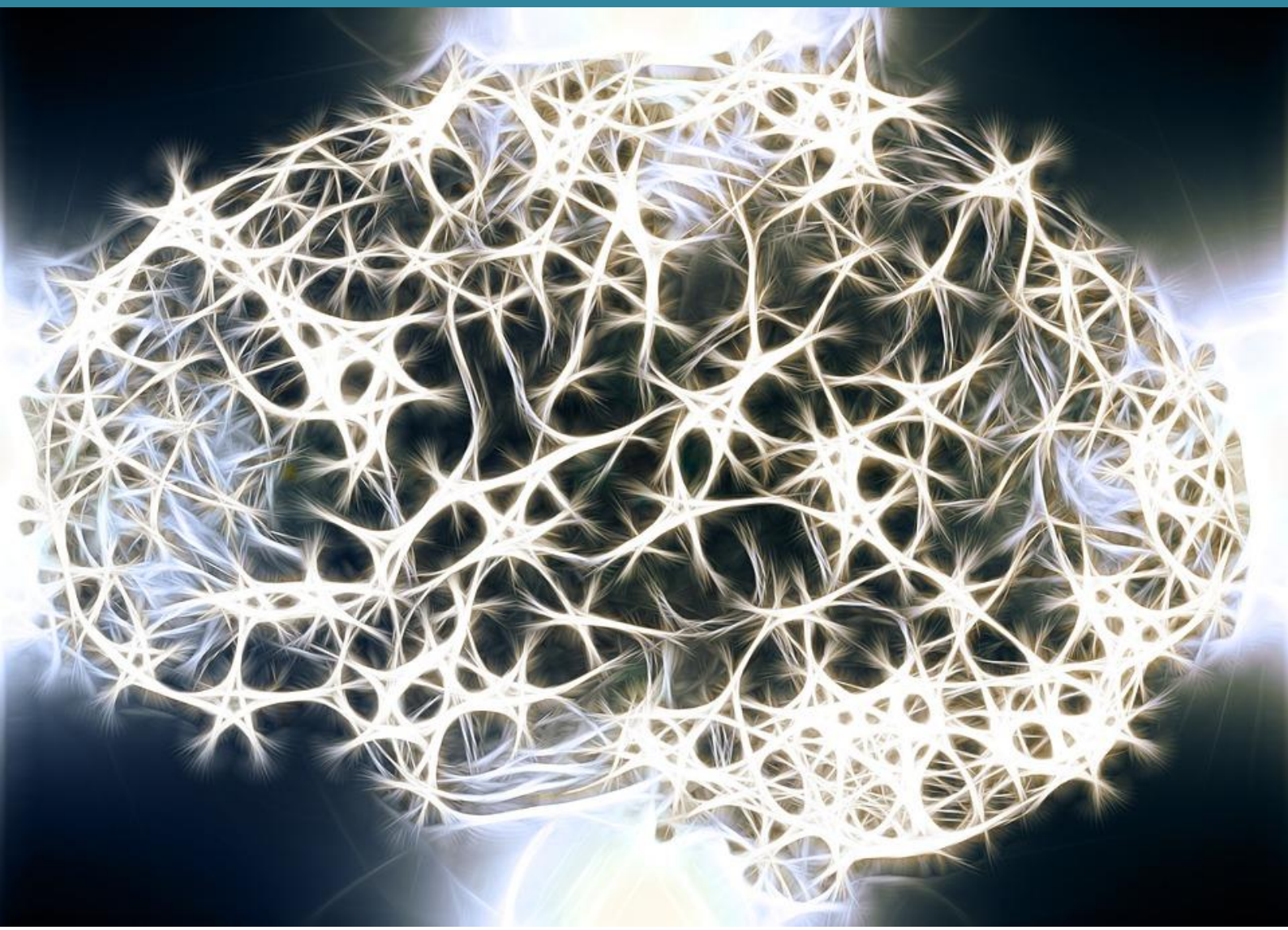
Biological Psychiatry
AUSTRALIA

8th Annual Scientific Meeting



Abstract Book

6th–8th November 2018

SAHMRI, Adelaide, South Australia

#BiolPsychAus18

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Program

Day 1

8th Annual Scientific Meeting, Adelaide	
Tuesday 6th of November SAHMRI Auditorium, North Terrace	
Time	Event
17:00-18:00	Registration opens
17:30-18:00	Welcome reception: SA food and drink showcase
18:00-18:40	Opening Address from Keynote Speaker Professor Urs Meyer, University of Zurich
18:40-20:40	Welcome Mixer

Join us in the SAHMRI auditorium and get to know your fellow conference attendees and speakers while you sample highly acclaimed local wine, beer and cider sourced from the Adelaide Hills, McLaren Vale and Barossa Valley. Meanwhile, local group Little Adelaide Catering Co. will serve a selection of South Australian delights, including internationally renowned seafood.

Day 2

Wednesday 7th of November SAHMRI Auditorium, North Terrace		
8:00-9:00	Registration opens	
8:45-9:00	Opening address: Professor Bernhard Baune, Chair, Local Organising Committee and Professor Darryl Eyles, President, Biological Psychiatry Australia	
9:00-10:00	9th Aubrey Lewis Lecture Dr Rachel A Hill, Florey Institute of Neuroscience and Mental Health / Monash University	
10:00-10:30	Data Blitzes Round 1 (5 x PhD Candidates presenting for 5 minutes each) Chaired by **Christin Weissleder**	**Ariel Dunn, University of Newcastle** Synergistic effects of maternal immune activation and adolescent cannabinoid exposure on schizophrenia-related behaviour and auditory processing responses in rats
		Alice Petty, The Queensland Brain Institute, The University of Queensland Enhanced Dopamine in the Prodrome of Schizophrenia; A Novel Animal Model
		Ellen Rose Cullity, The Florey Institute of Neuroscience and Mental Health Postnatal developmental trajectory of dopamine receptor 1 and 2 expression in cortical and striatal brain regions
		Ann-Katrin Kraeuter, James Cook University Chronic β-hydroxybutyrate administration normalises schizophrenia-like behaviours in a pharmacological NMDA hypofunction model
		Adrienne Grech, Monash University Characterising the cognitive consequences of disrupted BDNF-TrkB signalling at parvalbumin-expressing interneurons
10:30-10:50	Morning Tea	
10:50-12:20	Symposium 1 - Stress and trauma in psychopathology Dr Yann Quidé, Natasha Wood and Professor Anthony J Hannan Discussant: Dr Sarah Cohen-Woods Chair: Dr Yann Quidé	
12:20-12:50	Data Blitzes Round 2 (5 x Early Career Researchers presenting for 5 minutes each) Chaired by **Jessica Mills**	**Dr Adam K Walker, Neuroscience Research Australia / University of New South Wales / Peter MacCallum Cancer Center** The blood-brain barrier is a viable target to treat depression
		Dr Guiyan Ni, University of South Australia Age at first birth in women is genetically associated with the risk of schizophrenia
		Dr Xiaoying Cui, Queensland Brain Institute, The University of Queensland The role of long non-coding RNA in the development of dopamine systems: A convergent mechanism for schizophrenia
		Dr Tertia D Purves-Tyson, Neuroscience Research Australia / University of New South Wales Elevation of complement pathway-related transcripts in the midbrain of schizophrenia cases with high cytokine-related inflammatory profiles
		Dr Scott R Clark, University of Adelaide Probabilistic Modelling of Transition to Psychosis Using Clinical, Cognitive and MRI data in the PACE 400 sample
12:50-13:10	Lunch	

13:10-14:10	Group 1 Poster Presentations
14:10-15:40	Symposium 2 - What's wrong with my mouse? Deeper analysis of behavioural data in animal models towards modelling the human condition and disease By Dr Jess Nithianantharajah, A/Prof Tim Karl, Dr Rachel Hill and Professor Darryl Eyles Discussant: Professor Maarten van den Buuse Chair: Professor Urs Meyer
15:40-16:00	Afternoon Tea
16:00-17:00	Early Career Researchers Session: Report from one BPA ECR speaker awardee and panel discussion regarding new NHMRC funding guidelines, with a specific focus on ECRs
18:00-23:00	**Cocktail Function** **John Halbert Room, Adelaide Oval** Special presentation from Associate Professor Rohan Walker, The University of Newcastle: "A fuzzy overview of the random walk between failure, (moderate) success and survival in psychiatric neuroscience"

After our first full day of sharing ideas, we move across the river to The Adelaide Oval. Take in views of the oval itself as well as part of the riverbank, while you listen to local band The Blend and partake in an additional selection of locally produced food and beverages.

Day 3

Thursday 8th of November SAHMRI Auditorium, North Terrace		
9:00-10:00	6th Isaac Schweitzer Lecture Professor Christos Pantelis, The University of Melbourne	
10:00-10:30	Data Blitzes Round 3 (5 x PhD Candidates or ECRs presenting for 5 minutes each) Chaired by **Ilijana Babic**	**Salvatore Russo, University of Adelaide** Reconciling Mackintosh and Pearce-Hall: Evidence from human electrophysiology
		Elysia Sokolenko, University of Melbourne The mGluR2/3 agonist LY379268 reverses NMDA receptor antagonist effects on cortical gamma oscillations and coherence, but not working memory impairment in mice.
		Elizabeth Llewelyn, University of New South Wales Childhood trauma differentially moderates the association between inflammatory markers and cognitive performance in healthy individuals and psychotic disorders
		Jessica Mills, University of Wollongong Comfort Eating in Major Depressive Disorder: Links to Leptin and Ghrelin
		Dr Azmeraw Amare, SAHMRI Polygenic scores for traits of depression predict response to lithium in patients with bipolar disorder
10:30-10:50	Morning Tea	
10:50-12:20	Symposium 3 – Personalised approach to Major Depressive Disorder: the right treatment for the right person By Micah Kearns, Dr Matthew Knight and Dr Célia Fourrier Discussant: Professor Bernhard Baune Chair: Dr Adam Bayes	
12:20-12:50	Biological Psychiatry Australia's Annual General Meeting	
12:50-13:20	Lunch	
13:20-14:20	Group 2 Poster Presentations	
14:20-15:00	Presentations by recipients of Neuronal Signalling Travel Awards	**Dr Renata Pertile, Queensland Brain Institute** Developmental Vitamin D-deficiency affects DNA methylation and midbrain development
		Dr Yann Quidé, University of New South Wales / Neuroscience Research Australia Glutamate levels in the anterior cingulate cortex are associated with schizotypal personality traits and moderated by childhood trauma severity
		Katrina Bird, Illawarra Health and Medical Research Institute / University of Wollongong Maternal Methadone Treatment: Behavioural and Cognitive Deficits in Adolescent Rat Offspring
15:00-16:15	Q&A session – Biomarker discovery in psychiatry: fact or fantasy? By A/Prof K. Oliver Schubert, Professor Bernhard Baune and Professor Brian Dean Discussant: Professor Peter Hoffmann Chair: Professor Bernhard Baune	
16:15-16:30	Afternoon Tea	
16:30-16:45	Prizes and Awards	

16:45-17:00	Closing Address from Conference Discussant Dr Scott Clark, The University of Adelaide
17:00	Conference Close

Welcome

Dear Colleagues,

On behalf of the Local Organising Committee (LOC), I warmly welcome you to the Biological Psychiatry Australia (BPA) Conference in Adelaide! This is a first time visit of BPA to South Australia, and the conference will not only present excellent international and national research but also showcase world famous South Australian food and drinks.

I would like to thank our sponsors for their invaluable support. We would also like to thank and acknowledge the financial support of our Silver Sponsors, Otsuka/Lundbeck, Servier, and Janssen; and our bronze sponsors, the Fay Fuller Foundation and Neuronal Signalling. Their generosity ensures that these meetings are possible and provides support for our many Early Career Researchers and to acknowledge excellent research by providing support for various types of awards.

I would like to thank the BPA2018 LOC and the BPA Executive Committee as well as our graduate students, who have greatly assisted in organising the annual meeting in Adelaide. This year's program highlights the exciting and diverse range of biological psychiatry research that is being conducted in Australia. Major themes of the conference include Neuroinflammation and Precision Medicine in Psychiatry. We are excited to have an internationally renowned speaker, Prof. Urs Meyer, University of Zurich to give the opening keynote of the conference on Tuesday evening. We are equally delighted to have Professor Christos Pantelis and Dr Rachel A Hill presenting the Isaac Schweitzer Lecture and Aubrey Lewis Award Lecture. Featuring the conference themes, we have three outstanding symposia in this year's program, 3 data blitz sessions and two-days of poster presentations. Last year's highly successful interactive Q & A panel will be on the program again this year.

The BPA2018 LOC would like to offer a warm welcome to the new members of our society, and to our current members we would like to thank you for your continued support. We believe this year's program will provide opportunities to hear of the latest developments in biological psychiatry research from leading and emerging Australian researchers, engage in intellectual discussion and initiate new collaborations in biological-based research into mental illness. BPA2018 also provides an excellent platform for our Early Career Researchers to present their research and interact with the leaders in the field.

We are looking forward to welcoming you to our beautiful city, the outstanding food and wines and to a conference that promises to be a stimulating academic and social event to meet old friends, new colleagues and to engage in new ideas and collaborations.

Kind Regards,

Bernhard Baune

Chair, Local Organising Committee BPA 2018 Conference

Local Organising Committee

Chair: Professor Bernhard Baune

Dr Natalie Aboustate	A/Prof Jee Kim
Dr Scott Clark	Julie Morgan
Professor Darryl Eyles	Emma Sampson
Dr M. Catharine Jawahar	Dr Catherine Toben

Aubrey Lewis Award Lecture

Wednesday the 7th of November, 9:00am-10:00am

Dr Rachel A Hill

Psychoneuroendocrinology Laboratory, Florey Institute for Neuroscience and Mental Health, University of Melbourne; Department of Psychiatry, School of Clinical Sciences, Monash University

Dr Hill is an NHMRC Career Development Fellow and head of the Behavioural Neuroscience laboratory, Department of Psychiatry, Monash University. She completed her PhD in 2007 in biochemistry at Monash University and began postdoctoral training in neuroscience at The Burnham Institute, La Jolla, California, before accepting a NHMRC early career fellowship at the Mental Health Research Institute (now Florey Institute). In 2014 Dr Hill became an independent group head at the Florey Institute for Neuroscience and Mental Health, and in 2016 Dr Hill was recruited to Monash University, Department of Psychiatry to head the behavioural neuroscience program. She has made significant contributions to the fields of neuroscience, neuroendocrinology and psychiatry as demonstrated by her high quality / high throughput publication record (49 pubs, >1200 citations), several international and national invited seminars and funding success (>$3 million) from national (NHMRC) and international (Brain and Behavior Research Foundation USA) funding bodies.

Her research interests lie in behavioural neuroscience, with a particular focus on schizophrenia. She uses pre-clinical animal models to better understand the pathophysiology of mental disorders such as schizophrenia, and to design and test novel therapeutic strategies. She is investigating the origins of schizophrenia and how best to treat the various symptom presentations. These preclinical studies are aligned with collaborative human genetic studies. The long-term goal is patient-specific treatments that may be guided by both genetic and environmental patient profiles.

Isaac Schweitzer Award Lecture

Thursday the 8th of November, 9:00am-10:00am

Professor Christos Pantelis

The University of Melbourne

Professor Christos Pantelis is an NHMRC Senior Principal Research Fellow, Foundation Professor of Neuropsychiatry and Scientific Director of the Melbourne Neuropsychiatry Centre at The University of Melbourne and Melbourne Health. He holds an Honorary Professorial Fellow position at the Florey Institute for Neuroscience & Mental Health and heads the Adult Mental Health Rehabilitation Unit at Sunshine Hospital. He is an Honorary Adjunct Professor in the Centre for Neural Engineering (CfNE), Department of Electrical and Electronic Engineering at University of Melbourne. He leads a team of over 60 clinical and research scientists and students that have been undertaking neuroimaging and neuropsychological work in schizophrenia and psychosis, and other psychiatric and neurodegenerative disorders since 1993 in Australia.

His work has focused on brain structural and functional changes during the transition to psychosis. His group was the first to describe progressive brain structural changes at psychosis onset, with a seminal paper published in The Lancet in 2003. He has published over 500 papers and chapters, including papers in high-profile international psychiatry, neurology, radiology and medical journals. He published one of the first books on the neuropsychology of schizophrenia, a recently published book on "Olfaction and the Brain" and a book on "The Neuropsychology of Mental Illness". He has established a unique resource of over 5,000 multimodal brain scans in patients with schizophrenia and other neuropsychiatric disorders, including longitudinal imaging. Recent work focuses on early developmental disorders, including children with schizotypal features and autism.

Professor Pantelis has won a number of NHMRC grants, including four recent international collaborative EU-NHMRC grants and was a CI on a national NHMRC Enabling Grant to establish the Australian Schizophrenia Research Bank (ASRB). He was co-Chief Investigator on a NHMRC Program Grant, which commenced in 2005 (2005-2009: $7.4 million) and focuses on the neurobiology of emerging severe mental illness during late brain development. This grant was refunded for a further 5 years commencing (2009-2013: >$10 million). He is an investigator on a $23 million CRC grant examining biomarkers in neurodegenerative and psychotic disorders. In 2003 he won the Selwyn-Smith Medical Research Prize of The University of Melbourne for his work on progressive brain changes in early psychosis and, most recently, he was highly commended in the 2009 Victorian Minister of Health Award for Outstanding Individual Achievement in Mental Health. He was awarded an NHMRC Senior Principal Research Fellowship, which commenced in 2010, renewed until 2020. He was awarded a 2011 NARSAD Distinguished Investigator Grant from the Brain & Behavior Research Foundation (US). He was awarded the international 2013 Robert-Sommer Award from the Justus Liebig University School of Medicine, Germany. He was conferred a Doctor Honoris Causa from the National and Kapodistrian University of Athens in 2015. He was named in the Thomson Reuters list of "The World's Most Influential Scientific Minds" for 2014, 2015 and 2016, representing the top 1% of most highly cited scientists in his field. He is on the Editorial Boards of national and international journals, including Associate Editor for Psychological Medicine.

Symposium 1 - Stress and trauma in psychopathology

Wednesday the 7th of November, 10:50am-12:20pm

Speakers: Dr Yann Quidé, Ms Natasha Wood, Professor Anthony J. Hannan
Chair: Dr Yann Quidé
Discussant: Dr Sarah Cohen-Woods

Early-life stress, and trauma, have been consistently associated with poor mental health outcomes. This symposium will present mechanisms of this relationship, including human studies relating to inflammation, and DNA methylation, to mouse studies investigating transgenerational epigenetic inheritance. Dr. Yann Quidé will present his recent work investigating the relationship between markers of inflammation and childhood maltreatment, and if this impacts psychosis outcomes. He will be presenting with the Imaging Genetics in Psychosis cohort; unique in its depth of phenotypic, cognitive, neuroimaging, and biological data. Then Natasha Wood, a doctoral student, will present a systematic review of the relationship between early-life exposure to stress and DNA methylation outcomes in childhood and later life. Despite a huge interest in the stress-DNA methylation field, and multiple narrative reviews, to-date there has not been a systematic review. This is urgently required by a field where so much time and resources are being spent. Our final presenter is the esteemed Prof. Anthony Hannan who will introduce the concept of transgenerational inheritance of stress and trauma, and epigenetic mechanisms by which this may occur. Dr. Sarah Cohen-Woods will facilitate what will likely be a lively and topical discussion, considering how mechanisms such as inflammation and DNA methylation confer risk to psychopathology after early-life trauma exposure, and how transgenerational inheritance observed in mice may be observed in humans in the future.

1. Dr Yann Quidé, University of New South Wales

Dr. Yann Quidé is an early-career postdoctoral researcher in the School of Psychiatry UNSW Sydney, and affiliated scientist at Neuroscience Research Australia (NeuRA). Yann has a particular interest in identifying the neurobiological underpinnings of stress and trauma in relation to psychiatric conditions. His research particularly aims to identify the long-term neurobiological effects of childhood trauma exposure on the risk of developing schizophrenia and bipolar disorder. In addition, Yann is interested in identifying the early neurobiological changes occurring in the aftermath of sexual assault in females, and how these lead to the development of PTSD.

Elevated levels of pro-inflammatory cytokines are consistently reported in schizophrenia (SZ) and bipolar-I disorder (BD), as well as among individuals who have been exposed to childhood trauma. However, the association between trauma exposure, inflammation levels and brain morphology in these disorders is yet to be investigated. Participants were 71 cases with a diagnosis of schizophrenia/schizoaffective disorder (SZ), 72 cases with a diagnosis of psychotic BD and 74 healthy controls (HC). All participants underwent magnetic resonance imaging, serum levels of interleukin 6 (IL-6), tumour necrosis factor alpha (TNF-α) and C-reactive protein (CRP) were quantified, and childhood trauma exposure was assessed with the Childhood Trauma Questionnaire. In the context a higher IL-6, TNF-α and CRP levels in the SZ group compared to the HC group, and higher levels of TNF-α compared to the BD group, exposure to sexual abuse was positively associated with levels of CRP in the SZ group. There were no differences in levels of inflammatory markers between the BD and HC group, and childhood trauma exposure was not associated with inflammation in these groups. Preliminary results indicate that childhood trauma exposure differentially moderated the relationship between inflammation and grey matter volume in psychotic cases. Our results indicate that childhood trauma exposure is differentially associated with serum levels of pro-inflammatory markers across the diagnostic categories, and is a significant moderator of the relationship between inflammation and brain morphology. Together, this suggests that trauma may impact biological (stress and immune) systems differently in these patient groups.

2. Ms Natasha Wood, Flinders University

Natasha is a PhD candidate (Clinical Psychology) in the Behavioural Genomic and Environmental Mechanisms Lab at Flinders University. Natasha completed her Bachelor of Psychology (First Class Honours) in 2016 and commenced her PhD in 2018. Her research focuses on investigating the association between social disadvantage, genomic outcomes, and child and adult behaviour. As well as her research, Natasha is undertaking clinician training as a psychologist at Flinders University and develops her clinical skills through placements and skill-based assessments.

DNA Methylation and Childhood Adversity: A Systematic Review - There is a growing literature that presents evidence that adverse childhood events have potential to facilitate epigenetic changes, however findings are not completely consistent. Despite there being many narrative reviews on this topic, no systematic review has been published to date. Here we present a systematic review of the literature on the association between global DNA methylation, or site-specific DNA methylation, and exposure to childhood adversity. This systematic review also aims to give an overview of the potential link between mental health outcomes, DNA methylation, and childhood adversity. Three electronic databases were searched using keywords that aimed to capture any DNA methylation study related to childhood stressor exposure or experience. To be included articles had to be original research articles on humans, with at least one analysis of DNA methylation in relation to a change in the child's social environment. We will present the findings with DNA methylation by "type" of exposure (e.g. childhood maltreatment and/or trauma, socio-economic status, childhood exposure to war and war-related trauma). Inconsistent findings in the literature can be attributed in part to different exposures, evaluation of different regions of the epigenome, and use of different technologies. The findings presented are significant, as there have been no epigenomic systematic reviews on this frequently discussed topic in the scientific literature. Our conclusions can be used to identify and guide future research questions.

3. Professor Anthony J. Hannan, Florey Institute of Neuroscience and Mental Health

Professor Anthony Hannan is an NHMRC Principal Research Fellow and Head of the Epigenetics and Neural Plasticity Laboratory, Florey Institute of Neuroscience and Mental Health, University of Melbourne. Prof. Hannan received his undergraduate training and PhD in neuroscience from the University of Sydney. He was then awarded a Nuffield Medical Fellowship at the University of Oxford, where he subsequently held other research positions before returning to Australia on an NHMRC RD Wright Career Development Fellowship to establish a laboratory at the Florey Institute. He subsequently won other fellowships and awards, including an ARC FT3 Future Fellowship, the British Council Eureka Prize, the International Society for Neurochemistry Young Lecturer Award and the Federation of European Biochemical Societies Anniversary Prize. He currently serves on editorial boards (e.g. Neurobiology of Disease) and is President of the National Association of research Fellows. Prof. Hannan and colleagues provided the first demonstration in any genetic animal model that environmental stimulation can be therapeutic. This has led to new insights into gene-environment interactions in various brain disorders, including Huntington's disease, dementia, depression, schizophrenia and autism spectrum disorders. His research team explores how genes and environment combine via experience-dependent plasticity in the healthy and diseased brain. Their research includes models of specific neurological and psychiatric disorders which involve cognitive and affective dysfunction, investigated at behavioural, cellular and molecular levels so as to identify pathogenic mechanisms and novel therapeutic targets. He has published >150 journal articles, which have been cited >9,000 times (Google Scholar; h-index=47).

We have been investigating how various environmental manipulations selectively alter gene expression, cellular plasticity and associated cognitive processes and behaviours. Huntington's disease (HD) is one of over 40 tandem repeat disorders and involves a triad of psychiatric, cognitive and motor symptoms. In a transgenic mouse model of HD we have shown that expansion of the tandem repeat encoding a polyglutamine tract of the mutant huntingtin protein leads to a spatiotemporally specific cascade of molecular, cellular and behavioural abnormalities. We have also demonstrated that environmental enrichment can delay onset of the affective (depressive-like), cognitive and motor endophenotypes. Environmental enrichment and physical exercise induce changes in gene expression, which exhibit temporal specificity and regional selectivity. These findings have been extended to included stress and stress hormone (glucocorticoid) manipulation in HD mice and mouse models of psychiatric disorders, including depression and anxiety disorders. These approaches may also facilitate the development of 'enviromimetics' for a variety of brain

disorders known to be modulated by environmental stimuli. We have also explored the transgenerational effects of paternal environmental exposures. Our findings reveal significant experience-dependent effects on offspring via transgenerational epigenetic inheritance, which occurs via epigenetic modifications in the sperm of the fathers. We are exploring the impact of specific environmental and pharmacological factors, including stress hormone elevation, and the relevance of these discoveries in mice to human transgenerational epigenetics. Our findings, and their relevance to the proposed transgenerational inheritance of increased predisposition to various brain disorders, have major public health implications.

