluR7 protein compared to male controls (-20%, $p=0.040$). mGluR7 protein expression was elevated in schizophrenia subjects that died by suicide compared to schizophrenia subjects that died from other causes (groups were matched for sex) (+46%, $p=0.017$).

Conclusion
Our findings reveal sex-specific alterations of mGluR7 in the NAc in schizophrenia, suggesting that mGluR7 protein is consequently altered or potentially underlies the disrupted glutamate regulation within the ventral striatum. As mGluR7 can regulate both glutamate and GABA release, these findings suggest possible differences in glutamatergic and GABAergic signalling in the NAc between males and females with schizophrenia. Strategies to normalise mGluR7 within the NAc may differ in males and females with schizophrenia, indicating a need for sex-specific treatments. Further investigation of mGluR7 changes, particularly regarding cellular localisation and regulation of ventral striatal signalling, is warranted.

Poster Abstracts

Poster Session 2: Tuesday

P_11b Genetic correlations between Bipolar Disorder and co-morbid conditions across a broad array of body systems

Presenting Author: Samuel Brennan

Samuel Brennan - NeuRA

Bronwyn Overs - NeuRA

Kerrie Pierce - NeuRA

Jan Fullerton – NeuRA

Background
Bipolar Disorder (BD) is a major psychiatric illness primarily characterized by alternating episodes of depression and mania or hypomania. Apart from the direct impact these fluctuating mood symptoms have on the lives of BD patients, mounting epidemiological and clinical evidence suggests that people with bipolar disorder are more likely to develop additional psychiatric, neurodegenerative and somatic co-morbidities as they age. Shared risk estimated from global genetic correlations suggests that there may be common genetic contributors across these conditions. Identifying these specific pleiotropic risk factors will elucidate the molecular mechanisms underpinning these cross-disorder relationships.

Methods
Summary statistics from genome-wide association studies for conditions of interest were selected based on maximal sample size and power. Local Analysis of [co]Variant Association (LAVA) package was used to examine genetic correlations (rg) across 2945 quasi-independent linkage disequilibrium (LD) block partitions. Relationships between BD and comorbid conditions included: Schizophrenia, Anxiety disorder, Suicide attempt, Problematic Alcohol Use, Cannabis Use Disorder, Alzheimer's, Parkinson's Disease, Multisite Chronic Pain, Asthma, Sleep Apnoea, Essential Hypertension, Heart Failure, Diabetes, Irritable Bowel Syndrome. A significant rg was defined at: 1) a Bonferroni threshold [?=0.05/(n tests)] or 2) a false discovery rate (FDR) q<0.05.

Results
A total of 609 LD blocks exhibited univariate association (p<2e-05) and evidence of trait heritability, and underwent bivariate testing. Seventy five loci demonstrated Bonferroni-significant rg (P<8.21E-05), and 135 were FDR-significant (q<0.05). Out of 210 significant rg, 130 were between BD and Schizophrenia, highlighting extensive shared genetic risk. There were novel rg between BD and suicide (3 Bonferroni, 4 FDR), and BD and anxiety (2 Bonferroni, 7 FDR). Single bonferroni significant rg were identified between BD and Asthma (plus 10 FDR), and BD and hypothyroidism (plus 2 FDR). The genes in significant loci were identified and gene ontologies will be presented.

Conclusion
There are many genomic loci that demonstrate rg between BD and known psychiatric, neurological and somatic co-morbidities. Schizophrenia is strongly associated with BD at the genetic level, as were suicide attempt and anxiety disorders, albeit to a lesser extent. Many of the BD/SCZ loci have not been reported previously. This study provides a foundation from which we can identify specific genetic variants that influence the complex health issues impacting patients with BD. With proper knowledge of thesefeatures we can develop sensitive and accurate prognostics and provide personalised care to patients with BD to increase quality and quantity of life.

Poster Abstracts

Poster Session 2: Tuesday

P_23b Paclitaxel therapy induces sickness behaviour and microbiome changes in mice

Presenting Author: Sarah-Jane Leigh

Sarah-Jane Leigh - APC Microbiome Ireland; UNSW

Paula Sanchez-Diaz - APC Microbiome Ireland

Thomaz FS Bastiaanssen - APC Microbiome Ireland

Benjamin Valderrama - APC Microbiome Ireland

Cristina R Cardona - APC Microbiome Ireland

John F Cryan - APC Microbiome Ireland

Gerard Clarke - APC Microbiome Ireland

Background
Reciprocal microbiota-drug interactions are increasingly recognized as underlying some individual differences in therapy response and adverse events. Several cancer therapies are associated with long-last behavioural impairments for which there are no effective therapies, and also disrupt microbiota composition and function. However, the relationships between the gut microbiota, cancer therapies and associated behavioural impairments, and the underlying mechanistic changes along the gut-brain axis that drive these relationships, are not yet fully understood.

Methods
We examined how chemotherapeutic paclitaxel changed behaviour, hippocampal gene expression and microbiome composition and function in adult male C57Bl6 mice. Mice were exposed to low and moderate dose paclitaxel, and their behaviour was assessed using the open field test, novel object recognition test, 3-chamber social interaction test and nesting assessment.

Results
Both doses of paclitaxel disrupted nest-building, with no effects on novel object recognition, social behaviour or anxiety-like behaviour. Paclitaxel altered hippocampal gene expression of genes involved in blood-brain barrier integrity, neuroinflammation and myelination. Gut microbiota composition was altered by paclitaxel, with significant alterations observed in inferred gut metabolic functions. Specifically, paclitaxel increased microbial degradation of simple sugars. The mycobiome, or fungal species in the gut, were not altered by paclitaxel.

Conclusions
In summary, paclitaxel induced sickness behaviour and shifted the metabolic function of the microbiome. These changes were associated with altered gene expression in the hippocampus in genes relevant to blood-brain barrier integrity, and microglia and oligodendrocyte function.

Poster Abstracts

Poster Session 1: Monday

P_42a Subcortical modulation of the fronto-insular and cingulate functioning during negative emotional processing in mood and anxiety disorders

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Background
Dysfunctional processing of negative emotional events is a transdiagnostic feature of mood and anxiety disorders and is often associated with aberrant functioning of the fronto-insular/cingulate network involved in salience processing. Coordination of responses to negative emotional events in this network relies on dynamic interactions with subcortical regions, such as the amygdala and periaqueductal gray (PAG). However, the precise nature of these interactions is not well understood, specifically in mood and anxiety disorders.

Methods
Using dynamic causal modelling (DCM), in this study we investigated dynamic interactions between the amygdala, PAG and the fronto-insular/cingulate network, comprising anterior insula, dorsal anterior cingulate and ventrolateral prefrontal cortex, during negative emotional processing in mood and anxiety disorders. Thirty-seven participants with mood and anxiety disorders (29 Female) and 37 age and sex-matched healthy controls completed an emotional oddball paradigm during ultra-high field 7-Tesla functional magnetic resonance imaging scanning.

Results
DCM results revealed shared bi-directional interactions between the amygdala, PAG and fronto-insular/cingulate network during negative emotional processing. Specifically, while healthy control participants exhibited an inhibitory influence from the PAG to anterior insula, this effect was not detected in participants with mood and anxiety disorders (0.34 Hz, posterior probability=1.00). Leave-one-out cross validation revealed this effect was large enough to predict diagnostic status, negative affect, depression, and stress levels. Additional group differences emerged in modulatory amygdala-to-PAG intrinsic PAG self-inhibitory connections.

Conclusions
The current findings indicate that differences in PAG inhibition of the anterior insula likely contribute to maladaptive salience attribution, autonomic arousal, and affective response to negative emotionally salient events in mood and

anxiety disorders. Overall, these results highlight that incorporation of subcortical regions into our current network definitions would provide greater insight into the neurobiological underpinnings of dysfunctional negative emotion processing in mood and anxiety disorders.

Poster Abstracts

Poster Session 1: Monday

P_34a Investigating transitions between Goal-Directed, Habitual and Compulsive Behaviour

Presenting Author: Sophie Welch

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Dr Christopher Nolan - Decision Neuroscience Laboratory, School of Psychology UNSW

Dr Karly Turner - Decision Neuroscience Laboratory, School of Psychology UNSW

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Background
Compulsive behaviours persist in the face of negative feedback, thus are pivotal in the perpetuation of obsessive-compulsive, substance abuse and addictive disorders. One dominant hypothesis is that compulsive behaviours arise from an imbalance between goal-directed and habitual controls. Yet it remains unknown whether this is due to dysregulation in habitual or goal-directed control. It has proven difficult to pinpoint how compulsive behaviours develop, and to track shifts in behavioural control across time. Therefore, we will combine sophisticated behavioural tasks with multi-dimensional video and machine learning technology to conduct a more dynamic, high-resolution analysis to determine how these behaviours form.

Methods
To test dominant theories, our first goal was to characterise the habit formation via a single-lever, single outcome instrumental rodent paradigm. High-definition videos of training and test days following outcome devaluation were imported into automated pose estimation and tracking software, DeepLabCut. A supervised learning approach was used, where key body points were labelled manually before the remaining video dataset was processed for analysis. Relationships between these body parts and the environment in the form of feature representations of movements, paths, velocities and distances are then calculated using behavioural analysis software to test key hypotheses and characterise behavioural transitions of interest.

Results
This project aims to differentiate goal-directed, habitual, and compulsive behaviours in rodents using high-resolution movement tracking and machine learning analysis. We hypothesise that, if goal-directed behaviour is present, we will observe increased lever pressing variability and movement patterns following altered reward schedules. In contrast, if responding is under habitual control, then lever pressing will be consistent, with minimal pattern variability and stable movement trajectories. For compulsive behaviour, we expect to see persistent lever pressing during either non-reward phases or during negative feedback and we will compare performance with patterns of activity during habitual and goal-directed action control during these treatments.

Conclusions
Compulsive behaviours are a significant transdiagnostic symptom in obsessive-compulsive and substance-related disorders, likely arising from an imbalance between goal-directed and habitual controls (Robbins & Belin, 2024; Voon et al., 2015). By utilising high resolution tracking and machine learning analysis, this study aims to distinguish between these behaviours in rodents as they develop across time. The anticipated findings may provide deeper insights into the mechanisms driving compulsive actions, potentially refining therapeutic approaches and enhancing our understanding of addiction and compulsive disorders.

Poster Abstracts

Poster Session 2: Tuesday

P_13b Behavioural Stratification in animal studies – why its important

Presenting Author: Suzy Alexander

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Background
Individual variation to psychomimetic drugs in Sprague Dawley (SD) rats is well documented. Therefore, prior to starting a large chronic antipsychotic treatment experiment, we decided to screen 48 SD rats for their behavioural responses to two psychostimulants – Amphetamine and Apomorphine as well to assess their ability to learn a Condition Avoidance Response (CAR). This was to stratify individual animals prior to assigning them to treatment groups. These behaviours were chosen as both psychostimulants act on the dopamine system, amphetamine presynaptically and apomorphine postsynaptically, and CAR is D2 & 5-HT2A/c dependant and is a gold standard predictor of antipsychotic potential.

Methods
48 adult male SD rats were tested over a 2 week window for Amphetamine induced hyperlocomotion, Apomorphine impaired Prepulse Inhibition (PPI) and their ability to learn CAR. Locomotion: rats were observed in an open field for 120 minutes total, 30 minutes baseline and 90 minutes after Amphetamine (2mg/kg IP) on the same day. PPI: rats were tested for baseline response and again, 15 minutes after administration of Apomorphine (0.5mg/kg SC) on the same day. CAR training: rats received 40 trials once a day for 5 days in a two-way shuttle box with paired CS-US stimulus.

Results
There was no relationship between baseline locomotion and amphetamine induced hyperlocomotion in the open field ($r=0.15$, $p=0.33$), nor between baseline PPI and Apomorphine impaired PPI ($r=0.08$, $p=0.59$). Furthermore, to our surprise there was no relationship between Amphetamine induced hyperlocomotion and Apomorphine impaired PPI ($r=0.14$, $p=0.35$). Finally the ability to acquire adequate CAR (greater than 70% avoidance) was not related to either Amphetamine induced hyperlocomotion or Apomorphine impaired PPI.

Conclusions
As predicted, individual responses to psychostimulants was highly variable but normally distributed, highlighting the necessity to stratify individuals prior to intervention studies to avoid individual bias. In our planned chronic antipsychotic study, the response to these two psychostimulants will be repeatedly assessed and we predict initial behaviour will reflect an individual's behaviour over the experimental period. Apomorphine impaired PPI and locomotor sensitivity to amphetamine are routinely employed to establish subcortical hyperdopaminergia in animal models of relevance to schizophrenia. To our surprise, initial sensitivity to these two psychostimulants did not correlate, indicating pre- and postsynaptic dopamine are not initially coupled.

