4th APSAAR / 5th IDARS Conference
August 18-21, 2015
Australia

FRONTIERS IN ADDICTION

Conference Program

SPEAKERS INCLUDE:
Elizabeth Elliott, University of Sydney, Australia
Andrew Holmes, National Institute of Alcohol Abuse and Alcoholism, USA
Susumu Higuchi, KMAC, Japan
George Koob, National Institute of Alcohol Abuse and Alcoholism, USA
Andrew Lawrence, The Florey Institute, Melbourne, Australia
Barbara Mason, The Scripps Institute, California, USA
Ed Riley, San Diego State University, California, USA
John Saunders, University of Sydney, Australia
Ken Warren, National Institute of Alcohol Abuse and Alcoholism, USA
Frontiers in Addiction

CONFERENCE THEMES

- Fetal Alcohol Spectrum Disorder
- Treatment of Drug Addiction: Methamphetamine, Cannabis, Opiates
- Frontiers in Addiction Pharmacotherapy
- The Nature and Diagnosis of Addictive Disorders
- Anesthetics, Inhalants and Opiates
- Substituted Amphetamine Neurotoxicity
- MDMA/Ecstasy, GHB and Designer Drugs
- Novel behavioural and pharmacological approaches to preventing drug-seeking and relapse
- Novel Neurobiological Targets for the Treatment of Alcoholism
- Substance Use among Indigenous Peoples
- Internet Gaming and Social Media
- The Vulnerable Brain

THE VENUE

THE WESTIN SYDNEY
Confession Venue
1 Martin Place, Sydney 02 8223 1111

Experience an energising retreat in the centre of the city, surrounded by Sydney's most enticing fashion retailers and restaurants. The Westin is located only minutes from the Sydney Opera House, Darling Harbour, NSW Art Gallery, and Sydney Harbour.

HIGHLIGHTS

Sydney is Australia’s largest and most famous city. It’s home to beautiful beaches, iconic buildings, historic landmarks, award-winning restaurants, and a vibrant culture. From the breathtaking views of Sydney Harbour to the serene tranquillity of Hyde Park, Sydney has something for everyone. If you’re looking for high-energy adventure holidays, planning a honeymoon, or searching for a fun-filled getaway, Sydney delivers an extraordinary wealth of short and long-term holiday options.

MUST DO

- Relax in Hyde Park
- Stroll around Sydney Opera House
- Book in a BridgeClimb
- Enjoy a cruise on Sydney Harbour
- Explore the Royal Botanic Gardens
- Dine at one of Sydney’s best restaurants
WELCOME

We welcome you to Sydney, which we – and many others – think is one of the great cities of the world. We are gathering together on the occasion of the Joint Conference of the Asia-Pacific Society on Alcohol and Addiction Research (APSAAR) and the International Drug Abuse Research Society (IDARS), combined with a special day on Fetal Alcohol Spectrum Disorder (FASD). This is the first occasion at which the two societies have combined forces, and we hope that the combination of laboratory science, clinical science, public health and clinical management will be an enticing one.

Much is stated these days about the importance of translational research. This will be evident in specific symposia but also we hope that it will suffuse the conference as a whole. We have used the by-line “Frontiers in Addiction” to convey the sense of excitement when basic science interfaces with clinical management and contributes to developing our capacity to effectively respond to substance use and other addictive disorders.

There are streams throughout the conference which reflect the particular focus of the parent societies and also the special stream on FASD, a major problem in many of our countries. Although he would not allow us to say this, the FASD focus is a special tribute to the work and efforts of Dr Ken Warren, Deputy Director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and contributor to our understanding of FASD over more than a generation.

We hope that during your time in Sydney you will also take the opportunity of interacting with scientific and clinical colleagues, both within the Conference and by visiting the many renowned research centres working on addictive disorders in metropolitan Sydney. We know that for many of you this is your first visit to Australia and we also hope that you have an opportunity to sample the tourist delights of Sydney and possibly for some of you further afield such as Australia’s Outback and the Great Barrier Reef. For those of you who will stay entirely within Sydney, it is a very attractive city, which has one of the great deep water harbours of the world and two iconic structures in the form of the Sydney Harbour Bridge and the Opera House. We hope you will also enjoy our local hospitality both within the conference and the natural bonhomie of Australian people.

John B Saunders  
Conference Convenor

Peter Dodd  
Conference Convenor
GENERAL INFORMATION

BREAKFAST
A light ‘stand-up’ breakfast is provided daily, courtesy of the Conference, starting from 0730

CONFERENCE RECEPTION
Tuesday 18 August 1830-1930
Heritage Ballroom - Pre-Function Area
Cost: complimentary to all Conference delegates
Includes: beverages and canapes

CONFERENCE DINNER
Wednesday 19 August 1930-late
Heritage Ballroom - Pre-Function Area
Cost: $0 (included in ‘registration package’) or $150 per person
Includes: arrival beverages and canapes, 3 course dinner with drinks

POSTER PRESENTATIONS
During the catering breaks each day, posters will be available for viewing on the poster-boards which will be located at the back of the Heritage Ballroom.
## CONFERENCE PROGRAM OVERVIEW

<table>
<thead>
<tr>
<th>Time</th>
<th>Tuesday 18 August Stream 1</th>
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<td>Heritage Ballroom</td>
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<td>6: Psycho-stimulants</td>
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<td>3: FASD – Basic and Clinical Science</td>
<td>8: The Vulnerable Brain</td>
<td>12: The Victims of Alcohol Misuse: Impacts on Indigenous Children</td>
<td>16: Free Oral Communications</td>
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<td>Conference Dinner (until 22:00)</td>
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We were pleased to have had such a strong response from researchers wanting to present their work during the FASD Program.

Thank you to FARE and the University of Sydney for sponsoring registrations and prizes (respectively) for the best oral and poster presentation categories ($500 each).
<table>
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**Breakfast and registration**

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**Afternoon tea/coffee with posters**

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**Public Lecture in Heritage Ballroom**

- Prof Marc Potenza: Gambling and On-line Addictions
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<tr>
<th>Time</th>
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<th>Topic</th>
<th>Affiliation</th>
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<tr>
<td>07:30</td>
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<td>Breakfast and registration</td>
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<td>Conference opening, Welcome</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 1: Fetal Alcohol Spectrum Disorder – Overview</strong></td>
<td><strong>CHAIR:</strong> Dr Ken Warren (Deputy Director, NIAAA, USA)</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<tr>
<td></td>
<td>Ken Warren</td>
<td>A brief history of Fetal Alcohol Spectrum Disorder</td>
<td>University of Sydney, Australia</td>
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<td>Edward Riley</td>
<td>Fetal Alcohol Spectrum Disorder: brain and behavior</td>
<td>San Diego State University, CA, USA</td>
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<td></td>
<td>Elizabeth Elliott</td>
<td>Clinical and public health challenges in Fetal Alcohol Spectrum Disorder</td>
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<td></td>
<td>Sharman Stone</td>
<td>The role of governments in addressing Fetal Alcohol Spectrum Disorder</td>
<td>Federal Member of Parliament for Murray, Australia</td>
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<td><strong>Morning tea and coffee</strong></td>
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<td>11:00</td>
<td><strong>SESSION 2: Fetal Alcohol Spectrum Disorder (FASD) in the Asia-Pacific Region</strong></td>
<td><strong>CHAIR:</strong> Prof Elizabeth Elliott (Australia)</td>
<td>Angeles University, Philippines</td>
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<td>Olga Tulabut</td>
<td>FASD in the Philippines</td>
<td>University of Western Australia</td>
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<td>Carol Bower</td>
<td>Addressing FASD in Western Australia</td>
<td>Telethon Kid’s Institute, University of Western Australia</td>
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<td>Denis Lamblin</td>
<td>FASD in Reunion and Tahiti</td>
<td>FASD Program, Reunion</td>
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<td>Heather d’Antoine</td>
<td>Alcohol in pregnancy and FASD in Indigenous Australians</td>
<td>Menzies School of Health Research, Darwin, NT, Australia</td>
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<td></td>
<td>Ira Chasnoff</td>
<td>Prevention and intervention for FASD in Hawaii: developing a system of care</td>
<td>National Training Institute Upstream, Portland, OR, USA</td>
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<td>Christine Rogan</td>
<td>FASD in New Zealand</td>
<td>Alcohol Healthwatch, New Zealand</td>
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<td><strong>Lunch and poster viewing</strong></td>
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<td>14:00</td>
<td><strong>SESSION 3: Fetal Alcohol Spectrum Disorder – Basic and Clinical Science</strong></td>
<td><strong>CHAIR:</strong> Prof Jane Latimer (George Institute for Global Health, Australia)</td>
<td>University of Queensland, Australia</td>
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<tr>
<td></td>
<td>Karen Moritz</td>
<td>Long term outcomes of prenatal alcohol exposure – more than just effects on the brain</td>
<td>Rutgers University, NJ, USA</td>
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<td>Dipak Sakar</td>
<td>Endocrine, metabolic and immune disorders in fetal-alcohol-exposed adult animals</td>
<td>University of Otago, New Zealand</td>
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<td></td>
<td>Ruth Napper</td>
<td>Studies in animal models identify short and long term risks of prenatal binge alcohol exposure</td>
<td>University of Queensland, Australia</td>
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<td>Vicki Russell</td>
<td>FASD in regional Australia</td>
<td>NoFASD Australia</td>
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<td>Diana Zanfranche</td>
<td>The effects of maternal periconceptional ethanol exposure on long term cognitive outcomes in rat offspring</td>
<td>University of Queensland, Australia</td>
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<td>James Fitzpatrick</td>
<td>The Lilllian Project: neurodevelopmental outcomes and FASD in remote Aboriginal Australian children</td>
<td>University of Sydney and Telethon Kid’s Institute, Perth, W Australia</td>
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<td>Claire McCormack</td>
<td>Prenatal alcohol consumption prior to awareness of pregnancy</td>
<td>NDARC, University of NSW, Sydney, Australia</td>
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<td>16:30</td>
<td><strong>SESSION 4: Fetal Alcohol Spectrum Disorder - Selected Oral Presentations</strong></td>
<td><strong>CHAIR:</strong> Prof Ed Riley (San Diego State University, USA)</td>
<td>University of Sydney, Australia</td>
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<td>Barbara Lucas</td>
<td>Paediatric soft neurological signs in FASD: population-based study in remote Australia</td>
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<td>Heather Jones</td>
<td>Fetal Alcohol Spectrum Disorder educational resources for justice professionals</td>
<td>Telethon Kid’s Institute, Perth, Western Australia</td>
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<td>17:00</td>
<td><strong>SESSION 5: Fetal Alcohol Spectrum Disorder - Policy and Legal Perspectives</strong></td>
<td><strong>CHAIR:</strong> Dr Margaret Murray (NIAAA, USA)</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<td>Michael Thorn</td>
<td>Developing national approaches to address alcohol consumption in pregnancy and Fetal Alcohol Spectrum Disorder</td>
<td>Foundation for Alcohol Research and Education, Australia</td>
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<td>Margaret Murray</td>
<td>International initiatives in Fetal Alcohol Spectrum Disorder</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<td>Judge Linda Chezem</td>
<td>Legal perspectives on Fetal Alcohol Spectrum Disorder</td>
<td>USA</td>
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<td><strong>PANEL DISCUSSION – PANELLISTS:</strong></td>
<td>Denis Lamblin (Reunion, France); Sharman Stone (Australia)</td>
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<td>18:25</td>
<td><strong>Presentation of Prizes - best oral and best poster presentations</strong></td>
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<td><strong>Conference Reception – Heritage Ballroom Pre-Function Area</strong></td>
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<tr>
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<td>Breakfast and registration</td>
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<td>08:15</td>
<td>Conference opening, Welcome</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 6: Psychostimulants</strong></td>
<td><strong>CHAIR:</strong> Dr Jean Zwiller (France) and Prof Eliot Gardner (USA)</td>
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<tr>
<td></td>
<td>Ming Xu</td>
<td>DRD1, DRD3 and reconsolidation of cocaine memories in mouse self-administration model</td>
<td>University of Chicago, IL, USA</td>
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<td>Jean Zwiller</td>
<td>Cocaine self-administration and DNA methylation: a genome-wide study</td>
<td>Laboratoire de Neurosciences Cognitives, University of Strasbourg, France</td>
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<td>Eliot Gardner</td>
<td>Agonist replacement therapy for cocaine addiction – On the horizon?</td>
<td>National Institute on Drug Abuse, MD, USA</td>
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<td>Morning tea and coffee</td>
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<tr>
<td>11:00</td>
<td><strong>SESSION 7: Infection and Addiction</strong></td>
<td><strong>CHAIR:</strong> Dr Sulie Chang (USA) and Prof Dipak Sarkar (USA)</td>
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<td></td>
<td>Mark Hutchinson</td>
<td>The ‘other brain’: how knowing you are sick has implications for drug abuse liability</td>
<td>University of Adelaide, Australia</td>
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<td>Dipak Sarkar</td>
<td>Immune cells in the brain control alcohol programming effect on stress and addictive behaviors</td>
<td>Program of Endocrinology, Rutgers University, NJ USA</td>
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<td>Sulie Chang</td>
<td>NeuroHIV leading to the use of addictive substances</td>
<td>Seton Hall University, NJ, USA</td>
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<td>13:00</td>
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<td>14:00</td>
<td><strong>SESSION 8: The Vulnerable Brain</strong></td>
<td><strong>CHAIR:</strong> Prof Dan Lubman (Australia)</td>
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<td></td>
<td>Nadia Solowij</td>
<td>Cannabinoid effects on human brain structure and function: injury, protection, recovery</td>
<td>University of Wollongong, Australia</td>
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<td></td>
<td>Kelly Clemens</td>
<td>Nicotine and the brain</td>
<td>University of NSW, Australia</td>
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<td>Raimondo Bruno</td>
<td>Acute and residual effects of stimulant substances among young adults</td>
<td>University of Tasmania, Australia</td>
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<td>Subhash Pandey</td>
<td>Adolescent alcohol exposure: persistent epigenetic &amp; behavioral changes in adulthood</td>
<td>University of Illinois, IL, USA</td>
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<td></td>
<td>Dan Lubman</td>
<td>Substance use and brain development</td>
<td>Monash University, Australia</td>
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<td>16:00</td>
<td>Morning coffee and tea</td>
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<tr>
<td>16:30</td>
<td><strong>SESSION 9: Current Controversies in Internet Use Disorders</strong></td>
<td><strong>CHAIR:</strong> Prof Susumu Higuchi (Japan)</td>
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<tr>
<td></td>
<td>Wei Hao and Vladimir Poznyak</td>
<td>Position of behavioural addictions in ICD 11</td>
<td>Mental Health Institute, Central South University, China, and WHO, Geneva, Switzerland</td>
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<td>Marc Potenza</td>
<td>Neurodevelopmental features of Internet use and gaming problems</td>
<td>Yale University, CT, USA</td>
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<td>Chang Woo Han</td>
<td>Substance use disorder and internet addiction</td>
<td>Korea University, Ansan Hospital, Korea</td>
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<td></td>
<td>Susumu Higuchi</td>
<td>Clinical description and diagnostic guidelines</td>
<td>Kurihama Hospital, Japan</td>
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<td>18:30</td>
<td>Conference Reception – Heritage Ballroom Pre-Function Area</td>
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# OUTLINE OF SCIENTIFIC PROGRAM