Symposium 2 - What's wrong with my mouse? Deeper analysis of behavioural data in animal models towards modelling the human condition and disease

Wednesday the 7th of November, 2:10pm-3:40pm

Speakers: Dr Jess Nithianantharajah, Associate Professor Tim Karl, Dr Rachel Hill and Professor Darryl Eyles

Chair: Professor Urs Meyer

Discussant: Professor Maarten van den Buuse

Neuropsychiatric disorders are highly heterogenous, with significant variation in the cause, presentation and symptom severity even within a single disorder. Using animal models of disease to gain a clearer understanding of mechanisms that underlie how genetic, pharmacological and environmental insults impact a range of behaviours is essential. There is no doubt well-characterized preclinical behavioural paradigms are powerful research tools in the neuroscience community. Indeed, the face and predictive validity of animal models of psychiatric disorders rely upon a well-characterized battery of behavioural tests that examine distinct behaviours such as motivation, locomotor activity, startle reflex, anxiety, fear response, social behaviour, and many forms of learning and memory. However, the robustness and validity of the data gathered from these tests is only useful if the appropriate behavioural tests to address the research question are employed. Moreover, how we interpret behavioural phenotypes and analyse animal data to yield translationally relevant measures could benefit from deeper critical considerations. This symposium, consisting of four national leaders in the field of behavioural neuroscience, will lead a spirited discussion on pitfalls of experimental design, analysis and interpretation of rodent behavioural data and ways to move forward to get the most out of our disease models.

1. Dr Jess Nithianantharajah, Florey Institute for Neuroscience and Mental Health

Dr. Jess Nithianantharajah is an Australian Research Council Future Fellow and heads the Synapse Biology and Cognition laboratory at the Florey Institute of Neuroscience and Mental Health, University of Melbourne. She completed her doctorate in behavioural neuroscience at the University of Melbourne and commenced postdoctoral training at the Howard Florey Institute investigating gene-environment interactions on neural plasticity. She was recruited as a postdoctoral fellow by Prof. Seth Grant at the Wellcome Trust Sanger Institute, Cambridge UK during which time she also held a joint appointment at the University of Cambridge working with Professors Tim Bussey and Lisa Saksida on the development of the rodent touchscreen cognitive tests. She relocated to the University of Edinburgh before returning to the Florey Institute as an independent group leader. Her research interests lie in understanding the role of synaptic genes in cognition and disease.

Dissecting cognition in rodent models of disease: caveats, challenges and future perspectives Cognitive deficits are a core feature of psychiatric disorders and there is a need to effectively model and assess disease-relevant behavioural and cognitive phenotypes in rodent models. Human disorders are complex, and no single animal model can recapitulate an entire disorder. In recent years, clear recommendations from large research initiatives and frameworks to improve studies in mental health (including Research Domain Criteria (RDoc), Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS), Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia, CNTRICS) have highlighted key cognitive domains impacted in mental health disorders. A key approach towards translation from the lab to the clinic therefore requires the focus of animal studies to also be directed at assessing these same cognitive domains impacted in disorders. Towards addressing this, I will discuss our recent work employing the automated cognitive touchscreen assays as one approach for measuring distinct cognitive domains in rodent models. One key advantage of this system is it allows the assessment of a battery of tests within

the same testing environment to gain a comprehensive cognitive profile of an animal, analogous to that employed in the clinic. Although these assays have their own limitations, they provide a valuable platform from which to gain standardised, objective measures of behaviour. Combing this testing platform with in-depth analysis approaches to more closely mine our behavioural data, our work is providing deeper understanding towards dissecting complex cognitive behaviours in animal models.

2. Associate Professor Tim Karl, Western Sydney University

Tim Karl graduated from the Leipniz University of Hanover (Germany) in 2003 with a PhD in Zoology (Behavioural Neuroscience). Until 2008, he was a postdoctoral researcher at the Garvan Institute working on rodent models for anxiety and schizophrenia. In 2008, Tim Karl established his own research team at Neuroscience Research Australia (NeuRA). His research focused on the neurobehavioural consequences of gene-environment interactions in animal models for schizophrenia and the discovery of new therapeutic targets for Alzheimer's disease. Since 2016, Tim Karl is an Associate Professor for Behavioural Neuroscience at Western Sydney University, where he continues his preclinical research into schizophrenia and Alzheimer's disease. He also investigates the detrimental and potentially beneficial properties of cannabis constituents (in particular, cannabidiol) for brain disorders. Finally, Tim's research aims to enhance the validity of rodent models and the well-being of test animals in medical research by testing the effects of housing conditions, handling procedures, and test protocol specifics on established mouse model phenotypes. Assoc Prof Karl is currently funded by the National Health and Medical Research Council (NHMRC Project Grants & Dementia Research Team Initiative) and the Rebecca L Cooper Medical Research Foundation and has received funding from the Motor Neuron Disease Research Institute of Australia, the Brain and Behavior Research Foundation (USA), the German Research Foundation (DFG), and other funding bodies (e.g. Mason Foundation National Research Program, Ramaciotti Foundation) in the past.

Brain disorders such as schizophrenia are highly complex in nature, affected by a multitude of genetic and environmental factors, and symptom development significantly varies across patients. Furthermore, gender differences are evident in a number of these disorders including schizophrenia. The multi-factorial nature and our limited knowledge about the aetiology of these disorders makes the development of any highly standardised research strategies a challenge. Experimental animal research can provide focused, standardised model systems to increase our understanding of disease aetiology and potentially discover new therapeutic targets. Preclinical research utilising genetically modified mouse models has steadily increased over the last few decades with a particular focus on the analysis of endophenotypes rather than the full spectrum of disease characteristics. However, the majority of these research studies not only ignores the complexity of the human disease in question but also the sensitivity of the model system (i.e. laboratory mouse) to environmental factors. Furthermore, most phenotyping strategies do not adhere to the principles of comprehensive, in-depth testing of e.g. disease-relevant behavioural domains as suggested by J. N. Crawley in the 90s. Thus, I will present data on how core features of established mouse models for schizophrenia can be affected by test protocol specifics, conditions in the home cage, as well as specifics of the cage systems used. I will also provide evidence that multi-tiered, comprehensive test strategies can be more successful than simple approaches in discovering behavioural abnormalities with relevance to the clinical condition.

3. Dr Rachel Hill, Monash University

Dr Hill is an NHMRC Career Development Fellow and head of the Behavioural Neuroscience laboratory, Department of Psychiatry, Monash University. She completed her PhD in 2007 in biochemistry at Monash University and began postdoctoral training in neuroscience at The Burnham Institute, La Jolla, California, before accepting a NHMRC early career fellowship at the Mental Health Research Institute (now Florey Institute). In 2014 Dr Hill became an independent group head at the Florey Institute for Neuroscience and Mental Health, and in 2016 Dr Hill was recruited to Monash University, Department of Psychiatry to head the behavioural neuroscience program. She has made significant contributions to the fields of neuroscience, neuroendocrinology and psychiatry as demonstrated by her high quality / high throughput publication record (46 pubs, >800 citations), several international and national invited seminars and funding success (>$2 million) from national (NHMRC) and international (Brain and Behavior Research Foundation USA) funding bodies. Her research interests lie in behavioural neuroscience, with a particular focus on schizophrenia. She

uses pre-clinical animal models to better understand the pathophysiology of mental disorders such as schizophrenia, and to design and test novel therapeutic strategies. She is investigating the origins of schizophrenia and how best to treat the various symptom presentations. These preclinical studies are aligned with collaborative human genetic studies. The long-term goal is patient-specific treatments that may be guided by both genetic and environmental patient profiles.

Spatial memory can be investigated through a variety of tests on mazes such as the Cheeseboard Maze, and Morris Water Maze, to name a few. While common read-outs such as latency to find the platform/baited well/ are easily assessed and provide a basic measure of spatial memory, other, more complex aspects of performance, including navigation strategy are often overlooked. The current consensus is that spatial memory encompasses two distinct but related reference frames, egocentric and allocentric. I will outline the differences between these reference frames and discuss the merits of placing a stronger emphasis on distinguishing egocentric and allocentric search strategies in spatial memory tests. I will present recent data analysing the effects of a genetic and an environmental risk factor associated with schizophrenia on spatial navigation strategy. We found that both models displayed a switch in strategy from allocentric to egocentric dominance suggestive of impaired allocentric ability. This was associated with reduced hippocampal high frequency, 'gamma' oscillations, providing a functional correlate. Adding translational strength to this interrogation is the finding that people with schizophrenia show allocentric specific deficits and alterations in gamma power. Thus I support incorporation of this analysis when testing animal models with relevance to neuropsychiatric disorders.

4. Professor Darryl Eyles, Queensland Brain Institute

Professor Darryl Eyles is the Neurobiology laboratory director of the Queensland Centre for Mental Health Research based within the Queensland Brain Institute in Brisbane, Australia where he is also a senior faculty member. His research focuses exclusively on the neurobiology behind the non-genetic risk factor epidemiology of severe mental illness such as schizophrenia and autism. In particular his group is attempting to understand how adverse factors during the early (foetal) stages of brain development affect brain ontogeny to produce these disorders. Along with clinical researchers and epidemiologists he has established that low levels of vitamin D at birth increase the risk of schizophrenia in later life in two separate large Danish case/control studies and autism in separate Dutch and Swedish cohorts.

The core symptom clusters of the Autism Spectrum Disorder (ASD) in DSMV are impaired social behavior/communication and repetitive or stereotyped behaviours. Many animal models based on genetic or epidemiologically-proven environmental risk factors for ASD show such deficits. Behavioural neuroscientists often employ tests of social engagement or communication (ultrasonic vocalisations) and measures of stereotyped behaviours, (marble burying) as phenotypic readouts of these 2 major ASD symptom clusters. Any positive signs in such tests is often sufficient for the researcher to claim "face validity" with ASD. But is it? Here I will present convergent data we have obtained from two divergent developmental risk factors for ASD namely Maternal Immune Activation and Developmental Vitamin D Deficiency. Our findings basically align with certain dogmas regarding what other researchers show in their particular models. The question I wish to address in this presentation is whether replication of phenotypes described by others is good enough? What else could be learned from such behaviours by considering the ethology/housing/rearing conditions of the animal being tested? In addition could more relevant information be obtained from such tests if they were reassessed using appropriate ethological cues?

Symposium 3 - Personalised approach to Major Depressive Disorder: the right treatment for the right person

Thursday the 8th of November, 10:50am-12:20pm

Speakers: Micah Kearns, The University of Adelaide; Dr Matthew Knight, The University of Adelaide; and Dr Célia Fourrier, The University of Adelaide

Chair: Dr Adam Bayes, Black Dog Institute and University of New South Wales

Discussant: Professor Bernhard Baune, University of Melbourne

Personalised psychiatry aims to improve the treatment of psychiatric disorders, including Major Depressive Disorder (MDD), by individualising diagnosis and treatment through the identification of biological and clinical predictors of treatment response. This symposium will highlight some current developments in Australian clinical trials and applied machine learning research, which aim to provide more accurate treatment prediction, diagnostics, and prognosis of illness trajectories. The discussion will cover a range of biopsychosocial markers and computational methods that may help to facilitate this goal. This will include the use of machine learning and biomarkers in the prediction of treatment outcomes and relapse in MDD patients and the use of pre-treatment levels of biomarkers (e.g. immune biomarkers, neurotransmitters stress biomarkers and associated single nucleotide polymorphisms) to predict longitudinal response to either psychological or anti-inflammatory treatment of MDD. Professor Baune will then discuss the preliminary findings of these studies in the context of the field of personalised treatment of psychiatric disorders and lead an exciting discussion with the audience.

1. Micah Cearns, The University of Adelaide

Mr Micah Cearns is a doctoral student in the Discipline of Psychiatry, School of Medicine the University of Adelaide. His research focusses on the optimization of machine learning models in the prediction of treatment response in mood disorders. Mr Cearns has also completed an honours degree in psychology, focussing on category learning.

Machine learning (ML) models can learn what combinations of variables are optimal for a classification problem without the need for a-priori interaction specification. This task is carried out through the optimization of an objective function (e.g. maximising area under the curve (AUC) whilst penalizing a model to minimize overfitting on unseen data). Due to this ability, evidence suggests that ML may be effective for the diagnosis of complex traits and the personalisation of treatment through trajectory and treatment prognosis. For example, Chekroud *et al*. trained gradient boosted machines with data from the STAR-D cohort to predict response to Dulexotine in major depressive disorder (MDD) patients from COMED, attaining an AUC of 58. Further, Koutsouleris et al., successfully used support vector machines to predict 4 and 52-week outcomes on the global assessment of functioning in patients with first episode psychosis, attaining an AUC of 72.1 and 71.1, respectively. However, biomarkers were not integrated into either analysis, suggesting the potential for further increases in AUC with multimodal approaches. To investigate this potential in MDD, we have conducted diagnostics using ML and a set of biomarkers containing voxel-based morphometry data, a serum panel of 15 markers with tentatively established relationships to MDD, electrocardiography data, and the top 44 variants from the recent PGC mega-analysis. Further, using the same

biomarkers in unison with a range of clinical data, we've trained a range of ML models to predict relapse in a cohort of patients hospitalized for MDD. Preliminary results from these works will be presented.

2. Dr Matthew Knight, The University of Adelaide

Dr Matthew Knight completed his PhD in cognitive psychology at Flinders University. His doctoral research focussed on the role of working memory and interactivity (active control vs. passive observation) in map learning. The results demonstrated that active control of map exploration is not always beneficial to spatial memory, and that passive observation may be superior in highly demanding scenarios. It was also shown that map learning is reliant upon verbal processing and executive functioning, as opposed to visuospatial processing alone. Dr Knight is currently a post-doctoral research officer in the Discipline of Psychiatry, School of Medicine, at The University of Adelaide. His present research involves the development of a psychological treatment designed to improve cognitive, social, and emotional functioning in patients with Major Depressive disorder.

Major Depressive Disorder (MDD) is associated with psychosocial dysfunction in domains of occupational functioning, daily autonomy, interpersonal relationships, and self-perceived quality of life. Present treatments for MDD focus primarily on remediation of mood symptoms, resulting in psychosocial disability often persisting beyond the acute stage of illness. The CERT-D clinical trial, currently underway at the University of Adelaide, evaluates a treatment which targets psychosocial dysfunction in MDD patients. The CERT-D treatment involves participants completing training tasks designed to improve three domains which underly adaptive psychosocial functioning; cognition, emotion processing, and social cognition.

It is possible that treatment of psychosocial dysfunction will be improved by assessing participants' baseline profile of impairment, and personalising treatment plans to emphasise those domains which are most impaired. In the CERT-D study, the personalised approach is evaluated in comparison to a standard treatment which does not consider individual profiles of baseline impairment. In addition, the CERT-D study measures baseline levels of immune biomarkers (e.g., TNF-alpha and CRP), neurotransmitters, and stress biomarkers (e.g., BDNF, CRF) plus corresponding single nucleotide polymorphisms, to determine whether these markers can predict longitudinal treatment response, or whether biomarkers are sensitive to change over time owing to psychological treatment. This design enables evaluation of the efficacy of personalised psychological treatment of psychosocial dysfunction in MDD.

3. Dr Célia Fourrier, The University of Adelaide

Dr Célia Fourrier is a research officer in the Discipline of Psychiatry, School of Medicine, at the University of Adelaide. She completed her PhD in Bordeaux, France, where she investigated the role of neuroinflammation in emotional and cognitive alterations associated with obesity. She showed that inflammation, and particularly TNF-α, could be an important target in the treatment of mood disorders in obese individuals (Fourrier et al, 2018; Fernandez de Cossio et al, 2018). In addition, she investigated the effect of nutritional interventions with specific nutrients (i.e. n-3 polyunsaturated fatty acids and antioxidants) on metabolic, mood and cognitive alterations in inflammatory conditions (Larrieu et al, 2014) and on the regulation of inflammatory processes in the brain (Fourrier et al. 2017). Now, her research activities in the Discipline of Psychiatry encompass a new approach to personalised psychiatry with a focus on the role of the immune system in psychiatric disorders. She coordinates a clinical trial that investigates the efficacy of

using an antidepressant augmented with an anti-inflammatory medication in the treatment of major depressive disorder.

In patients with Major Depressive Disorder (MDD), antidepressant response and remission rates are low, highlighting the need for new treatment approaches. Recently, the abundant literature linking inflammatory processes and depressive symptoms have led to the hypothesis that selecting treatment for MDD based on the patient's inflammatory status could be a promising strategy to improve outcomes in patients suffering from MDD. The aim of the randomized control trial that will be presented is to investigate the antidepressant efficacy of the combined treatment of MDD with antidepressant medication plus anti-inflammatory medication in individuals with raised inflammation levels (C-reactive protein levels). Study participants assigned either into a "Depression with inflammation" stratum (CRP levels > 3 mg/L) or into a "Depression without inflammation" stratum (CRP levels ≤ 3 mg/L) randomly receive either antidepressant medication plus anti-inflammatory medication or antidepressant medication plus placebo for 6 weeks. For the first time, this study prospectively tests the efficacy of an antidepressant plus anti-inflammatory augmentation based on baseline inflammatory maker levels in MDD using a randomised controlled trial design. The current study will generate novel evidence for biomarker based personalized antidepressant treatment selection based on patient inflammatory status prior to treatment.

Special session – Early Career Researchers

Wednesday the 7th of November, 4:00pm-5:00pm

Chair: Alice Petty, Queensland Brain Institute, University of Queensland

BPA-ECRN Inaugural Travel Awardee Report

Presented by Kyna-Anne Conn, PhD Candidate, Queensland Brain Institute, University of Queensland

NHMRC changes and implications for ECRs, alternate avenues of funding and career trajectories

Speakers/Discussants:

Professor Darryl Eyles, Queensland Brain Institute, University of Queensland

Associate Professor Jee Kim, Florey Institute for Neuroscience and Mental Health, University of Melbourne

Dr James Kesby, Queensland Brain Institute, University of Queensland

Gareth Rees, Senior Research Grants Officer, Flinders University

Special symposium - Presentations by recipients of Neuronal Signalling Travel Awards

Thursday the 8th of November, 2:20pm-3:00pm

Chaired by Samuel Millard, University of Wollongong

Developmental Vitamin D-deficiency affects DNA methylation and midbrain development

Renata Pertile, Xiaoying Cui, Bellinda Yin, Xiang Li, Darryl Eyles

Queensland Brain Institute

Epigenetic events are critical for normal brain development. Dysregulation of DNA and histone methylation has been found in both the peripheral blood and post-mortem brain of patients with schizophrenia. We have shown in humans that the absence of vitamin D during gestation increases the risk of schizophrenia in offspring, and impairs various aspects of brain development in rodents. Considering the substantial difference between sexes on the prevalence and severity of schizophrenia, the aim of this study was to identify the epigenetic effects of vitamin D deficiency on the midbrain of males and females early in gestation.

We used DA-rich midbrain tissue from the well-established developmental vitamin D (DVD)-deficiency rat model at embryonic day 14 - a critical time point in the differentiation of embryonic dopaminergic neurons. We analysed the expression of several genes that code for epigenetic enzymes using quantitative PCR. We also assessed the accumulation of DNA methylation using dot blot against 5-methylcytosine in midbrain from DVD-deficient and control rat embryos.

Our results show that DVD-deficiency significantly increases the expression of the DNA methyltransferase DNMT3A in the midbrain of embryonic day 14 rats. However, the effects of DVD-deficiency were more profound in males; DNMT3A gene expression was 72.5% higher in male DVD-deficient embryos compared to controls, and 37.5% higher in DVD-deficient female embryos compared to controls. The DNA methylation analysis corroborates these results, with DVD-deficiency resulting in increased levels of methylated DNA in the midbrains of males when compared to controls. There was no significant difference in DNA methylation between female DVD-deficient and control embryos.

These results suggest that DVD-deficiency may modulate gene expression in the midbrain via epigenetic mechanisms in a sex specific manner. DNMT3A is highly expressed during embryonic brain development and is critical for neurogenesis, neuronal maturation and synaptogenesis. These findings therefore suggest that DVD-deficiency may alter the way early DA neurons develop via epigenetic processes and have sex-specific effects on the development of the dopaminergic system. This has profound implications for understanding the aetiology of a range of disorders of the DA system which demonstrate sex differences, including schizophrenia.

The author of this abstract was a recipient of a $250 Neuronal Signalling Travel Award

Glutamate levels in the anterior cingulate cortex are associated with schizotypal personality traits and moderated by childhood trauma severity

Yann Quidé, Martin Wilson, Stephen J. Wood, Melissa J. Green

School of Psychiatry, University of New South Wales (UNSW), Sydney, Australia; Neuroscience Research Australia, Sydney, Australia; Centre for Human Brain Health, School of Psychology, University of Birmingham, UK; Orygen, the National Centre of Excellence in Youth Mental Health, Melbourne, Australia; Centre for Youth Mental Health, University of Melbourne, Australia; School of Psychology, University of Birmingham, UK; School of Psychiatry, University of New South Wales (UNSW), Sydney, Australia; Neuroscience Research Australia, Sydney, Australia

Schizotypal personality characteristics are associated with disturbed neurochemistry in the anterior cingulate cortex (ACC) among healthy individuals. Childhood trauma exposure is associated with similar aberrations in ACC neurochemistry and, importantly, with the development of schizotypal traits. It is therefore possible that childhood trauma exposure might moderate relationships between ACC neurochemical integrity and schizotypal personality traits.

In a sample of 53 healthy individuals, childhood trauma exposure was measured using the Childhood trauma Questionnaire (CTQ), schizotypal personality was assessed using the Schizotypy Personality Questionnaire (SPQ) and magnetic resonance spectroscopy (MRS) indexed key metabolites in the ACC. First, using multiple hierarchical linear regression, we identified the ACC metabolite peaks associated with schizotypal traits (SPQ total score). Second, we investigated the role of childhood trauma (CTQ total score) as a moderator of the significant associations between SPQ Total scores and ACC metabolites.

Reported relative to the creatine (Cr) peak, the ACC peak of glutamate (Glu/Cr; Standardised β=0.319, t=2.103, p=0.042), glutamate+glutamine (Glx/Cr; Standardised β=-0.414, t=-2.778, p=0.008) and glutathione (GSH/Cr; Standardised β=-0.230, t=-2.111, p=0.041) were significantly associated with SPQ Total score. The moderation analyses indicated that childhood trauma was a significant moderator of the association between Glu/Cr (but not Glx/Cr of GSH/Cr) and SPQ Total score (B=0.986, t=2.160, p=0.037). In particular, increased Glu/Cr was associated with greater SPQ Total scores in individuals exposed to high levels of trauma (B=17.173, t=2.249, p=0.030), but not in individuals exposed to low levels of trauma (B=-7.937, t=-1.050, p=0.300).

These preliminary findings confirm the involvement of ACC glutamate in the development of schizotypal traits, consistent with previous findings reported in patients with schizophrenia. Importantly, this association was moderated by childhood trauma severity, indicating that childhood trauma survivors would benefit from early trauma-focused interventions known to normalise ACC morphology, function and neurochemistry.

The author of this abstract was a recipient of a $250 Neuronal Signalling Travel Award

Maternal Methadone Treatment: Behavioural and Cognitive Deficits in Adolescent Rat Offspring

Katrina Bird, Ian M. Wright, Jennifer Wilkie, Samuel J. Millard, Kelly A. Newell, Jeremy S. Lum

Illawarra Health and Medical Research Institute, Wollongong, NSW, Australia; School of Medicine, Faculty of Science, Medicine and Health, University of Wollongong, NSW, Australia

Opioid use during pregnancy has risen dramatically in recent years, reaching epidemic proportions. Methadone, a synthetic μ-opioid receptor agonist, is the most commonly prescribed medication for the treatment of opioid dependence. Due to its lipophilic nature, methadone can readily transverse the placenta, exposing the fetus to undesirable and deleterious effects at a critical period of brain development. Clinical studies thus far indicate that in utero exposure to opioids adversely affects a number of behavioural and cognitive parameters, including learning and memory. Given these findings, it is imperative to study the extent to which this agent influences adolescent offspring behaviour.

Adult female Sprague-Dawley rats were treated with vehicle (0.2% saccharin w/v) or methadone (30 mg/kg/day; 0.2% saccharin w/v) via drinking water for two weeks prior to conception, and throughout gestation and lactation. At postnatal (PN) day 35, rat offspring underwent a series of behavioural assessments, including open-field testing (OFT), novel object recognition (NOR) and rewarded T-maze alternation to examine locomotor activity, anxiety-like behaviour, and short-term recognition and working memory.

Vehicle- and methadone-treated rats displayed no significant differences in locomotor activity in the OFT. However, methadone-exposed offspring spent more time in, and displayed a greater number of entries into, the centre of the open-field arena, inferring reduced anxiety-like behaviour. In addition, methadone-treated offspring displayed significant recognition memory deficits when likened to their non-exposed counterparts, as measured using the NOR test. Furthermore, in the rewarded T-maze alternation task, the percentage of correct entries obtained during training was significantly lower in methadone-exposed females, with no differences detected upon testing. These results indicate that rewarded T-maze acquisition was impaired in methadone-exposed female rats.

These findings suggest that prenatal methadone exposure produces detrimental effects on adolescent rat offspring behaviour, namely recognition memory and learning. These novel results provide insight into the long-term consequences of maternal methadone treatment and allude to the need for additional research investigating these alterations. Furthermore, this study may aid in the identification of new effective treatments for opioid-dependent pregnant women and their fetuses.