Poster Abstracts

Poster Session 1: Monday

P_51a Effects of psychological trauma exposure in childhood or adulthood on brain morphology and function in chronic pain: a systematic review

Presenting Author: Tong En Lim

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Prof James H. McAuley - Centre for Pain IMPACT, Neuroscience Research Australia, Sydney, Australia; School of Health
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Prof Sylvia M. Gustin - NeuroRecovery Research Hub, School of Psychology, University of New South Wales, Sydney, NSW, Australia; Centre for Pain IMPACT, Neuroscience Research Australia, Sydney, Australia

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Background
Exposure to traumatic events is a risk factor for the development and maintenance of various mental and physical health conditions, including chronic pain. Trauma exposure is associated with more intense pain experience and increased pain-related disability. Similar morphological and functional brain alterations, including cognitive deficits, have been reported in separate studies of chronic pain and psychological trauma. Despite these similitudes, the changes in brain integrity associated with trauma exposure in chronic pain remain poorly understood. This systematic review aims to summarise the relationship of brain morphology and function with psychological trauma in childhood and adulthood in adults with chronic pain.

Methods
PubMed, Web of Science and Scopus were searched on 20/03/2024. Published articles of human adults were included if they reported changes in brain morphology or function, including cognitive performance, associated with exposure to trauma in childhood or adulthood, in people with chronic pain. Three independent reviewers screened titles/abstracts, full-texts and extracted data. Risk of bias (RoB) assessment was conducted using the Newcastle-Ottawa scale (one at high RoB; three at intermediate RoB; nine studies at low RoB). A narrative synthesis was used to present results due to inadequate number of studies for any one of the imaging modalities and cognitive measures.

Results
Thirteen studies were included: seven studies (one morphological; five functional; one cognition) examined the impacts of childhood trauma, and six studies (three morphological; two functional; one cognition) examined the impact of adulthood trauma. Childhood trauma exposure was associated with reduced insular grey matter volume (GMV),

resting-state functional connectivity among the insula, anterior cingulate cortex (ACC), parietal and frontal regions, and task-dependent ACC and hippocampal function in individuals with chronic pain. Exposure to adulthood trauma was associated with increased insula and superior temporal gyrus GMV, reduced white matter integrity in tracts connecting the hippocampus, thalamus and insula, and increased ACC activation.

Conclusions

This systematic review presents evidence for trauma-related brain alterations in people with chronic pain, particularly in key brain regions for emotion processing and regulation; processes commonly altered in separate studies of chronic pain and psychological trauma. Although this study is limited as no meta-analysis could be performed, our results demonstrated significant brain structural and function correlates of psychological trauma (childhood and adulthood) that may be related to increased risk of developing chronic pain later in life. Future research should consider the impact of psychological trauma to better understand underlying mechanisms and inform tailored intervention for trauma-exposed individuals with chronic pain.

Poster Abstracts

Poster Session 2: Tuesday

P_41b Gene Regulatory Networks: An Avenue for Drug Repurposing in Bipolar Disorder

Presenting Author: Trang Truong

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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
The lack of known singular pathophysiology of bipolar disorder presents significant challenges to the field of drug discovery, necessitating the exploration of alternative approaches. The implementation of computational techniques to biomedical data, offers promising avenues for uncovering innovative treatment strategies through drug repurposing. Network analyses thoroughly evaluate transcription factor regulatory effects operating through gene regulatory networks. This approach reflects interactions between transcription factors and target genes by integrating multiple lines of evidence, providing a comprehensive assessment of regulatory dynamics.

Methods
We employed gene regulatory networks to pinpoint noteworthy regulatory alterations in bipolar disorder, leveraging network-based signatures for drug repurposing. Utilizing the PANDA algorithm, we investigated variations in gene regulatory networks among individuals with bipolar disorder and unaffected individuals, incorporating binding motifs, protein interactions, and gene coexpression data. The differences in connection weights between bipolar disorder and control groups were subsequently utilized as differential network signatures. These signatures were employed to identify drugs that could potentially target the disease-associated mechanisms, utilizing the CLUEreg tool within the GRAND database.

Results
Leveraging a large RNA-seq dataset comprising 216 post-mortem brain samples from the CommonMind consortium, we identified gene regulatory networks based on co-expression for individuals with bipolar disorder and unaffected controls. This comprehensive analysis included 15,271 genes and 405 transcription factors. Our findings revealed significant influences of these transcription factors on pathways related to immune response, energy metabolism, cell signalling, and cell adhesion in the context of bipolar disorder. Utilizing drug repurposing, we identified 10 promising candidates with the potential for repurposing as treatments for bipolar disorder.

Conclusions

Continued exploration of repurposing candidates, particularly those with substantiated preclinical evidence of efficacy, such as kaempferol and pramocaine, is warranted to elucidate their mechanisms of action and assess their effectiveness in preclinical and clinical studies of bipolar disorder. Additionally, the identification of novel targets, including poly [ADP-ribose] polymerase-1 (PARP1) and adenosine A2b receptor, presents opportunities for future research to investigate their relevance to the disorder.

Poster Abstracts

Poster Session 1: Monday

P_60a Is activity of hypothalamic oxytocin neurons necessary or sufficient to reduce methamphetamine addiction behaviours?

Presenting Author: Tylah Doolan

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Alex Athanasopoulos - School of Psychology, Brain and Mind Centre, University of Sydney

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Nicholas Everett - School of Psychology, Brain and Mind Centre, University of Sydney

Background
No approved pharmacotherapies exist for methamphetamine (METH) addiction, highlighting an urgent need for therapies addressing neurobiological changes driving the development and maintenance of the disorder. Oxytocin (OXT) has gained interested as a potential treatment due to its interaction with addiction-relevant brain regions and promising preclinical results after exogenous OXT administration. While OXTs promising behavioural effects are known to result from binding to brain reward circuitry receptors, it remains unclear whether this is direct binding of exogenous OXT, or if exogenous OXT binds peripheral receptors and stimulates central release via a feed-forward mechanism in the paraventricular nucleus (PVN) of the hypothalamus.

Methods
We will utilise chemogenetics to activate or inhibit PVN OXT neurons in a METH and social self-administration model. Rats receive bilateral intracranial injections of either Otp-Gq-mCherry or Otp-Gi-mCherry into the PVN and jugular vein catheters for intravenous METH delivery. After METH acquisition, deschloroclozapine will be administered to modulate PVN OXT neuron activity. Subjects will be tested at multiple fixed-ratios to assess contribution of PVN OXT signalling at various efforts. Subjects will be split into two cohorts; 1 will undergo abstinence then cue-induced reinstatement, and 2 will acquire social operant behaviour and undergo deschloroclozapine testing on social reward.

Results
This experiment is currently underway, however, based on previous research, we anticipate chemogenetic activation of PVN OXT neurons will reduce METH self-administration. We also anticipate inhibition of PVN OXT neurons alone will not impact METH self administration, however, this inhibition will likely block the effects of low i.p. OXT doses, and potentially dampen the effects of high i.p. doses. Importantly, the subset of rats that continue onto the social self-administration phase will help inform us on whether chemogenetic modulation of the PVN OXT system affects social reward or is specific to METH.

Conclusions
Clarifying the contribution of the PVN to exogenous OXT signalling is crucial for developing effective OXT-based therapies. Given OXTs short half-life in the blood (~5 minutes), low blood-brain barrier penetrance (less than 1%), and poor drug-like properties, the molecule itself has little therapeutic utility. However, despite the mechanism of action being binding to OXT receptors in the brain reward circuity, if peripheral OXT receptor binding and subsequent PVN-mediated central endogenous release is sufficient to reduce drug-seeking behaviours, this could significantly influence the development of OXT-targeting pharmacotherapies.

Poster Abstracts

Poster Session 1: Monday

P_27a The effect of risperidone and voluntary exercise intervention on lipid metabolism in juvenile female rats: underlying mechanisms

Presenting Author: Weijie Yi

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Chao Deng - School of Medical, Indigenous and Health Sciences, and Molecular Horizons, University of Wollongong, Wollongong, NSW

Background
Risperidone is one of the most commonly used antipsychotics, however, it causes serious metabolic side effects. Our previous study found that voluntary exercise reduced plasma triglyceride and adipose tissue accumulation induced by risperidone treatment. This study will further explore the molecular mechanisms underlying these effects.

Methods
Thirty-two juvenile female Sprague Dawley rats were randomly assigned into four groups: Vehicle+Sedentary, Risperidone (0.9mg/kg; b.i.d)+Sedentary, Vehicle+Exercise (three hours daily access to running wheels), and Risperidone+Exercise groups for four weeks treatment. Liver was collected, snap-frozen in liquid nitrogen, and stored at -80°C until further analysis.

Results
Lipogenesis: Increased protein expressions of hepatic FASN and USF1 were observed in the risperidone-treated sedentary group, which were decreased by exercise intervention ($p<0.05$). Lipid uptake and storage: Risperidone-induced upregulations of PPAR? and CD36 were downregulated by exercise intervention ($p<0.05$). Lipolysis and ?-oxidation: Hepatic ATGL and HSL expression levels were higher in the Risperidone+Exercise group compared to Risperidone+Sedentary group ($p<0.05$). A reduced PGC1? expression was observed in the risperidone-only group ($p<0.05$), which was reversed by exercise intervention. Compared to the Vechicle+Sedentary group, a lower level of PPAR? expression level was observed in the Risperidone+Sedentary and Vehicle + Exercise groups.

Conclusions
Risperidone treatment increased fatty acid synthesis through the hepatic USF1/FAS signaling pathway, and elevated fatty acid uptake through the PPAR?/CD36 pathway, but reduced ?-oxidation by down-regulating hepatic PGC1? expression. Voluntary exercise intervention reversed these changes, thereby improving risperidone-induced lipid disturbances.

Poster Abstracts

Poster Session 1: Monday

P_49a What striatal cells control social reward? Investigating the effects of chemogenetic Gq-coupled activation of neurons or astrocytes in the nucleus accumbens in a social operant task in female rats.

Presenting Author: Wenxin Zhang

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Tylah Doolan - School of Psychology, Brain and Mind Centre, University of Sydney

Alex Athanasopoulos - School of Psychology, Brain and Mind Centre, University of Sydney

Nicholas Everett - School of Psychology, Brain and Mind Centre, University of Sydney

Background

Deficits to social motivation span psychiatric disorders, and therapies which treat social anhedonia do not exist. The brain regions which control social behaviour are well understood using rodent models of dyadic social interaction, however these lack volitional, reducing the ability to investigate motivation. The existing evidence implicates the nucleus accumbens (NAc) in social reward (motivation is currently unknown), however the cell types within the NAc are not well described, and there is emerging evidence for astrocytic modulation of reward processing. This experiment investigates the effects of chemogenetic Gq activation of astrocytes or neurons, on social operant motivation in female rats.

Methods

We will utilise chemogenetics to activate Gq-coupled receptors exclusively expressed in either astrocytes (GFAP promoter) or neurons (hSyn promoter) in the bilateral NAc of female rats. Rats will then acquire social operant conditioning, and then deschloroclozapine will be administered to modulate NAc astrocyte or neuron activity, using a behavioural economic model to model effort as the cost of social reward increases. This will be achieved by systematically increasing the fixed-ratio schedule of reinforcement.

Results

This experiment is still underway, however based on the literature we hypothesise that chemogenetic activation of NAc neurons will increase behavioural economic demand for social reward, as indicated by an increase in lever pressing for social reward at high effort. Given the scarcity of data surrounding the effects of NAc astrocyte signaling on social behaviour, it is challenging to predict what chemogenetic manipulation of astrocytes will do in this social motivation task.

Conclusions

Identifying whether neurons and/or astrocytes play a role in NAc-mediated social motivation will be crucial in understanding the neurobiology of social anhedonia, and in the development of novel pro-social pharmacotherapies. This social operant task, and its combination with behavioural economics, is highly translatable to human experimental tasks of social motivation, and so discovery of the neural mechanisms which underpin it could create a new field of translational social motivation research.

P_19b Developmental vitamin D deficiency increases DNA methylation in embryonic mesencephalon

Presenting Author: Xiaoying Cui

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Background
Schizophrenia is a debilitating neurodevelopmental disorder characterised by dysfunction of the dopamine system and abnormal brain development. Our previous research in humans has demonstrated that developmental vitamin D (DVD) deficiency increases the risk of schizophrenia later in life. Furthermore, our rodent model shows impaired brain development, including abnormal maturation of dopamine neurons. Vitamin D is known to modulate DNA methylation, a critical regulatory process essential for normal brain development. This study aims to elucidate whether alterations in DNA methylation within the ventral mesencephalon during early gestation play a role in the abnormal dopamine development observed in animals with DVD deficiency.

Methods
We used dopaminergic neuron-rich mesencephalic tissue from DVD deficient rats at gestational day (GD) 14 and analysed the transcript expression of several genes coding for epigenetic enzymes using a quantitative PCR assay. We assessed the effect of DNA methyltransferase (DNMT) 3A levels on dopaminergic neuron-associated and cell cycle-related gene expression in primary mesencephalic neural cultures. The methylation status of genes within the mesencephalon of DVD deficient embryos was examined using Nanopore sequencing and methylated DNA immunoprecipitation (MeDIP)-PCR. Dopaminergic neurite outgrowth was examined using an in vitro cell model, a human neuroblastoma cell line (SH-SY5Y) expressing exogenous vitamin D receptor (VDR).