## STREAM #1: HERITAGE BALLROOM

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Topic</th>
<th>Affiliation</th>
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<tr>
<td>07:30</td>
<td>Breakfast and registration</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 10: Preventing Drug-Seeking and Relapse: 1</strong>&lt;br&gt;CHAIR: Prof Andrew Lawrence (Australia) and Dr Antonio Noronha (USA)</td>
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<tr>
<td></td>
<td>Antonio Noronha (Introduction)</td>
<td>Alcohol dependence: a chronic relapsing behavioral disorder</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<td>George Koob</td>
<td>“Dark side” medications for treating addiction</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<td>Andrew Holmes</td>
<td>Neural circuits in punished alcohol-seeking</td>
<td>National Institute on Alcohol Abuse and Alcoholism, MD, USA</td>
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<tr>
<td>11:00</td>
<td><strong>SESSION 11: Preventing Drug-Seeking and Relapse: 2</strong>&lt;br&gt;CHAIR: Prof Andrew Lawrence (Australia) and Dr Antonio Noronha (USA)</td>
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<tr>
<td></td>
<td>Cavan McNally</td>
<td>From lapse to relapse: environment and neural circuits for drug seeking reacquisition</td>
<td>University of NSW, Sydney, Australia</td>
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<td>Nick Gilpin</td>
<td>Traumatic stress, nociception and drinking: CRF signaling in the amygdala</td>
<td>LA State University Health Science Center New Orleans, USA</td>
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<td>Bernard Baleine</td>
<td>Neural bases of drug-induced changes in behavioural control</td>
<td>BMRI, University of Sydney, Australia</td>
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<td></td>
<td>Paul Klenowski</td>
<td>Circuits modulating alcohol drinking</td>
<td>Queensland University of Technology, Australia</td>
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<td>13:00</td>
<td>Lunch and poster viewing</td>
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<td>14:00</td>
<td><strong>SESSION 12: The Victims of Alcohol Misuse: Impacts on Indigenous Children</strong>&lt;br&gt;CHAIR: Dr Richard Chenhall (Australia)</td>
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<td></td>
<td>Marcia Langton</td>
<td>The victims of alcohol misuse</td>
<td>Australian Indigenous Studies, University of Melbourne, Australia</td>
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<td>Elizabeth Elliott</td>
<td>FASD research in remote Aboriginal Australia</td>
<td>University of Sydney, Sydney, Australia</td>
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<td>Robyn Doney</td>
<td>Visual-motor integration impairment and FASD: a population-based study of children in the Fitzroy Valley</td>
<td>School of Public Health, Curtin University, Western Australia</td>
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<td>Emily Fitzpatrick</td>
<td>Starting the conversation: seeking consent for research with indigenous populations</td>
<td>University of Sydney, Sydney, Australia</td>
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<td>16:00</td>
<td>Afternoon tea and coffee with posters</td>
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<td>Poster viewing</td>
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<td>19:30</td>
<td>Conference Dinner</td>
<td>Heritage Ballroom Pre-Function Area</td>
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## STREAM #2: MEETING ROOM 1

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<th>Time</th>
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<tr>
<td>07:30</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 14: Genetics</strong>&lt;br&gt;CHAIR: Dr Alfreda Stadlin</td>
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<td></td>
<td>Mostofa Jamal</td>
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<td></td>
<td>Asheeta Prasad</td>
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<td>Ihn-Geun Choi</td>
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<td>10:30</td>
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<tr>
<td>11:00</td>
<td><strong>SESSION 15: Behavioural</strong>&lt;br&gt;CHAIR: Prof Kazutaka Ikeda</td>
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<td>James Kasper</td>
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<td>Kazutaka Ikeda</td>
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<td>Susan Schenk</td>
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<td>13:00</td>
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<td><strong>SESSION 16: Free Oral Co</strong>&lt;br&gt;CHAIR: Dr Snehasikta Swarnakar</td>
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<td>Huixi Dong</td>
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<td>Satoko Mihara</td>
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<td>16:00</td>
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<td>18:30</td>
<td><strong>SESSION 17: Free Oral Co</strong>&lt;br&gt;CHAIR: Dr Jyotshna Kanungo</td>
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<td>Ajeet Kaushik</td>
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<td>Frederico Pereira</td>
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<td>Jorge Campusano</td>
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<td>Peter Serrano</td>
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<td>Jyotshna Kanungo</td>
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**DAY 2**

- **SESSION 10: Preventing Drug-Seeking and Relapse: 1**
- **SESSION 11: Preventing Drug-Seeking and Relapse: 2**
- **SESSION 12: The Victims of Alcohol Misuse: Impacts on Indigenous Children**
- **SESSION 13: Comorbidity and Complications in Addiction**
- **SESSION 14: Genetics**
- **SESSION 15: Behavioural**
- **SESSION 16: Free Oral Co**
- **SESSION 17: Free Oral Co**
STREAM #2: MEETING ROOM 1

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<td>08:30</td>
<td>Jyotshna Kanungo</td>
<td>Free Oral Communications</td>
<td>Hunter College, USA</td>
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<td>09:00</td>
<td>Peter Serrano</td>
<td>Free Oral Communications</td>
<td>Católica de Chile, Chile</td>
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<td>Frederico Pereira</td>
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<td>University of Coimbra, Portugal</td>
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<td>Satoko Mihara</td>
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<td>International University NanoMed, FL</td>
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<td>Snehasikta Swarnakar</td>
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<td>11:00</td>
<td>In-Won Chung</td>
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<td>Kurihama National College of Nursing, Japan</td>
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<td>Huixi Dong</td>
<td>Free Oral Communications</td>
<td>National Center for Toxicological Research, USA</td>
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<td>Susan Schenk</td>
<td>Free Oral Communications</td>
<td>Teikyo University, Japan</td>
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<td>Kazutaka Ikeda</td>
<td>Free Oral Communications</td>
<td>Kagawa University, Japan</td>
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<td>James Kasper</td>
<td>Free Oral Communications</td>
<td>University of Tsukuba, Japan</td>
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<td>13:30</td>
<td>Asheeta Prasad</td>
<td>Free Oral Communications</td>
<td>Koryo Hospital, Japan</td>
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<td>14:00</td>
<td>Mostofa Jamal</td>
<td>Free Oral Communications</td>
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STREAM #3: MEETING ROOM 2

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<td>08:30</td>
<td>Hisatsugu Miyata</td>
<td>Substance Use and Relaxation (JSND Symposium)</td>
<td>Jikei University School of Medicine, Japan</td>
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<td>09:00</td>
<td>Keun Ho Joe</td>
<td>Substance Use and Relaxation (JSND Symposium)</td>
<td>Dasarang Central Hospital, Korea</td>
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<tr>
<td>09:30</td>
<td>Kohji Takada</td>
<td>Substance Use and Relaxation (JSND Symposium)</td>
<td>Teikyo University, Japan</td>
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<tr>
<td>10:00</td>
<td>Moritoshi Kido</td>
<td>Substance Use and Relaxation (JSND Symposium)</td>
<td>Osaka University of Commerce, Japan</td>
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<td>11:00</td>
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<td>Morning tea and coffee</td>
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<tr>
<td>12:00</td>
<td>Tomohiro Shirasaka</td>
<td>Internet overuse: comorbidity of high school students in Japan</td>
<td>Sapporo Medical University, Sapporo, Japan</td>
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<tr>
<td>12:30</td>
<td>Chia Chun Hung</td>
<td>Internet overuse: comorbidity of high school students in Japan</td>
<td>Yang Ming University, Taiwan</td>
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<tr>
<td>13:00</td>
<td>Woraphat Ratta-apha</td>
<td>Internet overuse: comorbidity of high school students in Japan</td>
<td>Mahidol University, Bangkok, Thailand</td>
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<tr>
<td>13:30</td>
<td>Masuo Tanaka</td>
<td>Internet overuse: comorbidity of high school students in Japan</td>
<td>Koryo Hospital Japan</td>
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<tr>
<td>14:00</td>
<td>Tetsuji Cho</td>
<td>Internet overuse: comorbidity of high school students in Japan</td>
<td>Mie Mental Care Centre</td>
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<td>15:00</td>
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<td>Lunch and poster viewing</td>
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<td>16:00</td>
<td>Hwei-Hsien Chen</td>
<td>Facial pain in the elderly</td>
<td>National Health Research Institute, Taiwan</td>
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<td>Facial pain in the elderly</td>
<td>University of Hermosillo, Mexico</td>
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<td>Nagoya University, Japan</td>
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<td>18:00</td>
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<td>Facial pain in the elderly</td>
<td>University of California, San Francisco, USA</td>
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<td>Facial pain in the elderly</td>
<td>University of Minnesota, USA</td>
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<td>20:00</td>
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<td>Facial pain in the elderly</td>
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Poster viewing
Conference Dinner
Heritage Ballroom Pre-Function Area
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<tr>
<td>07:30</td>
<td>Breakfast and registration</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 22: The Impact of Addictive Disorders in Asia. 1. Alcohol</strong></td>
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<td><strong>CHAIR:</strong> To Be Advised</td>
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<td></td>
<td>Soontaree Srikosai Attitudes of Thai nurses toward alcohol-dependent patients</td>
<td>Rajanagarindra Institute, Thailand</td>
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<td>Sathiarany Vong Alcohol misuse in Cambodia</td>
<td>MCH Ministry of Health, Cambodia</td>
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<td>Sung-Con Kim Culture and alcoholism</td>
<td>Pusan National University, Korea</td>
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<td>11:00</td>
<td><strong>SESSION 23: The Impact of Addictive Disorders in Asia. 2. Illicit Drugs</strong></td>
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<td><strong>CHAIR:</strong> Prof John Saunders (Australia)</td>
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<td>Roongnapa Kamplang and Sawitri Assanangkornchai Estimating the size of IDU</td>
<td>Prince of Songkla University and Health Innovation and Technology Assessment Programme, Thailand</td>
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<td>population and developing responses in Thailand</td>
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<td>Sawitri Assanangkornchai and Li Lei Methamphetamine use among IDUs and current</td>
<td>Prince of Songkla University, Thailand and Yunnan Institute of Drug Abuse, China</td>
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<td>harm reduction responses in a border area of Yunnan, China</td>
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<td>Civilai Wanaratwichit Prevention of methamphetamine addiction by rural health</td>
<td>Naresuan University, Thailand</td>
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<td>Narongsak Noosorn Drug addiction among hill tribe youth of lower Northern</td>
<td>Naresuan University, Phitsanulok, Thailand</td>
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<td>13:00</td>
<td>Lunch and poster viewing</td>
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<td>14:00</td>
<td><strong>FREE AFTERNOON</strong></td>
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### STREAM #2: MEETING ROOM2

#### THURSDAY 20 AUGUST

**DAY 3**

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<td>07:30</td>
<td>Breakfast and registration</td>
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<tr>
<td>08:30</td>
<td><strong>SESSION 24: Free Oral Communications</strong>&lt;br&gt; <strong>CHAIR:</strong> Prof Glen Hanson</td>
<td>Hypocretin neurotransmission mediates compulsive-like cocaine taking and seeking</td>
<td>National Institute on Drug Abuse, MD, USA</td>
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<td>Brooke Schmeichel</td>
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<td>Yuri Persidsky</td>
<td>CB2R agonists diminish inflammation and BBB injury in HIV infection and alcohol use</td>
<td>Temple University School of Medicine, USA</td>
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<td>Mohan Sopori</td>
<td>Airway epithelial cells in lung diseases</td>
<td>Lovelace Research Institute, USA</td>
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<td>10:30</td>
<td>Morning tea and coffee</td>
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<td>11:00</td>
<td><strong>SESSION 25: Free Oral Communications</strong>&lt;br&gt; <strong>CHAIR:</strong> To Be Advised</td>
<td>Effect of nicotine on the metabolism and locomotor activity of rats</td>
<td>PK Anokhin Research Institute, Russia</td>
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<td>Valentina Bashkatova</td>
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<td>Johnny He</td>
<td>HIV, HCV and alcohol: Role of HIV-1 Nef</td>
<td>University of Texas Health Science Center, TX, USA</td>
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<td></td>
<td>Emmanuel Onaivi</td>
<td>Endocannabinoid system alterations in an animal model of autism spectrum disorders</td>
<td>William Paterson University, NJ, USA</td>
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<td>Kiyofumi Yamada</td>
<td>The insula controls decision-making in healthy and methamphetamine-treated rats</td>
<td>Nagoya University, Japan</td>
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<td>13:00</td>
<td>Lunch and poster viewing</td>
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<td><strong>FREE AFTERNOON</strong></td>
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<td>07:30</td>
<td>Breakfast and registration</td>
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<td>08:30</td>
<td><strong>SESSION 26: The Nature and Diagnosis of Addictive Disorders</strong></td>
<td><strong>CHAIR:</strong> Prof John Saunders</td>
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<td></td>
<td>Vladimir Poznyak</td>
<td>ICD 11: overall approach and current status</td>
<td>World Health Organization, Geneva, Switzerland</td>
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<td>Marc Potenza</td>
<td>Gambling as an addiction</td>
<td>Yale University, CT, USA</td>
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<td>John Saunders</td>
<td>ICD 11: How do we describe and define substance &amp; other addictive disorders?</td>
<td>University of Sydney and University of Queensland, Australia</td>
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<td>Sawitri Assanangkornchai</td>
<td>ICD 11: how are substance disorders understood in different cultures?</td>
<td>Prince of Songkla University, Thailand</td>
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<td>Ben Teoh</td>
<td>What do clinicians need from a diagnostic system?</td>
<td>South Pacific Private Hospital, Sydney, Australia</td>
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<td>Morning tea and coffee</td>
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<td>11:00</td>
<td><strong>SESSION 27: Translational Research: Treatment of Alcohol Misuse</strong></td>
<td><strong>CHAIR:</strong> Prof Barbara Mason (USA)</td>
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<td></td>
<td>Leandro Vendruscolo</td>
<td>Dysregulation of glucocorticoid systems in alcohol dependence</td>
<td>National Institute on Drug Abuse, MD, USA</td>
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<td></td>
<td>Barbara Mason</td>
<td>Translational research on mifepristone: prospects for the treatment of alcohol dependence</td>
<td>The Scripps Institute, CA, USA</td>
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<td>Paul Haber</td>
<td>Update on alcohol pharmacotherapy</td>
<td>University of Sydney, Sydney, Australia</td>
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<td>Friedbert Weiss</td>
<td>Pharmacotherapies for relapse prevention</td>
<td>The Scripps Institute, CA, USA</td>
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<td>Carl Lin</td>
<td>Increased human DAT gene activity spurs alcohol</td>
<td>McLean Hospital, MA, USA</td>
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<td>Lunch with posters</td>
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<td>14:00</td>
<td><strong>SESSION 28: Cannabis and Medicinal Cannabinoids</strong></td>
<td><strong>CHAIR:</strong> Prof Eliot Gardner and Prof Emmanuel Onaivi (USA)</td>
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<td></td>
<td>Emmanuel Onaivi</td>
<td>THC pharmacotherapy &amp; potential treatments</td>
<td>WPM Paterson University, N, USA</td>
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<td>Iain McGregor</td>
<td>Development of medicinal cannabinoids</td>
<td>University of Sydney, Sydney, Australia</td>
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<td>Alex Wodak</td>
<td>Research on medicinal cannabis: practical steps and political influences</td>
<td>St. Vincent’s Hospital, Sydney, Australia</td>
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<td>16:00</td>
<td>Afternoon tea and coffee</td>
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<td>16:30</td>
<td>Public Lecture in Heritage Ballroom</td>
<td>Chair: Revd. Keith Garner, Superintendent Wesley Mission (Australia)</td>
<td>Prof Marc Potenza: Gambling and On-line Addictions</td>
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<td>Conference close</td>
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<td>Breakfast and registration</td>
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<td>08:30</td>
<td>SESSION 29: Anæsthetics, Psychostimulants, and Opiates</td>
<td>CHAIR: Prof Merle Paule and Dr Shilpa Buch (USA)</td>
<td>National Center for Toxicological Research, AR, USA, USA</td>
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<td></td>
<td>Merle Paule</td>
<td>Anæsthetics in pædiatric populations</td>
<td>National Center for Toxicological Research, AR, USA</td>
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<td>Glen Hanson</td>
<td>Broadening the dimensions methamphetamine preclinical studies: links with Parkinson's disease</td>
<td>University of Utah, UT, USA</td>
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<td>Cheng Wang</td>
<td>Sevoflurane-induced neuronal damage and its potential biomarkers</td>
<td>National Center for Toxicological Research, AR, USA</td>
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<td>Shilpa Buch</td>
<td>Cocaine mediates microglial activation via down-regulation of microRNA 124</td>
<td>University of Nebraska, USA</td>
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<td>Sabita Roy</td>
<td>Morphine induces distinct gut microbiome signatures via the TLR2 pathway</td>
<td>University of Minnesota, USA</td>
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<td>Morning tea and coffee</td>
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<td>11:00</td>
<td>SESSION 30: Pharmacology and Toxicology</td>
<td>CHAIR: TBA</td>
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<td>Jason White</td>
<td>Wastewater analysis as a tool in monitoring drug use</td>
<td>University of South Australia, Adelaide, SA, Australia</td>
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<td>Nadine Ezard</td>
<td>The case for incorporating drug checking into Australia’s drug trend monitoring systems</td>
<td>St. Vincent's Hospital, Sydney, Australia</td>
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<td>Nadine Ezard and Robin Butterfield</td>
<td>Casualties of an unknown substance in an inner Sydney hospital</td>
<td>St. Vincent's Hospital, Sydney, Australia</td>
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<td>Monica Barratt</td>
<td>Improving the monitoring on new psychoactive substances in Australia</td>
<td>St. Vincent's Hospital, Sydney, Australia</td>
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<td>Lunch with posters</td>
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<td>IDARS Panel Discussion: 14.00–16:00 [Panel members TBA]</td>
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| 16:30 | Public Lecture in Heritage Ballroom | Chair: Revd. Keith Garner, Superintendent Wesley Mission (Australia)  
Prof Marc Potenza: Gambling and On-line Addictions |                                                 |
| 18:30 | Conference close            |                                                    |                                                 |
TUESDAY 18 AUGUST

A Brief History of Fetal Alcohol Spectrum Disorders: How did this disorder go unrecognized for ¾ of the 20th Century; What we now understand about prevalence across the world

Dr Kenneth Warren

1National Institute on Alcohol Abuse and Alcoholism, Bethesda, United States

The teratologic consequences that arise from the consumption of alcohol during pregnancy were not recognized until late in the 20th century, even though a review of health issues surrounding alcohol in earlier periods of history should have alerted the medical community about these adverse effects. Our understanding of the range of deficits associated with prenatal alcohol exposure emerged gradually over the past 40 years as has our understanding of the prevalence of fetal alcohol spectrum disorders (FASD) across several countries and cultures. The attention afforded to FASD among different countries varies as well with a lack of understanding of the risks of prenatal alcohol exposure still prevalent in large parts of the world. There remain many challenges in achieving a full understanding of the mechanisms underlying FASD as well as the educational, policy, prevention and legal issue necessary to prevent and treat this major public health concern.