The author of this abstract was a recipient of a $250 Neuronal Signalling Travel Award

Q&A session - Biomarker discovery in psychiatry: fact or fantasy?

Thursday the 8th of November, 3:00pm-4:15pm

Speakers: Associate Professor K. Oliver Schubert, Professor Bernhard Baune and Professor Brian Dean

Discussant: Professor Peter Hoffmann

Chair: Professor Bernhard Baune

This session addresses important questions about the "valley of death" in biomarker research and the lack of translatable results in psychiatry. In this discussion, a systems biology approach that combines and integrates genomics, transcriptomics and proteomics is a proposed approach for a mechanism based biomarker discovery (Oliver Schubert). Furthermore, we address the important translational question of how such a biomarker can be validated across disease models and how it can be validated in randomised clinical trial settings as a marker of disease progression and a marker of treatment response (Bernhard Baune). Finally, we provide novel insights into the attempt to devise clinically useful tools to aid in managing people with psychiatric disorders and data underpinning such an approach to developing a tool will be presented and reviewed (Brian Dean). Hence, this session travels the entire road from a system-biology based discovery approach, to a biological validation and clinical validation in clinical trial settings and to the technical side of tool development and tool testing based on research findings. This symposium will provide insights into how competitively funded research can lead to discovery of clinically relevant mechanisms and biosignatures that may lead to the development of clinically usable biological tests. Importantly, the topic of the symposium will be controversially discussed (discussant Peter Hoffmann) to raise the question whether biomarker discovery in psychiatry is fact or fantasy.

1. Associate Professor K. Oliver Schubert, The University of Adelaide

Oliver Schubert is a Psychiatrist at the Northern Adelaide Mental Health Services and an Associate Professor at the Discipline of Psychiatry at the University of Adelaide. He trained in Medicine in Freiburg, Germany, and in psychiatry in Dublin, Ireland. He completed a PhD in psychiatric proteomics with Professor David Cotter at the Royal College of Surgeons in Ireland. Since moving to Australia in 2012, he has been studying the molecular underpinnings of mood- and psychotic disorders at the University of Adelaide, and is employing genetic, transcriptomic, and proteomic strategies towards biomarker development for diagnostic and therapeutic subtypes of psychiatric illnesses. He has a clinical special interest in severe mental illness in young people.

In order to accelerate the understanding of pathophysiological mechanisms and clinical biomarker discovery in psychiatry, approaches that integrate multiple –omics platforms are needed. This presentation introduces a workflow that investigates a narrowly defined psychiatric phenotypes, makes use of the potent and cost-effective discovery technology of gene expression microarrays, applies Weighted Gene Co-Expression Network Analysis (WGCNA) to better capture complex and polygenic traits, and finally links gene expression findings to the genetic and the proteomic levels. To illustrate the effectiveness of the workflow, examples exploring the phenotypes of cognitive dysfunction in major depressive disorder (MDD), and of lithium response in bipolar disorder (BD) are given. The examples demonstrate that that functional analysis of multi-omics data has the potential to point to cellular mechanisms and candidate biomarkers for complex psychiatric traits.

2. Professor Bernhard Baune, The University of Adelaide / The University of Melbourne

Bernhard Baune (PhD, MD, MPH, FRANZCP) is Professor of Psychiatry and holds the position of Chair of Psychiatry and Head, Discipline of Psychiatry, the University of Adelaide, Australia. He leads an inerdisciplinary research Program into Personalised Psychiatry, heads the Psychiatric Biomarker Centre and has developed the Psychiatric Clinical Research Facility (CRF) at the University of Adelaide. Bernhard Baune's research focusses on Personalised Psychiatry, Molecular Psychiatry, Experimental Psychiatry and Neuroimmunology. He has a particular interest in the severe course of mental illness and areas of major research activity include the clinical and neurobiological foundations of treatment response

and recovery. Bernhard Baune's research aims at the discovery of biological mechanism and related biomarkers that underpin the course and response to treatment of severe mental illness. Prof. Baune designs and conducts personalized randomized clinical trials that take clinical and biological information into account to inform treatments. He is developing novel treatments for improving emotion processing, cognitive function and functional outcomes in mood disorders. His work is supported by the National Health and Medical Research Council, Australia and other national and international funding bodies. Bernhard Baune currently leads an international study on the genomics of cognitive function in depression and directs a consortium on the genomics of severe depression and response to ECT in affective disorders. He has published more than 430 peer-reviewed articles, reviews and book chapters, edited several text books in Psychiatry and he is member of numerous editorial boards of international Journals in Psychiatry and related fields.

Translation of basic science research into human disease models of mental illness is an important but highly challenging first step for translation. Most often, clinical application of basic science in a sense of delineating a clinical mental disorder by its neurobiology and informing treatment decisions for psychiatric disorders by using biomarkers is practically non-existing. Among several reasons, biomarker validation is highly challenging and replication in independent samples is often failing or non-existing. Firstly, replication of prediction of treatment outcomes by using a biomarker requires large samples, comparable outcomes and similar methodological approaches including sufficient statistical power. These requirements will be reviewed in this presentation. Secondly, biological validation of a biomarker is an important step in underpinning the link of a biomarker to an underpinning biological mechanism. The use of different disease models (e.g. blood based biomarker to be tested in iPSC) for biological cross-validation of a biomarker and a related mechanisms presents as a promising route for biomarker validation. In this presentation, the view will be taken that a biomarker should be related to a disease mechanisms or to a mechanisms of treatment response. Thirdly, the important question of clinical validation of a biomarker will be discussed in terms of requirements for study designs of randomised controlled trials.

3. Professor Brian Dean, Florey Institute for Neuroscience and Mental Health / CMH Swinburne University

Brian Dean is Head of the Molecular Psychiatry Laboratory and Deputy Director of the VBBN at the Florey, Professorial Research Fellow at the Centre for Mental Health, Swinburne University and Honorary Professorial Fellow in the Department of Florey, University of Melbourne. Dean obtained a Doctoral Degree from the University of Melbourne since which he has sought to understand the causes of psychiatric disorders so as advance the approaches used to manage the treatment of people with such disorders. Hence, in over 240 peer reviewed publications there are significant bodies of work on understanding the role of muscarinic receptors in the aetiologies and treatment of schizophrenia and the role of cytokine-regulated pathways in the aetiologies of schizophrenia and mood disorders. His laboratory is developing diagnostic tests that will assist in the clinical management of psychiatric disorders. Dean is a Fellow of the Royal Society of Biology and the CINP and has presented the University of Melbourne Beattie Smith Lecture and the ASPR Lilly Oration. Dean is the Treasurer of the CINP, a Councillor of the Asian College of Schizophrenia Research (ACSR) and a Board Member and Chairman of the SAC of the Rebecca Cooper Medical Research Foundation. He was the Inaugural President of Biological Psychiatry Australia, has been Secretary of the ASCR, a Board member of the Asian College of Neuropsychopharmacology and President of the Melbourne Chapter of the Society for Neuroscience. He currently serves on 6 Editorial Boards and provides Ad Hoc Reviewer for 25 Journals.

Developing clinically useful tools to aid in the management of human disorders has relied on a growing understanding of the aetiology of these disorders and the innovative use of emerging technologies. An example of the use of emerging technologies to aspects of both the aetiology and treatment of a disorder in psychiatry was the use of PET neuroimaging to show the difference between percent blockade dopamine D2 receptor by antipsychotic drugs to gain optimum antipsychotic effect and that which used extra-pyramidal side effects [1]. However, the cost of such analyses was too high to allow wide-spread clinical use. More recently, a diagnostic test for schizophrenia was launched by Veripsych [2] but the complex nature of this test meant pricing was too high to allow a widespread uptake of the technology. My laboratory has utilised innovative bio-statistical approaches to analyse transcriptomic data to allow the separation of subjects with schizophrenia from bipolar disorder and both disorders from controls us a small sample

of blood. Discussions with an industry partner suggests, based on a market analyses, technology could be developed to cost this test at ~ US$ 100. In this presentation, lessons learned from attempts to devise clinically useful tools to aid in managing people with psychiatric disorders will be used and data underpinning our approach to developing such a tool will be reviewed.

Data blitz 1

Wednesday the 7th of November, 10:00am-10:30am

Chaired by Christin Weissleder, NeuRA

Synergistic effects of maternal immune activation and adolescent cannabinoid exposure on schizophrenia-related behaviour and auditory processing responses in rats

Ariel Dunn, Lauren Harms, Abbey Mateer, Ross Fulham, Gavin Cooper, Juanita Todd, Deborah Hodgson, Patricia Michie

University of Newcastle

The development of animal models that reliably recapitulate features of schizophrenia is essential for understanding the neurobiology of the disorder, as well as the preclinical development of new treatments. The neurodevelopmental multiple hit hypothesis suggests that schizophrenia is not caused by one factor alone, but rather a combination of risk factors across a lifetime. This series of studies investigated the impact of maternal immune activation (MIA) during prenatal life combined with a second 'hit' of adolescent cannabinoid exposure (ACE) on schizophrenia-related behavior, behavioural pharmacology and auditory processing responses commonly altered in schizophrenia.

Pregnant Wistar rats were exposed to either Poly(I:C) (MIA) or saline during late gestation (day 19). Offspring were then exposed to HU-210, a synthetic cannabinoid (ACE), or vehicle for 14 days during early adolescence. A cohort of adult animals underwent surgeries to implant skull electrodes to assess auditory processing responses using EEG, similar to the human mismatch negativity. A separate cohort of rats were tested on a variety of behavioural tasks, and another for behavioural pharmacology, or sensitivity to drugs such as MK-801 and amphetamine.

In the assay of mismatch responses, all rats exhibited repetition suppression, or decreased responses to repeating stimuli (neural adaptation). Two-hit animals (MIA-ACE) had reduced suppression responses compared to controls (CON-VEH), with the largest reductions in two-hit females. Prepulse inhibition and social recognition were reduced in two-hit females (MIA-ACE) versus controls (CON-VEH). Two-hit females (MIA-ACE) also had increased marble burying compared to females exposed to ACE alone. Similarly, female animals in all treatment groups travelled significantly less than controls following MK-801. No significant effects of MIA or ACE were observed in males for any behavioural task or behavioural pharmacology.

Our findings suggest that while MIA and ACE do have some separate effects, the largest effects in auditory processing, behavior and behavioural pharmacology are observed in the two-hit group, and are largely restricted to females. Previous work from our laboratory and others show that exposure to MIA produces schizophrenia-like alterations predominately in male animals. Given this and the lack of alterations in females in the single risk factor model, it is suggested that exposure to ACE and its interaction with MIA may have protective effects in males, but have additive or synergistic effects in females to exacerbate schizophrenia-like alterations.

Enhanced Dopamine in the Prodrome of Schizophrenia; A Novel Animal Model

Alice Petty, Dr. Xiaoying Cui, Prof. Deniz Kirik, Dr. Yas Tesiram, Dr. Oliver Howes, Prof. Darryl Eyles

The Queensland Brain Institute (UQ); BRAINS Unit, Lund University, Sweden; The Centre for Advanced Imaging, UQ; King's College London, UK; Queensland Centre for Mental Health Research (Wacol)

Although there are many useful animal models of schizophrenia, none so far have replicated perhaps the strongest neurochemical finding in the clinical population: increased synthesis and release of dopamine (DA) in the dorsal striatum (DS). A greater understanding of the molecular mechanism behind this clinical pathology might suggest novel therapeutics. We developed an animal model - Enhanced Dopamine in the Prodrome of Schizophrenia ("EDiPS") – to understand this mechanism. EDiPS also incorporates the potential to examine the course of schizophrenia, from the prodrome to the full disease. This could be crucial for studies of intervention.

We injected a viral vector coding for TH and GCH1 - critical DA-synthesis enzymes – into the pars compacta of P35 rats. These enzymes are transported to the DS, where they increase the capacity for DA synthesis. To confirm a schizophrenia-like phenotype, we assessed PPI, amphetamine(AMPH)-induced locomotion, and social interaction. To unpick the neurobiology underlying this model, we performed triple-probe microdialysis and 1H-MRS in separate cohorts. For both techniques, the DS, nucleus accumbens (NAc) and pre-frontal cortex (PFC) were assessed at baseline, after 0.6mg/kg AMPH, and finally after KCl (for microdialysis only). The locomotor response to quinpirole was also assessed.

EDiPS animals display deficient PPI, increased AMPH-induced hyperlocomotion, and a social novelty deficit. Microdialysis indicates increased DA turnover and increased levels of 5-HT at baseline, selectively in the DS of EDiPS animals. The 5-HT metabolite 5-HIAA was increased in all brain regions. EDiPS animals show increased AMPH-induced DA release in the DS and, to a lesser extent, the NAc, although KCl-induced DA release was unaffected. 1H-MRS indicates that EDiPS animals have an altered glutamine and NAA response to AMPH, specifically in the DS. EDiPS animals demonstrate normal responses to pre- and post-synaptic doses of quinpirole, suggesting normal D2/D3 receptor function.

This novel animal model successfully recapitulates the "positive" symptoms of schizophrenia. This model could therefore be crucial in understanding the mechanism by which increased pre-synaptic DA synthesis in the DS might result in the expression of schizophrenia phenotypes. The changes in the serotonergic and glutamatergic systems resulting from this pre-synaptic dopaminergic manipulation suggest that the complex interactions between these neurotransmitters may be key to understanding the neuropathology of schizophrenia. This model can also now be used to investigate the progressive onset of these abnormalities, and to trial new therapies to prevent or delay the onset of schizophrenia.

Postnatal developmental trajectory of dopamine receptor 1 and 2 expression in cortical and striatal brain regions

Ellen Rose Cullity, Heather Madsen, Christina Perry, Jee Hyun Kim

The Florey Institute of Neuroscience and Mental Health

Adolescence is a unique developmental period during which numerous biological and physiological changes occur. It is a period of heightened vulnerability for developing mental disorders, including substance use, schizophrenia, and anxiety disorders. Although the biological bases for this vulnerability are uncertain, they could be related to an imbalance in dopamine receptor levels in the adolescent brain compared to the adult brain. The precise postnatal developmental trajectory of these receptors is poorly understood, especially at key cognitive milestones. We hypothesised that adolescents express more cells with dopamine receptor mRNA in discrete neural regions compared to adults.

We used stereological software to investigate the development of dopamine receptor 1 (D1) and 2 (D2) gene-expressing neurons in the prelimbic and infralimbic cortices of the medial prefrontal cortex, insula cortex, dorsal striatum, and ventral striatum at postnatal day (P) 17 (juvenile), P25 (preadolescent), P35 (early adolescent), P49 (late adolescent) and P70 (adult), using transgenic mice expressing green fluorescent protein under the control of the D1 or D2 promoter. We estimated the total number and density of D1 and D2 positive neurons in these regions, as well as the volume of these regions.

D1:D2 density was the most erratic in the insula cortex. Specifically, there was a substantial increase from late-adolescence into adulthood in males but not in females. D1:D2 density in the prelimbic and infralimbic cortices were not affected by age, and in the dorsal and ventral striatum it increased across maturation. Additionally, D1:D2 density in all regions examined was higher in females compared to males.

Taken together, these results suggest that late-adolescent males may be more vulnerable to developmental disorders compared to adult males due to their lower D1:D2 density ratio in the insula cortex compared to adolescent females and adult males. That is, we have identified the insula cortex as a novel locus in which enhanced expression of D1 compared to D2 may be protective against certain developmental disorders.

Chronic β -hydroxybutyrate administration normalises schizophrenia-like behaviours in a pharmacological NMDA hypofunction model

Ann-Katrin Kraeuter, Maarten van den Buuse, Zoltán Sarnyai

Laboratory of Psychiatric Neuroscience, Australian Institute of Tropical Health and Medicine, College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, Queensland, Australia; College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, Queensland, Australia, School of Psychology and Public Health, LaTrobe University, Bundoora, Melbourne, Australia, Department of Pharmacology, University of Melbourne, Australia

Impaired cerebral glucose metabolism has been proposed as an underlying pathophysiology of schizophrenia. We demonstrated that ketogenic diet, which bypasses glycolysis via fatty acid oxidization by producing β-hydroxybutyrate, normalized schizophrenia–like behaviours in an acute murine model of schizophrenia. However, compliance issues and the long-term side effects of ketogenic diet make it essential to develop alternative approaches based on the metabolic mechanism of ketogenic diet. Preclinical trials show that β-hydroxybutyrate effectively treated symptoms of Alzheimers's diseases and Parkinson's disease. Therefore, we hypothesized that chronic administration of β-hydroxybutyrate reduces schizophrenia-like behaviours in an acute NMDA receptor hypofunction model of schizophrenia.

8 week old male C57Bl/6 mice were randomly divided into mice receiving daily intraperitoneal injections of 100 ul/mouse β-hydroxybutyrate (n=24) or saline (n=24) as control for 4 weeks. Throughout the experiment animals were weight weekly. After 3 weeks of treatment animals were tested in the open field and social interaction test. After 4 weeks of treatment animals were examined for sensory motor gating. Thirty minutes prior to behavioural testing animals received either 0.2 mg/kg MK-801 or saline as control. Animals were decapitated the following day after completion of sensory motor gating.

Animals treated with β-hydroxybutyrate had a reduced body weight gain compared to saline-treated animals. β-hydroxybutyrate normalized hyperlocomotion, impaired sociability and sensory motor gating in the acute NMDA receptor hypofunction model of schizophrenia.

Chronic β-hydroxybutyrate administration prevented the expression of key behavioural abnormalities related to schizophrenia in a validated pharmacological animal model. These results raise the possibility that β-hydroxybutyrate might be used effectively in the management of schizophrenia either in conjunction with antipsychotic drugs or possibly as a stand-alone approach, with good efficacy and no metabolic side effects.

Characterising the cognitive consequences of disrupted BDNF-TrkB signalling at parvalbumin-expressing interneurons

Adrienne Grech, Xin Du, Rachel Hill
Monash University

A main symptom category of schizophrenia is cognitive deficits. They emerge early in the disorder and can predict severity and course of illness, but current antipsychotic treatments do not address the cognitive symptoms. Post-mortem studies have found reduced parvalbumin (PV) and Tropomyosin receptor kinase B (TrkB) expression in schizophrenia patient brains (ref). PV, a calcium-binding protein, is expressed on GABAergic inhibitory interneurons. PV-expressing interneurons moderate excitatory cell activity for proper cognitive functioning. They receive neurotrophic support via TrkB, which has an important role in cognition. Thus, we hypothesize that disrupting this pathway will cause cognitive impairment.

The aims of this study were: 1) To generate transgenic mice where 50% of BDNF receptor (TrkB) gene is excised from PV-expressing neurons using the cre-lox recombination system and 2) To investigate the cognitive and behavioural consequences of disrupted BDNF signalling at inhibitory PV-expressing interneurons.

Male and female mice underwent a battery of tests including: Y-Maze, Elevated Plus Maze, Locomotor and Cheeseboard Maze. Immunohistochemistry and confocal microscopy were performed to confirm the percentage knockdown of TrkB receptors on PV-expressing interneurons.

Sex-specific spatial memory impairments were found in male PV-Cre x TrkB heterozygote floxed mice. This group showed no preference for the novel arm in the Y-maze paradigm. Furthermore, male PV-Cre x TrkB heterozygote floxed mice displayed a lack of cognitive flexibility in the Cheeseboard Maze for long term spatial memory. No significant differences were observed in measures of anxiety and activity, indicating that these were not confounding variables for observed cognitive behaviours. The extent of knockdown is currently being confirmed.

We show here male-specific impairments in spatial memory and cognitive flexibility induced by disrupting TrkB expression on PV interneurons. This male specific effect is in line with human data, whereby males with schizophrenia tend to exhibit more severe cognitive impairments. Our previous work suggests that the sex hormone estradiol may provide alternative support to PV interneurons in female mice allowing their memory performance to remain intact. While this was a global disruption to BDNF-TrkB signalling, future work would investigate hippocampal- and prefrontal cortex- specific knockdown. These are key regions for memory processes, and are highly implicated in schizophrenia pathophysiology.

Data blitz 2

Wednesday the 7th of November, 12:20pm-12:50pm

Chaired by Jessica Mills, University of Wollongong

The blood-brain barrier is a viable target to treat depression

Dr Adam K Walker, Emily E Wing, William A Banks, Robert Dantzer

Neuroscience Research Australia; University of New South Wales; Peter MacCallum Cancer Center; Geriatrics Research Education and Clinical Center, Veterans Affairs Puget Sound Health Care System; Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Washington School of Medicine; The University of Texas MD Anderson Cancer Center

Inflammation causes the metabolism of tryptophan into kynurenine, which leads to neurotoxicity and the development of depressive symptoms. Kynurenine is transported into the brain by the large amino transporter LAT1 at the blood-brain barrier. We hypothesized that administration of leucine, which has a high affinity for LAT1, would competitively inhibit the entry of kynurenine into the brain and attenuate the formation of neurotoxic kynurenine metabolites.

Mice were treated with lipopolysaccharide (LPS, 0.83 mg/kg IP) or saline and treated with leucine (50 mg/kg, IP) or vehicle before and 6 h after LPS. Depression-like behavior was assessed 24 -27 h after LPS once sickness behavior had attenuated using sucrose preference and forced swim tests. To confirm that leucine acts by interfering with kynurenine entry to the brain, mice were injected with leucine (300 mg/kg, IP) immediately before kynurenine (33 mg/kg IP). Brain kynurenine and depression-like behavior were measured 3 h later. In vitro modeling was used to examine influx and efflux mechanisms of kynurenine blood-brain barrier transport.

Leucine reduced brain kynurenine levels, blocked LPS-induced depression-like behavior and even caused antidepressant-like effects in control mice. Leucine did not affect sickness behavior or neuroinflammation. Leucine blocked the entry of exogenous kynurenine into the brain and eliminated kynurenine-induced depression-like behavior. In vitro modeling of the blood-brain barrier confirmed that kynurenine competes with leucine for LAT1 for brain uptake. We also revealed that efflux was the dominant direction of kynurenine transport, which is independent of LAT1 and leucine.

This is the first evidence that the blood-brain barrier can be targeted to treat depression. This is the first evidence that leucine works as an antidepressant under conditions of inflammation or not. Our findings show leucine impedes the ability for kynurenine to enter the brain by competing with LAT 1 transport across the blood-brain barrier. The discovery of a predominating efflux mechanism independent of LAT1 and leucine explains why leucine could block brain uptake of kynurenine without affecting brain clearance.

Age at first birth in women is genetically associated with the risk of schizophrenia

Guiyan Ni, Sang Hong Lee
University of South Australia

Studies in epidemiology have shown an increased risk for mental health problems (e.g., schizophrenia) in children born to both younger and older mothers, compared to children of average-aged mothers. However, it is unclear if this phenotypic association is fully explained by psychosocial factors associated with maternal age or if there is a latent genetic mechanism such that mothers at higher genetic risk for schizophrenia tend to have children at an earlier or later age. It is difficult to disentangle between the latent genetic and phenotypic associations in traditional studies where psychosocial factors are prone to be confounded with genetic effects.

In order to detect the latent genetic association, we used a novel design utilizing two independent genome-wide association studies (GWAS), which is free of such confounding between psychosocial and genetic factors. We used Psychiatric Genomics Consortium GWAS data (18,987 schizophrenia cases and 22,673 controls) to generate schizophrenia polygenic risk score (PRS) for each individual in an independent community sample, i.e. the UK Biobank (N=38,892) who had an age at first birth (AFB) record. We tested the genetic association between schizophrenia PRS and AFB, using group mean difference, linear prediction and genetic correlation analyses.

Using the PRS, we compared the mean difference of schizophrenia risk grouped by their AFB and observed a U-shaped relationship attributed to the latent genetic association. Linear prediction analysis showed that schizophrenia PRS could significantly predict AFB (p-value=1.12E-05). The estimated genetic correlation between schizophrenia and the younger AFB is -0.16 (SE=0.04) while that between schizophrenia and the older AFB is 0.14 (SE=0.08). The results show that schizophrenia risk in offspring associated with early and delayed maternal age, observed in epidemiological study, is partly explained by the genetic association between schizophrenia and AFB.

We show the significant genetic overlap between risk of schizophrenia and AFB in women, which suggests that early, and perhaps also late, AFB in women is associated with increased genetic risk for schizophrenia in the UK Biobank sample. These findings contribute new insights into factors contributing to the complex bio-social risk architecture underpinning the association between parental age and offspring mental health.

The role of long non-coding RNA in the development of dopamine systems: A convergent mechanism for schizophrenia

Dr Xiaoying Cui, James Kesby, Darryl Eyles

Queensland Brain Institute, The University of Queensland, Brisbane; Queensland Centre for Mental Health Research, Wacol, Qld 4076, Australia

Schizophrenia is a neurodevelopmental psychiatric disorder, and its aetiology is still poorly understood. PET studies have established that dopamine (DA) uptake and synthesis is increased in schizophrenia, and this is present prior to diagnosis. This suggests that developmental DA dysfunctions may be core to schizophrenia neurobiology. A comprehensive understanding of the developing DA system may be crucial to understanding the origins of this disorder. Long non-coding (Lnc) RNAs are emerging as factors that regulate brain development, and individual lncRNAs such as Hot AIRM1 have been implicated in schizophrenia. However, there is no direct evidence linking schizophrenia-related LncRNAs with DA ontogeny.

We knocked down HOTAIRM1 using RNAi, both in vitro in a human dopaminergic neuroblastoma cell line, and also in vivo in mouse DA progenitors using in utero electroporation. To examine the effect of this manipulation on the ontogeny of the DA system, we used quantitative PCR to examined the expression of DA neuronal markers; neurogenin 2 (Ngn 2), which represents an immature neuron, and tyrosine hydroxylase (TH, a rate limiting enzyme for DA synthesis), a marker of mature DA neurons. The levels of enzymes for DNA methylation and histone methylation were also assessed.