Results
DVD deficiency selectively increased DNMT3A expression from a panel of methylation enzymes in the GD 14 mesencephalon DNMT3A overexpression and silencing in mesencephalic neural cultures decreased and increased CCND1 (Cyclin D1) and CDKN1A (P21) expression, respectively, without altering dopamine-associated transcripts expression. MeDIP-PCR results revealed that DVD deficiency increased cytosine methylation (5mC) accumulation in the promoters (within 2kb from transcription start sites) of both CCND1 and CDKN1A. Finally, DNMT3A silencing in SH-SY5Y cells increased neurite length in differentiated dopaminergic neurons.

Conclusions
DVD deficiency is an established risk factor for schizophrenia. Hypermethylation of cell cycle regulators in the mesencephalon may represent an in utero mechanism behind the delayed differentiation of dopaminergic neurons in this model. It may contribute to the long-term functional abnormalities in the dopamine system observed in DVD deficient offspring, mirroring similar changes seen in individuals with schizophrenia.

Poster Abstracts

Poster Session 1: Monday

P_32a Exploring the Role of Ketamine in a Central Insulin Resistance Model of Depression

Presenting Author: Xinyuan Zhang

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Background
We have previously developed an animal model that demonstrates a depressive-like phenotype resulting from central administration of the diabetogenic drug alloxan. In addition to further validating this model, we aimed to investigate whether low-dose ketamine, a rapid acting antidepressant for treatment-resistant depression, can alleviate depressive-like symptoms in this model. This study explores potential mechanistic overlaps between the molecular pathways of central insulin resistance, ketamine therapeutics, and other relevant biomarkers.

Methods
Alloxan (0.5mg/kg) or artificial cerebrospinal fluid (aCSF) was delivered bilaterally via the intracerebroventricular (i.c.v.) route to six week-old male and female Wistar rats, followed by subcutaneous buprenorphine (0.03mg/kg) for analgesia for a subset of animals. Two weeks later, each treatment group received either physiological saline (0.9%) or ketamine (10mg/kg) intraperitoneally (i.p.). A subset of animals underwent a glucose tolerance test (GTT) or a battery of behavioural paradigms, including the Open Field (OF), two-hour interval Novel Object Recognition (NOR), and Forced Swim Test (FST). Data were analysed using two-tailed t-tests, one-way ANOVA, and two-way ANOVAs using Prism GraphPad.

Results
Changes in blood glucose values were significantly over time (p 0.22, Kruskal-Wallis test). Instead, Buprenorphine significantly increased immobility during the FST ($p = 0.0004$, Mann-Whitney test).

Conclusions
Centrally administered Alloxan did not induce peripheral insulin resistance, validating that it provides isolated actions within the central nervous system. Ketamine was found to impair short-term memory but did not significantly enhance stress-coping behaviour. The cognitive impairment effect of ketamine was blocked by the central administration of Alloxan, suggesting an interaction between the two in the CNS. The analgesic buprenorphine may have confounded results, impacting stress-coping behaviours. These findings suggest further research is needed on surgical effects on stress behaviours, interactions between ketamine and opioid pathways, and cognitive effects following ketamine administration.

Poster Abstracts

Poster Session 1: Monday

P_21a Glutamatergic dysfunction in dorsal striatum underlies compulsive eating in an animal model of binge eating

Presenting Author: Yan Li

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Robyn Mary Brown - Department of Biochemistry and Pharmacology, University of Melbourne, Victoria, Australia; Florey Institute of Neuroscience and Mental Health, University of Melbourne, Victoria, Australia

Background
Binge eating disorder is the most prevalent eating disorder and is associated with significant co-morbidities such as obesity. A hallmark feature of binge eating is a loss of control over eating 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.

Methods
Rats were provided either continuous (ad libitum) or intermittent access to high-fat/high-sugar ‘western diet’ (X% kcal from fat) 1h x 3 per week in a stochastic nature for 8 weeks. A control group were provided access only to standard chow. A modified conditioned suppression test was used to measure the level of compulsive eating (i.e. eating despite the threat of a negative consequence). The dorsal striatum and nucleus accumbens were collected and processed to examine protein levels of various glutamate receptors and proteins associated with glutamatergic plasticity.

Results
Intermittent access ‘binge’ rats showed a decreased latency to start eating on the conditioned suppression test i.e. were more compulsive towards the high-fat/high-sugar food compared to rats that had continuous access or only access to standard chow. They 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.

Conclusions
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.

Poster Abstracts

Poster Session 1: Monday

P_14a Alterations in Superficial White Matter and Their Association with Cognitive Function in Recent-Onset Psychosis: A Fixel-Based Analysis Study

Presenting Author: Yoshito Saito

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Background
Schizophrenia-spectrum disorders (SSDs) are associated with widespread changes in white matter (WM), including changes in superficial white matter (SWM), as demonstrated by post-mortem brain and imaging studies. Although a recent study showed an association between SWM and grey matter changes in SSDs, abnormalities in SWM can be difficult to quantify using standard diffusion imaging techniques. This study is the first to use fixel-based analysis (FBA), an advanced method for estimating WM microstructures at the sub-voxel level, to characterise SWM microstructural changes in recent-onset psychosis (ROP), and to investigate the relationship with adjacent grey matter, cognitive functions, and symptoms.

Methods
We used the Human Connectome Project for Early Psychosis and Development datasets, including MRI data from 78 nonaffective ROP individuals (age 22.01±3.02) and 78 matched controls (age 21.77±3.15). Using FBA, the average fibre density (FD) and fibre cross-section (FC) in the SWM were calculated for each brain region comprising the Desikan-Killiany atlas and compared between groups using linear regression. We examined associations of FD and FC with: (i)cortical thickness using correlation analysis based on ROP's deviation scores from controls for each brain region; and (ii)cognitive abilities and (iii)clinical symptoms using linear regression.

Results
ROP individuals showed widespread lower FD than controls, with the greatest difference in the lateral occipital gyri (right:pFDR=0.0006, left:pFDR=0.0060) and right pericalcarine cortex (pFDR=0.0047). FC reductions were less pronounced, with the greatest difference in the right superior parietal gyrus (pFDR=0.025). FD and FC in the SWM, we observed: (i)no significant relationship with cortical thickness; (ii)significant relationships of: whole-brain FD (p=0.0017) and FC (p=0.018) with processing speed; FC in temporal regions (p=0.015) and hippocampi (right:p=0.023, left:p=0.021) with working memory; FC in frontal (p=0.027) and temporal regions (p=0.0073) and left hippocampus (p=0.029) with premorbid IQ; and (iii)no significant associations with clinical symptoms.

Conclusions
We observed reductions in superficial white matter (SWM) in ROP, to a greater extent in the fibre density measure than fibre cross-section, suggesting more extensive microstructural than atrophic WM changes. The lower fibre density in these fully matured occipital regions may indicate impairments in neurodevelopmental maturation in SSDs. Previous studies have identified an association between working memory and grey matter structures in the temporal regions, as well as processing speed and the WM tracts. This study extends these findings to SWM, suggesting that SWM could be a biomarker for the severity of cognitive impairments in SSDs.

Poster Abstracts

Poster Session 1: Monday

P_28a The North Queensland Dietary Intervention Trial (NQDIT): A Randomized Controlled Clinical Trial investigating the effects of ketogenic metabolic therapy on psychiatric and metabolic outcomes in community patients with schizophrenia and bipolar disorder

Presenting Author: Zoltan Sarnyai

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Isabella Peachey - James Cook University, Townsville

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Background
Schizophrenia and Bipolar Disorder are psychiatric conditions characterized by a chronic pattern of emotional, behavioural, and cognitive disturbances. Cardiovascular, metabolic, infectious, and respiratory co-morbidities result in reduced life expectancy of up to 25 years. Nutritional ketosis has demonstrated efficacy in treating a range of neurological disorders and in animal models of psychosis. Recent evidence from open clinical trials has shown a dramatic reduction in psychotic, affective, and metabolic symptoms in both schizophrenia and bipolar disorder but no data from RCTs exist to date.

Methods
A randomized placebo-controlled clinical trial of 100 non-hospitalized adults residing in the Townsville Region and diagnosed with bipolar disorder, schizoaffective disorder, or schizophrenia. INTERVENTION: Dietitian-led and medically supervised ketogenic diet vs. Australian Guide to Healthy Eating for 14 weeks. OUTCOMES: Changes in the Positive and Negative Symptoms Scale(PANSS), Young Mania Rating Scale(YMS), Beck Depression Inventory(BDI), WHO Disability Schedule-2, Affect Lability Scale and the Cambridge Cognitive Battery. Metabolic outcomes include changes in body weight, blood pressure, liver and kidney function tests, lipid profiles and markers of insulin resistance.

Results
Ketone and glucose levels will study the correlation between primary and secondary outcomes. Hair cortisol analysis will assess long-term stress, and variations in faecal microbiome composition will be reported. Autonomic nervous system activity is measured via wearable devices (OURA ring and EMBRACE wristband) monitoring skin conductance, oximetry, continuous pulse monitoring, respiratory rate, movements and sleep quality. The study is currently recruiting and ongoing. We predict that ketogenic metabolic therapy will result in improved psychiatric, metabolic and social functioning. A correlation may exist between the level of ketosis achieved and the metabolic, cognitive, and psychiatric outcomes in the intervention group.

Conclusions
We expect this randomized controlled clinical trial to assess the feasibility, efficacy, and safety of ketogenic metabolic therapy in schizophrenia and bipolar disorder. To our knowledge, our proposed trial is the first of its kind worldwide.

We hypothesize that this study will reveal improvements in symptoms, overall quality of life, and better metabolic functioning for our participants. Results from this trial may inform future studies on more specific mechanisms of action, as well as introduce a novel treatment modality to manage psychiatric disorders that would otherwise have been considered as long-term, debilitating condition.

P_55b Establishing a causal relationship between inflammation and hyperdopaminergia in mammalian brain and behaviour

Presenting Author: Christian Chiha

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Background
The co-existence of neuroinflammation and hyperdopaminergia raises critical questions for schizophrenia research: “Does a causal relationship between inflammation and hyperdopaminergia exist, and if so which one comes first?” Answering this question would pave the way for development of early biomarkers and establish when anti-inflammatory treatments would be expected to have the most benefit. We hypothesized that inflammation can precede hyperdopaminergia in the mammalian brain. We tested this by determining if there is a bigger behavioural and/or striatal neuronal response to amphetamine challenge after peripheral injection of an inflammatory trigger.

Methods
Male C57BL/6JAusb mice (n = 40) received 0.83 mg/kg LPS or an equivolume of PBS intraperitoneally 24 hours apart. 72 hours post-first injection, mice were habituated to an open field chamber (OF) for 30 mins. Sickness responses (body weight change, body condition, activity) were assessed at 24 h intervals. To stimulate dopamine release, mice received intraperitoneal injections of dextroamphetamine (5 mg/kg), were returned to the OF chamber at 72.5 h, and distance travelled over 60 mins was analysed. Mice were euthanised, brains were extracted, and flash frozen in liquid nitrogen. Sections containing the NAc and CPu were stained for c-Fos.

Results
LPS-treated mice had lost significantly more body mass and body condition scores were higher compared to controls 24 h postinjection ($p < .05$) but gained significantly more mass than controls and improved in body condition in the 24 h pre-dexamphetamine testing ($p < .05$). Baseline activity was not significantly different between treatments. We found a significant main effect of treatment on activity and c-Fos+ cells, such that LPS-treated mice had increased ambulatory distance ($F(1, 36) = 4.32$, $p = .045$) and increased density of c-Fos+ cells across all striatal regions ($F(1, 10) = 7.00$, $p = .024$) compared to controls.

Conclusion
Here we provide behavioural and histological evidence to support the primacy of neuroinflammation in hyperdopaminergia. The fact that hyperdopaminergia was found during/after recovery of sickness behaviour extends previous findings by suggesting that hyperdopaminergia may be triggered or worsened even after the acute impact of inflammation subsides. Our findings require confirmation but, if true, this implies that neuroinflammation may play a causal role in the onset of hyperdopaminergia triggered psychosis in people with schizophrenia suggesting that more studies of inflammation prior to first break may be warranted.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_44b Three uncreased expressions in a proteomic pilot study in treatment-resistant schizophrenia: shedding light on the illness or clozapine?

Presenting Author: Dhamidhu Eratne

Dhamidhu Eratne - The University of Melbourne, Melbourne, Australia

Sam Olechnowicz - Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

Rory Bowden - Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

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Background
Treatment-resistant schizophrenia (TRS) is a severe condition associated with significant psychiatric and cognitive symptoms, functional impairment, and neurological and neuroradiological abnormalities. Clozapine is the most effective treatment currently available for TRS. Significant gaps remain in our understanding of underlying mechanisms and pathology in TRS, and our understanding of clozapine's mechanism of action, and improving our knowledge is critical for improved diagnosis, treatments, and outcomes for patients.