FASD: Face, Brain and Behavior

Dr Edward Riley

1San Diego State University, San Diego, United States

This presentation begins with a brief overview of the concept of FASD, discussing the relationship between prenatal alcohol exposure and a range of possible outcomes, with an emphasis on alcohol related neurodevelopmental disorders (ARND). Evidence of how prenatal alcohol exposure impacts the developing brain at various stages of development, even in persons without the obvious physical and facial characteristics of fetal alcohol syndrome (FAS) will be presented. An emphasis will be placed on changes in the frontal and parietal lobes, cerebellum, basal ganglia, and corpus callosum. In addition, finding from diffusion tensor imaging (DTI) and functional MRI studies will be presented, detailing changes in white matter and brain function. Behavioral changes that can occur as a result of these brain changes will then be discussed. An emphasis will be placed on alterations in global abilities, such as IQ, executive function, and motor performance. Finally, the relation between facial dysmorphology, brain changes, and behavioral alterations will be explored with an emphasis on how these might be useful in diagnosis.

Clinical and Public Health Challenges in Addressing FASD

Prof Elizabeth Elliott

1University of Sydney, Camperdown, Australia, 2Sydney Children's Hospitals Network, Westmead, Australia

Fetal Alcohol Spectrum Disorders (FASD) are as challenging as they are prevalent. Women worldwide continue to drink during pregnancy; FASD rates are unacceptably high; and delayed diagnosis and inadequate early intervention result in secondary disabilities for many living with FASD.

Barriers to recognition of children at risk of FASD include unwillingness of clinicians to ask about alcohol use in pregnancy; inadequate, non-standardised documentation of prenatal alcohol exposure (PAE); different definitions internationally for a standard drink; and lack of knowledge of potential harms from PAE.

Barriers to identifying FASD include clinicians’ lack of knowledge about physical features and lack of internationally agreed diagnostic criteria and a classification system for FASD. Clinicians are reluctant to consider a FASD diagnosis for fear of stigmatising children and because they perceive a lack of effective treatment.

FASD prevention is both our priority and biggest challenge, requiring attitudinal and behavioural change. Public health strategies required include community awareness campaigns; warning labels; targeted education of high risk groups; and availability of quality services for alcohol misuse. Underpinning these must be measures to restrict access to alcohol, such as appropriate pricing, taxation, restricted advertising and limits on the number and opening hours of liquor outlets.

The role of governments in addressing Fetal Alcohol Spectrum Disorder

Sharman Stone

Parliament for Murray, Australia

Abstract not supplied
Case illustrations and psychological profile of individuals with FASD
Olga Tulabut, Arvin Teopaco1, Elvira Balinas1
1Angeles University Foundation, Philippines, 2Colegio de Sebastian, City of San Fernando, Philippines

This study is an initial effort in understanding Fetal Alcohol Spectrum Disorder (FASD) in the Philippine context. It sought to present series of cases to determine the psychological profile of individuals with FASD. The profiles were gathered through psychological assessment in the areas of intelligence, academic achievement, executive functioning, visual perception, adaptive and behavioral functioning.

The respondents of the study were nine individuals suspected to have FASD, selected through purposive sampling. Diagnoses were made using the FASDPN 4 digit Code, through a multi-disciplinary team. The study utilized a descriptive case study research design and data gathered were analyzed based on the Domain Oriented Model. There is evidence from the current study that the effects of the impairment cut across domains, marked with difficulty in learning and behavior appropriately. These difficulties are a reflection of limitations in memory, problem solving, attention, comprehension, perceptual ability, and adaptive, behavioral and emotional functioning. On the other hand, respondents of the study showed abilities in solving non-verbal as compared to verbal problems. In general, academic achievement, most of the cases performed slightly higher on tasks that evaluated mathematical computation skills when compared with reading, comprehension and spelling difficulties. In general, results of the study are consistent with existing literature but with a few variations particularly in the mathematical computation skills.

Since this is an exploratory research in the Philippines, it is the researchers’ hope that the results of the paper will lead to public awareness cascading to prevention initiatives, as well as support and intervention strategies, to help both individuals with FASD and their families appropriately cope with the condition.

Addressing Fetal Alcohol Spectrum Disorders in Western Australia
Prof Carol Bower1
1Telethon Kids Institute, the University of Western Australia, West Perth, Australia

Introduction and Aims: Through the Alcohol & Pregnancy & FASD Research Group, the Telethon Kids Institute has led research and policy development in the area of FASD for over a decade. Our current program of research in FASD currently encompasses four research areas.


Results: 1. Two-fold increase in FASD case ascertainment; 2. Effective television advertisement, midwife training in use of AUDIT-C, feasibility of diagnostic instrument assessed and on-line training developed; 3. High rate of FASD, reduction in prenatal alcohol use; 4. Early information on assessment of FASD in juvenile justice setting.

Discussion and Conclusions: This presentation provides a brief overview of FASD research and research translation at Telethon Kids, conducted in collaboration with community, professional, government and non-government stakeholders. The research tackles alcohol use in pregnancy and FASD from several angles and has resulted in promising improvements in FASD prevention and management.

FASD in Reunion and Tahiti
Denis Lamblin
FASD Program, Reunion

Abstract not supplied

Alcohol in pregnancy and FASD in Indigenous Australians
Heather d’Antoine
Menzies School of Health Research, Darwin, NT, Australia

Abstract not supplied

Prevention and Intervention for FASD in Hawaii: Developing a System of Care
Dr Ira Chasnoff
1NTI Upstream, Evanston, United States

The use of alcohol by pregnant women and its effects on the child continue to generate crises across multiple systems of care in Hawaii: health, education, and social services; to name a few. To address these issues, Hawaii is developing an integrated system of care that begins with universal screening of pregnant women for alcohol use, the delivery of brief interventions within the prenatal care setting, linking the maternal screening results to newborn birth records, and ongoing screening and linkage to early intervention and treatment for any identified children not born to alcohol-exposed mothers.

This session will present current data on the prevalence of alcohol use among pregnant women in Hawaii and discuss the core components of a system of care that meets the needs of the alcohol-exposed children birth to five years of age.

FASD in New Zealand
Ms Christine Rogan
Alcohol Healthwatch, Auckland, NZ

The harm from alcohol use during pregnancy was first documented by New Zealand Maori in 1879. Today around a quarter of New Zealand women continue to consume alcohol after pregnancy confirmation, contrary to Government advice. Government policy has yet to progress beyond this basis advice to initiate strategic FASD prevention or intervention planning. Consequently all FASD-related activity in New Zealand is currently undertaken within communities where individual goodwill and small financial grants can be brought together. These activities have steadily grown since mid 2000, when efforts to establish FASD team diagnosis, was made a key focus. Following the Canadian FASD diagnostic approach, several hospital based paediatric teams were supported to undertake training to integrate FASD assessments into existing services. These had to fit within extra budgets and workforce capacity which remains a challenge and means assessments able to be carried out are few and far between. Nevertheless it has resulted in a good clinical base from which to develop and expand further initiatives to reduce FASD-related harm.

This presentation will describe a number of the key elements that helped to bring about these changes.

Long term outcomes of prenatal alcohol exposure - more than just effects on the brain
A/Prof Karen Moritz

The developmental programming of health and disease (DOHaD) hypothesis suggests early life events contribute to increased susceptibility to diseases in later life. Animal models have examined the effects of maternal undernutrition, glucocorticoid exposure and placental insufficiency but somewhat surprisingly, prenatal alcohol exposure has rarely been studied in the context of DOHaD.

We have developed rat models of alcohol consumption patterns during pregnancy and examined effects on fetal growth and long term renal, cardiovascular and metabolic outcomes. Rats were administered a liquid diet containing 6% ethanol throughout pregnancy (Low dose chronic ethanol exposure-LCE) or given a higher dose of ethanol around the time of conception (12%, periconceptional exposure - PCE). Both models resulted in fetal growth restriction and impairments in placental development. Offspring from the LCE model developed impairments in glucose homeostasis and renal function as well as altered blood pressure responsiveness and lung fibrosis. The PCE model resulted in profound insulin resistance, impaired renal and cardiac function and adiposity. These studies suggest that in addition to the well-known effects on the developing brain, alcohol exposure during pregnancy affects other developing organs and contributes to long term “programming” of adult disease.
A number of studies have shown that alcohol exposure during pregnancy results in a set of birth defects called fetal alcohol spectrum disorders (FASDs) and can result in neurodevelopmental deficits. The information about adult diseases in fetal alcohol exposed patients is lacking. We have recently shown that prenatal ethanol exposure produces hypermethylation of the POMC gene and reduces the expression of this gene in the hypothalamus of fetal alcohol exposed offspring. In this study, we determined physiological and behavioral abnormalities associated with the POMC neuronal defect in the adult fetal alcohol exposed offspring by studying anxiety behaviors, stress responses, metabolic and immune functions and cancer susceptibilities with or without the supplementation of POMC neuron via brain transplants. We found that adult fetal alcohol exposed rats showed increased anxiety-like behavior, elevated stress response, increased incidence of hyperglycemia, rheumatoid arthritis and cancers. POMC neuronal transplants in the hypothalamus reduced the incidence or the severity of these disorders in fetal-alcohol exposed animals. These data suggest that alcohol exposure in utero produces epigenetic modification of POMC gene that increases the susceptibility to many endocrine, metabolic and immune diseases during adult life. (Supported by Grants AA016695, AA08757, AA024330).

Animal model studies identify the risk of binge alcohol exposure during brain development; Short and long-term outcomes.

Dr Ruth Napper

1University of Otago, Dunedin, New Zealand

Ethanol exposure during in utero development may result a range of deficits classified within Fetal Alcohol Spectrum Disorder. Apoptotic cell death is a key event in ethanol induced developmental brain damage but the long-term impact from single binge exposure is not well established. We have used a neonatal rat model, to investigate acute and long-term effects of ethanol binge exposure on brain structure and function. Long Evans rat pups, were treated on a single day, postnatal days 0-8, with either alcohol, 67g/kg/day in artificial milk solution given in two feeds two hours apart, a sham intubation or as a suckle control group. Animals were perfused within 24 hours post ethanol or as adults and stereological methods used to determine the magnitude of acute apoptotic cell death or total cell number in regions including the cerebellum, hippocampus, cortical regions and midbrain nuclei. Data will be presented to show that acute apoptotic cell death and long-term cell deficits may differ but importantly, a single binge alcohol exposure can result in long-term neuronal deficits and consequent behavioural impairment. This indicates that binge drinking by pregnant women during the third trimester of pregnancy carries a significant potential risk to the developing fetus.

FASD in regional Australia

Mrs Vicki Russell

1NOFASD Australia, Wyndham, Australia

NOFASD Australia is the non-government peak body representing individuals and families living with Fetal Alcohol Spectrum Disorders. Our strategic objectives aim to raise public awareness through community education and advocacy, deliver training to service providers to build capacity to better respond to target groups who may be at increased risk for alcohol use in pregnancy or FASD, and offer consultation, advocacy and support for individuals and families whose lives are directly affected by FASD. A community development approach is used to engage with existing services in localities around Australia. This presentation will tell a different story about a harmful impact of alcohol use in Australia and the teachers, service providers and parents/carers who are struggling to help individuals living with FASD. In the absence of resources, it will describe the opportunity for prevention when champions stand up and communities work together.

The Effects of Maternal Periconceptional Ethanol Exposure on Long Term Cognitive Outcomes in Rat Offspring

Miss Diana Zanfrance, Dr Carlie Cullen, Associate Professor Karen Moritz

1University of Queensland - School of Biomedical Sciences, St Lucia, Australia

Little is known about the impact of alcohol during the periconceptional period (PC period) on the behaviour in offspring. The PC period has been recognised as a critical developmental window where changes to the epigene may occur. The aim of this study was to examine the effect of PC ethanol (PC ETOH) exposure on long term cognitive function; including memory and anxiety.

Rats were exposed to a liquid diet containing ethanol (ETOH) (12.5% vol:vol) or a control diet from 4 days prior to mating until day 4 of pregnancy. Offspring (8/group/sex) were put through a battery of behavioural tests to assess anxiety and spatial memory and the hippocampus was then collected and gene expression examined. PC ETOH resulted in a significant (P<0.0001) increase in directed exploring/ head dipping behaviour during holeboard testing. However, no anxiety like phenotype was observed. Interestingly, the female offspring exposed to PC ETOH demonstrated short term spatial memory impairment (P<0.05%) in the Y maze. Expression levels of epigenetic modifiers DNMT1, DNMT3a and HDAC2 was also altered by PC ETOH. In conclusion, PC ETOH did not lead to anxiety like behaviour in the aged offspring but may induce sex specific impairments in spatial memory.

The Lililwan Project: Neurodevelopmental outcomes and Fetal Alcohol Spectrum Disorders (FASD) in remote Australian Aboriginal children

James Fitzpatrick, Prof Jane Latimer, Prof Elizabeth Elliott

1Telethon Kids Institute, the University of Western Australia, West Perth, Australia, 2Discipline of Paediatrics and Child Health, Sydney Medical School, University of Sydney, Sydney, Australia, 3The Childrens Hospital at Westmead, Sydney, Australia, 4The George Institute for Global Health, Sydney Medical School, University of Sydney, Sydney, Australia

The Lililwan Project aimed to determine prevalence of Fetal Alcohol Spectrum Disorders (FASD) using active ascertainment in children born in 2002/2003 and living in the Fitzroy Valley in 2010/2011 (n=134). From this population, 127 consenting caregivers provided social, biomedical and antenatal data including alcohol use, with birth outcomes derived from medical records. Interdisciplinary assessments were conducted on 108 children. Prenatal alcohol exposure was objectively quantified. Prevalence of conditions in the FASD spectrum (Fetal Alcohol Syndrome (FAS), partial FAS (pFAS), and Neurodevelopmental Disorder – Alcohol Exposed (ND-AE)) were determined. Diagnoses were assigned using slightly modified FASD Canadian Guidelines. Alcohol was used in 55% of 127 index pregnancies, with 87% at high-risk levels and 88% during the first trimester. In 108 children assessed, 13 had FAS/pFAS (120 per 1000 (95% CI 70-196). Of these, 69% had microcephaly, 83% had growth deficiency, and all had facial dysmorphology and CNS impairment in 3-8 domains. Eight children were diagnosed with ND-AE. Overall FASD prevalence was 194 per 1000 (95% CI 130-280), which was higher than reported previously in Australia and amongst the highest worldwide. Alcohol use in pregnancy remains a major public health challenge throughout Australia, particularly in remote communities with high rates of alcohol consumption.