Knocking down HOTAIRM1 led to a reduction of TH and an increase of Ngn 2 in vitro, suggesting that the differentiation of DA neurons was delayed. We also observed a reduction in the vesicular monoamine transporter 2 (VMAT2) and monoamine oxidase (MAOA), proteins for DA packaging and metabolism. Additionally, we showed that reducing HOTAIRM1 led to a reduction of the epigenetic enzymes DNMT3a and JMJD3. This indicates that HOTAIRM1 potentially modulates DA ontogeny via these epigenetic mechanisms. In vivo we further showed that knockdown of HOTAIRM1 within the embryonic mesencephalon also reduced the levels of TH and VMAT2.

Our results indicate that the schizophrenia-related noncoding RNA HOTAIRM1 regulates DA ontogeny both in vitro and in vivo. These findings are crucial since they link an existing potential schizophrenia risk factor (noncoding RNAs) with disruption in a key neurotransmitter pathway implicated in this disorder. Noncoding RNAs are a recently discovered family of molecules that regulate brain development and function. Research on noncoding RNAs is rapidly evolving and represents one frontier of molecular neuroscience. Understanding of the role of LncRNAs in the development of the DA system has implications for schizophrenia and beyond.

Elevation of complement pathway-related transcripts in the midbrain of schizophrenia cases with high cytokine-related inflammatory profiles

Samantha J Owens, Tertia D Purves-Tyson, Cynthia Shannon Weickert

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Schizophrenia disproportionately affects males, with men having increased risk, more severe symptoms and worse prognosis than females. The peak age of onset in males occurs during adolescence to early adulthood which coincides with a rapid increase in testosterone production, suggesting a relationship between adolescent testosterone and disease pathophysiology. Subcortical hyperdopaminergia underlies the psychotic symptoms of schizophrenia and sex steroid hormones can modulate dopaminergic transmission. We aimed to determine whether testosterone modulates sex steroid and dopamine-related mRNAs in the mesolimbic dopaminergic pathway during adolescence via androgenic or estrogenic effects.

Male rats underwent sham surgery (Intact) or gonadectomy at 45 days old, prior to the adolescent surge in testosterone. Gonadectomised rats received a blank implant or sex steroid replacement via silastic implant (n=13-16/group) with testosterone (androgenic and/or estrogenic), dihydrotestosterone (androgenic only) or 17β-estradiol (estrogenic only). Rats were euthanised at 60 days old and brains dissected. Sex steroid-related (androgen receptor, 5α-reductase, estrogen receptor α and aromatase) and dopamine-related (tyrosine hydroxylase, dopamine transporter and dopamine D2 receptor) mRNAs were measured using quantitative PCR in the ventral tegmental area (VTA) and ventral striatum (VS).

Androgen receptor and 5α-reductase mRNAs were unchanged by sex steroid replacement in both regions. Estrogen receptor α [H(4)=11.41, p=0.02] and aromatase [F(4,71)=2.64, p=0.04] were decreased by dihydrotestosterone replacement compared to Intact, gonadectomised and estrogen-replaced rats in the VTA (all p<0.05). Aromatase [H(4)=12.57, p=0.01] was decreased by gonadectomy (p=0.02) in the VS and was further reduced by estrogen replacement (p=0.001) compared to Intact rats. Presynaptic tyrosine hydroxylase and dopamine transporter mRNAs were unchanged by sex steroid replacement. Postsynaptic D2 receptor [F(4, 67)=2.0, p=0.1] was increased by gonadectomy (p= 0.03) which was attenuated by dihydrotestosterone replacement compared to Intact rats (p=0.13).

During adolescence, androgens via androgenic effects may reduce the ability of the VTA to respond to estrogens. We speculate that increasing circulating testosterone levels during adolescence may reduce the neuroprotective capacity of estrogen in the VTA. Androgenic actions may also contribute to maintenance of dopamine D2 receptor levels in the VS during adolescence and changes in androgen levels may be important in altering dopaminergic signalling in the mesolimbic pathway in those developing schizophrenia.

Probabilistic Modelling of Transition to Psychosis Using Clinical, Cognitive and MRI data in the PACE 400 sample

Scott R Clark, Cali Bartholomeusz, John Gillam, Ashley Lin, K Oliver Schubert, G Paul Amminger, Christos Pantelis, Alison Yung, Bernhard T Baune, Patrick D McGorry, Barnaby Nelson, Steven Wood

University of Adelaide, Discipline of Psychiatry, Adelaide, Australia; Orygen, The National Centre of Excellence in Youth Mental Health, The University of Melbourne, Melbourne, Australia; Telethon Kids Institute, Subiaco, Australia; Melbourne Neuropsychiatry Centre, The University of Melbourne and Melbourne Health; Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, United Kingdom; University of Melbourne, Faculty of Medicine, Dentistry and Health Science

Clinical criteria for Ultra-High Risk of psychosis (UHR) show moderate specificity for the prediction of the first psychotic episode (FEP), with an average true positive rate of approximately 30% at 3 years. We have recently developed a multimodal probabilistic modelling approach using the odds ratio form of Bayes' rule that achieved sensitivity=73% and specificity=96% for FEP combining clinical data and biological data. To explore the validity of this approach we built a similar model using cognitive, clinical and MRI data from the Personal Assessment and Crisis Evaluation ('PACE 400') study.

430 patients presenting to a specialist psychosis service in metropolitan Melbourne, Australia were identified as UHR using the Comprehensive Assessment of At-Risk Mental State. Transition to FEP occurred in 114 within 13 years of presentation. Demographic and clinical data were available for the full cohort, cognitive data for 258 and MRI data for 151 cases. Positive and negative likelihood ratios (LRs) for FEP and poor function were calculated for clinical, cognitive and MRI variables with statistically significant receiver operating curves (ROCs). To calculate probability of outcome, LRs were combined using the odds ratio form of Bayes' Rule.

Ninety Nine cases had complete data, 23 transitioned to FEP and 19 had poor functional outcome. A model using significant clinical, cognitive and the top ten MRI predictors rated by AUROC was able to predict transition with a Sensitivity = 69.57%, Specificity = 84.21% and AUROC=0.82. A similar model designed to predict poor function was more sensitive but not specific (Sensitivity=84.21%, Specificity=63.75%, AUROC=0.738). Combining just cognitive assessment and MRI was a more accurate model for the prediction of functional outcomes (Sensitivity=73.68%, Specificity=81.25%, AUROC=0.791).

In a sample enriched by UHR criteria, multimodal modeling using simple Bayesian techniques can improve predictive power. Systematic use of clinical and cognitive assessment followed by MRI may facilitate personalised psychosis prevention strategies considering both risk of psychosis and long term functional outcome.

Data blitz 3

Thursday the 8th of November, 10:00am-10:30am

Chaired by Ilijana Babic, University of Wollongong

Reconciling Mackintosh and Pearce-Hall: Evidence from human electrophysiology

Salvatore Russo, Irina Baetu, Nicholas Burns

School of Psychology, University of Adelaide

Mackintosh (1975) proposed that attention is biased towards stimuli in our environment that reliably predict important outcomes so that we can exploit the information that these cues convey. Conversely, Pearce and Hall (1980) suggested that attention is biased towards cues that have an uncertain relationship with future events so that more information about these currently ambiguous stimuli can be obtained. The aim of this research was to reconcile these seemingly contradictory accounts by measuring attention in human participants while they learned simple cue-outcome relationships.

Participants were trained on a categorisation task where some stimuli were predictive of the correct response while others were non-predictive. The categorisation task was then combined with a dot probe task, in which participants had to respond as fast as possible to the location of a target that appeared randomly (and equally often) over the predictive or non-predictive stimuli. We varied the time between the onset of the categorisation cues and the onset of the target (i.e., the cue-target onset asynchrony; CTOA) to investigate the time course of attention. We obtained behavioural and electrophysiological (EEG) measures thought to reflect attention.

Our behavioural data all suggested a bias in responding towards predictive cues. Participants were faster to respond to targets that appeared over a predictive cue compared to a non-predictive cue. Errors made during the dot probe task suggested that participants were anticipating that the target would appear over a predictive cue. Participants also indicated that they thought the target appeared more often over predictive cues. Our EEG results showed that at short CTOAs it was easier to process the target when it appeared over a predictive cue compared to a non-predictive cue, but at long CTOAs this pattern was reversed.

It appears that predictive cues are preferentially processed as soon as they are perceived, consistent with Mackintosh's theory. However, after processing these predictive cues, attention shifts away from them and towards other stimuli. This shift of attention could allow for other currently ambiguous, but potentially important, stimuli to benefit from further processing, consistent with the Pearce-Hall theory. Our results offer a novel perspective that may help reconcile these two seemingly contradictory theories. This research could be beneficial for understanding clinical disorders characterised by abnormalities in attention, such as addiction, anxiety and schizophrenia.

The author of this abstract was a recipient of a $250 South Australian Student Excellence Award

The mGluR2/3 agonist LY379268 reverses NMDA receptor antagonist effects on cortical gamma oscillations and coherence, but not working memory impairment in mice.

Elysia Sokolenko, Matthew Hudson, Jess Nithianantharajah, Nigel Jones

Department of Medicine (Royal Melbourne Hospital), University of Melbourne, Melbourne Brain Centre, Parkville, Victoria, Australia; Department of Neuroscience, Central Clinical School, Monash University, The Alfred Centre, Prahran, Victoria, Australia; The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Parkville, Victoria, Australia.

Abnormalities in gamma oscillations may underlie cognitive impairment in schizophrenia. Both cognitive impairment and gamma oscillatory disturbances can be induced in healthy people and rodents with the administration of N-methyl-D-aspartate receptor (NMDAr) antagonists.

The aim of the current study was to assess whether a mechanistic relationship exists between the emergence of deficits in working memory and abnormalities in gamma activity following NMDAr antagonism. It was hypothesised that both working memory and gamma disturbances induced by an NMDAr antagonist would be reversed by the metabotropic glutamate receptor type 2/3 (mGluR2/3) agonist LY379268.

C57/Bl6 mice (n=11) were trained to perform the Trial-unique Nonmatching to Location (TUNL) test of working memory. They were then implanted with local field potential (LFP) recording electrodes in the medial prefrontal cortex and dorsal hippocampus. Mice were administered either LY379268 (3mg/kg) or vehicle followed by the NMDAr antagonist MK-801 (0.3 or 1mg/kg) or vehicle prior to testing on the TUNL task or recording LFPs during the presentation of an auditory stimulus.

Treatment with LY379268 prevented the increases in ongoing gamma power and regional gamma coherence induced by MK-801, but failed to improve the auditory-evoked gamma oscillatory deficit. In addition, LY379268 did not restore deficits in working memory, or perseverative behaviour caused by MK-801 in the TUNL task.

We conclude that NMDA receptor antagonism impairs working memory in mice, but that this is not reversed by stimulation of mGluR2/3 receptors. Since elevations in ongoing gamma power and regional coherence caused by MK-801 were improved by LY379268, it appears unlikely that these oscillatory abnormalities are responsible for working memory impairment caused by NMDAr antagonism.

Childhood trauma differentially moderates the association between inflammatory markers and cognitive performance in healthy individuals and psychotic disorders

Elizabeth Llewelyn, Yann Quidé, Chiara C. Bortolasci, Briana Spolding, Srisaiyini Kidnapillai, Oliver J. Watkeys, Sarah Cohen-Woods, Michael Berk, Ken Walder, Melissa J. Green

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Increased peripheral levels of various cytokines and acute phase proteins (inflammatory markers) are associated with cognitive impairment in schizophrenia and bipolar disorder. Exposure to childhood trauma is a risk factor for the development of these disorders and is also associated with increased circulating inflammatory marker levels in both psychotic and non-psychotic populations. It is therefore possible that childhood trauma might moderate the relationship between inflammatory markers and cognition.

Sixty-nine individuals with schizophrenia, 67 with bipolar disorder and 69 healthy controls completed the Spatial Working Memory task (SWMB) from CANTAB and the Trail Making Test B (TMTB). The Childhood Trauma Questionnaire (total score) provided an index of trauma severity. Serum levels of interleukin 6 (IL-6), tumour necrosis factor alpha (TNF-α) and C-reactive protein (CRP) were quantified using ELISA. Within each group, a series of multiple linear regressions were used to identify the associations between cognitive performance and inflammatory marker levels, severity of trauma exposure and their interaction. Moderation (by trauma exposure severity) was tested when significant interactions were observed.

Increased levels of IL-6 and CRP were significantly associated with poorer performance on TMTB in controls. In controls and bipolar disorder, severity of childhood trauma was significantly associated with decreased performance on both SWMB and TMTB. In controls exposed to high levels of trauma, increased levels of IL-6 and CRP were associated with poorer performance on both the SWMB and TMTB. In contrast, increased CRP levels were associated with better performance on the SWMB in schizophrenia exposed to low levels of trauma. Severity of childhood trauma did not moderate the association between inflammatory marker levels and cognition in bipolar disorder.

Increased levels of inflammatory markers were associated with impaired cognition in controls exposed to high levels of trauma. This association existed for individuals exposed to low, but not high levels of trauma in schizophrenia. As the immune and stress systems are closely linked, one potential mechanism underlying these results is a failure to regulate inflammatory markers by glucocorticoids in trauma-exposed individuals. Trauma-focused therapies may assist in normalising cognition in healthy individuals exposed to childhood trauma, while other strategies may be more suitable in schizophrenia. Future studies investigating the relationship between these systems may inform individualised treatment of these heterogeneous disorders.

Comfort Eating in Major Depressive Disorder: Links to Leptin and Ghrelin

Jessica Mills, Theresa Larkin, Chao Deng, Susan Thomas

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Disordered eating, including emotional eating, and food addiction, that is an increased dependency on or intake of highly palatable foods, are prevalent in Major Depressive Disorder (MDD) and comfort eating acting as coping mechanisms for low mood. Dysregulation of the hunger and satiety hormones ghrelin and leptin may contribute to this effect. Our previous pilot investigation identified links between emotional eating, food addiction and leptin in MDD. This current study aims to extend on our previous findings in a larger cohort study by examining these links in relation to both leptin and ghrelin.

Plasma total ghrelin and leptin levels, biometrics and psychopathology were compared between participants meeting the DSM-5 diagnostic criteria for MDD (n = 60) and healthy controls (n = 60). Participants were sub-categorised into those with increased, decreased or unchanged appetite/weight for a comparison by appetite/weight symptom profile. Psychological eating patterns were examined using the Dutch Eating Behaviours Questionnaire, and food addiction was assessed using the Yale Food Addiction Scale.

Emotional and Restrained eating were higher in MDD compared to controls, and higher in females compared to males. All twelve food addiction symptom subscale scores were also significantly higher in MDD, with nineteen (15.8%; 17 MDD) participants meeting the Yale criteria for food addiction. When compared by symptom profile, Emotional eating and all food addiction symptom scores were significantly higher in those with increased appetite/weight compared to decreased or unchanged appetite/weight. Leptin correlated positively with Restrained and Emotional eating, and the Failure to Quit, Continued Use and Adverse Consequences subscales of the YFAS; whereas ghrelin negatively correlated with Restrained eating.

Higher rates of comfort eating and food addiction in MDD compared to controls, and in females compared to males, indicate sex-specific coping mechanisms for depressed mood. Further, higher rates of such behaviours in those with increased appetite/weight suggests that these behaviours are specific to a subset of individuals with MDD; indicating symptom-specific coping mechanisms. Leptin and ghrelin correlated with problematic eating patterns, suggesting a possible role in the development of these behaviours. The results support the need for targeted interventions to prevent adverse consequences of increased food intake, such as weight gain, in MDD.

Polygenic scores for traits of depression predict response to lithium in patients with bipolar disorder

Azmeraw T. Amare, Klaus Oliver Schubert, International Consortium on Lithium Genetics (ConLi+Gen) authors, Thomas G. Schulze, Bernhard T. Baune

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Lithium is a first-line medication for bipolar disorder (BD), but only ~30% of patients respond optimally to the drug. Since genetic factors are known to mediate lithium treatment response, we asked whether polygenic susceptibility to the spectrum of depression traits is associated with treatment outcomes in patients with BD. In addition, we explored the potential molecular underpinnings of this relationship.

Weighted polygenic scores (PGSs) were computed for major depressive disorder (MDD) and depressive symptoms (DS) for BD patients from the Consortium on Lithium Genetics (ConLi+Gen; n=2,586). Lithium treatment outcome was assessed using the ALDA scale. Summary statistics from genome-wide association studies (GWAS) in MDD (130,664 cases and 330,470 controls) and DS (n=161,460) were used for PGS weighting. Associations between depression traits PGSs and lithium treatment response were assessed by binary logistic regression. For functional analysis of findings, we performed a cross-trait meta-GWAS, followed by Ingenuity® Pathway Analysis.

BD patients with a low polygenic load for depressive traits are more likely to respond well to lithium, compared to patients with high polygenic load (MDD: OR 1.64 [95%CI: 1.26-2.15], lowest Vs. highest PGS quartiles; DS: OR 1.53 [95%CI: 1.18-2.00]). Associations were significant for type 1, but not type 2 BD. Functional characterization

implicated voltage-gated potassium channels, insulin-related pathways, mitogen-activated protein-kinase (MAPK) signaling, and miRNA expression.

Genetic susceptibility to depression in BD type 1 patients lower their odds of responding optimally to lithium. Our findings support the emerging concept of a lithium-responsive biotype in BD.

Poster session 1

Wednesday the 7th of November, 1:20pm-2:20pm

Poster 1: Exposure to combination of early and chronic later-life stressors increase anxiety-, depressive-like behaviours as well as Nr3c1 gene expression and altered frequencies of CD4+ T cells in early adulthood

Magdalene C. Jawahar*, Catherine Toben*, Jason Izzo, Kate Pilkington, Bernhard T. Baune

**Equal first authors. Discipline of Psychiatry, Adelaide Medical School, University of Adelaide; Centre for Cancer Biology, SA Pathology and University of South Australia*

Early life stress (ELS) such as childhood maltreatment leads to persistent alterations in stress responsivity and altered immune responses. This 'early-life programming' has long-lasting effects on the developing brain increasing the risk to develop psychiatric disorders when exposed to later-life stressors through adolescence to adulthood. However, the neuro-immune-endocrine mechanisms that lead to the biological embedding of early and later-life stressors during adolescence are not clearly defined. In this study, we utilise a 2-hit stress model to investigate the effect of ELS and subsequent adolescent chronic stress on behavioural and neuroimmune changes in early adulthood.

Maternal separation (MS), an animal model of ELS was conducted for 3 hours between postnatal days (PND) 1-17 and adolescent unpredictable chronic mild stress (adol-uCMS) for 21 days from PND 30 – 51. The study groups were mice exposed to MS only (early-life stressor), adol-uCMS only (later-life stressor), MS+adol-uCMS (2-hit stress) and control (non-stressed). Locomotor, anxiety- and depression-like behaviours were assessed using open field (OF) and forced swim test (FST) between 8-10 weeks followed by neurobiological analyses at 10 weeks, including hippocampal candidate gene expression and immunophenotyping of lymphocytes from the cervical lymph nodes (CLN) draining the brain.

Mice exposed to MS and 2-hit stress showed significantly higher locomotion compared with controls and adol-uCMS only. Furthermore depression-like and anxiety-like behaviours were significantly increased within the adol-uCMS and 2-hit group compared with controls. Although total T lymphocyte numbers were not significantly different but meaningfully decreased across stress groups compared with controls, a significant increase in hippocampal Nr3c1 gene expression was found. While frequencies of naïve CD4+ T cells were significantly increased in cervical lymph nodes, CD4+ T cells expressing early activation marker CD25 were decreased in adol-uCMS and 2hit stress groups when compared with controls.

Our 2-hit animal model suggests there is a cumulative effect of early and later-life stressors on anxiety-, depression-like behaviours in addition to altered neuro-endocrine-immune pathways, as early as adolescence. While MS alone did not alter behaviour and immune cell phenotypes significantly compared to controls it increased susceptibility to later life stressors as seen in the altered frequencies of CD4+ T lymphocyte subsets of the 2-hit stress group. An increase in frequencies of naïve T lymphocytes and decrease in early activated T lymphocytes support the hypothesis of dysregulated CD4+ T cell responses to either uCMS alone or 2-hit stress during adolescence.

Poster 3: The Association Between Blood Haemoglobin and Ferritin and Mental Health and Cognition Outcomes in Iron Deficient Pregnant Women

Chnar Khoshnaw, Bernd Froessler, Natalie Aboustate, Tom Butler, Nicolette Hodyl, Oliver Schubert

Discipline of Psychiatry, University of Adelaide; Discipline of Acute Care Medicine, University of Adelaide; Northern Adelaide Local Health Network, Lyell McEwin Hospital; Robinson Research Institute, University of Adelaide

Iron deficiency (ID) is a common nutritional disorder in pregnancy, affecting up to 30% of pregnant women. ID in pregnancy is associated with adverse health outcomes including perinatal infection, pre-eclampsia, low birthweight and prematurity. Depressive and anxiety symptoms are also common during pregnancy, and pregnant women frequently report poorer cognitive function. The effect of ID on maternal mental health and cognition is incompletely characterised and can affect a woman's quality of life; physical activity, work performance and emotional life. Hence, we aimed to examine the relationship between measures of ID and mental health and cognitive function in iron-deficient pregnant women.

183 iron-deficient pregnant women in their second or third trimester were recruited for this study. Haemoglobin/ferritin measures were obtained from maternal blood at the time of clinical interview. Psychiatric symptoms were assessed using the Hamilton Anxiety and Depression Scale. Cognition function was measured using the THINC-It tool®; Choice Reaction Time (CRT), Digit Symbol Substitution Test (DSST), Trail Making Test (TMT-B), Working Memory Test (N-BACK) and the 5-item Depression of Perceived Deficits Questionnaire (PDQ-5D). Multiple linear regression was used to determine the correlation between Hb/ferritin levels and scores on HAM-D, HAM-A and THINC-it subtests, whilst adjusting for age, education and CRP.

Hb or ferritin levels were not associated with the severity of depressive or anxiety symptoms in iron-deficient pregnant women. However, DSST-Total Correct Numbers, predicted severity of Hb levels, b =.185, t(183)= 2.38, p=.018 with an R2 = .040, as did DSST-Average Completion Time, b=-.206, t(183)= -2.67, p=.008 with an R2 = .042, and planning ability, b=-.185, t(183)= -2.43, p=.016 with an R2 = .065. N-BACK-Average Completion Time, also predicted ferritin scores, b= -.194, t(156)= -2.33, p=.021 with an R2 = .042, We did not find an association between Hb and ferritin levels and other cognition test scores.

Pregnant women with low Hb levels exhibited poor scores on the task performance, reaction time and processing speed. Additionally, pregnant women with low ferritin levels also exhibited poor processing speed. Subjectively, an association was detected between low levels of Hb and poor planning and organization ability. We found no association between Hb or ferritin and depressive or anxiety symptoms in our cohort, indicating that mental health outcomes during pregnancy may be independent of Hb and ferritin levels. The present findings highlight the need for further exploration of the effect of antenatal ID on pregnancy-related cognitive difficulties.

FAY FULLER FOUNDATION

The author of this abstract was a recipient of a $250 South Australian Student Excellence Award

Poster 5: Sources of variation and reproducibility in rodent tests of cognition

Suzanne Alexander, Karly Turner, Thomas HJ Burne
Queensland Brain Institute, Queensland Centre for Mental Health Research

Genetic and environmental conditions are known to alter behavioural outcomes, yet animal models of neuropsychiatric disorders are typically developed using a single strain and standard housing conditions. This study examined two rat strains and the influence of different housing conditions on learning a simple discrimination in an operant chamber. We used two strains of rat, Sprague-Dawley (SD) and Long-Evans (LE), trained in operant chambers on a Signal Detection Task. The aim was to determine potential sources of variation and reproducibility to establish a stable baseline level of responding.

Rats were tested in an operant chamber with either a cue light or an LED screen showing either a signal or non-signal stimlus that cued pellet rewards in either left or right reward receptacles. Adult SD and LE rats were housed under standard or enriched conditions and drawn from two separate cohorts. The source of the SD rats was from ARC for both cohorts, whereas the LE rats were sourced from Monash (cohort 1) or ARC (cohort 2). The measures of interest were number of trials completed in a session and the number of sessions to reach criteria.

After baseline testing we found that enriched LE rats made more responses than standard housed LE rats. By contrast there was no effect of housing in SD rats. We also found a significant interaction between strain and cohort. LE rats from cohort 1 (LE-Monash) outperformed SD rats, whereas LE rats from cohort 2 (LE-ARC) were impaired compared to SD rats. We analysed data for multiple factors including strain, cohort, source, housing and stimulus used and show that the greatest source of variation was explained by the source of LE rats. SD rats had stable levels of performance across all variables

The results of this study demonstrate that SD rats show reliable and repeatable behaviour for a cognitive task using operant chambers. By contrast, LE rats showed highly variable responses that were dependent on housing and, in particular, breeding source. These data go part way to explain a lack of reproducibility across studies, which may be due to a combination of environmental and genetic differences between cohorts. We suggest that researchers need to establish stable baseline levels of responding to facilitate comparisons between studies.

Poster 9: TMS-EEG measures of Dorsolateral-Prefrontal Neuroplasticity as marker of Cognition and Function in Mood Disorders

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Neuroplasticity in the dorsolateral prefrontal cortex (DLPFC) has been associated with impaired cognitive function in Major Depressive Disorder (MDD). Transcranial magnetic stimulation (TMS) and Electroencephalography (EEG) can be used simultaneously as a non-invasive tool for exploring neural activity in cortical networks. Intermittent theta burst stimulation (iTBS) is a form of TMS capable of inducing neuroplastic change (long term potentiation) in cortical networks measured by increase in TMS-evoked potentials (TEPs). We present the development of a study protocol and preliminary data, exploring the feasibility of TMS-EEG measures of DLPFC neuroplasticity as biomarkers of cognition and function in mood disorders.