Methods
This pilot study performed proteomic analyses on plasma samples from patients with TRS and controls, using Olink Target 96 Neurology. As part of The Markers in Neuropsychiatric Disorders Study (The MiND Study) we have previously investigated blood biomarkers such as neurofilament light chain and glial fibrillary acidic protein in this well-characterised cohort of participants from the CRC Psychosis Study.

Results
Samples were analysed from 35 people with TRS (median age 39 years, 26% female, 17 years illness duration, all on clozapine), and 9 age- and sex- matched controls (median age 39 years, 33% female), . Three proteins were found to be very significantly upregulated in TRS compared to controls (all $p<0.005$): Fibroblast Growth Factor Receptor (FGFR2, which plays a critical role invarious cellular processes, including cell proliferation, differentiation, migration, survival, and development), SPARC-Related Modular Calcium Binding 1 (SMOC1, involved in extracellular matrix remodelling), and Asialoglycoprotein Receptor 1 (ASGR1, involved in metabolic processes such as cholesterol metabolism).

Conclusion
Upregulation of FGFR2 and SMOC1, related to neurodevelopmental and extracellular matrix remodelling processes, could reflect disease processes or compensatory mechanisms, or effects of clozapine treatment. Upregulation of ASGR1 could reflect the well known metabolic dysregulation associated with clozapine and TRS. These promising

preliminary findings from a small pilot study potentially shed light on disease and compensatory mechanisms and/or clozapine effects in TRS. Further studies are warranted and underway in the larger cohort and comparing to non-clozapine treated TRS and other psychiatric and neurological disorders, to further tease apart disease-related from treatment-related upregulation.

Late Breaking Abstracts

Poster Session 1: Monday

P_03a A Roadmap for Prader Willi Syndrome Research in Australia

Presenting Author: Diane Webster

Diane Webster - Prader Willi Research Foundation Australia

Background
Prader-Willi syndrome (PWS) is a rare neurodevelopmental disorder with an estimated incidence of 1 in 15,000. It is caused by the loss or dysregulation of the paternally expressed genes in the PWS imprinting region of chromosome 15 (q11.2-q13). Loss of the paternal genes results in significant hypothalamic dysfunction. The PWS phenotype changes across the lifespan. Babies present with hypotonia and developmental delays. Hyperphagia (intense hunger) emerges in childhood (~8yo). Quality of life is poor, marked by severe hunger, mental health issues, and low independence. Individuals may also experience temper outbursts, intellectual disability, autism, sleep disturbances, scoliosis and obesity-related conditions.

Methods
To develop a Roadmap for PWS research in Australia a systematic literature review was conducted, complemented by semi-structured interviews with scientific, clinical and live-experience PWS experts. Additionally, forward-facing interviews were undertaken with subject matter experts in emerging fields, including artificial intelligence, wearable technology, big-data in healthcare, -omics, RNA targets, neuroplasticity, and drug repurposing. These methodologies informed the development of the research roadmap.

Results
The PWS Research Roadmap: 1. Care: Developing innovative models for clinical care, such as a Centre of Expertise, embedding research into clinical care, and building clinical expertise across Australia. 2. Treat: Focusing research on the most debilitating symptoms, particularly hyperphagia and neurobehavioral challenges. 3. Transform: Researching ways to reactivate the silent PWS genes, including delivery approaches. To Activate and support these pillars, the roadmap emphasizes the need for a strong ecosystem, patient involvement, clinical trials, unlocking data insights, infrastructure (biobanks, model systems) and leveraging new technologies.

Conclusion
The Australian PWS Research Roadmap is a strategic, evidence-based document that: • Defines the research priorities identified by people with PWS and their families • Identifies where priority areas overlap with Australian research expertise • Outlines the resources available (and required) to accelerate PWS research in Australia The goal of the PWS Research Roadmap is to harness expertise and research advances to transform the quality of life for individuals with PWS and their families. https://praderwilli.org.au/

P_46b Inflammation, metabolic factors and sex differences in a clinical trial of raloxifene (estrogen receptor modulator) in people with schizophrenia

Presenting Author: Hayley North

Hayley F North - NeuRA; UNSW

Tomas Weickert - NeuRA

R Lenroot - University of New Mexico

S V Catts - UQ

M O'Donnell - NSW Health

C Galletly - University of Adelaide

D Liu - SA Health

D Pellen - NSW Health

J Curtis - Mindgardens

C S Weickert - NeuRA; UNSW; SUNY Upstate University

Background
Research highlights the role of hormonal pathways in schizophrenia; especially estrogen and its receptor. This led to clinical trials of raloxifene, a selective estrogen receptor modulator that exerts estrogen-like effects. In people with schizophrenia, adjunctive raloxifene performs better than placebo in reducing positive and negative symptom severity and improving cognition. However, the mechanisms remain unclear and controversy surrounds whether benefits are seen in both sexes. We tested the hypothesis that raloxifene treatment may exert effects though inflammatory or metabolic pathways. We will test whether there are sex differences in these pathways in schizophrenia and with raloxifene treatment.

Methods
We used blood samples from the published, randomized, double-blind, placebo-controlled clinical trial with raloxifene or placebo administered for 6 weeks alongside standard antipsychotic medications in people with schizophrenia. We quantified peripheral inflammatory marker CRP with ELISA in controls (only available at baseline) and in schizophrenia at baseline and after 6 weeks of either raloxifene (n=41) or placebo (n=42). Systemic inflammatory index (SII) was calculated using immune cell counts (neutorphils X platelets / lymphocytes). Blood levels of total cholesterol, LDL, HDL, glucose, triglycerides and SII were quantified in all people with schizophrenia in the trial but were not available in controls.

Results
CRP is higher in schizophrenia compared to controls ($p<0.0001$). In schizophrenia, immune markers were significantly elevated in females compared to males including CRP, IL6 mRNA, IL1R1 protein and SII (all $p<0.031$). Inflammation markers were not significantly changed after raloxifene treatment or placebo in this study. In schizophrenia, females had higher HDL ($p=0.011$) but there were no significant sex differences for total cholesterol, LDL, glucose or triglycerides. Interestingly, cholesterol was significantly reduced after treatment with raloxifene ($p=0.004$) but not placebo ($p=0.226$), when analysed by sex, this was the case for males ($n=21$; $p=0.007$) but not significant in females ($n=15$; $p=0.14$).

Conclusion

This study suggests that inflammation is elevated in schizophrenia and particularly females with schizophrenia. However, we were unable to detect an effect of raloxifene treatment on peripheral inflammation overall or in either sex. Six weeks of raloxifene treatment significantly reduced cholesterol, particularly in males with schizophrenia. We next plan to explore the relationship between cholesterol, raloxifene treatment and the previously identified improvements in cognition in this cohort. While most raloxifene studies focus on females, these results highlight that males, particularly those with heightened cholesterol may also see benefits, although further exploration is needed.

P_54b Neuronal Mitochondrial Dysfunction Induced by Herpes Simplex Virus Type 1 Infection via VDAC1 in Alzheimer's Disease

Presenting Author: Hongjuan You

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Xufeng Huang - School of Medical, Indigenous and Health Sciences, Faculty of Science, Medicine and Health, University of Wollongong, New South Wales, Australia

Background
Mitochondrial dysfunction leads to lower neuronal activity, which is a critical biological feature of early-stage Alzheimer's disease (AD). Herpes simplex virus type 1 (HSV-1) is a neurotropic virus that establishes lifelong latent infections in ganglia. Studies have shown that HSV-1 infection is associated with the pathology of AD, whereas the underlying mechanism remains unknown. The voltage-dependent anion channel 1 (VDAC1) protein is located in the outer mitochondrial membrane and is responsible for mitochondrial transport. Thus, it is essential to clarify the impact of HSV-1 on VDAC1 and mitochondrial dysfunction in neurons, which is crucial for unraveling the pathogenesis of AD.

Methods
HT22 cells, a mouse hippocampal neuronal cell line, were infected with HSV-1 for 72 hours. The mitochondrial membrane potential and reactive oxygen species (ROS) levels in the infected HT22 cells were assessed using flow cytometry. The adenosine triphosphate (ATP) levels in the infected HT22 cells were measured using a microplate reader. Western blot analysis was performed to examine the phosphorylation and oligomerization levels of VDAC1 in the infected HT22 cells.

Results
In this project, we found that HSV-1 infection resulted in reduced mitochondrial membrane potential, increased generation of ROS, and decreased synthesis of ATP in HT22 cells. Additionally, HSV-1 infection affects the outer mitochondrial membrane protein VDAC1, significant upregulating the phosphorylation and oligomerization levels of VDAC1 without altering its protein level. Increased oligomerization and abnormal phosphorylation of VDAC1 lead to mitochondrial damage. Furthermore, the small molecule NSC15364, which specifically inhibits VDAC1 oligomerization, significantly ameliorated the mitochondrial dysfunction in neurons infected with HSV-1.

Conclusion
Thus, our results confirm that HSV-1 induces neuronal mitochondrial damage through VDAC1, providing new therapeutic targets for AD as well as a new strategy for HSV-1 infection-induced neurological diseases.

P_49b The Effect of Maternal Immune Activation and Estrogen Receptor Modulation on Microglial Characteristics in the Adult Female and Male Ventral Midbrain

Presenting Author: Iveta Gavljak

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Background
Maternal Immune Activation (MIA) induces neuroinflammation, dopamine dysregulation, and behavioural changes comparable to those seen in people with schizophrenia. The selective estrogen receptor modulator, raloxifene, sometimes improves cognition and psychosis in men and women with schizophrenia, perhaps via modulating neuroinflammation. We propose that ventral midbrain microglia contribute to the pathological outcomes of MIA, and may partially mediate raloxifene's therapeutic effects. To test this, we induced MIA with the viral mimetic polyinosinic:polycytidylic acid [Poly(I:C)], treated offspring with raloxifene during adulthood, and measured alterations to microglial characteristics in the ventral midbrain, specifically within substantia nigra (SN) and ventral tegmental area (VTA) sub-regions.

Methods
Wistar dams were injected with high molecular weight poly(I:C) (4mg/kg) on gestational day 19. Offspring were administered raloxifene (5 mg/kg in cookies) between postnatal days 58-84 (chronic administration). The cohort consisted of four groups/sex (n=3-4/group): MIA/placebo, MIA/raloxifene, saline/placebo, and saline/raloxifene. Offspring were euthanised, and midbrain tissue blocks were dissected and snap-frozen. Anti-Iba-1 antibody and DAB was used to visualise microglia in 4 serial coronal sections (30?m thick) between Bregma -5.04 and –6.48mm. Microglial density, soma area, and staining intensity were quantified in subregions of the SN and VTA with QuPath and analysed using three-way ANOVAs (sex x MIA x treatment).

Results
Baseline sex differences in microglial soma area were detected in the lateral SN compacta (SNc). Saline-injected males displayed larger microglial soma area relative to females ($F(1,27)=5.67$, $p=0.025$). Furthermore, MIA increased microglial soma area in the lateral, but not medial, VTA ($F(1, 23)=4.91$, $p=0.037$) in both sexes. In contrast, MIA reduced soma area in the substantia nigra reticulata (SNr) ($F(1,23)=4.314$, $p=0.049$), but not in the medial or lateral SNc. Microglial density and staining intensity were unchanged by MIA in either sex. Raloxifene had no effect on any microglial parameters in any region examined (F ? 3.33, all p ? 0.08).

Conclusion
Baseline sex differences in microglial soma area suggests enhanced immune reactivity in the male lateral SNc.

MIA-induced increases in soma area in the lateral VTA in both sexes suggests a reactive, pro-inflammatory state, and that the VTA may be more susceptible to neuroinflammation. Conversely, MIA-induced decreases in soma area in the SNr may indicate “immune blunting”. Raloxifene did not alter the measured microglial parameters. This is the first study to suggest that a late gestational immune insult induces opposing effects on microglial state(s) in subregions of the ventral midbrain, which may impact dopaminergic neurotransmission in schizophrenia.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_45b Understanding impulsive actions through dopamine transients

Presenting Author: Karly Turner

Karly Turner - University of New South Wales

Background
Impulsive behaviour is rash, risky or premature, and often leads to negative consequences. High levels of impulsivity are associated with conditions such as ADHD and addiction. There are many hypotheses about the processes that could be driving impulsive behaviour. By examining dopamine signalling during impulsive behaviour, we aim to reveal whether reward is expected following premature actions and if dopamine transients differ in high impulsive individuals.

Methods
In this study we record dopamine transients in real-time while rat perform a task designed to measure impulsive actions. Using fiber photometry in the nucleus accumbens core, we can align changes in dopamine release with different behavioural events, such as premature actions and reward delivery. We find that dopamine signalling dips when rats make a premature response, consisted with a prediction error.

Results
We found dopamine signalling dips when rats make a premature response, consisted with a prediction error. This suggests that impulsive actions are not simply a discharge of motor activity, but that actions are made with the expectation of reward. Further, we find more exaggerated changes in dopamine signal associated with the presence and absence of reward in high impulsive rats as compared to low impulsive rats.

Conclusion
These results shed new light on the processes that support impulsive behaviour. By developing a deeper understanding of the psychological and neural processes underlying impulsive behaviour, it is hoped this fundamental knowledge will led to more effective intervention and treatment options in the future.