Prenatal alcohol consumption prior to awareness of pregnancy

Ms Clare McCormack1, Dr Delyse Hutchinson1,2,3,4,5, Dr Lucy Burns1, Dr Judy Wilson1, Prof Elizabeth Elliott1, Prof Steve Allop1, Prof Jake Najman1, Dr Craig Olsson1, Dr Sue Jacobs1, Prof Richard Mattick1

1NDARC, UNSW, Sydney, Australia, 2Australian Centre for Perinatal Science, UNSW, Sydney, Australia, 3Murdoch Childrens Research Institute, Melbourne, Australia, 4Centre for Social and Early Emotional Development, Deakin University, Melbourne, Australia, 5Department of Pediatrics, University of Melbourne, Melbourne, Australia, 6Paediatrics and Child Health, University of Sydney, Sydney, Australia

Animal model studies identify the risk of binge alcohol exposure during brain development; Short and long-term outcomes.

Prof Dipak Sarkar

1The State University of New Jersey, Program of Endocrinology, Rutgers, United States

We have recently shown that prenatal ethanol exposure produces hypermethylation of the POMC gene and reduces the expression of this gene in the hypothalamus of fetal alcohol exposed offspring. In this study, we determined physiological and behavioral abnormalities associated with the POMC neuronal defect in the adult fetal alcohol exposed offspring by studying anxiety behaviors, stress responses, metabolic and immune functions and cancer susceptibilities with or without the supplementation of POMC neuron via brain transplants. We found that adult fetal alcohol exposed rats showed increased anxiety-like behavior, elevated stress response, increased incidence of hyperglycemia, rheumatoid arthritis and cancers. POMC neuronal transplants in the hypothalamus reduced the incidence or the severity of these disorders in fetal-alcohol exposed animals. These data suggest that alcohol exposure in utero produces epigenetic modification of POMC gene that increases the susceptibility to many endocrine, metabolic and immune diseases during adult life. (Supported by Grants AA016695, AA08757, AA024330).
Aims: Many women consume alcohol during pregnancy. However, previous estimates of prenatal alcohol consumption may not take into account alcohol consumption prior to pregnancy recognition. The purpose of this study was to examine prevalence and predictors of alcohol use by women prior to awareness of their pregnancy, and factors predicting whether women will cease, reduce, or continue alcohol use following pregnancy recognition.

Methods: 1487 women and their partners from antenatal clinics completed detailed interviews about alcohol and drug use in each trimester. Alcohol consumption before and after awareness of pregnancy was recorded separately.

Results: Between conception and awareness of pregnancy, 59.4% of women consumed alcohol. Binge or heavy drinking was more common than light drinking during this period. Following awareness of pregnancy to the end of the first trimester, the rate of consumption decreased to 19.4% of women. Factors associated with alcohol use included income, age, education, smoking, and substance use.

Conclusions: Most women reduce or cease consumption after becoming aware of the pregnancy. Strategies to reduce drinking in early stages of pregnancy may be needed. Demographic and social factors are related to alcohol use during this period.

Paediatric soft-neurological signs: Population-based study in remote Australia

Ms Barbara Lucas1,2,3,4, Ms Jane Latimer1, Mr James Fitzpatrick1,2,3, Ms Robyn Doney1, Ms Rochelle Watkins1, Ms Tracey Tsang4, Ms Tracy Jirikowic5, Ms Heather Carmichael Olson6, Ms June Oscar7,8, Ms Maureen Carter9, Prof Elizabeth Elliott1,2,4

1Discipline of Paediatrics and Child Health, Sydney Medical School, The University of Sydney, The Children’s Hospital at Westmead, Westmead, Australia, 2The George Institute for Global Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 3Poche Centre for Indigenous Health, Sydney School of Public Health, The University of Sydney, Sydney, Australia, 4Physiotherapy Department, Royal North Shore Hospital, Sydney, Australia, 5Telethon Kids Institute, Perth, The University of Western Australia, Perth, Australia, 6School of Public Health, Curtin University, Perth, Australia, 7Department of Rehabilitation Medicine, Division of Occupational Therapy, University of Washington, Seattle, United States, 8Seattle Children’s Research Institute and University of Washington School of Medicine, Seattle, United States, 9Marninwarntikura Women’s Resource Centre, Fitzroy Crossing, Australia, 10University of Notre Dame, Broome, Australia, 11Nindilingarri Cultural Health Services, Fitzroy Crossing, Australia, 12The Sydney Children’s Hospital Networks, Westmead, Australia

The presence of soft neurological signs (SNS) was examined in children aged 7-9 years living in remote Australian Aboriginal communities in Fitzroy Valley, Western Australia in 2010-2011. SNS was assessed using the Quick Neurological Screening Test, Second Edition (QNST-2), and score outcomes were compared in those with and without (i) Fetal Alcohol Spectrum Disorders (FASD) and (ii) prenatal alcohol exposure (PAE). Significant SNS was defined as scores ≥ 5th percentile with higher scores indicating more SNS. Children were assigned FASD diagnoses using modified Canadian FASD Diagnostic Guidelines, while PAE was categorised using the Alcohol Use Disorders Identification Test-Consumption score. A total of 108 children (Aboriginal: 98.1%; males: 52.7%; mean age 8.7 years) were assessed with 52.2% exposed to “risky” levels of PAE. The median QNST-2 Total Score for all participants similar to population norms, but was significantly higher in children with than without an FASD (p=0.004) or PAE (p=0.02). Increased prevalence of significant SNS was also found in children with FASD (9.5%) and PAE (3.3%). Higher rates of SNS in children with an FASD or PAE suggest the QNST-2 may be a useful component in the evaluation of children with a diagnosis within the FASD category or with PAE.

FASD educational resources for justice professionals

Ms Heather Jones1, Associate Professor Raewyn Mutch1

1Telethon Kids Institute, the University of Western Australia, Subiaco, Australia

In 2011/2012 researchers from the Telethon Kids Institute surveyed WA judicial officers, lawyers, corrective services staff and police on their FASD knowledge and attitudes and practice. This research identified what information is required by justice professionals and how this information should be delivered. Since this research concluded we have been working closely with judicial officers and lawyers on developing an understanding of FASD and the legal implications for people engaging with the justice system. In Australia we are facing challenges from the high incarceration rates of Aboriginal people and people with cognitive impairments, and the introduction of mandatory sentencing which impacts on judicial officers ability to consider equality before the law particularly for people with disabilities.

The purpose of this project was to translate our research, by developing an educational intervention to prepare for the challenges facing judicial officers and lawyers so that they can:

- recognise cognitive impairments and possible FASD in young people engaging with the justice system
- identify legal implications
- consider referral for assessment if the disability is suspected
- consider decision making with respect to orders, sentencing and management

The resources include videos, on-line CPD module for lawyers and website

Developing national approaches to address alcohol consumption in pregnancy and Fetal Alcohol Spectrum Disorder

Michael Thorn

FARE, Act, Australia

Developing national approaches to address alcohol consumption in pregnancy and Fetal Alcohol Spectrum Disorder

In Australia there is no consensus about how to respond to the risks of consuming alcohol during pregnancy. There is no Australia-wide plan to address the high levels of consumption by pregnant women, and many in the community and government remain sceptical about the magnitude and incidence of harms and the need for strong action.

A modestly funded ($9 million over 4 years) Australian Government Plan was announced in 2014 by the Commonwealth Government and a number of jurisdictions have taken some action including establishing FASD clinics in New South Wales and Queensland, public awareness campaigns in Western Australia and various programs targeting Indigenous people around the country.

Prior to this, small amounts of funding had been provided by Governments’ and philanthropists to investigate prevalence in WA’s Kimberley and among heavy drinkers in NSW, and in the justice system.

The most comprehensive plan of action was devised by FARE (a charity working to stop harm caused by alcohol) in response to the need for focus and coherence in the pursuit of change. This detailed plan proposed action across five domains and was costed at $37 million over three years.

This plan was instrumental in activating governments and complemented the work of the 2012 Parliamentary Inquiry into FASD in Australia.

This presentation will focus briefly on the plan’s content and how it was put together, and describe in more detail how its development exploited opportunities that emerged to advocate for Australia-wide government action to prevent harm caused by drinking during pregnancy and to better support those born with Fetal Alcohol Spectrum Disorders and their carers.

International initiatives in Fetal Alcohol Spectrum Disorder

Margaret Murray

NIAAA, USA

Abstract not supplied

Legal perspectives on Fetal Alcohol Spectrum Disorder

Prof Linda Chezem

The session will give a brief high level overview of law and policy making around FASD in the United States. Key points will be the lack of coordination between states and federal government, an uninform ed justice system, and the detached judicial role taken by most judges. The overview will be followed by a discussion of the panel as a whole.
Dopamine D1 and D3 receptors mediate reconsolidation of cocaine memories in mouse models of drug self-administration

Prof Ming Xu1, Dr Yijin Yan2, Dr Amy Newman1
1The University of Chicago, Chicago, United States, 2The University of Chicago, Chicago, United States, (NIDA Intramural Research Program, Baltimore, United States

Memories of drug experience and drug-associated environmental cues can elicit drug-seeking and taking behaviors in humans. Disruption of reconsolidation of drug memories dampens previous memories and therefore may provide a useful way to treat drug abuse. We previously demonstrated that dopamine D1 and D3 receptors play differential roles in acquiring cocaine-induced behaviors. Moreover, D3 receptors contribute to the reconsolidation of cocaine-induced CPP. We have now examined effects of manipulating D1 or D3 receptors on reconsolidation of cocaine memories in mouse models of drug self-administration. We found that pharmacological blockade of D1 receptors or a genetic mutation of the D3 receptor gene attenuated reconsolidation that lasted for at least 1 week after the memory retrieval. In contrast, with no memory retrieval, pharmacological antagonism of D1 receptors or the D3 receptor gene mutation did not significantly affect reconsolidation of cocaine memories. Pharmacological blockade of D3 receptors also attenuated reconsolidation in wild-type mice that lasted for at least 1 week after the memory retrieval. These results suggest that D1 and D3 receptors and related signaling mechanisms play key roles in reconsolidation of cocaine memories in mice, and that these receptors may serve as novel targets for the treatment of cocaine abuse in humans.

Cocaine self-administration and DNA methylation: a genome-wide study

Dr Jean Zwiller1, Dr Mathieu Fonteneau1, Dominique Filliol1, Dr Katia Befort1, Dr Patrick Anglard1, Dr Pascal Romieu1
1CNRS UMR 7364, Université de Strasbourg, Strasbourg, France

Recent studies highlight the regulation of gene transcription in neurons by chromatin remodeling, a process governed by the interplay of DNA methylation and post-translational modifications of histones. To test the involvement of DNA methylation on drug reinforcing properties, we submitted rats to the cocaine intravenous self-administration paradigm. Using the fixed-ratio 5 schedule, we found that i.c.v. injection of the DNA methyltransferase inhibitors, 5-aza-2’-deoxycytidine and zebularin, dose-dependently increased cocaine self-administration. We then investigated genome-wide alterations in DNA methylation patterns in the median prefrontal cortex of those rats. About 189,000 differentially methylated genomic regions were identified in response to the treatment. Most of these regions were found inside and downstream of genes, while only 5% were located in promoter regions. Differential methylation occurred predominantly outside CpG islands. Cocaine was found to globally reduce DNA methylation, while treatment with the inhibitors actually increased the overall methylation. The differentially methylated regions were found to belong to 18,351 genes. Negative correlation between gene methylation and gene expression was found when methylation occurred in the promoter region, but not inside genes. The methylene approach was further validated by analyzing the methylation and expression of genes involved in neuronal plasticity.

Agonist replacement therapy for cocaine addiction - On the horizon?

Dr Eliot Gardner1, Dr Rui Song1, Dr Xia Li1, Dr Guan-Yi Lu2, Dr Xiao-Qing Peng1, Dr Guo-Ha Bi1, Dr Hong-Ju Yang1, Dr Yi He1, Dr Hai-Ying Zhang1, Dr Jin Li1, Dr Mark Froimowitz2, Dr Zheng-Xiong Xi1
1National Institute on Drug Abuse, Baltimore, United States, 2Beijing Institute of Pharmacology and Toxicology, Beijing, China, 3Massachusetts College of Pharmacy and Health Sciences, Boston, United States

Agonist replacement therapies are successful for opiate and nicotine addiction, but not cocaine addiction. We now report that a novel dopamine (DA) transporter (DAT) inhibitor, NIDA-32476, has a preclinical profile in rats arguably predictive of clinical utility. NIDA-32476: 1) is a highly potent and selective DAT inhibitor, and competitively inhibits cocaine binding to DAT; 2) augments brain-stimulation reward with slow-onset, long-acting profile; 3) augments extracellular nucleus accumbens DA with slow-onset, long-acting profile; 4) is not self-administered by cocaine-naïve rats; 5) shows progressive reduction in self-administration when substituted for cocaine; 6) shows a 50% lower progressive-ratio break-point than cocaine, which decreases with successive test days; 7) robustly inhibits cocaine self-administration; 8) significantly lowers progressive-ratio break-point for cocaine self-administration; 9) significantly inhibits cocaine-triggered and cue-triggered relapse to cocaine-seeking. We note that methadone is more than simply a slow-onset, long-acting opioid agonist; it internalizes the mu opioid receptor, making the receptor unavailable to subsequent heroin. We suggest that agonist therapy for cocaine addiction must do likewise, possibly by internalizing the cocaine binding site. NIDA-32476 is the first DAT blocker that we have tested that shows the profile noted above, and could be a promising pharmacotherapy for cocaine addiction.

The “other brain”: how knowing you are sick has implications for drug abuse liability

Prof Mark Hutchinson1
1University of Adelaide, ADELAIDE, Australia

The aetiology of “knowing you are sick” is comprised of a complex multi-factorial journey that culminates in the cardinal signs of the illness response. Advances in the basic science underpinning our mechanistic understanding of the illness response have embraced “the other brain” as an integrator of these multiple life stimuli that precipitate changes in higher order biological functions, ranging from altered mood to photosensitivity. This complex integration of life experiences, which are translated into neurokinine signals cause the neuroimmune cells of the central nervous system, or “the other brain” to adapt and change the environment in which the neuronal system operates. Critically, it is apparent that if these adaptations occur in motivation/reward centres of our brain then neuroimmune contributions to altered drug response may ensue. Importantly, the molecular triggers of these neuroimmune responses are being exposed, with the innate immune system playing a pivotal role. This presentation will summarise studies in this field and equip the attendees with further insights of the complexity and power that viewing the brain as a neuroimmune organ brings to understanding the motivational properties of drugs of abuse. Additionally, the implications that advances in biophotonics will have for moving this field forward will be discussed.

Immune cells in the brain control alcohol programming effect on stress and addictive behaviors

Dipak Sarkar1
1The State University of New Jersey, Program of Endocrinology, Rutgers, United States

Exposure to alcohol, during development or adulthood, results in damage to the nervous system, which underlies neurological and cognitive disruptions observed in patients with alcohol-related disorders, including fetal alcohol spectrum disorders and alcohol use disorders. Both clinical and preclinical evidence suggest microglia, the immune cells of the central nervous system, play a key role in modulating alcohol-induced neurotoxicity. We have shown that microglia participates in alcohol-induced killing of beta-endorphin (BE) neurons. We found that alcohol exposure stimulates microglia to produce inflammatory cytokines including TNF-z that activates the NF-kB pathway and NADPH oxidase to induce apoptotic signaling in developing BEP neurons. Furthermore, we found that BEP neurons influence the ethanol’s ability to increase inflammatory cytokines production by altering opioid receptors functions in microglial cells. We also found that early-life alcohol exposures program the microglial cell population to produce more inflammatory cytokines following a stress challenge during the adulthood. BEP neurons, localized in the hypothalamus, are involved in controlling stress function and alcohol-induced reward and reinforcement. Thus, the bi-directional communication between microglia and BEP within the hypothalamus following alcohol administration may predict the future risk for stress abnormality, anxiety and addictive behaviors (Supported by a NIH Grant R37 AA08757).
Cannabinoid effects on human brain structure, function and neurochemistry: injury, protection and recovery

A/Prof Nadia Solowij1, Dr Samantha Brody2, Dr Hendrika van Helle3, Dr Valentina Lorenzetti4, Dr Chao Suo5, Prof Dan Lubman6,7, Prof Murat Yücel2

1University of Wollongong, Wollongong, Australia, 2Monash University, Melbourne, Australia, 3Turning Point, Melbourne, Australia

Chronic cannabis use is associated with altered brain structure and function, with evidence for greater adverse effects of exposure during critical neurodevelopmental periods (e.g. adolescence). We have demonstrated dose-dependent reduction of hippocampal and amygdala volumes in long term heavy cannabis users, alongside elevated psychotic-like symptoms and poorer cognitive function, particularly memory being impacted more in adolescent users. Among the multiple compounds that comprise cannabis, Δ9-tetrahydrocannabinol (THC) is associated with worse outcomes, while cannabidiol (CBD) may ameliorate the adverse effects of THC and has intriguing therapeutic properties (e.g. anxiolytic, antipsychotic). We have evidence that prolonged exposure to CBD may protect against hippocampal volume loss in chronic users. The mechanisms of neuroprotection by CBD are currently not known. Acute administration of THC and CBD to frequent and infrequent cannabis users indicates differential modulation by each compound of the brain’s primary inhibitory and excitatory neurotransmitters, GABA and glutamate, in the hippocampus. GABA-ergic and glutamatergic response correlated with brain functional outcomes implicated in schizophrenia. Recovery of hippocampal volume and neurochemistry, but not functional measures, was observed following prolonged abstinence in former users. The implications of these findings will be discussed in light of shifting policies toward legalisation of cannabis for medicinal and recreational use.