The study protocol was designed across 3 sessions: an initial TMS titration followed by randomised active-iTBS and sham-iTBS conditions. Clinical assessments included Montgomery and Asberg Depression Rating Scale (MADRS), Brief Psychiatry Rating Scale (BPRS), Young Mania Rating Scale (YMRS), Global Assessment of Functioning Scale (GAF), and Functioning Assessment Short Test (FAST). The TMS-EEG procedure involved locating the appropriate motor cortex coil position, measurement of resting motor threshold (RMT), and stimulation of DLPFC using single-pulse TMS (to probe neuroplasticity) and iTBS (to induce neuroplasticity).

Thirty-three participants expressed interest; 5 met exclusion criteria, 10 did not follow up after further information. Eighteen participants (8 depressed, 6 controls, 4 bipolar) consented to participate in the experiment (17 TMS/EEG, 1 EEG only). Seven of 18 did not complete TMS: 3 were excluded for high RMT (>85% maximum stimulator output); 2 did not tolerate TMS; 1 risk of high MADRS score and chronic suicidal ideation; 1 reported adverse effects following titration (headache, mood fluctuation). Eleven participants completed the experiment (5 depressed, 2 bipolar, 4 controls). RMT did not differ significantly across groups (depressed 60%, controls 63.5%, bipolar 67%).

Most participants that consented to TMS-EEG were comfortable with TMS and finished the full study. The complexity of the protocol and technical difficulties occasionally required participants to be sitting for long durations (up to 4 hours with breaks). Time required to determine motor cortex coil position and RMT varied significantly, ranging from minutes to nearly an hour in one case (longer in participants that were more restless). The addition of MRI-guided neuronavigation could significantly improve the efficiency and tolerability of the protocol. An overall lesser duration for TMS-EEG processes would be beneficial in improving study design.

Poster 11: Maternal fluoxetine treatment alters glucocorticoid and glutamatergic receptors in the amygdala of adolescent offspring, in a sex-dependant and strain-specific manner

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Approximately 10% of pregnant woman are prescribed antidepressant drugs such as the selective serotonin reuptake inhibitor (SSRI), Fluoxetine (FLX; Prozac), for the treatment of depression. Emerging evidence suggests maternal FLX treatment can increase the risk of neurodevelopmental disorders in offspring. We have recently shown in an animal model that maternal FLX treatment increases anxiety-like behaviour in adolescent offspring. Glutamatergic and glucocorticoid signalling in the amygdala are both central to mediating anxiety-like behaviour. Therefore, this study aimed to determine if the glucocorticoid receptors and the glutamate NMDA receptor subunits were altered in the amygdala following developmental FLX exposure.

Wistar-Kyoto (established model of depression) and Sprague-Dawley (healthy model) rodent dams were treated with 10mg/kg/day FLX from gestational day (GD) 0 to postnatal day (PND) 14. Offspring were euthanised at adolescence (PND42) and the amygdala dissected. Immunoblotting was used to examine GR isoforms (GRα and GRβ) and NMDA receptor subunits (NR1, NR2A and NR2B) in male and female offspring. Two-way ANOVAs were used to determine the effects of FLX exposure and rat strain on protein measures in both sexes.

Male WKY offspring showed increased GRβ and NR2B subunit expression compared to SD offspring, while FLX exposure in the WKY strain returned GRβ and NR2B levels back to SD control levels. FLX exposure did not influence GR expression in the amygdala of female offspring, however WKY offspring showed reduced GRα compared to SD offspring. FLX exposure increased NR1 and NR2A subunit levels in the amygdala of both male and female offspring, but only in the SD strain.

This study highlights the sex specific effects of maternal FLX treatment on offspring glucocorticoid and glutamate receptor biology in the amygdala, and shows the potential protective effect of this exposure on GRβ and NMDA subunits in a depressive strain. This is in contrast to our previous reports in the prefrontal cortex, where FLX exposure potentiated the effects of maternal depression on glutamate NMDA receptor subunit expression in male adolescent offspring. While this study provides important insight into potential effects of maternal FLX on the amygdala, it's important for future studies to consider the functional and anatomical heterogeneity of this region.

Poster 13: Testosterone modulation of sex steroid and dopamine-related mRNAs in the mesolimbic pathway during adolescence

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Schizophrenia disproportionately affects males, with men having increased risk, more severe symptoms and worse prognosis than females. The peak age of onset in males occurs during adolescence to early adulthood which coincides with a rapid increase in testosterone production, suggesting a relationship between adolescent testosterone and disease pathophysiology. Subcortical hyperdopaminergia underlies the psychotic symptoms of schizophrenia and sex steroid hormones can modulate dopaminergic transmission. We aimed to determine whether testosterone modulates sex steroid and dopamine-related mRNAs in the mesolimbic dopaminergic pathway during adolescence via androgenic or estrogenic effects.

Male rats underwent sham surgery (Intact) or gonadectomy at 45 days old, prior to the adolescent surge in testosterone. Gonadectomised rats received a blank implant or sex steroid replacement via silastic implant (n=13-16/group) with testosterone (androgenic and/or estrogenic), dihydrotestosterone (androgenic only) or 17β-estradiol (estrogenic only). Rats were euthanised at 60 days old and brains dissected. Sex steroid-related (androgen receptor, 5α-reductase, estrogen receptor α and aromatase) and dopamine-related (tyrosine hydroxylase, dopamine transporter and dopamine D2 receptor) mRNAs were measured using quantitative PCR in the ventral tegmental area (VTA) and ventral striatum (VS).

Androgen receptor and 5α-reductase mRNAs were unchanged by sex steroid replacement in both regions. Estrogen receptor α [H(4)=11.41, p=0.02] and aromatase [F(4,71)=2.64, p=0.04] were decreased by dihydrotestosterone replacement compared to Intact, gonadectomised and estrogen-replaced rats in the VTA (all p<0.05). Aromatase [H(4)=12.57, p=0.01] was decreased by gonadectomy (p=0.02) in the VS and was further reduced by estrogen replacement (p=0.001) compared to Intact rats. Presynaptic tyrosine hydroxylase and dopamine transporter mRNAs were unchanged by sex steroid replacement. Postsynaptic D2 receptor [F(4, 67)=2.0, p=0.1] was increased by gonadectomy (p= 0.03) which was attenuated by dihydrotestosterone replacement compared to Intact rats (p=0.13).

During adolescence, androgens via androgenic effects may reduce the ability of the VTA to respond to estrogens. We speculate that increasing circulating testosterone levels during adolescence may reduce the neuroprotective capacity of estrogen in the VTA. Androgenic actions may also contribute to maintenance of dopamine D2 receptor levels in the VS during adolescence and changes in androgen levels may be important in altering dopaminergic signalling in the mesolimbic pathway in those developing schizophrenia.

Poster 15: Metabotropic glutamate receptor 7 shows age specific changes in schizophrenia and is altered following chronic antipsychotic and antidepressant treatment

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Mental illness is a growing global crisis. Severe psychiatric disorders such as schizophrenia occur in ~1% of the population. Poorly understood pathophysiology is associated with high rates of inadequate treatment. The glutamatergic system has been implicated in the pathophysiology of schizophrenia. The role of metabotropic glutamate receptor 7 (mGluR7) is of particular interest to the pathology and treatment of schizophrenia as it has repeatedly been identified as a candidate risk gene and has been associated with treatment response in patients.

Human post-mortem anterior cingulate cortex (ACC) was obtained from the NSW Brain Tissue Resource Centre. The cohort consisted of 40 subjects with schizophrenia and 40 Controls who had no history of psychiatric illness. To determine the potential effects of antipsychotic or antidepressant treatment, adult sprague-dawley rats were treated with the antipsychotics haloperidol (0.3 mg/kg/day) or olanzapine (3 mg/kg/day), the antidepressants fluoxetine (10mg/kg/day) or imipramine (10mg/kg/day) or vehicle (control) for 1 or 5 weeks (n=6/group). Brains were collected and the cingulate cortex dissected. Immunoblot analyses were performed across all cohorts to determine the level of mGluR7 expression.

mGluR7 expression was increased in schizophrenia subjects compared to controls, however this was restricted to those subjects who were less than 45 years of age. After controlling for age, mGluR7 levels were also increased in those schizophrenia subjects who died via suicide when compared to other causes of death. mGluR7 expression was increased in the rodent ACC following long-term treatment with the antipsychotic, haloperidol, however there was no effect of olanzapine. Similarly, long-term, but not short-term, imipramine and fluoxetine antidepressant treatment increased mGluR7 expression in the ACC.

These results reveal that mGluR7 is altered in schizophrenia in an age dependent manner in the ACC, a region which is highly associated with emotional and cognitive disturbances associated with schizophrenia. Considering the role of mGluR7 in inhibiting glutamate release, we speculate that this increase in mGluR7 could represent a compensatory response to control increased glutamatergic release in this region in schizophrenia, but further investigation is warranted. Chronic antidepressant and antipsychotic treatment was also associated with increased mGluR7 in the rodent cortex, suggesting they may mediate their effects via changes to mGluR7 in this region.

Poster 17: The antidepressant properties of agmatine are associated with a decrease in hippocampal pro-inflammatory cytokines

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Depression is a common, severe and chronic psychiatric disorder. However, the efficacy of currently available antidepressants in treating depression is often limited. There is growing evidence of a relationship between inflammation and psychiatric illness. Accumulating evidence suggests that up-regulation of pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) has an important role in the pathogenesis and treatment of the major depressive disorder. We sought to examine the effects of agmatine, a polyamine with antidepressant properties, on pro-inflammatory cytokines levels in the CNS.

Rats underwent olfactory bulbectomy and were treated with varying doses of agmatine or fluoxetine daily for 14 days. Locomotor and immobility time was assessed in the open field and forced swim test (FST), anhedonic behavior was assessed in the sucrose preference test (SPT). Following behavioural testing, hippocampal tissue was isolated and TNF-α, IL-1β, and IL-6levels were measured using ELISA.

Ablation of olfactory bulbs caused depression-like symptoms as evidenced by increased immobility time in FST, hyperactivity in open field arena, and anhedonia-like response in SPT. Administration of agmatine significantly reduced the immobility time in FST, attenuated the hyperactivity associated with the open field and restored the decrease in sucrose preference, comparable to the effects achieved by fluoxetine. Agmatine and fluoxetine treatment significantly decreased the level of TNF-α, IL-1β, and IL-6in the hippocampus.

Our study suggests TNF-α, IL-1β, and IL-6 may be involved in the antidepressant effects of agmatine. Our data also support a role for pro-inflammatory cytokines as a novel target for the treatment of MDD.

Poster 19: DNA Methylation of Immune Genes, Childhood Maltreatment and Psychosis

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Chronic inflammation is consistently associated with both schizophrenia (SZ) and bipolar disorder (BD). Childhood trauma is also associated with elevated inflammation and is a significant risk factor in developing psychotic disorders. However, the influence of childhood trauma on genes regulating inflammatory mechanisms in psychotic disorders remains unclear. We aim to investigate associations between epigenetic changes (DNA methylation) in genes coding for the inflammatory markers interleukin 6 (IL-6), tumour necrosis factor (TNF) and C-reactive protein (CRP), and diagnosis of a psychotic disorder (schizophrenia and bipolar disorder), and potential moderation of these associations by childhood trauma severity.

Participants were 114 cases (56 SZ, 58 BD) and 55 healthy individuals who completed the Childhood Trauma Questionnaire (CTQ) and provided blood samples for DNA methylation. DNA methylation was assessed using the Infinium HumanMethylation 450k BeadChip, for two inflammation genes (IL-6, TNF), and CRP-associated CpG sites. The CRP-associated CpG sites were used to calculate a CRP methylomic score. Logistic regressions were used to determine the relationship between DNA methylation of IL-6 and TNF, and the CRP methylomic score, and diagnosis of a psychotic disorder, and the potential moderating effect of trauma exposure on this relationship.

Logistic regressions revealed DNA methylation of the inflammation genes, and the CRP DNA methylation score, were not significantly associated with the diagnosis of a psychotic disorder. Furthermore, no association with childhood trauma exposure, or moderation by childhood trauma exposure, was observed. However, there was a significant main effect of childhood trauma exposure on psychotic disorder diagnosis, such that increasing maltreatment severity was associated with greater probabilities of a psychotic disorder diagnosis.

We investigated DNA methylation of genes regulating inflammatory processes, among psychiatric patients diagnosed with SZ or BD. Our findings indicate no changes in methylation at individual CpG sites. However we do demonstrate a new method with the use of a CRP methylomic score that may provide an alternative method to investigate inflammatory mechanisms in association with psychosis where CRP may not be readily available. This methodology has the potential to inform future research directions to improve our understanding of the epigenetic aetiology of SZ and BD, and the role of childhood trauma exposure in influencing the development of these disorders.

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Poster 21: Building an International Consortium on Geriatric Depression

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The aetiology and pathophysiology of late-life depression (LLD) and differences between early-onset and late-onset depression are not well understood. Given the increasing ageing population, it is crucial to understand the disorder and its implications in more detail to advance treatment and preventative strategies. We propose an international consortium to pool relevant data to investigate the aetiology and pathophysiology of LLD, with a focus on late-onset depression, by uncovering the genetic, biological, psychological and environmental determinants and their interactions.

National and international study leads of population and clinical studies will be/have been invited to join the consortium. We will perform joint or mega-analyses using combined, harmonised datasets that yield collated results with enhanced statistical power, in addition to comparisons across geographical regions, ethnicities and sociocultural groups. By combining studies and analysing pooled data, we will be able to examine environmental and bio-markers of LLD with sufficient statistical power.

We have contacted relevant international collaborators and received positive feedback. CHeBA contributes to the consortium with data from 3 ongoing, longitudinal studies: 1) The Older Australian Twins Study investigates healthy brain ageing in older twins (65+ years), 2) The Sydney Memory and Ageing Study examines clinical characteristics and prevalence of mild cognitive impairment and determines the rate of change in cognition over time, 3) The Sydney Centenarian Study investigates determinants of successful aging in a cohort of very old Australians (95+ years). All studies include measures of depression, cognition, physical health, genetics and biomarkers.

The consortium will address the global unmet health priority of understanding the aetiology of LLD through collaboration, innovation and partnership. By pooling data and knowledge, we will shed light on the aetiology and pathophysiology of LLD and will contribute to the knowledge base for the development of prevention and treatment strategies.

Poster 23: Epigenetic changes in a cross-disorder gene (NT5C2) and relationship with psychosis

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Recent genome-wide association studies (GWAS) have identified common variations in the 5'-Nucleotidase, Cytosolic II (NT5C2) gene in association with various psychopathologies. In parallel, childhood trauma has been recognised as a significant risk factor for multiple psychological disorders, and is associated with altered DNA methylation at specific genetic loci. This study ultimately aims to investigate whether DNA methylation of the NT5C2 gene mediates the relationship between severity of childhood trauma exposure and diagnosis of a psychotic disorder.

Participants were 116 psychotic disorder cases (schizophrenia or psychotic bipolar disorder), and 51 healthy controls. Severity of childhood trauma exposure was indexed using the total score from the Childhood Trauma Questionnaire (CTQ), and DNA methylation was assessed using the Infinium HumanMethylation450k BeadChip. Twenty-five individual CpG sites within NT5C2, and four means across the whole gene, promoter, TSS200 (0–200 nucleotides upstream of transcription start site), and enhancers, were analysed. Logistic regressions tested associations between trauma, NT5C2 DNA methylation, and diagnosis of a psychotic disorder. Covariates included age, sex, ethnicity, anti-psychotic and anti-depressant standardised dosages, slide, cell counts, and sample origin.

Severity of childhood trauma was positively associated with a psychotic disorder diagnosis; that is, people with psychotic disorder had higher CTQ total scores. DNA methylation of two CpG sites (in the TSS200 region), and two mean DNA methylation variables (TSS200 and promoter) were negatively associated with diagnosis, after correcting for False Discovery Rate (FDR). When also controlling for the use of mood stabiliser use (yes/no) in our model, results did not survive FDR correction. Severity of childhood trauma showed no significant association with DNA methylation of NT5C2. Mediation results will also be presented.

We demonstrate that both increased severity of childhood trauma exposure, and reduced DNA methylation of the NT5C2 promoter, are associated with psychosis; however, the latter association was no longer significant after adjusting for mood stabiliser use. Importantly, there were no associations between severity of childhood trauma and DNA methylation of NT5C2. To better understand these associations, future research including genetic risk variants and gene-expression data are required, ideally in first episode patients who have not yet taken any psychiatric medication.

Poster 25: Imaging Genetics in Psychosis study: Epigenetic Age Acceleration, trauma, and psychosis outcomes

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Schizophrenia (SZ) and bipolar disorder (BD) share cognitive and brain abnormalities, polygenic vulnerability, and common environmental risk factors such as childhood maltreatment. Childhood maltreatment has been associated with significant alterations in structure, function, and connectivity of the brain, as well as with advanced epigenetic age. Epigenetic processes (such as DNA methylation) function to regulate gene expression, and may be important mediators on the path between childhood maltreatment and psychosis.

The Imaging Genetics in Psychosis (IGP) cohort includes 171 individuals (n = 117 with psychosis [n=57 Schizophrenia/Schizoaffective, 59 bipolar], and 55 healthy controls) with completed clinical, cognitive, imaging, genetic, and DNA methylation assessments. Clinical measures include confirmation of diagnosis using the Diagnostic Interview for Psychosis, and the Positive And Negative Symptom Scale (PANSS) to evaluate current symptoms in cases. Childhood Trauma Questionnaire was administered to all. DNA was extracted from peripheral whole blood samples, with DNA methylomic data assayed using the Infinium HumanMethylation 450K BeadChip (Illumina, San Diego). Epigenetic age acceleration was calculated using the Horvarth epigenetic clock.

We find no association between epigenetic age acceleration and psychotic diagnoses. However, marginal support for epigenetic age acceleration was associated with trauma exposure ($t(171)=1.86$, $p=0.06$), which was attenuated when including standardised Imipramine and Chlorpromazine dosages in the model. There was also evidence of association between epigenetic age acceleration and negative symptoms in clinical cases from the PANSS ($t(117)=3.05$, $p=0.003$), independent of schizophrenia or bipolar diagnosis, and when standardised medication dosages were included in the model. Additional findings in relation to structural and cognitive changes will be presented.

The strongest association with peripheral DNA epigenetic age acceleration was revealed for current negative symptoms in the clinical cases, regardless of diagnosis and medication. This could reflect severity of psychosis, and potentially variation within individuals with a history of psychosis. The attenuation of associations with childhood trauma when accounting for medication dosages suggests that these clinical factors should be controlled as potential confounds in future methylation analyses of psychosis samples, and where possible first-episode psychosis samples identified prior to first medication.

Poster 27: Environmental interventions in a mouse model of depression/anxiety-like behaviours

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Globally, an estimated 350 million people suffer from depression (5% of the world's population). Notably, around 30% of patients with depression do not respond to current antidepressant medications. Both genetic and environmental factors play a role in the aetiology of psychiatric disorders. Interaction between polymorphisms in the serotonin transporter (5-HTT) and stress exposure is one of the most robust examples of gene-environment interaction in the context of depression and anxiety disorders. Critically, cognitive impairments are core symptoms of anxiety and depressive disorders and current medications do not target this aspect.

We investigated the effects of exercise and environmental enrichment (which does not include running-wheels) on affective behaviours and cognition, in wild-type (WT) and 5-HTT knock-out (KO) mice. At 8 week of age, mice were assigned to exercise (include 2 running wheels) or environmental enrichment (housed in larger cages with access to a variety of objects of different textures, shapes, and in differing configurations (changed weekly for novelty). Behavioural experiments were carried out from 12 weeks of age. Hippocampal synaptic plasticity was also assessed.

Using the elevated-plus maze and the light-dark box, we found that environmental enrichment ameliorated the abnormal innate anxiety of 5-HTT KO mice, by increasing the time spent in the open arms. Measuring the immobility time in the forced-swim test (a test sensitive to antidepressant drugs), we showed that exercise (but not environmental enrichment) exerted an antidepressant-like effect in 5-HTT KO mice. Notably, these behavioural effects of exercise were associated with changes in synaptic plasticity, including a restored long-term potentiation in the hippocampus of 5-HTT KO mice.

Mice with varying 5-HTT function are useful model systems to identify and understand the mechanisms mediating potential therapeutics. Overall, our data suggest that environmental enrichment specifically reduces innate anxiety of 5-HTT KO mice, whereas exercise is more efficient in reducing depressive-like behaviours. While the mechanisms mediating these effects remain unclear, our findings could have implications for patients with depression and anxiety disorders.

Poster 29: mGluR5 and associated proteins Homer1b/c, PSD95 and Neurochondrin in the anterior cingulate cortex in schizophrenia and major depression

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Schizophrenia and major depression are two of the leading causes of disease burden, with a lifetime prevalence of 1% and 15% respectively. Current treatment of these disorders is dominated by antipsychotic and/or antidepressant drugs. Recent evidence has implicated the glutamatergic system, specifically the metabotropic glutamate receptor subtype 5 (mGluR5), in the pathophysiology of these disorders. This study aimed to determine if protein expression of mGluR5 and its associated proteins Homer1b/c, PSD95 and Neurochondrin, were altered in the anterior cingulate cortex (ACC), a brain region mediating emotional and cognitive function, in schizophrenia and major depression subjects compared to controls.

ACC samples were obtained postmortem from 40 schizophrenia, 13 major depression and 40 matched control subjects from the NSW Brain Tissue Resource Centre. Relative protein levels of mGluR5, Homer1b/c, PSD95 and Neurochondrin were assessed via western blot, normalised to GAPDH. ANCOVAs were used to determine differences in protein levels between diagnostic groups. Spearman's correlations and two-way ANOVAs were used to examine any relationship with antemortem antipsychotic (measured chlorpromazine equivalents) and antidepressant treatment history. Spearman's correlations were used to examine protein-protein relationships in the diagnostic groups.

Protein levels of mGluR5 (dimeric and monomeric), Homer1b/c, PSD95 and Neurochondrin were not significantly different between controls and individuals with schizophrenia or major depression. As expected, dimeric mGluR5 was positively correlated with Homer1b/c, PSD95 and Neurochondrin (r>0.550, p<0.001) in control subjects. While the relationship between mGluR5 with Homer1b/c and PSD95 remained in schizophrenia and major depression subjects, the mGluR5-neurochondrin relationship was lost in schizophrenia (r=0.250, p=0.160) and major depression (r=0.333, p=0.347). PSD95 was 22% higher in subjects who had a history of antidepressant treatment (n=18) compared to those without (n=26). Protein expression was not associated with lifetime antipsychotic drug treatment.

The present study does not provide evidence of abnormalities in overall mGluR5 protein expression in the ACC in schizophrenia or major depression. However, the loss of the mGluR5 relationship with Neurochondrin raises the possibility that mGluR5 trafficking may be altered and warrants further investigation. The finding of increased PSD95 in subjects with a history of antidepressant treatment, suggest it may play a possible a role in mediating the effects of antidepressant drugs within this brain region.

Poster 31: Behavioural deficits following prenatal stress are reduced following stressful stimuli in the neonatal period and emapunil treatment

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Extensive evidence shows that the early developmental period is crucial in life-long programming, and that adverse environments and pregnancy compromises markedly increase the risk of emotional and behavioural disorders in later life. Neurosteroids provide optimal brain development through promotion of myelination and neurogenesis. Chronic stress in pregnancy has been shown to decrease neurosteroid synthesis, subsequently decreasing myelination and disrupting the GABAergic pathway in the fetal brain, resulting in long-term behavioural deficits such as anxiety and ADHD. We propose that stimulation of neurosteroid synthesis through administration of a ligand (Emapunil) of the mitochondrial translocator protein (TSPO) will reduce these adverse outcomes.

Pregnant guinea pigs were exposed to control-handling or stress (strobe light exposure for 2hrs/day on gestational age (GA) 50, 55, 60 and 65; term GA70). In the neonatal period, offspring were allocated to control or postnatal stress (maternal separation for 2hrs/day from postnatal day (PND) 2-8). Pups received emapunil (0.3mg/kg daily) or vehicle (45% β-cyclodextrin) on PND2-8 and underwent open field and elevated plus maze testing on PND 9 and 28. Mature myelination was assessed with myelin basic protein (MBP) immunohistochemistry and GABAA receptor α2, α4, and α5 subunit mRNA expression was assessed with real-time polymerase chain reaction (RT-PCR).

At PND9, the prenatal stress group and pre+postnatal stress group displayed hyperactive behaviour as assessed by the open field and elevated plus maze and this phenotype was reduced in offspring that received emapunil treatment. At PND28 only the prenatal stress group showed the hyperactive phenotype with the pre+emapunil group and pre+postnatal stress group displaying levels that were not different from controls. Myelination was decreased at PND30 in the prenatal stress group while the pre+emapunil and the pre+postnatal stress group displayed control levels of myelination. Similarly, only the prenatal stress alone group displayed increased mRNA expression of the GABAA receptor subunits.

This study further highlights the negative role of pregnancy compromises such as prenatal stress on programming the neurodevelopmental and neurobehavioural outcomes of the offspring. This work also shows that manipulation during the early neonatal period, whether it be further stress insults or therapeutic intervention, can reverse the negative outcomes seen in prenatal stress alone. Postnatal stimulation of the neurosteroid synthesis pathway with TSPO ligand emapunil may be a viable treatment option in those exposed to prenatal stress, thus warrants further investigation.