P_15b Is it spore than just serotonin? The effect of psilocybin on neurotransmitter release in a corticostriatal pathway

Presenting Author: Kaspar McCoy

Kaspar McCoy - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Felicia Reed - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Alex Reichenbach - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Claire J Foldi - Monash Biomedicine Discovery Institute, Monash University Clayton, Australia.

Background
Psilocybin has shown promise in treating a wide range of mental health conditions with increased cognitive flexibility and reward processing being proposed mechanisms. Two brain regions integral to these processes are the medial prefrontal cortex (mPFC) and the nucleus accumbens (NAc). We have preliminary data suggesting that psilocybin acutely increases NAc dopamine release to food reward and we aimed to explore the role of the serotonin 2A receptor in this effect. Given the importance of mPFC serotonin release in cognitive flexibility and that psilocybin improves cognitive flexibility, we also aimed to investigate whether psilocybin changes serotonin release in the mPFC.

Methods
We performed fibre photometry in female C57Bl6/J mice with a dopamine sensor (GRAB_DA) expressed in the NAc, and recorded repeated responses to food reward 24 hours before, acutely (20-60 min) after, and 24 hours after psilocybin (1.5 mg/kg) administration in the presence or absence of 5-HT2A antagonist (MDL 100907; 0.1 mg/kg). We also trained a separate cohort of mice in a probabilistic reversal learning task (the two-armed bandit; 2AB) and recorded fluorescence from a serotonin sensor (GRAB_5-HT) expressed in the mPFC during the task; 24 hours before, acutely after, and 24 hours after psilocybin administration.

Results
Contrary to previous findings, psilocybin slightly, but not significantly, attenuated NAc DA response to food reward retrieval, though this was not affected by the presence of MDL, suggesting this process is non 5-HT2A dependent. We also show a decrease in mPFC 5-HT release in response to sucrose reward under baseline (normal) conditions, which was flattened by psilocybin acutely and may underlie the improvements in cognitive flexibility reported in humans and rats. There was no sustained effect of psilocybin on NAc DA release or mPFC 5-HT release 24 hours after administration, suggesting effects are limited to the acute actions of psilocybin.

Conclusion
These findings suggest that psilocybin impacts both DA and 5-HT signalling in this corticostriatal pathway, which may relate to improved cognitive flexibility after psilocybin treatment. However, whether this effect occurs via direct actions on DA neurons or receptors, or indirectly through the 5-HT system remains unknown. Similarly important to understand is whether the changes in mPFC serotonin are related to changes in NAc dopamine. Ongoing studies aim to parse out the mechanisms behind this interaction using viral tracing, cre-dependent expression of photometric biosensors in specific neuronal populations and a version of the 2AB task optimised for use with mouse photometry.

Late Breaking Abstracts

Poster Session 1: Monday

P_46a The heterogenous default mode network in major depressive disorder: A systematic review of diffusion tensor imaging

Presenting Author: Kevin Hou

Kevin Y C Hou - Imaging and Phenotyping Laboratory, Resonait Medical Technologies

Yoong K Ang - Imaging and Phenotyping Laboratory

Avanti Shrikumar - Imaging and Phenotyping Laboratory

Thao Mi Tran - Imaging and Phenotyping Laboratory

Stuart M Grieve - Imaging and Phenotyping Laboratory, Lumus Imaging

Background
A core paradigm of biological psychiatry is synthesising the causal features of clinical disease manifestations into biomarkers. The capabilities of neuroimaging have stimulated biomarker research, generating functional and structural markers in disorders including Major Depressive Disorder (MDD). Popular theories of dysfunction in MDD have emerged from network research, with overactivity in the Default Mode Network (DMN) being related to rumination. However, the field is marked with heterogeneity and poor replicability of results. We review the current state of diffusion imaging DMN findings in MDD, asking the question: How consistent are network measures and what are their applicability as clinical biomarkers?

Methods
Using the PRISMA reporting guidelines, this review searched five databases published from inception until June 2024: PubMed, Web of Science, PsycINFO, Cochrane Library, and EMBASE, using a pre-registered protocol (PROSPERO CRD42024557466). Studies were included if they: examined a cohort of MDD and healthy controls, used diffusion MRI, included a network-related measure, referenced the DMN, and had sufficient imaging quality, measured by a modified scale. 14 studies met this criteria.

Results
There is variance in how the DMN is defined and analysed across studies. 7 papers explored edge-based differences, with the most DMN-involved nodes including the anterior cingulate cortex, posterior cingulate cortex, thalamus, dorsomedial prefrontal cortex. 6 papers explored nodal property differences, implicating the precuneus, thalamus, caudate, and cingulate cortex. 10 papers analysed networks through graph analysis, which largely found no correlation or decreased graph parameters in MDD, including decreased feeder connections. 5 studies found correlations between these properties to clinical scales.

Conclusion
This review highlights the need to come to an anatomical and technical consensus in defining and exploring the DMN of MDD in diffusion imaging. Psychiatric clinical translation of these results still struggle from both replicability and construct validity. Transdiagnostic cohorts, methodological consensus, and higher quality diffusion imaging are needed to advance the field.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_31b The Effects of Early Life Inflammation on Maternal Behaviour and Fear Expression in Infant Rats

Presenting Author: Lauren Sams

Lauren Sams - University of New South Wales

Tayla McCutcheon - University of New South Wales

Rick Richardson - University of New South Wales

Background
Early life adversity leads to an array of detrimental mental and physical health outcomes throughout the lifespan. It accelerates both neural and behavioural maturation, often resulting in long-term effects on emotion regulation. Psychosocial stress during infancy has been shown to lead to a precocious engagement of neurocircuitry during fear expression. Similarly, early life inflammation (ELI) accelerates emotion regulation, suggesting a shared mechanism underlying various forms of early adversity. Here, we examined whether ELI affects the expression of learned fear (with the aim of examining the neural circuitry involved). We also examined whether such adversity affected maternal behaviour.

Methods
Whole litters were assigned to receive lipopolysaccharide, an endotoxin that elicits an inflammatory response, or saline injections on postnatal days (P) 3 and 5. Maternal behaviour was assessed by measuring the dam's latency to retrieve the pups immediately after injections, and again on P7 (when no injections occurred). Infant male and female rats were fear conditioned to an auditory cue (on P17), and fear to the cue was tested the following day. One hour after the test, rats were perfused, and their brains were extracted for later analysis of neural activation in the prelimbic cortex (PL).

Results
Preliminary results show that pup retrieval was faster in ELI than saline controls on P5 and P7 (ps < .004). No effect of ELI on fear expression was observed, with paired animals in both conditions exhibiting higher, and comparable, levels of learned fear than an unpaired control group. We predict that infants in the ELI group will have higher levels of neural activity in the PL compared to saline controls, indicating accelerated maturation. These results would align with previous findings showing that standard-reared animals do not recruit the PL when expressing fear, whereas early adversity leads to premature PL engagement.

Conclusion
These preliminary findings suggest that ELI has a significant impact on maternal behaviour, at least in terms of pup retrieval. Should our predictions about ELI leading to premature recruitment of the PL during fear expression be confirmed, then this would align with previous findings from other early adversity models. This research builds on evidence that early adversity accelerates neural maturation, potentially leading to long-term changes in emotion regulation. Understanding these effects may provide insight into how early inflammatory experiences shape both caregiving behaviour and emotional responses throughout life.

P_13a Exosomes derived from microglia exposed to oxidized low-density lipoprotein impair healthspan, learning, and memory in Caenorhabditis elegans

Presenting Author: Lei Zhu

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Background
Patients with schizophrenia demonstrate impaired cognitive performance. Exosomes, which are extracellular vesicles responsible for transporting genetic materials such as mRNA and miRNA, as well as proteins, play a role in the modulation of cognitive function. Nonetheless, the involvement of exosomes in cognitive dysfunction among individuals with schizophrenia remains uncertain. Additionally, individuals with schizophrenia exhibit a high prevalence of lipid metabolism dysregulation during the early stages of the disease. Elevated levels of oxidized low-density lipoprotein (ox-LDL), indicative of lipid metabolism dysfunction, have been detected in their blood serum.

Methods
In this study, Caenorhabditis elegans (C. elegans) was used as an experimental animal model to examine the potential effects of exosomes derived from BV2 microglial cells following exposure to ox-LDL (ox-Exos) on healthspan, learning, and memory.

Results
We found that the pharyngeal pumping rate and the frequency of body bends significantly decreased from day 1 to day 9 of adulthood after ox-Exos treatment from the L4 stage. Additionally, a significant increase in lipofuscin autofluorescence intensity was observed in 9-day-old worms following ox-Exos exposure. Furthermore, ox-Exos induced short-term learning and memory deficits in L4-stage worms.

Conclusion
Our findings confirmed the detrimental effects of ox-Exos on healthspan, learning, and memory in C. elegans, suggesting the potential role of exosomes induced by ox-LDL in the pathology of psychiatric disorders.

Late Breaking Abstracts

Poster Session 1: Monday

P_57a The Impact of Gestational Timing of a Prenatal Immune Insult on Behavioural Patterns of Adolescent Male and Female Offspring

Presenting Author: Maral Jkorkozian

Maral Jkorkozian - Cornish-Perry Laboratory, Macquarie University, NSW, Australia; Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia (NeuRA), Sydney, NSW, Australia

Christina Perry - Cornish-Perry Laboratory, Macquarie University, NSW, Australia

Jennifer L. Cornish - Cornish-Perry Laboratory, Macquarie University, NSW, Australia

Tertia Purves-Tyson - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia (NeuRA), Sydney, NSW, Australia; Discipline of Psychiatry and Mental Health, UNSW Sydney, NSW, Australia

Background
Epidemiological studies indicate that infection during pregnancy increases the risk for neurodevelopmental disorders. The rat maternal immune activation model (MIA) of dopamine dysregulation, induced by the viral mimic polyinosinic:polycytidylic acid [Poly(I:C)], is relevant to disorders including schizophrenia and autism spectrum disorder. However, similarly to these disorders, MIA offspring exhibit heterogeneous behaviours. Few studies have examined sex differences in behavioural phenotypes across adolescence following immune insult on different gestational days (GD). This study aims to assess behavioural patterns of male and female adolescent MIA offspring, compared to control, following immune insult on GD15 or GD19.

Methods
Pregnant Wistar dams received tail vein injection of 5 mg/kg high molecular weight (HMW)-poly(I:C) or saline on GD19 (n=2 dams) or GD15 (n=3 dams), yielding 14/16 male/female MIA and 14/11 male/female control offspring. MIA was confirmed by dam weight loss and sickness behaviour 3-24 hours after injection. Behavioural tests were conducted during adolescence (PND40-64), including the attention set-shifting task (ASST, PND40-44) to measure problem solving, novel object recognition (NOR, PND45-46), social preference task (object versus unfamiliar rat, PND48), and amphetamine-induced locomotion (PND62, 1mg/kg females; 1.5 mg/kg males). Results were analysed using ANOVA (GD, sex, behaviour) followed by post-hoc comparisons.

Results
GD15 and GD19 MIA males and females spent less time exploring the novel object compared to control (GD15: males $t(21)=-3.32$, $p=.002$; females $t(21)=-2.24$, $p=.029$; GD19: males $t(22)=-3.35$, $p=.001$; females $t(22)=-2.34$, $p=.023$). Male and female GD19 and female GD15 MIA offspring did not differ from controls in social preference. However, GD15 MIA males spent less time interacting with the unfamiliar rat compared to control males ($t(18)=-4.250$, $p=.048$). No significant differences were found in amphetamine-induced locomotion. No significant differences were seen in the ASST task completion ability. GD15 MIA females required more trials to complete the tasks compared to control.

Conclusion
The preliminary behavioural data show some different effects of MIA on GD15 or GD19 at the time points tested during adolescence. While differences in spatial memory were apparent after prenatal immune activation on either gestational day, social behaviour differed only in GD15 MIA males. Hence, MIA-induced adolescent behavioural phenotype differs between sexes. Though MIA on GD15 or GD19 did not alter problem-solving ability, MIA females required a higher number of repetitions to solve the tasks. These results suggest utilising GD15 may induce a more robust phenotype to investigate interventions that may alter these behaviours.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_03b Neuronal integrity in adolescent psychosis over the first 5 years after the first episode: A longitudinal proton magnetic resonance spectroscopy study

Presenting Author: Marta Rapado-Castro

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Background

Early-onset Psychosis (EOP) is a severe debilitating condition including a broad range of both affective and non-affective psychosis disorders with onset before the age of 18. EOP impacts an estimated 11-18% of individuals later diagnosed with schizophrenia spectrum disorders and is associated with several developmental and functional impairments. N-Acetyl-Asparte (NAA) concentration, a non-invasive marker for neuronal health or integrity using proton magnetic resonance spectroscopy (H-MRS), has shown to be reduced in psychosis.