Prolonged exposure to nicotine self-administration increases sensitivity to nicotine, motivation to seek nicotine, and the reinforcing properties of nicotine-paired cues

Dr Kelly Clemens1, Ms Belinda Lay2, Dr Nathan Holmes3

1University of New South Wales, Sydney, Australia, 2Monash University, Melbourne, Australia

An array of pharmacological and environmental factors influence the onset and maintenance of tobacco addiction. The nature of these influences likely changes across the course of development, and with an extended smoking history. The present study used an animal model to examine the factors that drive nicotine seeking behavior after either brief (10 days) or extended (40 days) self-administration training in young rats. In Experiment 1, extended training increased rats’ sensitivity to nicotine, indicated by a leftward shift in the dose-response curve, and their motivation to work for nicotine, evident as an increase in the break point achieved under a progressive ratio schedule. In Experiment 2, extended training imbued the nicotine-paired cue with the capacity to maintain responding to the same high level as nicotine itself. However, Experiment 3 showed that the mechanisms involved in responding for nicotine or a nicotine-paired cue are dissociable, as treatment with the partial nicotine receptor agonist, varenicline, suppressed responding for nicotine but potentiated responding for the nicotine-paired cue. Hence, across extended nicotine self-administration, pharmacological and environmental influences over nicotine seeking increase such that nicotine seeking is controlled by multiple sources, and therefore, highly resistant to change. Therefore early intervention is crucial to reduce the prevalence of tobacco dependence in young adults.

The vulnerable brain: acute and residual effects of stimulant substances among young adults

A/Prof Raimondo Bruno1, Dr Amy Peacock2

1University of Tasmania, Hobart, Australia

Consumption of stimulant substances by young adults is increasing internationally. In Australia, 8.6% of 20-29 year-olds have used ‘ecstasy’ in the past year. Large-scale surveys suggest 46% of young adults report mixing highcaffeine energy drinks with alcohol in the past year.

We will present a series of laboratory studies examining the acute effect of stimulant energy drinks when consumed with alcohol on the experience of intoxication, cognition, and risky decision making. These demonstrate that high doses of energy drinks decrease subjective perception of intoxication, and increase perceived ability to drive. While energy drinks in combination with alcohol can increase risky decision making, these effects have not been identified on simulated driving tasks.

Impaired performance of ‘ecstasy’ consumers on numerous cognitive tasks is well-established, with neuroimaging suggesting this relates to compromised serotonergic functioning. The visual cortex receives serotonergic input and appears vulnerable to ‘ecstasy’-mediated impacts. Three interlinked studies applying visual illusions demonstrate specific impairments in abstinent ‘ecstasy’ consumers: compromising orientation processing of stimuli processed at the primary visual cortex (VI) but not those involving prestimate cortex (V2), and impairing motion processing on tasks tapping both VI and area MT (V5). These studies aid interpretation of driving impairments identified among ‘ecstasy’ consumers.

Adolescent alcohol exposure and persistent effects on epigenetic and behavioral changes in adulthood

Dr Subhash Pandey1

1Center for Alcohol Research in Epigenetics, Dept. of Psychiatry, University of Illinois at Chicago & Jesse Brown VA Medical Center, Chicago, United States

DNA methylation and histone acetylation/methylation are important epigenetic mechanisms that regulate gene expression. We investigated the effects of adolescent intermittent ethanol/n-saline (AIE/AIS) exposure in rats during postnatal days (PND) 28-41 with a 2-day on/off paradigm on epigenetic mechanisms in the amygdala in adulthood. It was found that DNA methyltransferase (DNMT), histone deacetylase (HDAC) activity, HDAC2 and DNMT3b expression, and histone lysine demethylating enzyme LSD1 were altered in the amygdala of AIE rats during adolescence; some of these changes persisted into adulthood. Neuropetide Y (NPy) and brain derived neurotrophic factor (BDNF) expression were decreased in the central and medial amygdaloid structures of AIE adult rats as compared to AIS adult rats. Interestingly, chromatin was condensed at the break point achieved under a progressive ratio schedule. In Experiment 2, extended training imbued the nicotine-paired cue with the capacity to maintain responding to the same high level as nicotine itself. However, Experiment 3 showed that the mechanisms involved in responding for nicotine or a nicotine-paired cue are dissociable, as treatment with the partial nicotine receptor agonist, varenicline, suppressed responding for nicotine but potentiated responding for the nicotine-paired cue. Hence, across extended nicotine self-administration, pharmacological and environmental influences over nicotine seeking increase such that nicotine seeking is controlled by multiple sources, and therefore, highly resistant to change. Therefore early intervention is crucial to reduce the prevalence of tobacco dependence in young adults.

Intervening early to reduce developmentally harmful substance use among youth populations

Prof Dan Lubman1,2

1Turning Point, Melbourne, Australia, 2Monash University, Melbourne, Australia

Over the past decade, research highlighting the links between early onset substance use and later mental health problems has increased public and political concerns regarding the use of alcohol and illicit drugs among young people. Despite robust evidence for a link between early onset substance use and later mental health problems, over the past decade, research highlighting the links between early onset substance use and later mental health problems has increased public and political concerns regarding the use of alcohol and illicit drugs among young people. Despite robust evidence for a link between early onset substance use and later mental health problems, recent research has highlighted the need for early intervention approaches to reduce the prevalence of tobacco dependence in young adults.
use and the development of problem use or other psychopathology in late adolescence and early adulthood, the mechanisms that underlie such associations are not fully understood. The extent to which such relationships may be explained by individual, family or social characteristics of those young people who begin using at an early age, the neurobiological effects of substance use on the developing brain, or some combination of the two, remains to be determined. Early intervention approaches are required that inform young people about the link between drugs and mental disorder and encourage early help-seeking for those developing problems, as well as assisting current users to minimise or reduce risky patterns of use while effectively treating any underlying mental health issues. This presentation will provide an overview of early intervention work in this area, as well as discussing the implications for service delivery and policy development.

Position of behavioural addictions in ICD-11

Dr Vladimir Poznyak

Text: Currently the World Health Organization is in the process of development of its 11th edition of the International Classification of Diseases (ICD-11) which is expected to be submitted for approval of the World Health Assembly in 2017. Field testing of suggested diagnostic categories and their diagnostic criteria will take place during 2015 and 2016. In the beta version of Chapter 6 of ICD-11 “pathological gambling” is included in the section of “impulse control disorders”, which also includes diagnostic category for “other specified impulse control disorders” that can be used for “internet gaming disorder” and the like in the absence of a specific section in the classification established for “behavioral addictions” including internet use (gaming) disorder. Currently the term “behavioral addictions” is not a part of WHO nomenclature. The WHO meeting on public health implications of behavioural addictions associated with excessive use of internet, computers, smart phones and similar electronic devices held in Japan in August 2014 and hosted by Kurihama Medical and Addiction Centre, highlighted clinical utility of such diagnostic categories as “internet gaming disorder”, “gaming dependence”, “internet use disorder”, and emphasized their conceptual and clinical similarity to the concepts of ‘dependence syndrome’ and ‘harmful use’ of psychoactive substances. There is a need to test in different cultural and health care settings feasibility, clinical and public health utility of diagnostic categories commonly described as “behavioral addictions” including “internet gaming disorder”, “internet use disorder” and potentially other related disorders which share conceptually common clinical and diagnostic features. The development of the ICD-11 by the World Health Organization provides additional rationale for developing international consensus on clinical descriptions and diagnostic guidelines for the key diagnostic categories of “behavioral addictions” and testing their public health utility as well as diagnostic validity and reliability in clinical settings around the world. Expected outcomes of the above-mentioned process will form the basis for data-driven recommendations that can be taken into consideration in the process of ICD-11 finalization.

Neurodevelopmental features of Internet-use and gaming problems

Prof Marc Potenza

*Yale University, New Haven, United States

Internet use and video-gaming represent two prevalent behaviors, particularly amongst adolescents and young adults. With recent changes in the availability and use of the Internet for gaming and other purposes, questions have been raised regarding the how Internet use and gaming may influence development and what constitutes problematic or addictive engagement. To investigate, we used survey and neurobiological approaches to investigate problematic Internet use (PIU) and problematic video-gaming (PVG) in adolescents and adults. Findings indicate associations between both PIU and PVG and substance-use disorders, depression and other mental health conditions. Neurobiological studies suggest similarities between PIU and substance use disorders. Findings will be discussed within public health and clinical contexts.

Relationship between substance use disorder and internet addiction

Prof Changwoo Han, Prof Young Sik Lee

*Department of Psychiatry, Chung Ang University Hospital, Seoul, South Korea

Conclusion:
The relationship between substance use disorder and internet use has been of particular interest recently. Most prominently, the study of the relationship between pathological gambling and addiction has been the focus of significant research. Indeed, pathological gambling has been included as a separate diagnostic category in the DSM-5, which is the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders. The inclusion of pathological gambling as a separate diagnostic category highlights the importance of understanding the relationship between substance use disorder and internet addiction.

Clinical description and diagnostic guidelines for Internet use disorders

Susumu Higuchi, Hideki Nakayama, Hiroshi Sakuma, Satoko Mihara

National Hospital Organization Kurihama Medical and Addiction Center, Yokosuka, Kanagawa, 239-0841, Japan

Behavioural addictions produce health and social consequences of some magnitude in many parts of the world today. Unfortunately, we are poorly served by existing definitions provided by established diagnostic guidelines. Indeed, only pathological gambling is included as a discrete clinical entity in ICD-10 and DSM-5. In the case of Internet use disorders (IUDs), several diagnostic criteria or guidelines have been proposed, which are essentially modified versions of existing criteria of substance use disorders and pathological gambling, or alternatively are unique criteria based on empirical data. Recently published criteria included in DSM-5 focused on Internet gaming disorder. However, further research and clinical experience will be required prior to its acceptance as a formal disorder. Our presentation begins with a brief review of the epidemiological findings of IUDs globally, followed by a review of the published diagnostic criteria and guidelines for IUDs. When constructing the diagnostic guidelines for IUDs, several key questions need to be addressed: 1) are IUDs a discrete clinical entity with clear boundaries in relation to normal behaviour? 2) what type of structured guidelines are most appropriate? e.g. only one guideline with several subtypes such as gaming, gambling, SNS, other; and 3) what symptoms should be included to best reflect actual clinical experiences? These will be presented and discussed in the symposium.

WEDNESDAY 19 AUGUST

Alcohol dependence: a chronic relapsing behavioral disorder

Antonio Noronha

NIAAA, USA

Abstract not supplied

Medications for Treatment of Addiction that Derive from the “Dark Side” of Addiction

Dr George Koob

*National Institute on Alcohol Abuse and Alcoholism, Bethesda, United States

Addiction is a disorder characterized by compulsive drug intake, loss of control over intake and emergence of a negative emotional state during withdrawal manifest in 3 stages of an addiction: Binge intoxication, withdrawal-negative affect and preoccupation-anticipation (“craving”). The binging-toxication stage includes enhanced habit (stimulus- response) activity in involving the neuropathology of the basal ganglia. The withdrawal-negative affect stage reflects reward deficits and recruitment of the brain...
stress systems in the extended amygdala. The preoccupation-anticipation stage reflects impairments in self-regulation mediated by dysregulation of executive function in the frontal cortex. Each of these stages provides a heuristic framework for treatment; however, the identification of excellent and validated animal models, human laboratory models and neuropharmacological mechanisms specifically related to the withdrawal/negative affect stage have provided numerous viable, unique and untapped targets for future medications. Neurotransmitter systems known to modulate withdrawal/negative affect in the extended amygdala function include corticotropin releasing factor, dynorphin, norepinephrine, hypocretin (orexin), substance P, vasopressin, neuropeptide Y, nociception and endocannabinoids. Future medications that focus on the withdrawal/negative affect stage and preoccupation-anticipation stage to restore the reward-stress dysregulation characterizing this stage of the addiction cycle may have high potential as novel approaches to medications development for addiction.

Neural circuits in punished alcohol-seeking

Dr Andrew Holmes

This presentation will show data from behavioral, genetic and in vivo single-unit recordings that implicate NMDA receptor-mediated neuronal circuits in the prefrontal cortex and amygdala in regulating alcohol self-administration following shock-induced punishment. Addictions including alcohol use disorders (AUDs) are characterized by the loss of control over the substance seeking and consumption, but the neural circuits and signaling mechanisms responsible for the transition from controlled use to uncontrolled abuse remain incompletely understood. Prior studies have developed measures of ‘compulsive-like drug-seeking’ in rodents that measure persistent responding for ethanol (EtOH) despite footshock or adulteration with an unpleasant taste. We have performed chronic single-unit recordings of neurons in the mouse prefrontal cortex and amygdala during punished-suppression of responding for EtOH. We have also assessed the effects of chronic intermittent EtOH (CIE) and tested, post-withdrawal, for (footshock) punished-suppression of responding for EtOH. Mice exposed to CIE exhibited attenuated suppression of EtOH-seeking during punishment, as compared to air-exposed controls. By contrast, CIE exposure was not found to affect punished food reward-seeking behavior, nor other putative measures of compulsive-like EtOH-seeking (progressive ratio and persistent responding for EtOH). Analysis of brain tissue extracts found reduced sensitivity to punished EtOH-seeking after CIE exposure was accompanied by a significant increase in the gene expression of the NMDA receptor, specifically in the medial orbitofrontal cortex. Mice genetically engineered to lack GluN2B-containing NMDA receptors in cortical principal neurons exhibited partial resilience to stress effects on EtOH seeking. We have also performed single-unit recordings that implicate NMDA receptor-mediated neuronal circuits in cortical principal neurons exhibited partial resilience to stress effects on EtOH seeking.

Mapping and manipulating neural circuits for (re)lapse and abstinence

Prof Gavan McNally

1 UNSW, NSW, Australia

Alcohol-use disorders and other drug addictions are chronically relapsing conditions, characterised by cycles of use, abstinence, and relapse. I will describe behavioural approaches to modelling lapse and relapse in animal models, the mapping and identification of discrete neural circuits promoting and preventing such relapse, including those providing inhibitory control over craving and drug seeking, and the impact of bidirectional optogenetic as well as chemogenetic manipulation of these circuits on abstinence from, and relapse to, drug seeking.