Poster 33: Enhanced latent inhibition of conditioned fear in adolescent rats

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Latent inhibition refers to how exposure to a stimulus reduces subsequent learning to that stimulus. When modelled using Pavlovian fear conditioning, it is thought that repeated non-reinforced presentations of a tone (pre-exposure) form a safe memory of the tone, which inhibits subsequent memories of aversive tone-shock pairings (conditioning). This is like extinction - the reduction in learned fear that occurs following repeated tone presentations after conditioning. Both latent inhibition and extinction recruit dopamine signalling in the medial prefrontal cortex. Adolescents display deficits in extinction due to immaturity in this system, however latent inhibition in adolescence has not been investigated.

Experiment 1 examined developmental differences in latent inhibition. On day 1, adult or adolescent rats were placed in conditioning chambers and presented with a tone either 45 or 0 times. The next day they were conditioned to fear the tone through repeated pairing with a foot-shock. Learning was assessed on day 3, by presenting the tone alone a further 45 times in the same chambers. The role of dopamine receptors in the medial prefrontal cortex was tested by injecting D1 agonist eticlopride or D2 agonist quinpirole bilaterally into this region before conditioning in adults (Experiment 2) and adolescents (Experiment 3).

In Experiment 1 we found that fear to tone at test was reduced in rats that had received preexposure, confirming latent inhibition in our model. The effect was greater in adolescents compared to adults, suggesting that adolescents are more sensitive to the inhibitory effects of preexposure. Furthermore, infusion of eticlopride into the medial prefrontal cortex did not affect expression of fear during conditioning, but did impair latent inhibition in adults.

These results highlight important differences between latent inhibition and extinction, and suggest that the mechanisms underlying latent inhibition are dissociated across development. The findings of this study help to understand anxiety disorders in adolescence and highlight a mechanism through which adolescents may be resilient.

Poster 35: Oxytocin genetics and family adversity in the development of substance use disorders

Linda Gowing, Murthy Mittinty, Femke Buisman-Pijlman

Drug and Alcohol Services South Australia-WHO Collaborative Centre, University of Adelaide; School of Public Health, University of Adelaide; Adelaide Medical School and Robinson Research Institute, University of Adelaide

Early adversity can increase the risk of mental health problems and addiction. Oxytocin is a neuropeptide which impacts on behaviour, stress regulation and mental health. Individual differences in the oxytocin system have been identified as a possible mechanism in the association between stressful life events in early childhood and development of substance use disorders. This study aimed to investigate the impact of genetic variation in the oxytocin receptor and gene specifically on this interaction.

This study uses data from the UK Avon Longitudinal Study of Parents and Children to investigate SNPs for the oxytocin receptor gene (rs53576, rs2254298, rs4564970 and rs1488467) and oxytocin gene (rs4813625). The genotype of SNPs in the oxytocin receptor and oxytocin genes, and a measure of cumulative family adversity in early childhood were related to age at first use and risky use of alcohol and nicotine at age 21-23 for a subset of 8795 participants. Logistic and ordinary least squares regression were used with multiplicative interaction, with coefficients being used to assess additive interaction in a sufficient cause approach.

The results strongly support an association between family adversity in early childhood and nicotine dependence at age 21 to 23 years, particularly for males. There is also strong support for an association between maternal smoking during pregnancy and nicotine dependence in the offspring at age 21 to 23. The results provide only weak support for a similar association with alcohol use disorders. No consistent association was found between substance use outcomes and the SNPs investigated, either alone or in interaction with family adversity.

The results confirm the association between family adversity and nicotine use disorders, but do not support the role of these specific oxytocin SNP's in mediating these effects. The effects of early adversity on alcohol use were less pronounced.

The dataset permits us to continue our research to separate out specific early factors, such as trauma, general adversity and prenatal exposure to drugs. The current study did not rule out oxytocin as a mediator, but merely these SNP's. New studies can look at methylation of the genes and the functional measures of the functioning oxytocin system impacting on susceptibility to addiction.

Poster 37: Altered behavioural phenotypes in a developmental vitamin D deficient rat model of autism

Asad Ali, Mia Langguth, Suzanne Alexander, Xiaoying Cui, Darryl Eyles
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Emerging evidence suggests that developmental (both gestational and early postnatal) vitamin D (DVD) deficiency is associated with an increased risk of autism. Autism is a neurodevelopmental disorder characterized by impairments in social interaction, lack of verbal and non-verbal communications, stereotyped repetitive behaviours and hyper-activation. There are several other conditions that are comorbid with autism, including olfactory impairments, anxiety, and delays in motor development. Here we investigate the effects of DVD-deficiency on behavioural phenotype relevant to autism in the DVD-deficient rat at different developmental stages.

DVD-deficiency in female Sprague-Dawley rats was induced by feeding vitamin D deficient diet for the period of 6 weeks before mating. DVD-deficiency was maintained until weaning to produce animals that experienced both gestational and postnatal vitamin D deficiency. Pups were sexed by anogenital distance. To avoid repeated handling, pups were randomly divided into three behavioural cohorts. Cohort 1 was assessed for righting reflex, ultrasonic vocalizations and pup retrieval. Cohort 2 was tested for negative geotaxis and olfactory discrimination. Cohort 3 was assessed for marble burying, social play, social interaction, and anxiety-like behaviour. Data was analysed by multivariate analysis of variance.

DVD-deficient pups are physiologically normal, having normal weight gain and developmental milestones. However DVD-deficient male pups had impaired righting reflex at postnatal-day (P) 5 ($p=0.012$). Negative geotaxis was delayed in DVD-deficient pups of both sexes at P7 ($p=0.001$). Both male and female DVD-deficient pups emitted louder and a higher number of ultrasonic vocalizations at P7 ($p=0.0001$) and 9 ($p=0.023$). DVD-deficient animals buried significantly fewer marbles compared to control animals in both adolescence ($p=0.041$) and adult ages ($p=0.008$). These animals also travelled significantly ($p=0.001$) further in an elevated plus maze. There was no effect of DVD-deficiency on sociability or anxiety-like behaviour.

DVD-deficient pups have delayed motor development. Increased ultrasonic vocalizations and calling intensity suggests that DVD-deficient pups may have heightened anxiety levels. Reduced digging behaviour at both adolescent and adult ages may reflect long-term impairments in normal stereotypic behaviour in DVD-deficient animals. The reduced digging behaviour is unlikely to be due to motor impairments as DVD-deficient animals were hyperactive in the elevated plus maze. In conclusion, the current study shows broad-spectrum behavioural abnormalities in DVD-deficient neonates, adolescents and adult rats which may reflect some developmental symptoms seen in young children with autism.

Poster 39: Role of NMDA receptors on Parvalbumin Interneurons and Pyramidal Cells in Behaviour and Electrophysiology

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Recent models of schizophrenia propose that abnormalities in gamma (30-80Hz) oscillations may be closely tied to the pathophysiology of the disorder, with hypofunction of NMDAr implicated as having a crucial role. NMDAr antagonists induce disturbances to gamma frequency oscillations akin to abnormalities reported in schizophrenia. We sought to investigate the role PV+ neurons and pyramidal cells play in NMDAr antagonist induced disturbances in gamma activity and behaviour by utilising two transgenic mouse lines in which cell-type specific deletion of the obligatory NMDA receptor subunit (NR1) in parvalbumin positive neurons (PV:NR1 KO mice) and pyramidal neurons (CaMKIIα:NR1 KO mice) was achieved.

Two separate cohorts of animals were used in this experiment: Cohort 1[(adult PV:NR1 KO mice(n=26) and wild-type littermates (n=28)) and cohort 2[(adult CaMKIIα:NR1 KO mice(n=25) and wild-type littermates(n=20)) were first used to assess behavioural outcomes. Specifically, %PPI and locomotor activity were assessed following administration of the NMDAr antagonist MK-801(1.0mg/kg) or vehicle (saline). Following behavioural assessment, all mice were implanted with electrodes in the medial prefrontal cortex (mPFC) and dorsal hippocampus (dHPC) to allow for LFP measures to be obtained. Assessment of ongoing and auditory evoked gamma activity, as well as mPFC-dHPC coherence were then obtained from these LFP measures.

In control mice, MK-801 increased ongoing gamma power, reduced auditory evoked gamma power and increased gamma band coherence between the mPFC and dHPC. These consequences of NMDAr antagonism were differentially regulated in PV:NR1 KO mice and CaMKIIα:NR1 KO. The MK-801induced increase in ongoing gamma power was significantly attenuated in both PV:NR1 KO mice and CaMKIIα:NR1 KO mice, but deficits to auditory evoked gamma activity were unaffected by genotype. Interestingly, in contrast to PV:NR1 KO mice, the emergence of abnormal gamma band hyperconnectivity between the mPFC and dHPC following MK-801 treatment was completely absent in CaMKIIα:NR1 KO mice.

The results of this study suggest that while disturbances to local gamma synchrony can be caused by NMDAr antagonism on both PV interneurons and pyramidal neurons, NMDAr blockade on pyramidal neurons is crucial for inducing disturbances to long-range coherence and regional communication.

Poster 41: Prenatal Alcohol Exposure and Offspring Adolescent Alcohol Use: A Longitudinal Study

Daniel Cooper, Femke Buisman-Pijlman

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Prenatal exposure to alcohol can have lifelong effects on development and mental health. Excessive alcohol exposure can result in Foetal Alcohol Spectrum Disorders, but more subtle effects on social, emotional and cognitive development are being shown. Distal effects, such as adolescent drinking and addictive behaviour, can also be impacted by this exposure. Data from animal models highlights that the biological effect of prenatal alcohol varies between trimesters, an effect which has yet to be investigated in humans. This study aims to identify the impact of alcohol exposure in the three trimesters on drinking in young adults.

Prenatal exposure to alcohol can have lifelong effects on development and mental health. Excessive alcohol exposure can result in Foetal Alcohol Spectrum Disorders, but more subtle effects on social, emotional and cognitive development are being shown. Distal effects, such as adolescent drinking and addictive behaviour, can also be impacted by this exposure. Data from animal models highlights that the biological effect of prenatal alcohol varies between trimesters, an effect which has yet to be investigated in humans. This study aims to identify the impact of alcohol exposure in the three trimesters on drinking in young adults.

Data on maternal drinking in each trimester and drinking habits were available for 4743 participants. Rates of maternal drinking were consistent across all three trimesters, 70% reported any drinking in the first trimester, 70% in the second and 68% in the third. Interestingly, 17% of women who did not drink during the first trimester reported drinking in the third trimester. Data showed a range of alcohol use behaviours; 42% drinking monthly or less and 16% drinking more than twice a week. Approximately 4% of offspring had results suggestive of dependence. Results from this study are still pending advanced statistical analysis.

Despite widespread medical advice to avoid drinking during pregnancy, 30% of mothers in this cohort still did so. This sample size allows isolation of trimesters, so the individual effect of drinking alcohol in each of these periods can be compared. There are also high numbers of mothers who either drank low levels (<1 drink/week) of alcohol in pregnancy or did not drink at all. This allows direct comparisons between the two groups, and adjustment for any cofounding factors. Findings from this project could guide future obstetric advice and may improve our understanding of life trajectories that lead to addiction.

Poster 43: Behavioural characterization of a novel rat model of the Brain-derived Neurotrophic Factor (BDNF) Val66Met polymorphism

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The val66met polymorphism is a common variant of the BDNF gene (rs6265) which reduces activity-dependent release of this neurotrophin and has been suggested as a risk factor for anxiety and affective disorders. The met/met genotype has also been associated with positive symptoms in patients with schizophrenia. Previous studies using mice with the BDNF val66met polymorphism have shown impaired memory and differences in prepulse inhibition (PPI) behaviour. Here we present a behavioural characterization of a novel rat model of the BDNF val66met polymorphism.

The rat line was originally generated by Sortwell et al. using CRISPR/Cas-9 induced valine to methionine substitution at codon 68, equivalent to position 66 in humans. We used rats that were either val/met or met/met and compared them to control littermates without the substitution (val/val). Animals underwent a battery of behavioural tests to investigate anxiety, cognition and psychosis-like behaviours.

All rats showed normal learning and memory in a fear conditioning and extinction protocol, as well as the Y-maze and novel object recognition tests. Met/met rats tended to show increased anxiety in the open field but not the elevated plus maze. While baseline PPI was not altered, met/met rats showed a significantly reduced disruption of PPI by MK-801, but not apomorphine. In contrast, methamphetamine-induced locomotor hyperactivity was unaltered.

BDNF met/met rats showed reduced effects of NMDA receptor antagonism in PPI. While there were few other differences between genotypes in the baseline behaviours investigated, further studies with these rats using different ‘two hit’ gene-environment interaction models are warranted to further investigate the role of BDNF in schizophrenia and affective disorders.

Poster 45: Antipsychotic Induced Metabolic Side-effects in Juvenile Poly (I:C) Rats

James Kenneth Hodgson, Jiamei Lian, Chao Deng

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Background: Second generation antipsychotic (SGAs) prescription such as risperidone and olanzapine have been sharply increased in juvenile patients with various mental disorders. These treatments however, cause adverse side effects including obesity and other metabolic disturbances. Whilst research has been performed in health juvenile animal model pertaining to these metabolic effects, mental disorders often present with metabolic disturbance that is evidenced in drug naïve patients. Therefore, this study investigates the metabolic disorders induced by risperidone and olanzapine in a juvenile Poly I:C rat model.

Method: 14 Time mated female Sprague Dawley rats (320-430g) were treated with either Poly IC (2mg/kg; N=7) or 0.2ml Saline on gestation day 15. Female offspring pups from the Poly I:C or saline treated pregnant rats were treated with (1) Vehicle only (0.3g cookie dough pellet, b.i.d; n=12), (2) Olanzapine (3mg/kg) or (3) risperidone (0.9mg/kg) from postnatal day (PD) 31-55. Weight gain, food/water intake, body temperature were measured pre-treatment , and throughout the antipsychotic treatment period. Intraperitoneal glucose tolerance test and open field test were conducted. Blood, liver, brown and white adipose tissue were collected and analysed.

Results: Offspring pups of Poly IC treated rats demonstrated increased weight gain and water intake, and a higher fasting blood glucose level. Risperidone- and olanzapine- treated poly IC rodents displayed increased weight gain, food intake and water intake, higher feeding efficiency, decreased activity compared to both Saline and Poly IC vehicle treatment groups. There were also statistically significant increases in liver weight, inguinal fat, mesentery fat and total white fat in both Poly IC treated SGA cohorts against both vehicle groups.

Conclusions: Our results have demonstrated that Poly IC treatment significantly increases weight gain, water intake and fasting glucose in offspring rats. SGA administration exacerbates t body weight gain, water intake, food intake, feeding efficiency, and fat accumulations, while decreased activity in Poly IC treated animals. Further analysis of the liver brawn adipose tissue for various regulatory and thermogenic biomarkers is currently underway. Our results demonstrated that poly I:C rat model is suitable for investigating mechanisms of antipsychotic-induced metabolic side-effects in juveniles.

Poster 47: Mitigating severe metabolic side-effects associated with olanzapine and risperidone use through betahistine co-treatment: a juvenile rodent study

Thomas Spunar, Jiamei Lian, Chao Deng

School of Medicine, University of Wollongong, Wollongong, NSW; Antipsychotic Research Laboratory, Illawarra Health and Medical Research Institute, Wollongong, NSW

Second generation antipsychotic drugs (SGAs) have increasingly prescribed to children and adolescents, which is associated with a myriad of clinically reported metabolic disturbances; such as weight gain, dyslipidaemias, hormonal imbalances, and chronic sedation. The SGA-induced blockage of several key neurotransmitters, including the histaminergic H1 and serotonergic 2C receptors plays key roles in the development and progression of these metabolic disorders and as such are key candidates for mediation. Through use of a well-developed juvenile rat model, we have investigated the effects of Betahistine (a histaminergic H1 receptor agonist and H3 antagonist) in ameliorating these metabolic disorders induced by SGAs.

Seventy-two juvenile female Sprague Dawley (SD) rats were separated into six treatment groups (n= 12/ group): (1) olanzapine-only (2mg/kg), (2) risperidone-only (0.6mg/kg), (3) betahistine-only (5mg/kg), (4) olanzapine-betahistine (O+B), (5) risperidone-betahistine (R+B), and (6) vehicle (control), 3 times/day. Body weight, food/ water intake, and core body temperature of the rats was measured at four-day intervals. Locomotor activity was measured using an open field test. The protein expression of thermogenesis biomarkers UCP 1 & 3, PGC 1 α/β in brown adipose tissue (BAT) was examined utilising immunoblotting techniques. Furthermore, levels of blood-borne lipids and hormones were measured followed the established protocols

Our results revealed that weight gain, and food intake was significantly elevated in both the sole Olanzapine- and Risperidone-treated groups. These gains were accompanied with associated elevations in the appetite-mediating hormone ghrelin, as well as plasma triglyceride and total cholesterol; with decreases in core body temperature and locomotor activity. Both the Olanzapine-Betahistine (O+B) and Risperidone-Betahistine (R+B) co-treatment groups reported significant increases in core body temperature, with elevated BAT PGC1 α/β, and UCP 1 & 3 expression. Interestingly, the R+B and not the O+B co-treatment group reported significant increases in locomotor activity when compared to risperidone-only or olanzapine-only groups.

This study was the first in a juvenile animal model to investigate the therapeutic potential of betahistine co-treatment for reducing metabolic side-effects associated with the use of both Olanzapine and Risperidone. Our results support previous findings that have shown SGA-induced elevations in weight gain, ghrelin, and plasma lipid levels; with accompanied decreases in locomotor activity and core body temperature. In the context of a juvenile rodent model, betahistine co-treatment is largely effective in ameliorating Risperidone-induced degeneration in locomotor activity and decreases in core body temperature, which over long-term treatment may culminate in decreases in SGA-induced weight gain.

Poster 49: Neurite repair for severe mental disorders

Xu-Feng Huang

Illawarra Health and Medical Research Institute, University of Wollongong

Neurites are projections from the cell body of neurons, which allow neurons to connect to each other. Neurite deficits impair neural connectivity and alter brain function. Importantly, neurites are not fixed structures and are changeable to form the bases for neuroplasticity throughout lifespan. Neurites are regulated by many intrinsic genes and proteins including neurotrophins, membrane receptors, calcium channels etc. D2R/NR2B regulate neurites, synaptogenesis and connectivity and are also major antipsychotic drug targets. We have investigated the molecular mechanisms of neurite lesion and repair using a number of animal models as well as preliminary human studies.

We have used the following methods in this project. 1) cell cultures including human cell lines and primary cells from gene knockout mice; 2) Fluorescence Resonance Energy Transfer to examine signalling molecular interaction; 3) siRNA down regulation of targeted gene expression; 4) Nrg1-TM +/-, DISC1-FI, PCP mouse models; 5) targeted gene insertion for over expression; 6) clinical trials in 1st episode schizophrenia patients on risperidone treatment; 7) RT/PCR-16s microbiota gene sequence.

Our studies showed that: 1) D2R and DISC1 interaction/dimerization regulates neurite outgrowth which responds to anti-psychotic drug treatment; 2) D2R and NR2B show a direct reciprocal regulatory mechanism; 3) 3D cell culture showed that Nrg1-FI induced neurite lesion could be repaired by physiological level of electrical stimulation, but not antipsychotic drug; 4) neural adhesion molecule-PSA form responsible for neural plasticity is significantly reduced in first episode schizophrenia patients; 5) identification of altered microbiome species in the first episode schizophrenia patients; 6) beneficial effect of gut microbiome metabolites.

From above studies, we conclude that dopamine D2 receptor plays important role in the regulation of neural connectivity and plasticity. D2R directly interacts with DISC1 gene at a specific site. When there was D2R hyperactivity, D2R-DISC1 forms dimerization disrupting intracellular molecular trafficking and causing neurite withdraw. When D2R is down regulated by siRNA, NMDAR-NR2B specific phosphorylation sites were activated possibly involving the receptor internalisation. Altered gut microbiota in patients can lead to their metabolites changes including short chain fatty acids. A supplementation of specific short chain fatty acid is capable of repair neurites in vitro.

Poster 51: Aberrant intrinsic functional connectivity in female victims of sexual assault

Yann Quidé, Frédéric Andersson, Wissam El-Hage

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Females exposed to sexual assault are at high-risk to develop posttraumatic stress disorder (PTSD). However, the changes in functional connectivity arising early following sexual assaults and leading to the development of PTSD are unclear.

Participants were 25 adult females recruited 3 weeks following their exposure to sexual assault (T1) and 19 age-matched Controls. Among the Victims, 10 participants met (PTSD+) and 15 did not meet (PTSD-) DSM-IV criteria for PTSD 6 months post-trauma (T2). At both visits, patterns of intrinsic connectivity (IC), a whole-brain measure of network centrality at each voxel, were derived from resting-state functional magnetic resonance imaging using the CONN toolbox, and were compared at T1 between groups at T1, at T2 between groups at T2, and at T1 between groups at T2.

At T1, Victims showed significantly weaker IC in the posterior cingulate cortex (PCC; pFWE=0.019) and stronger IC in the right occipital pole (rOP; pFWE=0.025) than Controls. At T2, there were no between-group differences in IC. However, compared to Controls, the PTSD+ group showed stronger IC at T1 in both the rOP (pFWE<0.001) and left OP (pFWE=0.013), and the PTSD- group showed weaker IC at T1 in the PCC (pFWE<0.001). There were no differences in IC at T1 between the PTSD- and PTSD+ groups.

This study indicates that stronger IC in the OP early following sexual assault in females is associated with the development of PTSD, while weaker IC in the PCC is associated with trauma exposure.

Poster 53: Antenatal depression as a predictor of cognitive and psychosocial dysfunction in women with iron deficiency

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Major Depressive Disorder (MDD) affects 20% of women during the perinatal period. Low iron is the most common nutritional deficiency encountered during pregnancy and is associated with depressive symptoms. Iron deficiency is the most common cause of anaemia during pregnancy. Both MDD and iron deficiency can lead to cognitive dysfunction, which negatively impacts psychosocial function including maternal bonding and caregiving. Identifying specific cognitive deficits associated with iron deficiency and depression in pregnancy will allow clinicians to better support these women. This study investigates whether cognitive function and iron deficiency anaemia (IDA) affect specific domains of psychosocial function in pregnancy.

A cohort of iron-deficient pregnant women, with or without IDA (n=274) were assessed using a clinical interview including a history of depression and for current depressive symptoms using the HAM-D assessment tool and FAST questionnaire. Participants were administered the THINC-It cognitive battery test (CRT, DSST, Nback, TMT) to assess five domains of cognition: attention, executive function, working memory and a perceived deficits questionnaire for depression-5-item (PDQ). Laboratory data were collected regarding haemoglobin, iron stores and CRP. Multiple linear regressions were performed using domains of psychosocial function, which also modelled for age, education and anaemia as predictors of cognitive function.

Preliminary analysis of our dataset shows several measures of psychosocial dysfunction are predicted by cognitive dysfunction in iron-deficient pregnant women with MDD. Poor performance on the DSST was a predictor of total FAST score ($\beta=0.949$, $p<0.001$), autonomy ($\beta=0.226$, $p=0.004$), subjective cognition ($\beta=0.461$, $p<0.001$), leisure time ($\beta=0.112$, $p=0.016$) and interpersonal relationships ($\beta=0.166$, $p=0.033$). Contrastingly, women without MDD demonstrated a positive association between DSST performance and financial issues ($\beta=0.009$, $p=0.034$). We performed a sub-analysis on women with MDD and anaemia and found poor performance on the DSST predicted total FAST score ($\beta=-0.468$, $p=0.004$) and autonomy ($\beta=-0.196$, $p=0.001$).

As a composite measure of executive functioning, processing speed and attention; poor performance on the DSST in pregnant women with MDD was indicative of several difficulties in psychosocial functioning overall. As such, cognitive performance indicated deficits in independence, social capabilities and undertaking physical or leisure activities. The added presence of anaemia in MDD was associated with overall psychosocial dysfunction and decreased independence. These preliminary findings support that cognitive training may be a useful therapeutic target for women who suffer from MDD during pregnancy.

Poster 55: Maternal vitamin D supplementation rescues dopamine developmental abnormalities in maternal immune activation

Wei Luan, Suhailah Ali, Suzy Alexander, Darryl Eyles
Queensland Brain Institute, University of Queensland

Maternal immune activation (MIA) and developmental vitamin D (DVD)-deficiency induce mesencephalic dopamine (mesDA) developmental abnormalities relevant to schizophrenia.

In this study, we investigated whether maternal administration of the vitamin D hormone (1,25OHD) could rescue MIA-altered early mesDA neurogenesis. We administrated the viral mimetic polyriboinosinic-polyribocytidylic (poly (I:C)) to pregnant mouse dams at gestational day (GD) 9 simultaneously with 1,25OHD and/or their vehicles. At GD11 and GD14, mesDA cell expression of various maturation factors specific for DA neurons was assessed at a single-cell level by a novel immunochemical method.

The results showed MIA treatment decreased the mesDA progenitor (Lmx1a + Sox2+) cells at GD11. MIA treatment also reduced the protein expression of mesDA maturation factors Lmx1a, Nurr1 and the enzyme tyrosine hydroxylase (TH) in mesDA cells at GD11. In contrast, 1,25OHD treatment increased the expression of these proteins. MIA also altered the mediolateral position of post-mitotic (Lmx1a + Sox2-) neurons an outcome that was also rescued by 1,25OHD treatment at GD11. However, there were no noticeable effects of MIA or 1,25OHD on these outcomes at GD14.

Our data demonstrate the acute effects of MIA and maternal 1,25OHD treatment on developing mesDA cells. This suggests vitamin D is neuroprotective for fetal mesDA neurons. Maternal vitamin D supplementation in the dietary form, cholecalciferol, therefore may be considered as a future strategy for the prevention of MIA-induced neurodevelopmental abnormalities.