Methods
We aimed to examine NAA concentrations in the dorsolateral prefrontal cortex in adolescents with EOP (n=67) and controls (n=65) over time (i.e. at baseline, two years, and five years after the onset of the first episode). Functional brain images were acquired using H-MRS. Absolute NAA concentrations were extracted using LCModel. Lineal mixed models were used to explore the time x group interaction and secondary models were conducted to explore the potential influence of covariates such as age, gender, severity of symptoms, and accumulative dose of anti-psychotic medication.

Results
We found no significant time x group interaction in the non-adjusted main model (F=9.846; p=0.432), however, we found lower concentrations of NAA in adolescents with EOP than in the control group at 2 years follow-up (p=0.060) and significantly lower NAA concentrations at 5 years (p=0.030) follow-up.

Conclusion
We found decreased NAA concentrations in adolescents with EOP in comparison to matched controls. Our findings suggest lower levels of neural integrity as measured by NAA may be related to the progression of the disease over the first five years after onset of the first psychotic episode.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_04b Neuronal integrity and cognitive development in early onset psychosis: A five years follow-up study using proton magnetic resonance spectroscopy

Presenting Author: Marta Rapado-Castro

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Background
Early Onset Psychosis (EOP) involved psychosis onset before 18s. EOP can evolve into a range of clinical conditions, including schizophrenia spectrum disorders, affective and non-affective psychotic disorders. Its onset in important neurodevelopmental stage caused that cognitive development seems to be arrested in EOP (specifically cognitive functions associated with DLPFC), while in controls cognitive functions continue developing until late adolescence and

early adulthood. In DLPFC, there is a reduction of NAA levels in EOP compared to controls. Aim: To analyse the relationship between NAA DLPFC concentration and the development of cognitive functions in EOP over the first -years follow-up by diagnosis.

Methods
The sample were 65 EOP and 67 matched controls adolescents. Function of cognitive domains of interest (attention, working memory, executive function) was performed by neuropsychological assessment, raw scores from specific subtests were standardised into z-scores for the calculation of mean average cognitive domains indexes. In vivo NAA levels were obtained by single-voxel H-MRS in DLPFC, and metabolites quantification was done using LC Model software. Mixed models were used to determine the effect of changes in NAA on cognitive function development, including metabolite levels over time as covariate. NAA changes and cognitive development correlation was analysed using Pearson's correlation.

Results
For attention development: the difference between EOP and control becomes significant at 5-years follow-up (difference=0.722, p=.002) considering NAA. For working memory, controls had a significant development from baseline to 5-years follow-up considering NAA (difference=0.437, p=.010). Executive function development showed differences between schizophrenia and schizoaffective individuals at 2-years follow-up, with and without NAA (diff=0.753, p=.03 without NAA; diff=0.871, p=.022 NAA). In whole EOP group, executive function development correlated with NAA change (r=0.24, p=.05) The global DLPC cognitive index, differed in controls from 2-5 years follow-up considering NAA (diff=0.329, p=.001). There was correlation between NAA changeand cognitive development inschizoaffective disorder (r=0.593, p=.025).

Conclusion
There were differences in the effect of change in NAA levels over time in cognitive development as a function of psychosis diagnosis, with an specific relation between NAA brain metabolite and cognition in controls and schizoaffective individuals that wasnot present in other psychotic disorders. NAA can be considered as plausible cognitive biomarker that could aid to explain different trajectories of cognitive development in different psychosis early onset psychotic disorders. It may be useful to guide specific interventions to target different diagnosis within the psychosis spectrum.

Late Breaking Abstracts

Poster Session 1: Monday

P_56a CAN N-ACETYL ASPARTATE BE A USEFUL BIOMARKER FOR COGNITIVE DEVELOPMENT IN EARLY ONSET PSYCHOSIS BY SEX?

Presenting Author: Marta Rapado-Castro

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Background

Early Onset Psychosis (EOP) involves a heterogeneous group of psychotic disorders which emerges at a decisive stage for neurodevelopment. EOP can evolve into a chronic and clinically variable form of the psychotic disorder characterised by functional and cognitive impairments. We have found a specific relationship between cognitive arrest

and a reduction of N-acetyl aspartate (NAA) in EOP in Dorsolateral Prefrontal Cortex (DLPFC) compared to matched controls. We aim now to ascertain if there are differences by sex in the relationship of biochemical and cognitive development in EOP and matched controls over the first 5-years after the onset of psychosis.

Methods

The study sample are 65 EOP and 67 adolescent matched controls. The assessment of cognition (attention, working memory, executive function) was performed by neuropsychological assessment and raw scores were standardising into z-scores. A global cognitive index related to the DLPC was calculated as a mean average of all three cognitive domains. In vivo NAA levels were obtained by single-voxel H-MRS in the DLPFC, and metabolites quantification was performed using LC Model software. Mixed models were used to determine the effect of NAA changes over time on cognitive function. And correlation between NAA and cognitive changes was analysed using Pearson's correlation.

Results

Males with EOP presented a correlation between NAA and attention changes over time (r=0.306, p=.038), that was not present in control males neither in females. For working memory there were differences in males EOP and control ones at 5-years follow-up, without NAA (difference=0.718, p=.005) and with NAA (difference=0.861, p=.008). In females there were not differences. Executive functions correlated with NAA in EOP males (r:0.33, p=.027) but not in control males neither in females. The global cognitive DLPC index development showed sex-differences, in control males NAA caused an effect in 2-5 years cognitive trajectory (difference=0.388, p=.005), while not occurred in females.

Conclusion

NAA variation correlates with attention and executive function development over time in EOP males, but not in females neither in control males. Also, in control males, global cognitive DLPC index showed a significant variation from 2 to 5 years follow up when we consider NAA as covariate. Sexual hormones and/or other sex-related factors may be implicated in the effect of the NAA on cognitive development. NAA as possible cognitive biomarker could explain the abnormal neurodevelopment in EOP males. It can be key to improving the effectiveness of interventions, future targets, and the early detection and prognosis.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_53b Polygenic Contributions to Cognitive Dysfunction in Schizophrenia and Bipolar Disorder

Presenting Author: Megan Man

Megan Man - University of New South Wales

Melissa Green - University of New South Wales

Yann Quidé - University of New South Wales

Oliver Watkeys - University of New South Wales

Background
Cognitive dysfunction is common in schizophrenia (SCZ) and bipolar disorder (BD), is independent of clinical symptomology, and is associated with poor outcomes and prognoses. Investigating the polygenic contributions to cognitive dysfunction in SCZ and BD may reveal clinically significant research regarding their genetic underpinnings, and therefore may inform early intervention strategies and novel pharmacological treatments which specifically target the physiological basis of cognitive dysfunction in these disorders. This study aimed to investigate whether associations between polygenic variation and cognitive ability varied between individuals with SCZ and BD compared to healthy controls.

Methods
Participants were 112 clinical participants (SCZ = 55, BD = 57) and 53 healthy controls. We derived PRSs for three separate cognitive domains (including general cognitive function [PRS-GCF], executive function [PRS-EF] and processing speed [PRS-PS]) by summing risk alleles of individuals weighted by the effect sizes of risk alleles from summary statistics of previously published genome-wide association studies for cognition. Cognitive performance across these same three domains was assessed using a variety of batteries. Direct associations between PRSs, clinical group, and their interactions in association with cognitive performance, were evaluated via linear regression. Significant interactions were probed using moderation analyses.

Results
In all participants, there was a direct positive association between PRS-GCF and general cognitive function, but none between PRSEF and executive function or between PRS-PS and processing speed. Both clinical groups showed significant deficits in general cognitive function and processing speed, but only individuals with SCZ showed significantly poorer executive function. A significant interaction between PRS-PS and the clinical group of SCZ in relation to processing speed reflected a higher PRS-PS in line with better processing speed exclusively among individuals with SCZ, revealed via moderation analyses. There were no interaction effects for general cognitive function or executive function.

Conclusion
Processing speed deficits were uniquely associated with polygenic variability only in SCZ. Higher PRS-PS was related to better processing speed exclusively among individuals with SCZ, suggesting that genes associated with this cognitive domain are operating to influence the heterogeneity of cognitive performance in this clinical group. Further research into the genetics of cognitive dysfunction in BD is required, with greater same sizes. Future studies may also explore the polygenic contributions of and interaction between brain morphology, processing speed, and genetic risk for SCZ and BD.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_56b Dissociated activity and neurotransmitter release within basolateral amygdala during punishment and fear learning

Presenting Author: Michelle Shen

Michelle H. Shen - University of New South Wales

Luke J. Keevers - University of New South Wales

Gabrielle Lambert-Bridges - University of New South Wales

Colin W.G. Clifford - University of New South Wales

Gavan P. McNally - University of New South Wales

Philip Jean-Richard-dit- Bressel - University of New South Wales

Background
When aversive events are response-dependent, animals can learn about behavioural antecedents to avoid these actions in the future (punishment learning). When aversive events are response-independent, animals can learn about environmental antecedents to emit defensive responses to predictive cues (Pavlovian fear learning). Basolateral amygdala (BLA) is known to be critical for both these forms of learning.

Methods
To assess how neural dynamics in BLA underpin these processes, we used fibre photometry to record calcium activity of principal neurons (PNs), parvalbumin neurons (PVs), serotonin (5-HT) release, or norepinephrine (NE) release, during a “co-yoking” task that permits within-subjects comparisons of punishment and fear learning.

Results
Animals exhibited contingency-specific learning during co-yoking sessions, suppressing lever-presses on the punished lever only. However, when presented with the Pavlovian and instrumental aversive-associated auditory stimulus, animals indiscriminately suppressed lever-pressing on both levers. Concurrently, we observed dissociated task-related dynamics in PNs, PVs, 5-HT, and NE, representing distinct computations for adaptive behaviour.

Conclusion
The BLA has dual roles in punishment and fear learning, but how it achieves this is unclear. Using a co-yoking task that permits direct comparison of punishment and fear, we first demonstrate that animals are sensitive to contingency. Next, recordings of BLA during the co-yoking task revealed dissociable activity of PNs during punishment and fear-associated events. Opposing patterns of activity in PV interneurons and 5-HT and NE release, which have known neuromodulatory effects, may represent one mechanism that underpins the dual role of BLA in aversion coding.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_57b A scoping review on serotonergic psychedelics for obsessive compulsive and body image disorders

Presenting Author: Nicole Acevedo

Nicola Acevedo - Swinburne University, St Vincent's Hospital Melbourne

Susan Rossell - Swinburne University, St Vincent's Hospital Melbourne

David Castle - University of Tasmania, Statewide Mental Health Service, University of Melbourne

Background
Obsessive compulsive disorder (OCD), body dysmorphic disorder (BDD), and anorexia nervosa (AN) are debilitating and often chronic conditions. These conditions share overlapping psychopathological determinants in terms of cognitive-behavioural dysfunction and neurobiological underpinnings involving aberrant neurocircuitry. Further treatment resistance (40-60%) and lack of treatment engagement is common across these conditions. Psilocybin assisted psychotherapy (PAP) has been shown to be highly effective for treatment-resistant depression (with large effect sizes) and there is additional empirical and theoretical evidence to support applications in OCD, BDD and AN. PAP fosters in engagement in psychotherapy, and a multitude of changes to cognition, beliefs, perceptions and behaviours.

Methods
A scoping review of all previous investigations (randomised controlled trials, open label, retrospective studies, surveys, case reports) and protocols of classical serotonergic psychedelics for OCD, BDD and AN symptomology was conducted. Also, clinical trial registries were reviewed for unpublished investigations currently being conducted.

Results
One pilot trial of PAP was identified for each of the patient cohorts demonstrating efficacious outcomes. Methodological limitations suggest optimised outcomes can be achieved with more robust implementation. Randomised, and controlled investigations with long term data were lacking. Additional case reports, and qualitative investigations provide useful insights into the lived experiences of psychedelic effects. Further, 12 ongoing trials of PAP were identified across conditions, through clinical trial registries. Thus, preliminary evidence was identified to support the therapeutic use of PAP in OCD, BDD and AN patients.

Conclusion
Currently, there is a lack of evidence on serotenergic psychedelics for OCD, BDD, and AN, however preliminary findings support the potential of PAP in treating obsessive compulsive and body image disorders. Conclusions cannot be made in relation to other psychedelic therapies. Across conditions, it is recommended to implement multiple doses of PAP with long-term follow up. Additional recommendations for AN participants include comprehensive education, briefing and support, and therapeutic focus on psychological recovery (i.e., identify, purpose) rather than solely on weight restoration.

Late Breaking Abstracts

Poster Session 2: Monday

P_58a Multimodal characterization of deep brain stimulation for obsessive compulsive disorder

Presenting Author: Nicole Acevedo

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Susan Rossell - Swinburne University, St Vincent's Hospital Melbourne

David Castle - University of Tasmania, Statewide Mental Health Service, University of Melbourne

Peter Bosanac - St Vincent's Hospital Melbourne, University of Melbourne

Background
The symptomology and prognosis of obsessive-compulsive disorder (OCD) is complex and debilitating. First-line treatment achieves response in 40-60% of patients, thus a large majority are left with a lack of therapeutic options. Considering OCD is underpinned by impaired neural networks, the psychopathology lends itself to modulation via neurostimulation. Deep brain stimulation (DBS) is an invasive neurostimulation therapy that can lead to profound changes to the lives of severe patients in a personalised and adjustable manner. Yet within OCD investigations, patterns and predictors of response have not been well elucidated, treatment protocols are not yet standardized, and thus outcomes are heterogeneous.