Dr Paul Klenowski

1 Brain & Mind Research Institute, University of Sydney, Sydney, Australia

Changes in neuronal morphology and synaptic connectivity are key components underlying alterations in the activity of neural pathways. In order to understand how long-term ethanol consumption alters neural circuits implicated in the development of addiction, we have adapted a technique that allows for morphology, electrophysiology and the distribution of neurochemical synapses within a three-dimensional neuronal arbor to be determined. We have applied this technique to investigate the effects of long-term ethanol consumption on neuronal morphology, basal synaptic activity and neurochemical synapse density of principal neurons from the medial prefrontal cortex (mPFC), a brain region implicated in addiction, decision making and executive functions. We show that long-term ethanol consumption increases total dendritic arbor length of basal but not apical dendrites in layer V mPFC neurons. We also show increased spontaneous excitatory post-synaptic current frequency and neurochemical glutamatergic synapse density, suggesting that long-term ethanol consumption induces changes in synaptic connectivity and enhances basal excitatory synaptic transmission in mPFC neurons. These results provide insights into the morphological and neurochemical changes that accompany differences in physiology following prolonged exposure to ethanol. Furthermore we can apply these methods to investigate changes in the connectivity of other brain circuits involved in the development of alcohol dependence.
The victims of alcohol misuse
Marcia Langton
University of Melbourne
Abstract not supplied

FASD research in remote Aboriginal Australia
Prof Elizabeth Elliott1,4

1University of Sydney, Camperdown, Australia, 2Sydney Children’s Hospitals Network, Westmead, Australia
Aboriginal children living in remote Australian communities face significant disadvantage and have poor health outcomes. In some of these communities alcohol misuse is widespread, including during pregnancy. Women say that they drink to deal with the stress of historical trauma and adverse living conditions. As a result many children have been exposed to alcohol in utero and some have Fetal Alcohol Spectrum Disorders.

In this presentation some of the challenges, pitfalls and results from FASD research in remote Australia will be presented, as will be a suggested approach to working collaboratively in partnership with Indigenous people to address their priorities through action research.

Visual-motor integration impairment and FASD: A population-based study of children in the Fitzroy Valley
Ms Robyn Donen1, Ms Barbara R Lucas1,2,3,4, Dr Rochelle E Watkins5, Dr Tracey W Tsang5, Dr Kay Sauer1,2, Professor Peter Howat5, Professor Jane Latimer1, Dr James P Fitzpatrick1,2,6, Ms June Oscar8,9, Ms Maureen Carter10, Professor Elizabeth Elliott1,4

1School of Public Health, Curtin University, Perth, Australia, 2Discipline of Paediatrics and Child Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 3The George Institute for Global Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 4Poche Centre for Indigenous Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 5Physiotherapy Department, Royal North Shore Hospital, Sydney, Australia, 6Telethon Kids Institute, University of Western Australia, Perth, Australia, 7Centre for Behavioural Research in Cancer Control, Curtin University, Perth, Australia, 8Marninwarntikura Women’s Resource Centre, Fitzroy Crossing, Australia, 9University of Notre Dame, Broome, Australia, 10Nindilingarri Cultural Health Services, Fitzroy Crossing, Australia, 11The Sydney Children’s Hospitals Network (Westmead), Sydney, Australia

We assessed visual-motor integration (VMI), visual perception, and fine motor coordination in children who participated in the Lililwan Project (n = 108, 7.5 - 9.6 years). We compared scores between children i) without prenatal alcohol exposure (PAE); ii) with PAE but not Fetal Alcohol Spectrum Disorder (FASD); and iii) with FASD, and reported the prevalence of ‘moderate’ (≤ 16th percentile) and ‘severe’ (≤ 2nd percentile) impairments. In the cohort, VMI scores were ‘below average’ (M = 87.8), and visual perception scores were ‘average’ (M = 97.6), with no significant differences between groups. Fine motor coordination scores were ‘below average’ for children with FASD (M = 87.9), but ‘average’ for children without FASD (No PAE M = 95.1; PAE (no FASD) M = 96.1, p = .02). Few children had severe VMI impairment (0.9%), but the prevalence of moderate VMI impairment was very high (42.2%). Aboriginal children living in remote Western Australia have VMI skills that are below average regardless of PAE or FASD, and high rates of moderate impairment. For children with FASD, fine motor coordination problems may have contributed to VMI impairment, highlighting the need to assess both fine motor and VMI in populations with high levels of PAE.

Starting the conversation: seeking consent for research with indigenous populations
Dr Emily Fitzpatrick1,2, Associate Professor Alexandra Martinuik1,4, Ms Heather D’Antoine1, AO June Oscar4, Ms Maureen Carter10, Professor Elizabeth Elliott1,4

1Discipline of Paediatrics and Child Health, Sydney Medical School, University of Sydney, Sydney, Australia, 2The Sydney Children’s Hospital Network, Sydney, NSW, Australia, 3Sydney, Australia, 4Sydney Medical School, University of Sydney, Sydney, Australia, 5The George Institute for Global Health, Sydney, Australia, 6The Sydney Children’s Hospitals Network (Westmead), Sydney, Australia

In response, The Picture Talk Project, working in partnership with Aboriginal communities of the Fitzroy Valley, W.A. interviewed Aboriginal leaders about community engagement and conducted focus groups with community members about individual consent. Transcriptions were analysed and validated by local leaders and interpreters. Themes and rich quotes from Aboriginal leaders and community members are explored and discussed.

Results: Interviews (n=20) conducted with Aboriginal leaders and focus groups (n=6). The interviews and focus groups were conducted in the setting most preferred by participants in the presence of a local Community Navigator, who was well known and respected by the community. Participants involved were different ages, both males and females and from the main language groups of the Fitzroy Valley. Themes such as reciprocity, respect, integrity, responsibility, equality, trust, cultural protocol and language where highlighted in these discussions.

Conclusion: It’s time to consult communities directly about research, how consent could be sought and to evaluate this.

Alcoholism comorbidity with other substance dependence and behavioral addiction
Prof Hisatsugu Miyata1

1Department of Psychiatry, Jikei University School of Medicine, Tokyo, Japan

The National Epidemiological Survey on Alcohol and Related Conditions (NESARC) conducted in the United States using the DSM-IV diagnostic criteria showed that 13.1% of persons diagnosed with alcohol dependence experienced other substance dependence whereas among persons diagnosed with substance abuse or dependence more than half (55.2%) were diagnosed with an alcohol dependence. This type of comorbidity is particularly observed in an alcohol and tobacco use disorder. A serious clinical issue is that alcoholism comorbidity with other substance dependence or behavioral addiction forms the treatment-resistant factors for alcoholism. Recent advances in the research on the risk factors of alcohol dependence have demonstrated that high vulnerability is associated with preexisting schizophrenia or bipolar disorder, as well as impulsivity (producing enhanced rates of all substance dependence and gambling disorder), and a high risk specifically for alcohol dependence is associated with a low level response (low sensitivity) to alcohol. A number of studies have indicated that the dysfunction of the brain dopamine reward system are involved in low response to alcohol. In this presentation, the latest findings of this issue and the several treatment options will be discussed with the introduction of Japanese conditions of alcoholism.

The biological understanding of alcohol effect on Diabetic Mellitus
Prof Dai-Jin Kim1

1Catholic University of Korea, Seoul, South Korea

Alcohol has deleterious influences on glucose metabolism which may contribute to the development of type 2 diabetes mellitus (T2DM). Insulin-like growth factor I (IGF-I) and growth hormone (GH), which interact with insulin to modulate metabolic control, have been shown to be related to impaired glucose tolerance. Brain-Derived Neurotropic Factor (BDNF) plays a major role in insulin resistance, a pathogenic feature of T2DM. In animal study, T2DM model were fed chronic alcohol diet (O-E) and pair-fed control diet to non-diabetic model (L-C). IGF-I, GH and BDNF levels were measured. The serum IGF-I and BDNF levels were significantly lower in the diabetic model than in the control group. Diabetic model show lower IGF-1 level and higher anxiety-like behavior. The biological understanding of alcohol effect on Diabetic Mellitus was then studied.
assessed using the Korean-Mini Mental Status Examination (K-MMSE), digit symbol test. Diabetes group showed significantly lower score in language of K-MMSE and digit symbol test than non-diabetes group.

Comorbidity of alcoholism with depression

Prof Yoshihisa Sato

1Miki Mental Clinic, Sapporo, Japan

Alcohol use disorders (AUDs) have a high prevalence rate of depression. However, the relationship between AUDs and depression has not yet been thoroughly examined in Japan. The present study was designed to investigate the influence of alcohol problems on depression.

Method: 122 new patients were divided into 2 groups: Depression group (D-Gr: n=64) and Alcohol group (A-Gr: n=58) according to their chief complaint at the first visit by using the Hamilton Rating Scale for Depression (HAM-D), Beck Depression Inventory (BDI) and the Alcohol Use Disorders Identification Test (AUDIT). The treatment course was monitored over 12 weeks.

Results: About 20% of D-Gr showed alcohol problems (AUDIT score ≥12) at the first visit. There was no significant difference in the HAM-D score between D-Gr and A-Gr at the first visit. 69% patients of D-Gr and 54% of A-Gr showed moderate depression (HAM-D score ≥14), respectively. In addition, 46% of both groups showed almost the same degree of moderate depression from the respect of BDI score (≥20).

Conclusion: The above results suggest that some of the patients who complained depression had alcohol problems. And the converse is also true, the patients who complained alcohol problems had moderate depression like D-Gr.

Neuroticism tendency as a risk factor for the development of alcohol use disorders: findings from the Alcohols with Inactive ALDH2 Study (AIA Study)

Dr Mitsuru Itoh1, Ms Tomoko Yonemoto1, Ms Satoko Mihara1, Dr Tsuyoshi Toyama2, Dr Yosuke Yumoto2, Dr Chie Iwahara2, Dr Tsuyoshi Takimura3, Dr Atsushi Yoshimura1, Dr Hiroshi Sakuma4, Dr Hideki Nakayama5, Dr Yasunobu Komoto5, Dr Tsuyoshi Takimura6, Dr Mitsuru Itoh1, Ms Tomoko Yonemoto7, Ms Satoko Mihara8, Dr Tsuyoshi Toyama9, Dr Yosuke Yumoto9, Dr Chie Iwahara9, Dr Tsuyoshi Takimura10, Dr Atsushi Yoshimura11, Dr Hiroshi Sakuma12, Dr Hideki Nakayama13, Dr Yasunobu Komoto14, Dr Hitoshi Maesato15, Dr Mitsuru Itoh16, Dr Sachio Matsushita17, Dr Susumu Higuchi18

1National Hospital Organization Karuizawa Medical and Addiction Center, Yokosuka, Japan

Introduction: Despite the potentially severe reactions, some individuals with inactive ALDH2 go on to become alcoholics, and it is hypothesized that they have risk factors for developing alcohol use disorders (AUDs). Hence alcoholics with inactive ALDH2 (AIA) could serve as a useful model for identifying novel risk factors as well as confirming the effects of existing factors. In this study, we attempted to identify possible risk factors regarding personality tendencies with this model (AIA model).

Methods: The subjects were Japanese male AIA (N=104), those with active ALDH2 (AAAS) (N=86) and age-matched healthy males (N=201). To assess personality tendencies, we used the Maudsley Personality Inventory, an 80-item self-reporting measure to assess individual differences in dimensions of neuroticism and extraversion-introversion.

Results: Alcoholics in total showed higher scores for neuroticism than healthy males. In terms of the neuroticism tendency, the scores clearly decreased according to the order of AIA, AAAs, and controls. However, we could not detect any significant differences in the scores of the extraversion-introversion tendency among the three groups.

Conclusion: Using the AIA model, this study identified neuroticism as one of the risk factors for AUDs.

High ethanol and acetaldehyde exposure differentially alters extracellular levels of dopamine and serotonin in the dorsal striatum of Aldh2-knockout mice: a reverse microdialysis study

Dr Mostofa Jamal1, Dr Kiyoshi Ameno1, Ms Naoko Tanaka1, Dr Asuka Ito1, Ms Ayaka Takakura1, Dr Hiroshi Kinoshita2

1Kagawa University, Takamatsu-Shi, Japan

The aim of this study was to describe the in vivo effects of local ethanol (EtOH) and acetaldehyde (ACh) perfusion on extracellular dopamine (DA) and serotonin (5-HT) in the dorsal striatum of Aldh2-knockout (Aldh2-KO) and wild-type (WT) mice. Aldh2-KO mice were used as models of aldehyde dehydrogenase 2-deficient human to examine ACh effects. Mice were perfused with saline, EtOH (100, 200 or 500 mM) or ACh (100, 200, or 500 μM) into the striatum. Dialysate samples were collected every 5 min, and then analyzed with HPLC coupled to an ECD. We found that local perfusion with 500 mM EtOH increased extracellular levels of DA (p<0.05) in both Aldh2-KO and WT mice compared to control, while 5-HT levels remain unchanged. In contrast, perfusion with 100, 200 or 500 μM ACh decreased both DA and 5-HT (p<0.05) in Aldh2-KO mice, but this decrease was not found in WT mice at any of the ACh doses, indicating a role of ACh on DA and 5-HT levels. There was no genotype effects on basal levels of DA and 5-HT. These results indicate that high EtOH can stimulate DA, whereas ACh can depress both DA and 5-HT in the dorsal striatum of mice.

Effects of chemogenetic manipulation of the nucleus accumbens shell on the renewal and reacquisition of extinguished alcohol seeking

Dr Asheeta Prasad1, Professor Gavan McNally

1University of New South Wales, Kensington, Australia

The nucleus accumbens shell (AcbSh), located in the ventral striatum, and is a key brain region for drug seeking behaviour. We transcended AcbSh neurons with an adeno-associated virus expressing designer receptor exclusively activated by a designer drug (DREADD); hM3Dq (excitatory) and hM4Di (inhibitory) under the control of synapsin promoter. Rats were trained to self-administer alcoholic beer in one context (A), extinguished in a second context (B), tested in the extinction (ABB), in context (A) for renewal and reacquisition. Prior to test, rats were administered with clozapine N-oxide (CNO, 3mg/kg i.p.) to activate the DREADDs. There was ABA renewal of alcohol seeking yet no effect of activation or inhibition of AcbSh on the ABA and ABB. Yet, when tested for reacquisition of alcoholic beer seeking only excitatory effect of hM3Dq showed enhanced levels of reacquisition. To further identify the explicit effect on reacquisition, we also tested the rats on a progressive ratio schedule. The break point was unaffected by the DREADD manipulations. Here we show activation of AcbSh using pharmacogenetic manipulation of excitatory Qq-hM3D-DREADD selectively increases reacquisition of drug seeking.

Association analysis of BRAP polymorphisms on the risk of Alcohol Dependence and Alcohol Use Disorders Identification Test (AUDIT)

Prof Ihn-Geun Choi1, Prof Jee Wook Kim2

1Hallym University, Seoul, South Korea

Background: Alcohol dependence (AD) is a common disorder with both environmental and genetic factors. Previous studies have shown that the genomic region from chromosome 4q22-q32 is closely associated with AD. To identify new candidate genes, the present study used GWAS and replication studies in a Korean cohort with AD.

Methods: We conducted a follow-up replication study of association between BRAP polymorphism and AD with 459 alcoholics and 455 normal controls, all of Korean descent. To rank the AD of the subjects, Alcohol Use Disorders Identification Test (AUDIT) was utilized. Using the TaqMan assay, 5 SNPs of BRAP, 53 SNPs of PRMT8 and 39 SNP of TSPAN18 were genotyped.

Results: In the case-control analysis, BRAP rs3782886 showed the most significant association with the risk of AD (p = 1.29 × 10-16, OR = 0.19). Further association analysis in normal controls showed that BRAP rs3782886 was strongly associated with overall AUDIT score (p = 1.40 × 10-16, pcorr = 6.30 × 10-24 in co-dominant model). Both SNPs of PRMT8 and TSPAN18 which were associated with AD showed negative results that were not replicated from the follow-up study.

Conclusion: We found BRAP rs3782886 to be significantly associated with alcohol consumption in normal controls.

A novel neuropeptide regulator of behavioral sensitization to cocaine

Dr James Kasper1, Mr David McCue1, Ms Adrianna Milton1, Ms Catherine Sampson1, Dr Zhixia Ding2, Dr Mei Huang3, Dr Susan Carlton1, Dr Herbert Meltzer1, Dr Johnathan Hommel1

1University of Texas Medical Branch, Calvaston, United States, 2Northwestern University, Chicago, United States
This study evaluates the effect of accumbal neuromedin U (NMU) and its receptor NMU receptor 2 (NMUR2) on behavioral sensitization to cocaine and explores the underlying neurocircuitry. The expression of behavioral sensitization was tested by pretreating rats with cocaine (15 mg/kg) or saline twice a day for five days. Following seven days of no treatment, locomotor activity was measured after rats were microinjected with NMU (0.5 nmoles) into the nucleus accumbens shell (NAcSh) and received cocaine or saline challenge. NMU blocked the expression of cocaine-evoked locomotion in non-sensitized rats but had no effect on sensitized rats. NMU treatment blocked the development of cocaine sensitization when administered during pretreatment as opposed to on challenge day. Electron microscopy localized NMUR2 to presynaptic neurons in the NAcSh. Knockdown of presynaptic NMUR2 in the NAcSh potentiated cocaine sensitization. Using immunohistochemistry, presynaptic NMUR2 in the NAcSh colocalized with a viral-vector tracer injected into the dorsal raphe nucleus (DRN) and GAD67. We then studied the effect of NMU on GABAergic neurons using microdialysis and found that NMu microinjection to the NAcSh decreases local GABA concentrations. These results suggest that NMU blocks development of cocaine sensitization possibly by inhibiting GABAergic projections from the DRN to the NAcSh.