Poster session 2

Thursday the 8th of November, 1:20pm-2:20pm

Poster 2: Assessing decision-making in people with schizophrenia: an update on task-specific factors

James P Kesby, Matilda Mackay-Sim, Alex Ryan, James G Scott

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Even though our knowledge of the neurobiology of schizophrenia has advanced considerably, novel targets for interventions are needed to facilitate drug discovery. We are interested in the associative striatum (aSTR) because it may represent a common area involved in both the psychotic and cognitive symptoms of schizophrenia. Increased dopaminergic transmission in the aSTR underlies psychotic symptoms and this region is densely innervated by the cortical areas underlying many of the cognitive symptoms in schizophrenia. Goal-directed behaviour is highly dependent on aSTR function. Therefore, we are assessing goal-directed action in people with schizophrenia and those experiencing a first episode of psychosis.

To assess goal-directed action we are using the outcome-specific devaluation task (ODT). This ODT features an instrumental learning phase whereby participants move a joystick left or right to attain one of two outcomes (learning the action-outcome association). A devaluation procedure is then used to reduce the value associated with one outcome. Subsequently, a choice phase allows participants to respond and attain either outcome (although no feedback is given). Healthy subjects show a bias in their responding toward the outcome that was not devalued. We are also testing premorbid and current IQ, alongside the Positive and Negative Syndrome Scale (PANSS).

We are trialling two versions of the ODT, one based off a prior study that uses food rewards and aversion-based devaluation (video) and another that features a credit system with a direct credit-value reduction to devalue. Our results from pilot studies and control participants suggest the ODT with food rewards is highly sensitive to motivational influences. The hunger of the participant is critical to obtain outcome-specific devaluation and personal personal experiences to the devaluation method influence responses in an unpredictable manner. Our studies using the second version of the ODT are currently underway.

Our data suggest the ODT is a cognitive task that is sensitive to a range of factors that can complicate the interpretation of goal-directed behaviour. As such, certain versions of this task work well in specific contexts but may be problematic when conducted in different settings. However, if the optimal context-specific parameters are identified, the task is simple and quick to administer. Thus, it is a useful addition to test batteries in studies of neuropsychiatric disorders.

Poster 4: Understanding the efficacy of GLP-1 receptor agonist, liraglutide, to prevent olanzapine-induced weight gain in rats: examining neuropeptide Y in the hypothalamus

Ilijana Babic, Nagesh Pai, Katrina Weston-Green

School of Medicine, Faculty of Science, Medicine and Health, University of Wollongong; Illawarra Health and Medical Research Institute, Wollongong, NSW, Australia; Illawarra and Shoalhaven Local Health District.

Second-generation antipsychotic drugs such as olanzapine are used to treat schizophrenia; however, they can cause serious metabolic side-effects such as weight gain and obesity. Liraglutide is a synthetic glucagon-like peptide-1 (GLP-1) receptor agonist with anti-obesity properties. We have recently shown that liraglutide prevents olanzapine-induced weight gain in rats; however, the mechanisms are unclear. Hypothalamic neuropeptide Y (NPY) plays an important role in olanzapine-induced weight gain. The aim of this study was to examine the effect of chronic olanzapine and liraglutide treatment on hypothalamic NPY expression.

Female Sprague-Dawley rats were administered olanzapine (2mg/kg), liraglutide (0.2mg/kg) and olanzapine+liraglutide co-treatment or vehicle (control) (n=12/group) for six weeks. Body weight was recorded. Hypothalamic brain sections were collected and NPY immunoreactivity was examined in the arcuate nucleus (ARC) and ventromedial hypothalamic nucleus (VMH) using DAB (3,3'-diaminobenzidine) immunohistochemistry (n=4-6/group).

Olanzapine treatment significantly increased body weight gain (p<0.05 vs control), whilst liraglutide co-treatment prevented body weight gain (p<0.001 vs olanzapine). Total NPY optical density, the number and intensity of immune-reactive NPY cells and the percentage of NPY coverage in both ARC and VMH hypothalamic regions did not differ between treatment groups.

This study suggests that obesogenic NPY levels reach a new homeostasis with chronic olanzapine and liraglutide administration. Further research into the mechanisms of liraglutide's prevention of weight gain is required.

Poster 6: Fronto-Parietal Connectivity as a Marker of Cognition in Affective Disorders

Diana Bol, Kai Tit Tan, Lynton Gratez, Oliver Shubert, Michael Ridding, Bernhard T Baune, Mitchell Goldsworthy, Scott Clark

University of Adelaide, Discipline of Psychiatry; University of Adelaide, Robinson Institute, Neuromotor Plasticity and Development (NeuroPAD); University of Melbourne, Faculty of Medicine, Dentistry and Health Science.

Fronto-parietal connectivity, reflected as synchronised neural oscillatory activity between key brain regions as measured by electroencephalography (EEG), is positively associated with higher cognitive functions in both healthy individuals and those with neurodegenerative and psychiatric disorders. Affective disorders including major depressive and bipolar disorder, are associated with cognitive impairment that persists after symptomatic remission, impacting on functional recovery. This study aims to compare resting-state functional connectivity with key executive functions and psychosocial functioning between individuals with affective disorders and healthy controls.

Participants were recruited via treating teams and advertisements. Participants were screened to confirm diagnostic groups. Mood symptoms were assessed using the Young Mania Rating Scale and Montgomery-Asberg Depression Rating Scale. General function was assessed using the Functional Assessment Short Test and Global Assessment of Functioning. Cognitive testing was performed using the THINC integrated tool, including tests on working memory, cognitive updating and set-shifting. EEG was recorded at rest with eyes open (3 minutes) and closed (3 minutes). Functional connectivity was measured with imaginary coherence between frontal (F3/F4) and parietal (P3/P4) electrodes.

A sample of 18 healthy controls (CT n=6; 33.33% female) and individuals with a confirmed diagnosis of major depressive disorder (MDD n=8; 62.5% female) and bipolar disorder (BD n=4; 100% female) met inclusion criteria. Participants with affective disorders had higher symptom measures compared to healthy controls. Healthy controls had more psychosocial and functional stability (mean FAST 1.16; GAF 83.33) compared the participants with MDD (mean FAST 13.38; GAF 66.88) and BD (mean FAST 20.25; GAF 70.25). We will present pilot data comparing fronto-parietal connectivity, cognitive and general function between these groups.

Patients with a diagnosis of mood disorder have symptomatic and functional deficits. EEG connectivity provides a novel biomarker to enable further understanding of the neural mechanisms of impaired cognition in affective disorders and may be useful to improve diagnosis and predict functional outcomes.

The author of this abstract was a recipient of a $250 South Australian Student Excellence Award

Poster 8: Multisystem allostatic load is associated with poor functional capacity in youth at ultra-high risk for psychosis

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Current pathophysiological models of psychotic disorders suggest that stress contributes to the aetiology and trajectory of the disorder. Allostatic load (AL), a multisystem index of immune, neuroendocrine and metabolic dysregulation, is thought to represent the cumulative biological impact of stress. Two recent studies suggest that AL is elevated in patients with first-episode psychosis and related to psychotic symptoms and poor social and occupational functioning. Here, we investigate the relationship between AL and clinical outcomes in individuals at ultra-high risk for psychosis.

We quantified AL in a sub-group of participants of the NEURAPRO study, a multicentre randomized-controlled trial of omega-3 polyunsaturated fatty acids versus placebo in people aged 13 - 40 at UHR for psychosis. A total of 106 participants underwent additional biomarker analysis and were included in the present study. AL was measure at baseline and clinical outcomes were assessed 6 and 12 months after study intake. Multivariate linear and logistic regression models were used to test the relationship between AL and clinical outcomes.

AL at baseline was associated with impaired social and occupational functioning at 6 months (β =-0.224, p=0.025) and with more severe manic symptoms at 6 months (β=0.207, p=0.026), taking into account relevant covariates including age and smoking. No significant associations were observed at the 12-month follow-up assessment or with any other clinical outcome measures.

Our data provide initial evidence for a link between AL and impaired functioning in individuals at UHR for psychosis. These observations are consistent with recent research demonstrating elevated AL in patients with psychotic disorders that is related to reduced functioning. Further studies are needed to evaluate AL as a potential predictor of early treatment response.

Poster 10: Age is a predictor of change in locomotor activity, anxiety- and cognitive-like behaviours, neuroimmune response and hippocampal gene expression

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Ageing has significant progressive effects on the brain affecting sensory, motor and cognitive functions. A large body of research in the past have investigated the effects of age on various behaviours and reported ageing-related behavioural dysfunctions, especially during old age. However, less is known on the effects of age during early to late middle stages of life and in the absence of all external interventions. Hence, we investigated the effects of ageing on locomotion, cognition-, anxiety- and depressive-like behaviours, and associated changes in gene expression and molecular biology in the brain of early to late middle age C57BL/6 mice.

Healthy C57BL/6 mice that were raised under controlled environmental conditions and in the absence of all interventions underwent behavioural testing at 4, 9 and 14 months of age using an established behavioural battery, which included the following behavioural tests: Home Cage (HC), Open Field (OF), Elevated Zero Maze (EZM), Barnes Maze (BM) and Forced Swim Test (FST). Following this, we conducted the molecular analysis of brain tissues and cervical lymph nodes using Immunohistochemistry and Reverse Transcriptase qPCR, and Fluorescence-activated sorting analysis respectively.

The 14-month-old mice showed significantly less baseline locomotion in the HC, significantly less exploration time and head dips in the open arms of EZM, and significantly higher latency in finding the escape box on days 1 and 4 of training and during the probe trial on day 5 in BM when compared to 4- and 9-month-old mice. Microglia numbers in the dentate gyrus and CD8+ memory T cells in the cervical lymph nodes increased towards late middle age. Age also altered the expression of some of the genes in the hippocampus selected for analysis.

Age is a predictor of change in locomotor activity, cognition- and anxiety-like behaviours, neuroimmune response and hippocampal gene expression. However, age alone (i.e., in the absence of all external interventions) may not be a regulating factor for depressive-like behaviour.

Poster 12: Impact of chronic early life adversity on fear extinction in juvenile and adolescent rats

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Early life is viewed as a developmental period in which adversity could cause long-term impairments in fear inhibition. Exposure to adversity in both the neonatal period (Postnatal Day (P) 2-13) and adolescence period (P21-42) has previously been shown to cause robust changes to fear-related behaviours. We hypothesized that chronic adversity early in life would be deleterious to fear inhibition throughout development in male and female Sprague-Dawley rats.

In Experiment 1: We subjected male and female neonatal rats to a limited bedding stress environment from P2-13. Five days later, animals underwent fear conditioning, extinction and were tested to see whether their fear would renew. In Experiment 2: We reared rats in social isolation from P21-42, at which they were either tested or resocialized and then tested in adulthood at P70. All animals underwent fear conditioning, extinction and were tested for their extinction retrieval ability.

In Experiment 1, we found that juvenile male rats exposed to a limited bedding stress environment displayed a robust relapse of fear following extinction compared to controls. However, juvenile female rats behaved no differently to controls as both groups displayed a relapse of fear. In Experiment 2, relative to group-housed controls, both male adolescent and resocialized adult rats displayed higher freezing at test. In contrast, female adolescent and resocialized adult rats displayed enhanced extinction acquisition compared to controls but showed similar levels of freezing at test.

Conclusions: Overall, these results demonstrate that exposure to adversity during early post-natal and adolescent development sex-specifically impacts the ability of rats to inhibit fear. Future work will determine whether exposure to adverse environments during development led to alterations in the activity of transposons (particularly long interspersed nuclear elements) in the rat genome.

Poster 14: Caught in the net: The role of perineuronal nets in rodent spatial memory.

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Emerging evidence suggests involvement of perineuronal nets (PNNs) in cognitive deficits seen in schizophrenia. PNNs are specialized aggregates of extracellular matrix (ECM) molecules that encapsulate the soma, dendrites and proximal axon segments of primarily GABAergic parvalbumin (PV+) interneurons, known to be responsible for mediating cortical oscillatory activity. It is thought that dysfunction of PNNs alters the synaptic integrity of PV+ interneurons, resulting in the presentation of cognitive deficits. The aim of my PhD is to elucidate the role that PNNs play in cognition and synaptic plasticity, and, using animal models, identify possible mechanisms that might cause their dysregulation in schizophrenia.

Twelve adult male BALB/c mice will undergo a bilateral craniotomy, receiving either local injections of the enzyme chondroitinase ABC (chABC), to degrade the PNNs, or saline, as a control. They will receive injections in the Retrosplenial cortex, a node of the Default Mode Network, and essential for spatial memory integration. The mice will then undergo a one day training session on Active Place Avoidance (APA), a task that assesses spatial memory, to examine whether PNNs are necessary for learning, followed by a reversal learning test to examine cognitive flexibility. The extent of PNN's will be quantified using immunohistochemistry.

It is expected that animals receiving chABC will have impaired performance compared with those receiving saline in the learning task. Furthermore, it is expected that chABC injected animals will also be impaired on the reversal learning compared with the saline-injected animals. With the prospective application of in vivo two-photon imaging, we aim to be able to develop a protocol to visualise the PNNs in a live animal to examine the role of the PNNs in dynamic synaptic remodelling that occurs during memory consolidation.

My projects will contribute significantly to understanding the role of PNNs in cognition and synaptic plasticity. This work will also increase our knowledge about brain mechanisms that are involved with complex behaviours, such as memory consolidation. Given that post mortem tissue from schizophrenia patients reveals disrupted PNNs and synaptic plasticity, this research may provide new insights into the pathophysiology of schizophrenia, leading to the identification of novel therapeutic targets with the potential of restoring cognitive function in the brain of patients afflicted by this illness.

Poster 16: Reduced GABAergic-related Gene Expression in the Midbrain in Schizophrenia

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Dopamine dysfunction in schizophrenia contributes to the pathophysiology of the disorder. In the cortex and hippocampus, gene expression associated with GABAergic interneurons, which modulate the function of dopamine, is reduced. The midbrain is the point of origin for the nigrostriatal pathway, which is implicated in the positive symptoms of schizophrenia. We hypothesised that GABAergic-related gene expression would be decreased in the midbrain, with the resulting loss of inhibition leading to increased dopamine action, and negative correlations between GABA-related and dopamine-related gene expression in schizophrenia.

Gene expression of vesicular GABA transporter (VGAT) and glutamate decarboxylase 67 kDA (GAD1), as well as GABA(A) receptor subunits α1 (GABRA1), α2 (GABRA2), and α5 (GABRA5), was measured with qRT-PCR in post-mortem midbrain tissue from 28 schizophrenia cases and 29 healthy controls (tissue supplied by the New South Wales Tissue Resource Centre). Analysis was conducted using student's t- tests or ANCOVA when genes correlated with covariates, RIN, PMI, or age. Correlations between GABAergic genes and tyrosine hydroxylase (TH), the dopamine synthesis enzyme, and dopamine transporter (DAT), were investigated.

Gene expression of VGAT ($F(1,53)=14.448$; $p=0.0004$) and GAD1 ($F(1,53)=11.487$; $p=0.001$) was reduced in schizophrenia relative to controls (27 and 35%, respectively). There were corresponding reductions in gene expression (between 17 – 42%) of GABRA1 ($U=192.0$, $p=0.001$), GABRA2 ($F(1,54)=1.389$; $p=0.022$), and GABRA5 ($F(1,53)=6.143$; $p=0.016$). There were no correlations between any genes and estimates of antipsychotic dose (p>0.05). Whilst none of the GABAergic and dopaminergic markers correlated in control cases, significant positive correlations between TH and GAD1 were observed in schizophrenia cases ($r=0.630$, $p=0.001$). GABRA2 correlated with DAT ($r=0.590$, $p=0.001$) and TH (0.589, $p=0.001$) in schizophrenia, but not controls.

Reductions in VGAT and GAD1 suggest reduced synthesis and packaging of GABA in neurons of the midbrain, and changes in GABA(A)R alpha subunits may indicate reduced inhibition of nigrostriatal dopamine neurotransmission. These results provide the first evidence for altered inhibitory neurotransmission in the midbrain in schizophrenia. Contrary to our hypothesis, positive correlations between markers of resident GABA neurons and dopamine neurons suggest concomitant loss of function in both neurotransmitter systems in the midbrain in schizophrenia. Future studies should explore mechanisms, such as oxidative stress or inflammation, or altered glutamate input, that may contribute to the decrease in both systems.

Poster 18: Reduced CXC chemokine family member expression predicts adult neurogenesis marker expression in the human subependymal zone in schizophrenia and bipolar disorder

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The human subependymal zone (SEZ) is the largest reservoir of newly-born inhibitory interneurons in the adult brain. Stem cell maintenance, progenitor proliferation and neuronal differentiation are regulated by signalling of the CXC motif chemokine 12 (CXCL12) through CXC motif chemokine receptors 4 (CXCR4) and 7 (CXCR7). Given decreased expression of neural stem cell, cell proliferation and neuronal progenitor markers in the SEZ in schizophrenia or bipolar disorder, we aimed to determine whether altered CXC chemokine family member expression may contribute to impaired neurogenic capacity in these psychiatric disorders.

Post-mortem tissue was obtained from 33 schizophrenia, 32 bipolar disorder and 33 control cases from the Stanley Medical Research Institute. SEZ tissue was dissected from 60 µm thick sections for RNA isolation and cDNA synthesis. Gene expression of CXCL12, CXCR4 and CXCR7 were measured by quantitative polymerase chain reactions using Fluidigm Biomark HDTM. Analyses of covariance were performed to assess diagnostic differences for each target gene. Semi-partial correlations were performed to assess whether CXC chemokine family member mRNAs may correlate with expression of different cellular developmental stages of neurogenesis in the SEZ. CXCL12 mRNA was decreased in schizophrenia compared to both controls (24%, $p=0.001$) and bipolar disorder (14%, $p=0.03$). CXCR4 and CXCR7 mRNAs were decreased in schizophrenia (9% and 33%, all $p\leq0.05$) and bipolar disorder (26% and 33%, all $p\leq0.007$) compared to controls.

CXCL12, CXCR4 and CXCR7 expression positively correlated with neural stem cell (GFAPδ, all $p\leq0.008$) and neuronal progenitor marker mRNAs (ASCL1, all $p\leq0.001$). CXCL12 and CXCR4 expression positively correlated with cell proliferation marker mRNA (MKI67, all $p\leq0.03$).

These findings provided the first molecular evidence of decreased CXC chemokine family member expression in the adult SEZ in schizophrenia and bipolar disorder, reinforcing the overlap of neuropathological abnormalities in these psychiatric disorders. Disease-specific reductions in CXCL12 expression indicate that schizophrenia cases may have exacerbated deficits in CXCL12 signalling capacity compared to bipolar disorder cases. Dysregulated CXC chemokine family member expression may hamper neurogenesis in the SEZ and potentially contribute to inhibitory interneuron deficits in cortical and subcortical brain regions in schizophrenia and bipolar disorder.

Poster 20: Amphetamine improves attention on a rodent signal detection task in a baseline-dependent manner

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Psychostimulants, such as low dose amphetamine, are commonly used to improve attentional deficits. Previous research indicates that amphetamine may improve performance in a baseline-dependent manner. We used Long-Evans (LE) rats administered dexamphetamine while being tested on a Signal Detection Task (SDT adapted from Turner and Burne, 2016, Psychopharmacology 233:3383-94). The aim was to compare whether low-performers benefited more from low dose amphetamine administration on this task compared to high-performers that had a high baseline level of attentional accuracy.

The SDT was used to examine changes in attention after dexamphetamine administration. Rats were tested in an operant chamber with an LED screen showing either a signal (grey) or non-signal (black) screen at varying durations that cued pellet rewards in either left or right reward receptacles. Intraperitoneal injections of dexamphetamine were delivered to 16 LE rats in 0.05mg/kg and 0.1mg/kg doses. Injections were delivered in a repeated measures design over four days of SDT testing. Saline injections were given on day 1, 0.05mg/kg of dexamphetamine on day 2, saline on day 3, and 0.1mg/kg of dexamphetamine on day 4.

After 5 days of baseline testing on the SDT, rats were split into high-performers and low-performers depending on whether they had scored above or below 80%. A paired comparison analysis validated that low-performers and high-performers showed statistically significant accuracy scores on the SDT. However, after administration of intraperitoneal dexamphetamine in either 0.05 mg/kg or 0.1 mg/kg doses, no significant difference in performance accuracy on the SDT remained between low-performers and high-performers. Furthermore, no significant differences in accuracy improvement were discovered between the two doses of dexamphetamine used in the experiment.

The results of this study demonstrate that dexamphetamine reliably improves performance on a task measuring attention and that this improvement is baseline-dependent. LE rats that previously showed poor baseline-performance on the SDT improved performance on this task resulting in a boost in performance to the level of the high-performers. However, the high-performers did not benefit from the same doses of dexamphetamine. These results support the hypothesis that dopamine levels follow an 'Inverted U-shaped' function whereby too much or too little dopamine impairs performance. In conclusion, this finding may be useful in predicting the efficacy of certain drugs through individual performance.

Poster 22: Building an International Consortium on Geriatric Depression

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The aetiology and pathophysiology of late-life depression (LLD) and differences between early-onset and late-onset depression are not well understood. Given the increasing ageing population, it is crucial to understand the disorder and its implications in more detail to advance treatment and preventative strategies. We propose an international consortium to pool relevant data to investigate the aetiology and pathophysiology of LLD, with a focus on late-onset depression, by uncovering the genetic, biological, psychological and environmental determinants and their interactions.

National and international study leads of population and clinical studies will be/have been invited to join the consortium. We will perform joint or mega-analyses using combined, harmonised datasets that yield collated results with enhanced statistical power, in addition to comparisons across geographical regions, ethnicities and sociocultural groups. By combining studies and analysing pooled data, we will be able to examine environmental and bio-markers of LLD with sufficient statistical power.

We have contacted relevant international collaborators and received positive feedback. CHeBA contributes to the consortium with data from 3 ongoing, longitudinal studies: 1) The Older Australian Twins Study investigates healthy brain ageing in older twins (65+ years), 2) The Sydney Memory and Ageing Study examines clinical characteristics and prevalence of mild cognitive impairment and determines the rate of change in cognition over time, 3) The Sydney Centenarian Study investigates determinants of successful aging in a cohort of very old Australians (95+ years). All studies include measures of depression, cognition, physical health, genetics and biomarkers.

The consortium will address the global unmet health priority of understanding the aetiology of LLD through collaboration, innovation and partnership. By pooling data and knowledge, we will shed light on the aetiology and pathophysiology of LLD and will contribute to the knowledge base for the development of prevention and treatment strategies.

Poster 24: CRP DNA methylomic score and depressive symptom outcomes in adolescents and young adults

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Depression is a complex condition, for which the underlying aetiology is still being understood. There is significant heterogeneity in the development of depressive symptoms through adolescence, with adolescents falling into identifiable trajectories including: low consistent, increasing, high consistent, and decreasing. C-reactive protein (CRP) is a marker of systemic inflammation, and has been consistently associated with depression and/or depressive symptoms. However, the mechanism (and causality) of elevated inflammation in depression is not yet established. Alterations in DNA methylation have also been associated with depression outcomes, and with CRP expression.

Whole blood DNA methylation from the Brisbane Longitudinal Twin Study (n = 606) was analysed using the Illumina 450K array. Using multiple regression we establish if CRP-associated DNA methylation risk scores predict depression symptoms at ages 12, 14, and 16, and depression diagnosis in early adulthood. We also investigate if CRP-associated DNA methylation risk scores at age 12 (n = 200) predict high and increasing depressive symptom trajectories through adolescence.

Our results demonstrate if CRP-associated DNA methylation loci predict current depression symptoms, and/or if they predict future depressive symptom trajectories through adolescence. We will also present exploratory analyses of the impact of discordant CRP-associated DNA methylation risk scores within twin pairs on depression outcomes.

This is the first study to investigate CRP associated DNA methylation scores in relationship with depression, and with adolescent depressive symptom trajectories. This will provide a more accessible method to investigate CRP and depressive symptoms in large cohorts with epigenomic data available.

Poster 26: Association between the age of onset of methamphetamine use and cue-extinction behaviour in people with methamphetamine use disorder

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Among illicit substances, methamphetamine (meth) represents one of the greatest global health threats. Meth-related deaths have doubled in Australia in recent years, and over 4% of Australians aged 14-19 have reported using meth in the past year. This is a major concern as adolescence is a period of heightened vulnerability to addiction. To further understand adolescent vulnerability to addiction, we investigated whether the age of onset of meth use is associated with cognition, extinction, and dopamine-related single-nucleotide polymorphisms (SNPs) in people with meth use disorder.

Four current meth users and matched-controls underwent a 3-hour session at St Vincent's Hospital Melbourne, in which they were administered the MINI International Neuropsychiatric Interview, the Positive and Negative Syndrome Scale (PANSS), several drug use questionnaires, a short cognitive task battery, and a 20-min cue-extinction task. The cue-extinction task consisted in the presentation of 35 meth-related cues, counterbalanced with 35 neutral (food-related) cues, matched for colour, quality, and modality.

We measured cue-induced cravings using skin-conductance response (SCR) throughout the task, and a 0-10 self-report scale. Whole blood, plasma and serum samples were collected immediately following testing. We measured physiological craving as the difference in SCR between meth and neutral cues. We found that meth users displayed higher physiological and objective cravings than controls at the start of the task. In addition, meth users' SCR decreased throughout the task, whereas there was no change in response in controls. When split into adolescent onset (first use 22 years-old; n=2), adolescent-onset users displayed significantly higher SCR to meth cues compared to adult-onset users.

Overall, these results show that cue-induced cravings may be extinguished upon repeated presentation of meth-related cues in current meth users. Additionally, these results provide evidence that the age of onset of meth use plays a role in cue-extinction behaviour, which may be why adolescent-onset users are more resistant to treatment and more liable to relapse. Future steps include investigating the association between SNPs in certain genes, age of onset of meth use, cognitive performance, and cue-extinction behaviour in meth users.