Methods
The presentation aims to provide a multimodal evaluation of DBS efficacy and mechanisms for optimised and standardised care. All previous investigations of DBS therapy for OCD and related conditions were systematically reviewed. Eight treatment refractory OCD (TR-OCD) patients underwent DBS therapy in an open label trial, clinical outcomes were analysed with mixed linear modelling (MLM). Responders completed a follow up open-ended qualitative interview evaluated using interpretive phenomenological analysis (IPA). Evidence was combined with clinical expertise to propose a series of evidence-based recommendations for OCD DBS care.

Results
7 randomised controlled trials (RCTs) and 17 open label trials demonstrate DBS response in at least 60% in otherwise refractory patients. Our cohort trial achieved response in 6 out of 8 patients, on average obsessions and compulsions improved by 45% (10 months- 7 years). MLM identified insight into symptoms as a significant predictor of changes in symptom severity. Patients experienced profound psychopathological changes as well as shifts in self and identity constructs. Theoretical frameworks are proposed describing a common progression of DBS induced changes and how alterations in the cognitive appraisal of intrusions contributed to recovery.

Conclusion
The effectiveness of DBS for OCD treatment is demonstrated in dramatic improvements to symptom severity, comparable or greater than first line therapies. Also, global changes to psychosocial functioning and phenomenological experiences can be achieved. DBS should be appreciated as an established therapeutic option for refractory-OCD, yet barriers to treatment access remain. Thus, we demonstrate a high level of evidence to support DBS therapy for OCD and advocate for greater access to care. Clinical and research protocols should implement a multidisciplinary and biopsychosocial approach. Future investigations should evaluate mediators of response by large-scale data pooling.

P_06b Maternal immune activation and raloxifene effects on behaviour across adolescence in male and female offspring

Presenting Author: Priscila Costa

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Tertia Purves-Tyson - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia (NeuRA), Sydney, NSW, Australia; Discipline of Psychiatry and Mental Health, UNSW

Background
Adolescence is a critical period for behavioural changes in schizophrenia, and psychotic symptoms frequently present at this age. Raloxifene, an estrogen receptor modulator, can improve cognition and symptom severity in women and men with schizophrenia. Maternal immune activation (MIA) is a preclinical model of dopamine dysregulation that results in sensorimotor gating deficits and increased psychostimulant sensitivity in adulthood. Few studies have examined whether there are behavioural sex differences in the MIA model across adolescence or in response to raloxifene. We investigated the impact of chronic raloxifene treatment on schizophrenia-relevant behaviours across adolescence in male and female MIA offspring.

Methods
Wistar dams received a tail vein injection of 4 mg/kg high molecular weight -polyinosinic:polycytidylic acid [HMW-poly(I:C)] or saline (n=3-4/group) on gestational day 15. Adolescent offspring (females, n=7-10/group; males, n=5-8/group) were treated daily with raloxifene (5mg/kg) or placebo via cookie dough between postnatal days (PND) 30-57, a total of 4 groups per sex: Saline/Placebo, Saline/Raloxifene, Poly(I:C)/Placebo and Poly(I:C)/Raloxifene. Open field test was performed on PND43 as an anxiety-like behavioural measure. Prepulse inhibition (PPI), a measure of sensory motor gating, was conducted on PND47-48. On PND50-52, 2-hour locomotor activity was recorded after intraperitoneal injection of amphetamine (AMPH, females, 1.0mg/kg; males, 1.5mg/kg).

Results
There was a main effect of sex ($P<0.001$) and a trend interaction between sex and treatment ($P=0.053$) in the open field, with raloxifene increasing time spent in the centre by control and MIA females compared to males (simple effects, P?0.013). In males, %PPI was increased by raloxifene in MIA-offspring compared to placebo-treated MIA-offspring ($P=0.041$), whereas raloxifene reduced %PPI in female MIA-offspring compared to MIA-offspring treated with placebo ($P=0.02$). AMPH-induced locomotor activity was unaltered by MIA in males ($P=0.162$) and females ($P=0.404$), but was reduced by raloxifene in MIA-exposed compared to control males ($P=0.029$).

Conclusion
We show sex-specific differences in anxiety-like behaviour during adolescence in healthy offspring, and suggest that the anxiety-like behaviour evident in females at early-adolescence is modifiable with raloxifene. At mid-adolescence, raloxifene ameliorated sensorimotor deficits in male MIA-offspring. Conversely, raloxifene-induced sensorimotor deficits in female MIA-offspring suggests sex-specific considerations for its use. MIA did not increase AMPH sensitivity at late-adolescence, suggesting MIA-induced AMPH sensitivity precipitates later. However, raloxifene-induced reduced AMPH sensitivity in male MIA-offspring suggests that MIA-offspring do have an underlying difference in the

dopaminergic neurotransmission. This study highlights the importance of considering sex-specific effects of raloxifene on dopamine-related symptoms in clinical studies.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_52b The impact of transient adolescent food insecurity on metabolic, reward, and mood-related behaviour.

Presenting Author: Ruchi Jayasinghe

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Felicia Reed - Monash University Department of Physiology, Biomedicine Discovery Institute

Erika Greaves - Monash University Department of Physiology, Biomedicine Discovery Institute

Claire J Foldi - Monash University Department of Physiology, Biomedicine Discovery Institute

Background
Food insecurity, defined as inconsistent access to sufficient and nutritious food, affects more than 800 million people worldwide and disproportionately impacts the mental health of adolescents. The prevalence of food insecurity is rising in response to socioeconomic challenges, geopolitical instability and climate change. Food insecurity affects weight regulation, mood, reward-related behaviour, and cognition, but the underlying mechanisms remain unclear. In this study, we established a model transient food insecurity in adolescent mice to examine its effects on weight gain, feeding behaviour, and reward processes in adulthood. We hypothesized that food insecurity triggers metabolic and behavioural changes in a sex-dependent manner.

Methods
Adolescent C57Bl/6 mice of both sexes were transiently exposed to unreliable access to food (standard laboratory chow), involving variability in the quantity and timing of scheduled feeding across a 4-week period (between 5-9 weeks of age). Metabolic phenotyping including assessment of body composition, glucose tolerance and insulin sensitivity was followed by a series of maze-based anxiety tests and intermittent access to a high-fat, high-sugar (HFHS) diet. A progressive ratio task (PRT) was conducted using home-cage operant devices, the Feeding Experimentation Device 3 (FED3) to investigate the impact of food insecurity on reward processing and motivation.

Results
Despite comparable intakes following ad libitum access, both FI groups gained weight compared to controls that were maintained on ad libitum food access, with females ($p= 0.0004$) gaining more than males ($P=0.0089$) FI females demonstrated binge-like patterns of feeding in the intermittent access paradigm ($p= 0.0004$), a phenotype that was not observed in males. However, both male ($p= 0.0260$) and female ($p= 0.0805$) FI groups showed improved insulin sensitivity compared to controls and increased exploratory behaviour in an elevated plus maze (males $p= 0.0800$; females, $p = 0.0090$). The PRT data will be presented in the poster.

Conclusion
Food insecurity leads to alterations in metabolic parameters, promotes maladaptive feeding behaviours, and may differentially impact decision-making and reward-related behaviours based on sex. These findings underscore the need for further investigation into the long-term consequences of food insecurity on metabolic health, cognition and behaviour, with a focus on sex-specific differences. Future research will include operant tasks to assess various aspects of behaviour and cognition, as well as fiber photometry and histological techniques to explore the neurobiological changes resulting from food insecurity.

P_48b PSILOCYBIN TREATMENT FOR EATING DISORDERS: A FOCUS ON PROSOCIAL EFFECTS

Presenting Author: Sheida Shadani

Sheida Shadani - Monash University

Background
Psilocybin, traditionally valued for enhancing social cohesion and conflict resolution, shows promising prosocial effects in recent human and rodent studies. Deficits in social behaviour are core features of numerous mental disorders, including anxiety, depression, obsessive-compulsive disorder and anorexia nervosa (AN). A Phase 1 clinical trial recently demonstrated its safety in treating AN, yet its therapeutic mechanisms remain unclear. Social interaction potentially plays a role in psilocybin's efficacy for AN, since social withdrawal is common among this population. To explore this, we studied social behaviours in mice exposed to activity-based anorexia (ABA), using tasks for social motivation, novelty, and helping behaviour.

Methods
To assess the effects of a single psilocybin dose (1.5 mg/kg) on social behaviour, female C57BL/6J mice underwent the ABA paradigm (n=15), which consists of time-restricted (2h) food access and unlimited access to a running wheel. Control groups included food restriction only (n=14), running wheel access only (n=15) and single housing only (n=12). After sufficient body weight loss in the ABA group had been achieved, mice received psilocybin (n=29) or saline (n=27) and testing in the 3-chamber sociability test occurred 4 hours post-administration. Behaviour was analysed in two phases: social exploration (first half) and social choice (second half).

Results
Interestingly, psilocybin did not elicit a significant effect on the mice, so the data for the treatment groups were combined. Exposure to the ABA paradigm increased the preference for social novelty compared to control groups, including the food-restricted group ($p_{ABA} = 0.032$), those with access to running wheels ($p = 0.058$), and socially isolated mice ($p_{ABA} = 0.0416$). Additionally, a positive correlation was observed between body weight in the ABA and food-restricted groups and their preference for social novelty.

Conclusion
Together, these data highlight the importance of using appropriate mouse models to study different aspects of psychiatric conditions as the ABA mouse model did not replicate the social deficits seen in individuals with AN. Although psilocybin did not produce social behavioural changes relevant to eating disorders, it remains important to investigate potential molecular changes. We are currently examining the effects of ABA and psilocybin treatment neuroplasticity biomarkers, including brain-derived neurotrophic factor (BDNF) and Tropomyosin receptor kinase B (TrkB), in specific brain regions of mice subjected to food restriction and wheel running. This may help uncover mechanisms driving prosocial behaviour.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_60b Food brand logos and their association with dietary habits

Presenting Author: Simone Rehn

Simone Rehn - University of Technology Sydney

Michael Kendig - University of Technology Sydney

Poppy Watson - University of Technology Sydney

Background
Our environment is full of advertisements featuring distinctive food brand logos that are associated with tasty food rewards. These logos are argued to capture attention and bias our behaviour, but to date there has been limited experimental work examining individual differences in learning about these food logos or the degree to which they interfere with goal-directed behaviour.

Methods
Across three experiments in young adults we examined how ratings of food-logos were associated with self-reported dietary fat and sugar consumption and patterns of appetite control. Participants categorised different brand logos as food or non-food related and rated them on a variety of dimensions including liking, familiarity and health. These measures were then linked to individual variations in fat and sugar intake. Finally, we examined the degree to which food-brand logos interfered with performance when used as task-irrelevant distractors in cognitive tasks and explored associations with individual differences in eating habits.

Results
Overall, individuals who reported eating more dietary fat and sugar rated the food brands as being more likeable, exciting and healthy. Notably, when used as distractors in cognitive tasks, food-brand logos exerted stronger interference effects in participants reporting issues with food and appetite control.

Conclusion
These preliminary results suggest that food brand logos interfere with goal-directed behaviour, particularly for those who regularly consume foods high in fat and sugar. These studies offer a promising avenue for future investigations into how advertising and brand exposure can bias decisions about food and health.

Late Breaking Abstracts

Poster Session 1: Monday

P_08a Using spatially resolved single-nucleus multi-omics to understand how stress contributes to psychiatric disorders

Presenting Author: Tamim Ahsan

Tamim Ahsan - Charles Perkins Centre, University of Sydney, NSW, Australia; School of Medical Sciences, University of Sydney, NSW, Australia; Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia; Department Genes and Environment, Max Planck Institute of Psychiatry, Munich, Germany

Dominic Kaul - Charles Perkins Centre, University of Sydney, NSW, Australia; School of Medical Sciences, University of Sydney, NSW, Australia; Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia

Amber Curry - Charles Perkins Centre, University of Sydney, NSW, Australia; School of Medical Sciences, University of Sydney, NSW, Australia; Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia

Katrina Z. Edmond - Charles Perkins Centre, University of Sydney, NSW, Australia; School of Medical Sciences, University of Sydney, NSW, Australia; Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia

Nathalie Gerstner - Department Genes and Environment, Max Planck Institute of Psychiatry, Munich, Germany; International Max Planck Research School for Translational Psychiatry, Munich, Germany; Institute of Computational Biology, Helmholtz Zentrum München, Neuherberg, Germany

Anna S. Fröhlich - Department Genes and Environment, Max Planck Institute of Psychiatry, Munich, Germany; International Max Planck Research School for Translational Psychiatry, Munich, Germany; Institute of Computational Biology, Helmholtz Zentrum München, Neuherberg, Germany

Michael J. Ziller - Department of Translational Research in Psychiatry, Max-Planck Institute of Psychiatry, Munich, Germany; Department of Psychiatry, University of Münster, Münster, Germany

Elisabeth B. Binder - Department Genes and Environment, Max Planck Institute of Psychiatry, Munich, Germany; Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, USA

Lezanne Ooi - Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia

Janine Knauer-Arloth - Department Genes and Environment, Max Planck Institute of Psychiatry, Munich, Germany; Institute of Computational Biology, Helmholtz Zentrum München, Neuherberg, Germany

Natalie Matosin - Charles Perkins Centre, University of Sydney, NSW, Australia; School of Medical Sciences, University of Sydney, NSW, Australia; Molecular Horizons and School of Chemistry and Molecular Bioscience, University of Wollongong, NSW, Australia

Background

Despite affecting millions of people worldwide, psychiatric disorders are inadequately treated. Understanding how stress, one of the major risk factors for these disorders, raises risk to psychopathology is essential for identifying new treatments. The orbitofrontal cortex (OFC), a sub-region of prefrontal cortex (PFC), is involved in higher cognitive processes and is highly vulnerable to stressors. However, the impacts of stress on various cell-types across the cortical layers of the OFC are largely unknown. Here, we explored human postmortem OFC (BA11) samples to unravel stress-induced cell-type-specific transcriptomic and epigenomic changes in psychiatric disorders and their spatial distribution.