**GIRK channel as a candidate target for pharmacotherapy of drug and alcohol dependence**

Prof Kazutaka Ikeda1, Dr Nagisa Sugaya1,2, Dr Yasukazu Ogai1, Dr Daisuke Nishizawa1

1Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan, 2Yokohama City University, Yokohama, Japan, 3Tsukuba University, Tsukuba, Japan

G-protein activated inwardly rectifying potassium (GIRK, Kir3) channel is one of the effectors in signal pathways from G/Gi coupled receptors such as opioid and dopamine receptors. In addition, GIRK channel is directly activated by ethanol. Therefore, GIRK channels play roles in mediating signals of various addictive substances. We found associations between genetic polymorphisms in the GIRK subunit genes and sensitivity to addictive substances in mice and humans. We looked for compounds which inhibit GIRK channels to find medicines for substance misuse and dependence. We found that fluoxetine and paroxetine, selective serotonin reuptake inhibitors (SSRIs), but not fluvoxamine, another SSRI, inhibited GIRK channels in Xenopus oocyte expression assays and reduced preference for methamphetamine in conditioned place preference tests using mice. In addition, we found that relapse rate and relapse risk scores were lower in alcoholics who received GIRK inhibition treatment than alcoholics with non-GIRK inhibition treatment. These results suggest that GIRK channels are important molecules in the reward system and candidate targets for pharmacotherapy of drug and alcohol dependence.

**The selective D2 dopamine receptor antagonist eticlopride prevents the development of MDMA-induced behavioural sensitisation in rats**

Prof Susan Schenk

Victoria University of Wellington, NZ

Rationale: We hypothesise that MDMA self-administration proceeds as a result of neuroadaptations in brain dopamine and GSH mechanisms. Objectives: Determine the impact of repeated MDMA self-administration on behavioural indices of dopamine and serotonin activation. Methods: In some groups, rats were pretreated with MDMA (10.0 mg/kg) once daily for 5 days. The acquisition of MDMA self-administration and the locomotor activating effects of MDMA were subsequently measured. For other groups, the effect of MDMA self-administration on MDMA-produced hyperactivity and serotonin syndrome were measured. Results: MDMA pre-treatment decreased the latency to acquisition of MDMA self-administration and increased the percentage of rats that met a criteria for acquisition of self-administration. The dose-effect curve for MDMA-produced hyperactivity was shifted leftward following self-administration and this sensitized response was persistent. MDMA self-administration increased MDMA-produced rearing, an indication of an enhanced dopaminergic response. In contrast, components of the serotonin syndrome were decreased following self-administration. Conclusions: These data suggest that dopaminergic substrates become sensitised and serotonin substrates become desensitised following MDMA self-administration.

**Comparison of co-morbid DSM-IV Axis I mental disorders between heroin dependent and methamphetamine dependent adult males in Hunan Province, China**

Dr Huixi Dong1, Dr Wei Hao1

1Mental Health Institute, Second Xiangya Hospital, Central South University, Changsha, China

**Purpose:** This study compared current prevalence (CP) and lifetime prevalence (LP) of co-occurring mental disorders between heroin dependent and methamphetamine (MA) dependent adult males in Hunan, China.

**Method:** We assessed demographic and drug related conditions based on a psychological interview using the Chinese version of the Structured Clinical Interview for DSM-IV-TR Axis I Disorders-Patient Edition (SCID-I/P) in 739 heroin dependent and 552 MA dependent males from several rehabilitation centers.

**Findings:** Study results indicated MA users were younger and had lower educational level, higher separated/divorced rate and more family history of substance use than heroin users were. MA users were more likely to suffer from independent mental disorders (CP:18.0% vs.10.8%, p=0.004; LP: 26.5% vs.20.5%, p=0.033), but less likely to have substance-induced mental disorders (CP:6.6% vs.36.4%, p=0.001; LP: 16.2% vs.46.6%, p<0.001). The two groups varied widely in co-occurring substance use disorders, except for lifetime alcohol use disorder. It is remarkable that 21.38% heroin users and 16.12% MA users had polysubstance use disorder.

**Conclusions:** Substantial differences of co-occurring mental disorders were detected between heroin dependent and MA dependent adult males. This study call for targeted intervention and prevention, and develop treatment services and policies for drug-specific users in China.

**Anti-Inflammation and neuroprotective drugs benefit of opioid dependent patients undergoing methadone maintenance treatment**

Prof Ru-Band Lu1,2, Assistant Prof Sheng-Yu Lee1,3, Assistant Prof Shou-Lan Chen1,4, Assistant Prof Yun-Hsuan Chang1,2

1Department of Psychiatry, College of Medicine and Hospital, National Cheng Kung University, Tainan, Taiwan, Taiwan, 2Addiction Research Center, National Cheng Kung University, Tainan, Taiwan, Taiwan, Taiwan, 3Department of Psychiatry, Kaohsiung Veterans’ General Hospital, Kaohsiung, Taiwan, Kaohsiung, Taiwan, 4Department of Neuroscience, Kaohsiung Medical University, Kaohsiung, Taiwan, Kaohsiung, Taiwan, 5Department of Psychology, Asia University, Taiwan, Taichang, Taiwan

Memantine and dexamethorphan might possess anti-inflammatory and neuroprotective effect. In a randomized, double-blind, controlled 12-week study, we investigated whether using low dose of memantine or dexamethorphan to reduced cytokine levels and treat opioid dependent patients with methadone maintenance treatment (MMT). Patients were randomly assigned to a group 1: DM60 (dexamethorphan [60 mg/day]) (n = 65), DM120 (dexamethorphan [120 mg/day]) (n = 65), or Placebo (n = 66). Memantine (5 mg/day) (n = 53) or Placebo (n = 75). The methadone dose required and retention in treatment were monitored. Plasma tumor necrosis factor (TNF)-α, C-reactive protein (CRP), interleukin (IL)-6, IL-8, transforming growth factor (TGF)-β1, and brain-derived neurotrophic factor (BDNF) levels were examined during week 0, 1, 4, 8, and 12. After 12 weeks, the DM60 group had significantly longer treatment retention and lower plasma morphine levels than did the Placebo group. Plasma TNF-α was significantly decreased in the DM60 group than in the Placebo group. Memantine group required a significantly lower methadone dose than Placebo group did. They also had significantly lower plasma TNF-α and significantly higher TGF-β1 levels. We provide evidence of the benefit of dexamethorphan and memantine in opioid dependent patients undergoing MMT.

**Electroencephalographic Characteristics of Alcohol Dependent Patients: 3-Dimensional Source Localization**

Prof In-Won Chung1, Dr Sandchul Seo2, Dr Sungjin Im3, Dr Sang-Gu Lee1, Professor Chul-Jin Shin4

1Mental Health Institute, Second Xiangya Hospital, Central South University, Changsha, China

**Objective:** To develop treatment services and policies for drug-specific users in China. We looked for compounds that activate by ethanol. Therefore, GIRK channels play roles in mediating signals of various addictive substances. We found associations between genetic polymorphisms in the GIRK subunit genes and sensitivity to addictive substances in mice and humans. We looked for compounds which inhibit GIRK channels to find medicines for substance misuse and dependence. We found that fluoxetine and paroxetine, selective serotonin reuptake inhibitors (SSRIs), but not fluvoxamine, another SSRI, inhibited GIRK channels in Xenopus oocyte expression assays and reduced preference for methamphetamine in conditioned place preference tests using mice. In addition, we found that relapse rate and relapse risk scores were lower in alcoholics who received GIRK inhibition treatment than alcoholics with non-GIRK inhibition treatment. These results suggest that GIRK channels are important molecules in the reward system and candidate targets for pharmacotherapy of drug and alcohol dependence.
The power spectral analysis of electroencephalogram has been widely used to reveal the pathophysiology of the alcoholic brain. However, the results were not consistent and the three dimensional study could be hardly found. This study was to investigate characteristics of the three dimensional electroencephalographic (EEG) activity of these dependent patients using standardized low resolution electromagnetic tomography (sLORETA).

The participants consisted of 30 alcohol dependent patients and 30 healthy controls. All the participants were males who had refrained from alcohol at least one month and not taken any medication. 32-channel EEG data was collected in the resting state with eyes-closed during 30 seconds. The three dimensional data was compared between two groups for the frequency bands.

sLORETA revealed significantly increased brain cortical activity in alpha, beta, beta2, and beta3 bands in alcohol dependent patients compared to normal data was compared between two groups for the frequency bands. In the resting state with eyes-closed during 30 seconds. The three dimensional one month and not taken any medication. 32-channel EEG data was collected in the resting state with eyes-closed during 30 seconds. The three dimensional study could be hardly found. This study was cross-sectional in design, the causal relationship between IUD and these factors could not be determined, and further studies aimed to address this issue are warranted.

Additive effect of tobacco over promoter polymorphism of matrix metalloproteinase7 in gastric cancer risk

Dr Snehasikta Swarnakar

CSIR-Indian Institute of Chemical Biology, Kolkata-700032, India, Kolkata, India

Gastric cancer is the second largest cause of global cancer related mortality and its pathogenesis involves host susceptible genetic factors, exogenous risk factors and H. pylori infection. Genetic factors including single-nucleotide polymorphisms (SNPs) within the promoter region of certain genes regulates respective protein expression that relates to cancer susceptibility. We found elevated expression of matrix metalloproteinase7 (MMP7) in association with gastric cancer invasion. We performed a case-control study (n=520) to evaluate the association of MMP7+181C/G polymorphism and gastric cancer risk, and dependence on age, sex as well as tobacco addiction. Our results suggest that MMP7+181C/G genotype is associated with significant risk of gastric cancer in eastern Indians. The frequency of GG genotype in the eastern Indian gastric cancer patients is much higher (17.5%) compared to control (10%) that strongly associated with disease susceptibility (p=0.02, OR=1.9). Tobacco addiction enhances gastric cancer risk in GG than AA carrier (p=0.03, OR=2.46, 95% CI=1.07-5.68) by facilitating transcription factor binding to GG promoter sequences. Meta-analysis shows that tobacco enhances the risk for cancer more pronouncedly in AG and GC carriers. Our study may provide better diagnosis and therapy of gastric cancer risk by monitoring the association between predisposition marker and exogenous factor.

Internet Use Disorder and Associated Factors among Adolescents in Japan

Ms Satoko Mihara

National Hospital Organization Kurihama Medical and Addiction Center, Yokosuka, Kanagawa, Japan

Japan is assumed to have serious health and social problems due to Internet overuse, but the data has been scarce. The present study was intended to reveal the magnitude of problems arising from excessive Internet use, especially Internet use disorder (IUD) and its associated factors, using a large number of students from randomly selected junior and senior high schools in Japan. The result revealed that 6.2% of male junior and senior high school students and 9.8% of female students were estimated to have IUD. The prevalence of IUD correlated significantly with female gender, school grades and the number of hours spent on Internet. Both common and gender-specific application programs that contributed to the occurrence of IUD were identified. While the downloading application was common to both genders, online gaming played a significant role for males and applications for communication. Finally, this study revealed that IUD was associated with adverse effects on school and daily lives, sleep status, and mental and physical health among adolescents. Because this study was cross-sectional in design, the causal relationship between IUD and these factors could not be determined, and further studies aimed to address this issue are warranted.

Magnetically guided delivery of Methanadamide across blood brain barrier to block cannabinoid induced effects in HIV patients

Ajeet Kaushik

Center of Personalized Nanomedicine, Institute of Neuroimmune Pharmacology, Department of Immunology, Herbert Werheim College of Immunology, Florida International University, USA

Abstract not supplied

Speeding and crashing: methamphetamine induces anhedonia and disrupts frontal cortical energetics in mice

Dr Frederico Pereira-1,2,3, MSc Raquel Fonseca1, PhD Rui Carvalho1,2,3,4, MSc Cristina Lemos1, MSc Ana Sequeira5, MSc Inês Pita1, MSc Fábio Carvalho1, MD Carlos Silva1, PhD Rui Prediger1, Ivana Jarak1,2, PhD Rodrigo Cunha1,2, MD, PhD Carlos Fontes Ribeiro1, PhD Attila Kofávi1,3,5

1Pharmacology and Experimental Therapeutics/IIBLI Faculty of Medicine, University of Coimbra, Coimbra, Portugal, 2Department of Life Sciences, Faculty of Sciences and Technology, University of Coimbra, Coimbra, Portugal, 3Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, 4Institute for Interdisciplinary Research, University of Coimbra, Coimbra, Portugal, 5Department of Farmacology, Centro de Ciências Biológicas, Universidade Federal de Santa Catarina, UFSC, Florianópolis, Brazil, Florianópolis, Brasil

We showed that a single high dose of methamphetamine (METH) induced a persistent frontal cortical monoamine depletion that is accompanied by a depressive-like phenotype in mice. This recapitulates a METH addiction scenario in humans. However, the brain metabolic alterations underlying both neurochemical and mood alterations remain unknown.

Inhere, adult C57BL/6 mice were injected with METH (30 mg/kg, i.p.) and their frontal cortical metabolic fingerprint was characterized after probing their anhedonic profile 3 days post-injection. METH triggered anhedonia, as indicated by the decreased grooming time in the splash test. At this time, METH did not alter anxiety-like behavior or motor functions. Depolarization-induced glucose uptake was reduced in frontocortical slices from METH-treated mice compared to controls. Consistently, astrocytic glucose transporter (Glut1) density was lower in the METH group. A proton high rotation magic angle spinning (HRMAs) approach revealed a significant decrease of the levels of N-acetyl aspartate (NAA), suggesting that METH decreased neuronal function in the frontal cortex. Additionally, METH also decreased the lactate/alanine ratio indicative of an increased oxidative stress. In conclusion, we report for the first time that a single METH injection impairs neuroenergetics, leading to neuronal dysfunction in frontal cortex, which underlies an anhedonic-like behavior.

Increased serotonin release underlies the effect of 4-MTA on olfactory responses in drosophila

Dr Jorge Campuzano1, Mr Sergio Hidalgo1, Ms Daniela Molina1, Dr Angelica Fierro1, Dr Patricio Iturriaga-Vasquez1, Dr Rodrigo Varas1, Mr Nicolás Fuenzalida-Urbe1

1Pontificia Universidad Católica De Chile, Santiago, Chile, 2Universidad de la Frontera, Temuco, Chile, 3Universidad Autónoma, Talca, Chile

4-MTA (4-Methylthioamphetamine) is a “designer drug” which induces prolonged stimulation and euphoria, and has been associated with neurotoxicity and even death. It was designed to specifically block the serotonergic plasma membrane transporter (SerT), leading to an increase in extracellular content of this amine. However, it also acts on other targets. Thus, the behavioral consequences of 4-MTA exposure depend on the effects induced by this drug on all these targets. As mammals, invertebrates exposed to drugs of abuse display a set of behaviors that depend on the activation of amnergic systems. In our lab, we are using the behavioral, physiological and genetic tools available in the fly Drosophila melanogaster to dissect out the contribution of amine systems to the effects induced by 4-MTA.