Poster 28: Elevated dopamine transmission impairs goal-directed action in mice: implications for schizophrenia

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Symptoms of schizophrenia include impaired motivation and cognitive deficits, and one of the most robust pathophysiological findings is increased striatal dopamine neurotransmission. The striatum is involved with the coordination of motor- and action-planning, decision-making, reinforcement and reward perception. Many of these cognitive deficits are not ameliorated by antipsychotic treatment. Thus, increased brain dopamine levels may contribute to cognitive dysfunction in schizophrenia in a D2 receptor independent manner, providing a potential avenue for interventions to improve daily functioning. The aim of this project was to assess the effects of elevated dopamine transmission on reward learning and goal-directed action in mice.

Using the Outcome-specific Devaluation Task (ODT), we were able to investigate learning of action-outcome associations (instrumental training), goal-directed action (choice testing) and reward valuation (value testing) in 24 adult male C57BL/6J mice. To manipulate baseline brain dopamine levels, mice were administered a systemic injection of either saline, 0.1, 0.5 or 1 mg/kg of amphetamine during instrumental training (n=6/dose group). Value testing was conducted twice, with and without a drug challenge. Locomotor activity during the amphetamine challenge was also observed using a 2-hour Open-Field Test pre- and post-operant testing.

Only the highest dose of amphetamine (1mg/kg) altered performance during action-outcome learning (instrumental training) driven by a reduction in the response rate. All doses of amphetamine (0.1, 0.5 & 1 mg/kg), impaired goal-directed action (choice testing) as demonstrated by no significant bias in responding to the newly valued outcome. In contrast, amphetamine did not alter reward valuation (value test) indicating that the deficits in goal-directed behaviour were due to the inability to update reward values into action after outcome-devaluation. Finally, only 1mg/kg amphetamine elevated locomotor behaviour and there was no evidence of a sensitisation due to repeated amphetamine administration.

The experimental results suggest that increased striatal dopamine transmission may underlie the deficits in goal-directed behaviour observed in people with schizophrenia. Therefore, the ODT represents a translational approach to examine complex cognitive processes relevant to schizophrenia such as goal-directed action and reward learning, and the ability to probe the underlying neural mechanisms in mice. The interactions between the cognitive and negative symptoms in schizophrenia are poorly understood and there are currently no efficacious treatments. Identifying the underlying neurobiology that contributes to these functional impairments will help to identify approaches to improve the quality of life in people with schizophrenia.

Poster 30: Personalising treatment for inflammation-associated depression: a randomised, controlled trial

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Major Depressive Disorder (MDD) is still poorly understood at a biological level and has poor treatment efficacy. New treatments must account for variation in pathophysiology between individuals. Inflammation has emerged as a relevant factor in some cases of MDD, and anti-inflammatory treatment has been shown to ameliorate symptoms. C-Reactive Protein (CRP) is an acute phase reactant in the inflammatory process and can be used as an effective marker of inflammation in peripheral blood. It has been shown to be present at concentrations above the normal range in individuals with current or past major depressive episodes.

PREDDICT is a randomised, controlled trial (n=200) of antidepressant treatment (vortioxetine) augmented with anti-inflammatory medication (celecoxib) or placebo. Celecoxib/placebo is allocated in a 1:1 randomised ratio to participants with high baseline CRP and with low baseline CRP respectively (four total groups; n=50). The celecoxib/placebo treatment lasts 6 weeks while vortioxetine is taken for 8 weeks with an optional 6 month follow-up period of continued administration. Participants are assessed for symptomatic, functional and cognitive changes fortnightly. Blood is collected at baseline, the conclusion of celecoxib/placebo treatment, and the conclusion of the follow-up period, allowing measurement of biological changes due to treatment.

The study aims to demonstrate that MDD symptoms and serum concentration of selected pro-inflammatory cytokines will decrease with treatment, and to demonstrate that the largest decrease will be found in participants with acute MDD and a high baseline CRP level treated with combination therapy of an antidepressant and anti-inflammatory. The study further aims to conduct an exploratory analysis of gene expression levels in blood samples provided by study participants and to correlate this with symptom change information as well as protein biomarkers from pre- and post-treatment time points.

This study is the first to account for the confirmation of inflammation prior to anti-inflammatory treatment allocation. If successful in its hypothesis, the study will demonstrate that anti-inflammatory medication is useful in MDD treatment, but only among those who are demonstrated to have inflammation-associated MDD. This distinction can help clinicians to recognise the benefit of anti-inflammatory treatments in MDD. Furthermore, they can understand and treat those who will likely respond to the intervention, but spare those who are unlikely to benefit from unnecessary polypharmacy, in a step towards personalisation of psychiatric treatment.

Poster 32: Perinatal Fluoxetine (Prozac) treatment causes alterations in neuronal maturation of exposed male offspring at adolescence: a correlation with anxiety-like behaviours.

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Approximately 10% of pregnant woman are prescribed antidepressant drugs such as the selective serotonin reuptake inhibitor (SSRI), Fluoxetine (FLX; Prozac), for the treatment of depression. Emerging evidence suggests maternal FLX treatment can increase the risk of neurodevelopmental disorders in offspring. We have recently shown in an animal model that maternal FLX treatment increases anxiety-like behaviour in adolescent offspring. Glutamatergic and glucocorticoid signalling in the amygdala are both central to mediating anxiety-like behaviour.

Therefore, this study aimed to determine if the glucocorticoid receptors and the glutamate NMDA receptor subunits were altered in the amygdala following developmental FLX exposure. Wistar-Kyoto (established model of depression) and Sprague-Dawley (healthy model) rodent dams were treated with 10mg/kg/day FLX from gestational day (GD) 0 to postnatal day (PND) 14. Offspring were euthanised at adolescence (PND42) and the amygdala dissected. Immunoblotting was used to examine GR isoforms (GRα and GRβ) and NMDA receptor subunits (NR1, NR2A and NR2B) in male and female offspring. Two-way ANOVAs were used to determine the effects of FLX exposure and rat strain on protein measures in both sexes.

Male WKY offspring showed increased GRβ and NR2B subunit expression compared to SD offspring, while FLX exposure in the WKY strain returned GRβ and NR2B levels back to SD control levels. FLX exposure did not influence GR expression in the amygdala of female offspring, however WKY offspring showed reduced GRα compared to SD offspring. FLX exposure increased NR1 and NR2A subunit levels in the amygdala of both male and female offspring, but only in the SD strain.

This study highlights the sex specific effects of maternal FLX treatment on offspring glucocorticoid and glutamate receptor biology in the amygdala, and shows the potential protective effect of this exposure on GRβ and NMDA subunits in a depressive strain. This is in contrast to our previous reports in the prefrontal cortex, where FLX exposure potentiated the effects of maternal depression on glutamate NMDA receptor subunit expression in male adolescent offspring. While this study provides important insight into potential effects of maternal FLX on the amygdala, it's important for future studies to consider the functional and anatomical heterogeneity of this region.

Poster 34: The effects of N-methyl-D-aspartate receptor hypofunction on sociability and mirror-directed behaviours in mice

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Impaired sociability is a symptom of various neuropsychiatric disorders including schizophrenia. N-methyl-D-aspartate receptor (NMDAR) hypofunction is hypothesised to underlie the pathogenesis of schizophrenia. MK-801 (dizocilpine) is a non-competitive NMDAR antagonist used to model the abnormal behaviours associated with this disorder including social deficits.

In the current study, we further investigated this pharmacological model and extended it to the salience of a mirror, as a potential social conspecific. MK-801 induced a dose- and time-dependent impairment in behavioural engagement with the mirror, when it was presented alone in a modified open field arena. Furthermore, mirror-directed sniffing failed to habituate over time in MK-801-treated mice. MK-801 (0.2 mg/kg) appeared to disrupt social and mirror preference in the three-chambered social approach task.

Overall, this study provided support for MK-801, at the dose of 0.2 mg/kg, to be used to induce impaired sociability. Although the lack of olfactory and auditory information limited some preference towards the mirror, it still appeared to be a salient social stimulus, which may provide insight into schizophrenia-like social impairments.

Poster 36: A systematic review and meta-analysis of 271 PCDH19-variant individuals identifies psychiatric comorbidities, and association of seizure onset and disease severity

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Girls Clustering Epilepsy (GCE) is an infantile onset disorder characterized by clusters of seizures. GCE is due to mutations in the X-chromosome gene PCDH19, and is underpinned by cellular mosaicism due to X-chromosome inactivation in females or somatic mutation in males. ID is present in approximately 70% of cases. The prevalence of psychiatric comorbidities is unknown, however, reports suggest that autism spectrum disorder is a common feature. No association has been established between the severity of epilepsy and ID. This review characterizes the neuropsychiatric profile of this disorder and examines the association of clinical and molecular factors with neuropsychiatric outcomes.

Studies were included if they met the following criteria: 1) reported the cDNA or protein change, 2) were peer-reviewed and written in English, and 3) were original cases only. For a study to be included in the meta-analysis, information regarding cognitive function or the degree of impairment, or the presence or type of psychiatric comorbidity was also required. A computerized search of public databases Embase, PubMed, Google Scholar, and Scopus from January 2008 to August 2017 was conducted. The search terms were: pcdh19, pcdh 19, protocadherin19, and protocadherin 19. Data were extracted from 38 original articles including 271 individual cases.

We found that seizure onset ≤12 months was significantly associated ($p = 4.127 \times 10-7$) with more severe intellectual disability, compared with onset >12 months. We identified two recurrent variants p.Asn340Ser and p.Tyr366Leufs*10 occurring in 25 (20 unrelated) and 30 (11 unrelated) cases, respectively. PCDH19 mutations were associated with psychiatric comorbidities in approximately 60% of females, 80% of affected mosaic males, and reported in nine hemizygous males. Hyperactive, autistic, and obsessive-compulsive features were most frequently reported. There were no genotype–phenotype associations in the individuals with recurrent variants or the group overall.

This review provides some insight into the type of psychiatric comorbidities that likely exist in association with PCDH19 mutations. In line with previous reports, we observe that autistic features are most prominent. A novel finding to emerge is that hyperactivity is frequently observed. We have shown that seizure onset within the first 12 months is significantly associated with more severe ID. Therefore, knowledge of an individual's seizure onset will aid prognostic counseling, providing valuable information for clinicians managing affected individuals and their families.

The author of this abstract was a recipient of a $250 South Australian Student Excellence Award

Poster 38: Exploring the origins of GABAergic dysfunction associated with schizophrenia in the maternal immune activation model uncovers a role for the Arx gene

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Schizophrenia is associated with GABAergic dysfunction and disrupted neural synchrony. More specifically, high frequency neural oscillations, particularly in the gamma frequency, modulated by parvalbumin-positive GABAergic interneurons are disrupted in schizophrenia. Epidemiological data identifies infection during pregnancy as a risk factor for the child to develop schizophrenia and in rodent models of maternal immune activation the offspring develop core behavioural and neurochemical features with relevance to schizophrenia, including reduced expression of parvalbumin. This study sought to further explore the prenatal origins of disrupted GABAergic function associated with schizophrenia using the maternal immune activation (MIA) model.

Pregnant dams received the viral mimetic, poly-I:C (20mg/kg, i.p.), at gestational day 17. In adult offspring, local field potentials from the CA1 hippocampus were simultaneously recorded during pre-pulse inhibition testing to assess auditory-evoked gamma and theta power. Foetal (24 hr post-poly-I:C) and adult brains were collected for mRNA (96.96 Biomark) and protein expression analysis. Gene expression findings were aligned with human genomic data from the Australian Schizophrenia Research Bank (ASRB) consisting of 500 schizophrenia patients, as well as from the Psychiatric Genomics Consortium 2 (PGC2) (over 900,000 patient samples) to identify commonalities between the rodent model and the human condition.

Acoustic-evoked gamma and theta power were reduced during the pre-pulse response in poly-I:C exposed mice, with impaired PPI performance. Poly-I:C exposure reduced expression of mRNA transcripts for GABAergic cell migration/specification, (Arx, Nkx2.1) in the foetal brain and reduced protein levels of parvalbumin and somatostatin, in adult forebrain. From the ASRB data set we identified a female patient with schizoaffective disorder with a missense mutation in the Arx gene. Furthermore, using a targeted hypothesis-driven approach, we found a nominal association of proximal single nucleotide polymorphisms within a 6.5Kb region surrounding the Arx gene and schizophrenia from the PGC2 data set.

Poster 40: Excitatory Amino Acid Transporter (EAAT)1 and EAAT2 mRNA levels show region-specific increases in the prefrontal cortex of subjects with schizophrenia

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Excitatory Amino Acid Transporter (EAAT)1 and EAAT2 are proposed to mediate the duration of glutamate receptor activation and prevent spill-over or glutamate excitotoxicity, through the perisynaptic binding and transportation of glutamate into glia. Using an Affymetrix™ microarray, we observed a 1.36 fold increase in EAAT1 mRNA expression in the prefrontal cortex (Brodmann's area (BA) 9) from subjects with schizophrenia. The aim of the current study was to determine whether changes in EAAT1 and EAAT2 mRNA levels occur in other cortical regions from subjects with schizophrenia.

cDNA was prepared from tissue extracted post-mortem from BA44, BA46 and BA10 of subjects with schizophrenia (n=20) and non-psychiatric controls (n=18), obtained from the Victorian Brain Bank Network. mRNA levels were measured using the Bio-Rad iQ5 qPCR Detection System with SYBR Green 1 dye technology. Reactions were measured in triplicate with results normalised to the geometric mean of two stably expressed reference genes – transcription factor B1, mitochondrial (TFB1M) and S-phase kinase-associated protein 1A (SKP1A).

Normalised levels of EAAT1 mRNA were significantly higher in BA44 and BA10, but not BA46, from subjects with schizophrenia compared to age and sex matched controls (Mann Whitney test, BA44 median fold increase: 1.24, p = 0.002; BA10 median fold increase: 1.70, p < 0.001; BA46 median fold increase: 0.73, p = 0.15). Normalised levels of EAAT2 mRNA were significantly higher in BA10, but not BA46, from subjects with schizophrenia compared to age and sex matched controls (Mann Whitney test, BA10 median fold increase: 1.66, p = 0.002; BA46 median fold increase: 1.41, p = 0.16).

Our data suggests that region-specific increases in EAAT1 and EAAT2 mRNA in the prefrontal cortex are involved in the pathophysiology of schizophrenia. These findings support a role for glia in glutamatergic dysfunction in schizophrenia and may have important implications for the treatment of the disorder.

Poster 42: Differential effects of chronic 17β-estradiol treatment on behaviours relevant to depression

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Neurobiological sex differences play an important role in the pathophysiology of psychiatric disorders, such as major depressive disorder which affects women at a higher incidence than men. Research indicates that the most potent endogenous estrogen, 17β-estradiol, may have therapeutic potential in treating depression. This study aimed to investigate the effects of chronic 17β-estradiol on behaviours relevant to depression.

This study used adult female Sprague-Dawley rats that were ovariectomised and treated with chronic 17β-estradiol or vehicle, via a subcutaneous silastic implant. Rats were assessed in the forced swim test, saccharin preference test, novel object recognition memory test and for possible confounding behaviours, including locomotion and anxiety (open field test) and motivation and anxiety (novelty supressed feeding test).

Treatment effects were verified using body and uterus weight, as well as serum concentrations of 17β estradiol, progesterone and testosterone. Compared to ovariectomised rats, chronic 17β estradiol treatment enhanced saccharin preference and novel object recognition performance, with results unlikely to be due to group differences in confounding behaviours. There were no group differences in passive or active coping behaviour when assayed using the forced swim test.

Taken together, these results support an antidepressant-like action of estrogens but highlight that the beneficial effects of chronic 17β-estradiol treatment are on specific depression-related symptoms, particularly anhedonia and memory.

Poster 44: miRNA expression signature of cognitive dysfunction in the peripheral blood of patients with schizophrenia

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Schizophrenia (SZ) is a neuropsychiatric disorder affecting 1% of the population. Patients display various symptoms, including cognitive impairments. While the diagnosis is currently based on signs and symptoms, by understanding SZ molecular determinant, we may be able to identify biomarkers and better direct treatment to the underlying causal factors. Genomic analyses indicate SZ as a complex developmental disorder involving many genes and epigenetic factors. MicroRNAs (miRNAs), a class of small non-coding RNAs that appear to be associated with SZ etiology, are explored in this study with the aim of identifying a miRNA expression signature associated with phenotypic subtypes of SZ.

We conducted small RNA-Seq on peripheral blood mononuclear cells (PBMCs) of male patients with severe cognitive deficits (CD group), collected by the Australian Schizophrenia Research Bank (ASRB), and compared it to those with moderate impairments (CS group). Raw sequencing reads were aligned to the reference genome (hg38) and analysed further through a customized pipeline, including the software FastQC, Cutadapt, Bowtie2 and Htseq. edgeR package of RStudio and ToppFun of the ToppGene Suite were employed for differential expression and pathway analyses, respectively.

We could detect several differentially expressed miRNAs with P-value<0.05. Pathway analysis for the most highly differentiated miRNA suggested the molecule is involved in several pathways related to the brain function and development, such as synaptic signaling, regulation of synaptic plasticity, neurogenesis, neuron differentiation and axonogenesis.

These pilot data suggest there may be miRNA expression changes associated with the cognitive deficit subtype of SZ to explore as an interesting candidate biomarker worthy of further investigation.

Poster 46: dietary β-glucan fiber improves cognition and gut microbiota in obese mice

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Excess fat and lower dietary fiber intake contributes to the development of obesity, which is associated with cognitive decline. Dietary fiber has beneficial effects in improving microbiota dysbiosis and cognition. This study examined effects of two types of soluble dietary fibres (beta-glucan) on gut microbiota, post-synaptic density, and cognition in mice.

Mice were fed 1-3,1-4 beta-glucan (oat bran) or 1-3,1-6 beta-glucan (curdlan) for 3 days (acute study) and 15 weeks (chronic study), mixed in high-fat (HF) or low-fat diet (LF). Gut microbiota in cecum content were examined by 16S sequencing in acute study. Temporal order test, novel object recognition test Y-maze test were performed in chronic study. The synapse morphology was examined in prefrontal cortex (PFC) and hippocampus by transmission electron microscopy (TEM).

Acute 1-3,1-4 beta-glucan and 1-3,1-6 beta-glucan supplementations decreased the abundance of Firmicutes and increased Bacterioides in the gut microbiota of mice on both LF and HF diets. In chronic study, these two beta-glucans increased the temper-order memory in LF mice. Chronic HF diet impaired temper-order memory, novel object recognition memory, and spontaneous alteration in Y maze test. Chronic 1-3,1-4 beta-glucan improved these three cognition scores in HF mice, while chronic 1-3,1-6 beta-glucan only improved the first two impairments in cognition. These two beta-glucan diets increased the post-synaptic density in the hippocampus and prefrontal cortex of HF mice examined by TEM.

Increasing the beta-glucan dietary fibre intake prevents alterations of gut microbiota and post-synaptic morphology in the brain regions involved in cognitive function. This maybe the neurobiological basis for improving altered cognitive function associated with obesity.

Poster 50: Smaller hippocampal volume predicts the development of posttraumatic stress disorder following sexual assault in females

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Exposure to sexual assault is a significant risk factor to develop posttraumatic stress disorder (PTSD) in females. However, the early neurobiological changes leading to the development of PTSD remains understudied and unclear in this population.

Participants were 25 victims of sexual assault recruited 1 month following exposure to sexual assault (T1) and 20 age-matched healthy controls. Among the victims, 10 participants met (PTSD+) and 15 did not meet (PTSD-) DSM-IV criteria for PTSD 6 months post-trauma (T2). At both visits, participants underwent magnetic resonance imaging and salivary cortisol samples were collected. Hippocampal volumes were extracted and areas under the curve relative to the ground (AUCg) were calculated (total diurnal cortisol changes). Measures at T1 were compared between groups at T1, measures at T2 between groups at T2, and measures at T1 between groups at T2.

At T1, victims had significantly smaller hippocampal volumes than controls (left: $p=0.004$, $r=-0.43$; right: $p=0.022$, $r=-0.34$), but AUCg did not significantly differ between groups. At T2, neither hippocampal nor AUCg significantly differed among the groups. However, hippocampal volumes at T1 were significantly smaller in the PTSD+ group relative to the control group (left: $p=0.021$, $r=-0.50$; right: $p=0.029$, $r=-0.48$), but not the PTSD- group.

This study indicates that having smaller hippocampal volumes is a risk factor to develop PTSD for females exposed to sexual assault.

Poster 52: Breast cancer induces cognitive impairment which is prevented by aspirin

Adam K Walker, Erica K Sloan

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70% of cancer patients report a decline in cognitive function and 40% have observable cognitive impairment with objective testing. For decades chemotherapy was considered the sole cause of cancer-associated cognitive impairment but recent clinical evidence shows that some patients present with cognitive impairment before chemotherapy. Indeed, studies show up to 50% of patients have cognitive impairment at diagnosis and after surgery but before adjuvant chemotherapy. One may expect that the anxiety caused by a life-threatening diagnosis or the impact of surgical stress causes this impairment. However, we hypothesised that the tumour itself can hijack the brain and impair its function.

To investigate if a non-CNS tumour can cause cognitive impairment in the absence of a cancer diagnosis and cancer surgery, we used mouse models of metastatic breast cancer. Syngenic mammary adenocarcinoma cells vs PBS were injected into the mammary fat pad of female mice and episodic memory was assessed. Cancer progression was measured using bioluminescence imaging. To determine if soluble factors secreted by tumour cells cause memory impairment, we injected mice with tumour cell-conditioned medium and assessed memory performance. The anti-inflammatory drug aspirin was delivered to mice in drinking water to determine if inflammation is causal in tumour-induced cognitive impairment.

Tumours caused memory impairment within 4 days after tumour cell injection prior to tumour palpability and metastasis, and independent of tumour-induced sickness or malaise. To confirm generalisability of this phenomenon, tumour-induced cognitive impairment was confirmed in an additional tumour cell line injected into a different strain of mice. Tumour cell-conditioned medium was sufficient to induce memory impairment. Multiplex analysis confirmed that an array of cytokines and chemokines were secreted by tumour cells into the medium and this inflammatory profile was consistent with the plasma and hippocampal inflammatory profile of tumour bearing mice. Aspirin abrogated tumour-induced cognitive impairment.

Our findings demonstrate that non-CNS tumours can hijack the brain to cause cognitive impairment. The fact that cognitive impairment was present within 4 days after tumour cell injection and prior to the development of sickness behaviour suggests that tumours may induce cognitive impairment before it is palpable and before patients experience symptoms that prompt them to seek medical advice. The ability of low dose aspirin to abrogate memory impairment demonstrates that inflammation mediates tumour-induced cognitive impairment, and implies the potential for this affordable and safe anti-inflammatory to be repurposed as an intervention for cancer-associated cognitive impairment.

Poster 54: Effect of lurasidone on cognitive impairment: from the lab to the clinic

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Sunovion Pharmaceuticals Inc, Fort Lee, New Jersey and Marlborough

Cognitive impairment is common in patients with schizophrenia. The aim of this review is to summarise results of pre-clinical and clinical data on the effect of lurasidone on cognitive function. In the pre-clinical battery, lurasidone restored MK-801-induced memory impairment in the passive avoidance and Morris water maze tests, improved working memory in the radial-arm maze test, improved PCP-induced deficits in novel object recognition test, and increased the success rate of marmosets in the object retrieval with detour task. In the first clinical trial, treatment with lurasidone 160 mg was significantly superior to both placebo and quetiapine XR 600 mg on the CogState composite score at week 6 ($p<0.05$), while lurasidone 80 mg, quetiapine XR, and placebo did not differ. In the double-blind extension phase, lurasidone treated patients performed significantly better than patients taking quetiapine XR on the CogState at month 6 ($p<0.01$). In the second clinical trial, lurasidone patients demonstrated significant within-group improvement from baseline on the MCCB composite score ($p=0.026$) and on the SCoRS ($p<0.001$). Taken together, these pre-clinical and clinical findings provide preliminary evidence to suggest that lurasidone may help improve cognition in patients with psychotic illness.

Awards

We would like to congratulate all recipients of awards in this year's scientific meeting. This includes attendees who have already received awards based on the quality of their abstracts, as well as the awards that will be presented at the conclusion of the meeting to the best presenters.

The five recipients of the Fay Fuller Foundation awards for the best abstracts by a HDR student studying at a South Australian institution were Salvatore Russo, Chnar Khoshnaw, Brock Harley, Kristy Kolc and Diana Bol. These 5 students will be reimbursed for the conference attendance cost ($250).

The three recipients of the Neuronal Signalling travel awards were Renata Pertile, Yann Quidé and Katrina Bird. They have each been given the opportunity to present their work to the entire conference for 10 minutes each, and will each receive $250.

The remaining awards to be allocated on the day are listed in the table below.

Number available	Award Sponsor	Award criteria	Value
1	Biological Psychiatry Australia	Best Data Blitz Presentation	$250
1	Neuronal Signalling	Best Data Blitz Presentation	$250
1	The Fay Fuller Foundation	best presentation by a South Australian-based HDR student (oral or poster)	$250
1	Biological Psychiatry Australia	Best poster presentation	$250
2	Servier	Best poster presentation	$250

Maps and locations

The welcome night function and the 2 days of the scientific meeting will be held at SAHMRI, North Terrace, Adelaide. The social event on the evening of Wednesday the 7th will be held at The Adelaide Oval.

The oval is accessible on foot walking from SAHMRI, taking about 15 minutes. Alternatively, take the tram one stop towards the Botanic Gardens for free, and walk from the Adelaide Railway Station in 7 minutes.

SAHMRI is easily reached from anywhere in Adelaide by AdelaideMetro services. For more details, see our website.