Methods
We examined 86 individuals (n=32 controls vs n=54 cases with mixed major psychiatric disorders: schizophrenia, major depression and bipolar disorder) with or without history of profound psychological stress exposure (n=23 with severe stress and n=31 without). To capture the cell-type-specific effects, we generated single-nucleus Assay for Transposase-Accessible Chromatin sequencing (snATAC-seq) and single-nucleus RNA sequencing (snRNA-seq) datasets using 10x Chromium (10x Genomics, USA). To dissect spatial heterogeneity, we produced spatial transcriptomic dataset using Visium (10x Genomics, USA). We performed compositional and differential gene expression analyses, followed by gene ontology and disease enrichment analyses, on the snRNA-seq data.

Results
After filtering out the low-quality nuclei, about ~800,000 nuclei from 15 different cell types were retained. The proportions of inhibitory neurons and astrocytes were significantly lower in individuals exposed to stress vs those without stress, while the proportion of oligodendrocytes was higher (Log2FoldChange of -0.51, -1.02 and 0.33, respectively). We identified a large number of differentially expressed genes (DEGs) in oligodendrocytes and reelin-expressing inhibitory neurons (160 and 265, respectively) only when the contrast was performed among cases based on their history of stress. These DEGs showed significant enrichment of psychopathology-associated metabolic processes and phenotypes.

Conclusion
These results highlight the striking cell-type-specific impacts of psychological stress on gene expression and cellular abundance in the OFC of individuals with psychiatric disorders. Experiments and analyses are underway to further disentangle the regulatory changes affecting transcription by delineating epigenomic modifications and gene co-expression network within these cell types and to unmask the changes in transcript, as well as cellular, abundances across the cortical layers. We hypothesise that transcriptomic dysregulation and alterations in cellular composition across multiple neuronal and glial cell types are localised to specific cortical layers in the OFC of psychiatric patients with a history of stress exposure.

P_51b The effect of raloxifene on anxiety and stress-related gene expression in the ventral hippocampus of rat offspring exposed to maternal immune activation

Presenting Author: Tsz Ho Timothy Wong

Tsz Ho - Timothy Wong Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia, Randwick, 2031, NSW, Australia

Sophie Debs - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia, Randwick, 2031, NSW, Australia; and Discipline of Psychiatry and Mental health, UNSW Sydney

Priscila A. Costa - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia, Randwick, 2031, NSW, Australia

Samantha Owens - School of Biotechnology and Biomolecular Sciences (BABS), UNSW Sydney

Margaret Morris - Department of Pharmacology, School of Biomedical Sciences, UNSW Sydney Australia, New South Wales, Australia

Tertia Purves-Tyson - Preclinical Neuropsychiatry Laboratory, Neuroscience Research Australia, Randwick, 2031, NSW, Australia; and Discipline of Psychiatry and Mental health, UNSW Sydney

Background
Dysregulation of glucocorticoid-signalling in the hippocampus may contribute to the development of schizophrenia. Changes in stress signalling molecules including glucocorticoid receptor (GR, Nr3c1 gene), and GR cofactors FKBP51 (Fkbp5) and FKBP52 (Fkbp4), have been identified in the hippocampus and other regions in schizophrenia. As raloxifene, an estrogen receptor modulator, may improve schizophrenia symptoms, understanding its underlying molecular mechanisms may provide novel therapeutic targets. We used the rat maternal immune activation (MIA) model to investigate the effect of raloxifene on anxiety-like behaviours and stress-related transcripts in the ventral hippocampus (vHPC) of male and female MIA and control offspring.

Methods
Pregnant Wistar dams received 4mg/kg high molecular weight-poly(I:C) or saline on gestational date 15 (adolescent study, n=38, n=3-7 per group) or 19 (adult study, n=116 n=13-17 per group). Offspring were randomized into four groups/sex: saline/placebo, MIA/placebo, saline/raloxifene, MIA/raloxifene; oral raloxifene/placebo treatment from postnatal date (PND) 30-57 (adolescence) or PND56/57-81/82 (adulthood). Anxiety-like behaviours were measured using elevated plus maze (EPM) during early adolescence (PND33/34) and late adolescence (PND54/55). Data were analysed by two-way ANOVA (raloxifene, MIA), sexes separately. Stress-related transcripts (Nr3c1, Fkbp4, Fkbp5) in the vHPC were measured using qPCR and analysed by three-way ANOVA (sex, raloxifene, MIA).

Results
MIA significantly increased maternal sickness behaviours [F(1,12)=7.893, p=0.016]. MIA increased the time male offspring spent in the closed arm of the EPM and decreased their central crosses on PND33/34 [all F(1,11)?4.958, p0.05]. There was no effect of MIA on EPM anxiety measures at either age in females [all F(1,19)?2.859, p>0.05]. There was no effect of raloxifene on any anxiety measures at either time investigated [males: all F(1,11)?1.190, females: all F(1,19)?2.962, all p>0.05]. Nr3c1, Fkbp4 and Fkbp5 mRNA levels were unaltered by MIA or raloxifene in the vHPC during adulthood [all F(1,105)?1.090, all p>0.05].

Conclusion
Our findings suggest that a mid-late gestational prenatal immune insult promotes anxiety-like behaviour in adolescent male offspring that resolves in adulthood but is not modified by raloxifene. Additionally, the effects of raloxifene and prenatal immune stress on stress-responsivity are not reflected by changes in stress-signalling transcripts (Nr3c1, Fkbp4 and Fkbp5) in the vHPC of adult rats. Thereby, further investigations are needed to explore the molecular

mechanisms of raloxifene to individuals exposed to a prenatal immune insult and whether these are relevant to the management of schizophrenia.

Late Breaking Abstracts

Poster Session 1: Monday

P_31a Orexin signaling in ventral tegmental area as a common mediator of sleep and drug seeking during acute cocaine abstinence

Presenting Author: Utsav Gyawali

Utsav Gyawali - Rutgers University

Shayna O' Connor - Rutgers University

Charlie Olson - University of Tennessee

Michelle Bilotti - Rutgers University

David De Sa Nogueira - Rutgers University

Morgan James - Rutgers University

Background
Sleep disturbances are common in individuals with cocaine use disorder (CUD) and worsen during withdrawal. Poor sleep often leads to relapse, indicating a biological link between these disorders. Preclinical studies show that uncontrolled drug use is associated with increased orexin neuron activity, which influences both reward and wakefulness. As a result, targeting orexin signaling could improve sleep and reduce relapse risk. Here, we tested whether normalizing orexin signaling during cocaine abstinence in rats would improve sleep and reduce drug-seeking behavior, with a focus on the ventral tegmental area (VTA) as a key site for orexin-driven reward and arousal.

Methods
We trained rats to self-administer cocaine before extinguishing lever pressing over 7 days. Another group was trained to develop conditioned place preference (CPP) for cocaine injections (10 mg/kg), which was extinguished over 5 days. Both groups were treated with the dual orexin receptor antagonist suvorexant (0 vs. 30 mg/kg; p.o) 1 hour before the inactive period during extinction. In a subset of CPP rats, sleep was monitored overnight using EEG/EMG. In a separate group of CPP rats, we collected brain samples from reward and arousal regions, including VTA, after 48h abstinence and measured orexin and receptor mRNA changes using qRT-PCR.

Results
Cocaine abstinence led to increased time in Wake and reduced NREM sleep during the first 3 days of extinction, which was reversed by suvorexant: D1 (Wake, p=0.02; NREM, p=0.043), D2 (Wake, p=0.008; NREM, p=0.009), and D3 (Wake, p=0.004; NREM, p=0.007). Suvorexant administration during the inactive period also facilitated next-day extinction of cocaine seeking in both self-administration (p=0.034) and CPP (p=0.040) rats. In CPP rats, abstinence increased orexin mRNA expression in the LH (p=0.026) and Ox1R levels in the VTA (p=0.002), with no changes in other brain regions. Preliminary data show arousal events (waking) increase orexin binding in VTA (p=0.002).

Conclusion
Inhibiting orexin signaling through suvorexant administration during cocaine abstinence helps restore normal sleep patterns and reduces drug-seeking behavior. Changes in orexin receptor levels and peptide binding in the VTA suggest that this region may be a key target for orexin signaling during abstinence. Ongoing research is exploring the causal role of orexin signaling in the VTA in regulating both sleep and drug-seeking behaviors.

P_59b Adrenergic Modulation of Inputs to the Paraventricular Thalamus

Presenting Author: Wendi Gao

Wendi Gao - School of Biomedical Science, UNSW Sydney

Eun A. Choi - School of Psychology, UNSW Sydney

Si Yin Lui - School of Biomedical Science, UNSW Sydney; School of Psychology, UNSW Sydney

Gavan P. McNally - School of Psychology, UNSW Sydney

John M. Power - School of Biomedical Science, UNSW Sydney

Background
Overeating contributes to health issues like obesity and type 2 diabetes, burdening healthcare systems. Noradrenaline (NA) is known to modulate feeding in reward-associated brain regions, including the hypothalamus and nucleus accumbens. NA also affects the paraventricular thalamus (PVT), a gateway node for appetitive motivation that merges cortical and subcortical inputs. Previous studies have found that exogenous NA application increases the frequency of spontaneous excitatory postsynaptic currents (EPSCs) in PVT neurons, however, how its effect on specific input pathways is unknown. Here we examined the effect of NA on two major PVT input pathways: the prefrontal cortex (PFC) and hypothalamus.

Methods
Two-month-old male C57BL/6J mice received viral injections to express the excitatory opsin channelrhodopsin-2 in PFC or hypothalamic neurons. After allowing 4-12 weeks for viral expression, mice were anesthetised, decapitated, and coronal brain slices were prepared. Whole-cell patch-clamp recordings were made from PVT neurons. Pharmacologically isolated EPSCs and inhibitory postsynaptic currents (IPSCs) were evoked using brief pairs (1 ms 20 Hz) of 470 nm light pulses. NA (10 μM) was applied via bath application.

Results
Photostimulation of hypothalamic terminals evoked synaptic currents with both inhibitory and excitatory components with no topographical bias. Currents evoked by PFC terminal photostimulation were excitatory and topographically biased toward the posterior PVT. NA reduced the amplitude of EPSCs evoked by PFC terminals and the paired-pulse ratio (PPR, EPSC2 / EPSC1). NA also decreased the EPSC amplitude evoked by hypothalamic stimulation, however the PPR increased. NA had a limited effect on inhibitory hypothalamic inputs with no apparent change in either the PPR or the IPSC amplitude.

Conclusion
Our findings indicate that the PVT neurons integrate descending excitatory inputs from the PFC with ascending excitatory and inhibitory inputs from the hypothalamus. These inputs were differentially affected by NA, selectively suppressing the excitatory inputs. While PFC and hypothalamic excitatory inputs were reduced by NA, differences in the PPR suggest NA increases transmitter release at PFC synapses and decreases transmitter release at hypothalamic synapses. Together these data suggest that adrenergic signalling biases PVT inputs altering the way the PVT merges cortical and subcortical inputs to influence motivated behaviour.

Late Breaking Abstracts

Poster Session 2: Tuesday

P_50b Olanzapine accelerates aging through impaired mitophagy via dysfunctional lysosomes and defective SNARE complexes

Presenting Author: Xi Chen

Wendi Gao - School of Biomedical Science, UNSW Sydney

Eun A. Choi - School of Psychology, UNSW Sydney

Si Yin Lui - School of Biomedical Science, UNSW Sydney; School of Psychology, UNSW Sydney

Gavan P. McNally - School of Psychology, UNSW Sydney

John M. Power - School of Biomedical Science, UNSW Sydney

Background
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Conclusion
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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
2024	14th meeting at Mercure, Sydney

BPA 2025 will be held at the Florey Institute, Melbourne, VIC

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