Our data show that 4-MTA affects fly olfaction and locomotion at different concentrations. Chronoamperometry studies indicate that 4-MTA induces the release of endogenous amines in the fly brain. Experiments in mutant flies suggest that the amine whose release is modified by 4-MTA is serotonin. We further show that the effects on olfaction are not observed in mutants for SerT. Altogether, this data support the proposition that 4-MTA induces the release of serotonin to modulate olfactory responses in Drosophila.
Acute methamphetamine produces long-term deficits in spatial learning and memory retention involving decreased PKMζ and increased COX-2 and ubiquitinated protein levels in the hippocampus

**Prof Peter Serrano**, Mr Stephen Braren

1Hunter College, New York, United States

We evaluate MA (methamphetamine) effects on spatial learning and memory using the radial 8-arm maze (RAM). Hippocampal tissues were quantified for the memory-related protein kinase M zeta (PKMζ), the Dr receptor and inflammatory markers, cyclooxygenase-2 (COX-2), microglia (IBA-1), including ubiquitinated protein levels. COX-2 catalyzes the conversion of arachidonic acid into prostaglandins. Several prostaglandins are catalyzed by COX-2, but one is very toxic, prostaglandin J2 (PGJ2). Thus, we are interested in how MA toxicity activates this inflammatory pathway perpetuating the toxicity. Our results show that two bolus doses (to 2g/kg) of MA delivered 1 week apart produces deficits in learning the RAM 6 weeks later. Additionally, delivering these two bolus doses after acquiring the RAM memory results in retention deficits identified 2 weeks after the end of training. These results show that MA disrupts learning and memory. The MA effects in the hippocampus identified a decrease in PKMζ and the Dr receptor while increasing COX-2, IBA-1 (a marker for microglia) and levels of ubiquitinated proteins (marker for ubiquitin proteosome pathway, UPP function). Our data suggest that acute MA initiates an inflammatory response that continues over time impairing the trafficking of PKMζ to the synapse leading to spatial learning and memory deficits.

Mechanistic studies on the reversal of ketamine-induced toxicity in zebrafish

**Dr Jyotshna Kanungo**, Ms Melanie Dumas, Dr Xiaoxing Guo, Dr Syed Ali, Dr Merle Paule, Ms Bonnie Robinson

1National Center for Toxicological Research, USFDA, Jefferson, United States

Ketamine, an antagonist of the N-methyl-d-aspartate (NMDA) receptors, is a pediatric anesthetic. Ketamine is cardiotoxic and neurotoxic in zebrafish embryos. We show that acetyl l-carnitine (ALCAR) protects zebrafish embryos against ketamine-induced toxicities. Since NMDA receptors are calcium permeable, ketamine’s toxic effects are likely due to blockade of calcium entry into the cells. ALCAR is known to open the L-type calcium channel and generate ATP. We tested whether this presence of calcium chelators and L-type calcium channel blockers (e.g., verapamil). ALCAR was ineffective in reversing ketamine’s effect. Microarray studies also revealed that gene expression involved in ATP synthesis was altered in the embryos exposed to ketamine. Based on this genomic data, we interfered with the ATP synthesis pathway using specific inhibitors. We show that mitochondrial function is a target of ketamine. Verapamil and ketamine together are more toxic than each drug alone. ALCAR was effective in counteracting the effects of verapamil or verapamil and ketamine, but not in presence of an inhibitor of ATP synthesis. ALCAR also reversed ketamine’s effects on serotonin levels and metabolism. Our combined in vivo and in vitro studies suggest that alteration in energy metabolic pathway and neurotransmitter levels may play critical roles in ketamine-induced toxicity.

Proper use of alcohol: Can alcohol become a relaxation-promoting item?

**Prof Hisatsugu Miyata**

1Department of Psychiatry, Jikei University School of Medicine, Tokyo, Japan

Alcohol has a negative effect on human health. At the same time, humans have used alcohol as a tool for stress reduction or a lubricant of human relations. In general, not a few people have enjoyed alcohol without producing significant problems. The theme of this presentation is to discuss whether or not alcohol can promote any beneficial effects on mental function under the so-called proper use. For that purpose, we investigated whether ethanol (EtOH) could decrease impulsivity in the doses producing neither dependence nor motor performance by rats. In an intracranial self-stimulation (ICSS) paradigm, the rats were trained to hold a lever for 4 seconds to obtain an ICSS reward, and to release the lever immediately after they had obtained a reward. As for estimating impulsivity, a number of reward gain per min is regarded to reflect impulsivity related to “action restraint”; whereas a time for releasing the lever is regarded to reflect impulsivity related to “action cancellation”. The results of the experiment indicated that EtOH had a potential to decrease impulsivity related to “action restraint” at a dose producing neither dependence nor motor performance. Together with these findings, a concept of the proper use of alcohol will be discussed.

Nicotine: beneficial for stress relief?

**Dr Keun Ho Joe**, Dr Jeong Seok Seo

1Dasanong Central Hospital, Euiwang, South Korea, 2Kunkuk University, Chungju, South Korea

In 2015, the Korean government raised the price of cigarette and expand the medical insurance coverage to quit-smoking. Because the smoking rate of adult male was stagnant for several years over 40 percent. Many people have a myth that cigarette smoking is one of the effective tool to relief stress. They say that they feel real comfort after smoking. However, many studies supports that the ease feeling after smoking is no more than the relief of nicotine withdrawal. Furthermore, studies about stress coping revealed that the quit smokers are more positively perceive their stress and overcome it. We will deal with the significance of smoking on managing stress by reviewing research outcomes and clinical experiences. And we will discuss about the clinicians’ or counselors’ attitude toward stress during quit smoking counselling.

Is caffeine “addictive”?

**Prof Kohji Takada**

1Teityo University, Tokyo, Japan

Caffeine-containing beverages and foods have been used over centuries in humans, and nearly 90% of the population in the US over 2 or more years of age is said to consume caffeine regularly. As such, these reference-containing materials are clearly reinforcing, by definition of the term. Caffeine itself exhibits physiologic effects (e.g. increased blood pressure), CNS stimulant effects, and positive subjective effects, and can serve as a discriminative stimulus. Moreover, acute toxic effects and withdrawal symptoms of caffeine have been well-documented. However, the evidence that pure caffeine, unaccompanied by e.g. sensory aspects of caffeine-containing materials, serves as a positive reinforcer is ambiguous. In this presentation whether caffeine should be defined as “addictive” will be discussed. Further, the role of other materials contained in caffeine-containing edibles and drinks (e.g. glucose), as well as sensory aspects of these, will also be discussed from the viewpoint of harm reduction.

Casino in Japan, to do or not to do?

**Dr Moritoshi Kido**

1Osaka University of Commerce, Osaka, Japan

People spend their leisure time to improve their lives. And entertainment creates a refreshment and a peace of mind. As a kind of demotic entertainments, there are various gambling industries all over the world and gambling facilities provide the leisure time. On the other hand, gambling has negative effects like “gambling disorder”. In recent years, Japanese government is planning to attract casinos to have a stimulative effect on the economy. This presentation is aimed to provide the information of present situation of gambling disorder and industry in Japan, and consider future direction to cope with the negative effect.

The relationship between problematic internet use and social withdrawal among senior high students in Japan

**Dr Tomohiro Shirasaka**, Dr Masaru Tateno, Masaya Tayama

1Teine Keijinkai Hospital, Sapporo, Japan, 2Tokivara Hospital, Sapporo, Japan, 3Miki mental clinic, Sapporo, Japan, 4Sapporo Medical University, Sapporo, Japan

The Internet was originally designed to facilitate communication and research activities. However, there has been a dramatic increase in the use of the Internet in recent years for education, entertainment, including video games. Problematic Internet use of a phenomena has been described by researchers as excessive or compulsive use of computers that interferes with daily life. The prevalence of adults with tendencies towards
The prevention of alcohol use disorder among working persons with habitual drinking “Young Psychiatrist Symposium”.

Dr Masuo Tanaka1,2, Prof Junichiro Ota1, Ms Etsuko Doki1, Ms Norie Kishi1, Dr Nozomu Hashimoto2, Dr Takashi Sunami2, Prof Shigeo Hori1

1Department of Psychiatry, Koyo Hospital, Ube, Japan, 2Ziiei Institute of Psychiatry, Ziiei Hospital of Psychiatry, Okayama, Japan, 3Mental Health and Welfare Center of Okayama City, Okayama, Japan, 4Okayama Psychiatric Medical Center, Okayama, Japan

We studied the effectiveness of the two-steps interventions, first ones conducted after the lecture, and the second in about 6 months after them, to prevent working persons with habitual drinking from suffering from alcohol use disorder. We took self-administered questionnaires about their frequencies and quantities of alcohol, their self-efficacy in drinking, and their motivation for moderation in drinking, before and after the first interventions, and after the second one. 79 working persons responded our questionnaires. 43 participants (54.5%) had habitual drinking more than 4 times per week. 24 participants (30.4%) drank more than 6.1 drinks. Except for 9 ones chose less than once drinking per month and unanswered, we investigated 70 persons about their changes in amount of alcohol (Participation; once 22, twice 48). 8 of 22 first participants and 25 of 48 ones in the both reduced amount of alcohol. Regarding their attitudes about their habitual drinking and their frequencies and quantities of alcohol, those who tried to change their alcohol related habits were significantly higher among participants in both sessions than ones in the first (P<0.05). Although the both participants had high motivation for their improvements of drinking, we suggested the booster interventions were more effective on them.

Alcohol use disorder in a stricken area

Dr Tetsuji Cho1, Dr Masuo Tanaka1, Dr Kazuki Kuno2, Dr Seiichiro Obata2, Dr Takashi Egami2, Dr Takahiro Fukuda2, Dr Keizo Hara3, Dr Sachio Matsushita3, Dr Masayuki Morikawa3, Prof Toshifumi Kishimoto4

1Mental Care Center, Prefecture of Mie, Tsu, Japan, 2Department of Psychiatry, Nara Medical University, School of Medicine, Kashihara, Japan, 3Koyo Hospital, Ube, Japan, 4National Hospital Organization Rikuyu Hospital, Kin, Japan, 5Hara clinic, Sendai, Japan, 6National Hospital Organization Kanhami Medical and Addiction Center, Yolosuka, Japan

Objectives: The large complex disasters at 11th March 2011 caused a breaking up families and communities. Therefore, alcohol related problems have increased and the people with alcohol related problems have distrest large stigma in temporary housings. This study aimed to compare the change patterns of perceived stigma for alcohol use disorder among supporters in a stricken area.

Methods: We demonstrated a series of three lectures among 66 supporters in Ishinomaki area, where is one of the worst tsunami-devastated regions in Tohoku area. We investigated the changes in the attitude of supporters to the people with alcohol related problems using Alcohol and Alcohol Problems Perception Questionnaire (AAPPQ) and Nawata Visual analogue scale (N-VAS), before and after the programs.

Results: These activities induced statistically significant improvements of participants’ motivation, confidence, and attitudes. The total mean score (standard deviation) of AAPPQ from 127.2 (24.7) before the intervention to 137.2 (21.2) after the intervention. In addition, the score of N-VAS also induced statistically significant improvements.

Conclusion: As an antistigma program, These activities for alcohol use disorder in a stricken area were effective. These programs might be helpful for not only the supporters but also the people with alcohol related problems in a stricken area.

Effects of the glutamatergic modulating agents on toluene-induced enhancement of brain-stimulation reward and behavioral disturbances

Prof Hwei-Hsien Chen1,2, Prof Ming-Huan Chan1,4, Ms Yi-Ling Tsai5, Mr Chia-Yu Lin6, Dr Astrid K Stoker5, Prof Athina Markou5

1Center for Neuropsychiatric Research, National Health Research Institutes, Zhunan, Miaoli County Taiwan, Zhunan, Miaoli County, Taiwan, 2Master/PhD Program in Pharmacology and Toxicology, Tzu Chi University, Hualien, Taiwan, Hualien, Taiwan, Hualien, Taiwan,
Morphine and HIV induced bile acid imbalance leads to gut barrier compromise and systemic inflammation in NSG-BLT humanized mice.

Dr Santanu Banerjee, Dr Jingjing Meng, Ms Li Zheng, Dr Umakanth Sharma, Dr Joseph Dalluge, Dr Peter Southern, Prof Sabita Roy

University of Minnesota, Minneapolis, United States

Despite being predominant drugs of choice for anti-nociception, morphine and its pharmacological derivatives result in severe co-morbidities studied both in humans and several animal disease models. Opioids and HIV infection have been shown to promote bacterial translocation across the gut mucosa, leading to systemic inflammation/sepsis. HIV infection is independently known to alter microbial composition and causing biliary problems/diseases in infected patients, independent of their immune status. Recent studies have strongly correlated bile-acid dysbiosis (increased ratio of hydrophobic to hydrophilic bile acids) to gut barrier disruption and host systemic inflammation. In this context, role of hepatic cholesterol-7-hydroxylase (CYP7A1; catalyzes rate-limiting first step of cholesterol to bile conversion) and Farnesoid-x-receptor (FxR; regulator of hepato-enteric bile circulation) has been strongly implicated in gut pathologies due to altered bile composition.

Here, using a Blood-Liver-Thymus (BLT) model of humanized mice, we show for the first time that morphine causes significant alteration in cholesterol/bile acid metabolism. Next, we show the role of bile acid changes due to HIV infection and chronic morphine in gut barrier dysfunction in the context of CYP7A1/FxR. Precise understanding of this phenomenon would open up the prospect of devising minimally invasive adjunct treatment strategies for managing morphine-mediated inflammation in the host.

Oleoylthanolamide prevents neuroimmune HMGB1/TLR4/NF-kB danger signaling, oxidative stress and pro-apoptotic caspase-3 in frontal cortex after ethanol binge administration

Dr Laura Orio, Ms María Antón, Dr Francisco Alén, Dr Raquel Gómez de Heras, Dr Antonia Serrano, Dr Javier Pavón, Dr JuanCarlos Leza, Dr Fernando Rodríguez de Fonseca, Dr Borja García-Bueno

Universidad Complutense De Madrid, Pozuelo De Alarcón, Spain, Instituto IBIMA, Málaga, Spain

Alcohol abuse is frequently characterized by a specific pattern of intake in binge drinking episodes, inducing neuroinflammation and brain damage. Here, we characterized the temporal profile of neuroinflammation in rats exposed to intragastric binge ethanol administrations (3 times/day x 4 days) and tested the anti-inflammatory/neuroprotective properties of the satefy factor oleoylthanolamide (OEA). Pre-treatment with OEA (10 mg/kg, i.p) previous each alcohol gavage blocked the expression of High mobility group box 1 (HMGB1) danger signal and the innate immunity Toll-like receptors 4 (TLR4), inhibiting the Nuclear factor-kappa B (NF-kB) proinflammatory cascade induced by alcohol binge in frontal cortex. OEA reduced the levels of Interleukin-beta (IL-1β), the monocyte chemoattractant protein-1 (MCP-1), and the enzymes cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in ethanol binged animals. Elevation in plasma Tumor necrosis factor alpha (TNF-α) and IL-1β after ethanol were also inhibited by OEA. Additionally, OEA prevented ethanol-induced lipid peroxidation, caspase-8 and pro-apoptotic caspase-3 activation in frontal cortex. Finally, OEA blocked the rise in blood corticosterone levels after ethanol with no alteration in blood ethanol levels. Altogether, results highlight a beneficial profile of OEA as a potent anti-inflammatory/neuroprotectant compound to treat alcohol abuse.

GHB receptor antagonist reverses GHB-induced amnesia in adolescent rat

Prof Ratna Sircar, Keita Ishiwa

The City College Of New York, New York, United States, Albert Einstein College Of Medicine, Bronx, NY

Gamma-hydroxybutyric acid (GHB) is abused by adolescents and young adults. In humans GHB produce anterograde amnesia, and memory impairments in experimental animals. GHB binds to GHB receptors as well as GABAB receptors. While many of the behavioral effects of relatively high doses of GHB have been attributed to its effects on the GABAB receptor, it is unclear which receptors mediate its low dose amnesic effects. The present study examined the ability of the GHB receptor antagonist NCS-382 to block the amnesic effects of GHB in adolescent female rat. Separate groups of rats received either NCS-382 or vehicle before training for fear conditioning. Followed by either GHB or saline injection, and tested for contextual fear memory and auditory cued fear memory. The results demonstrated that NCS-382 produced a dose-dependent reversal of deficits in the acquisition of contextual fear memory induced by GHB. When animals were tested for cued fear memory, treatment groups did not differ in freezing responses to the tone. Since contextual fear conditioning is thought to be mediated by the hippocampus, where GHB receptors are particularly abundant, the present results suggest that GHB may exert its amnesic effects via hippocampal GHB receptors.

The Role of ABCB1 Drug Transporter in Psychostimulants and Nicotine-induced Neurotoxicity

Dr Beverly Lyn-Cook, Graduate Student Lascelles Lyn-Cook, Jr, Dr Wei Ding, Biologist Beverly Word, Dr George Hammons, Biologist Susan Lantz-McPeak, Dr Syed Ali

1FDA/National Center for Toxicological Research, Jefferson, United States, 2University Arkansas Medical Sciences, Little Rock, United States

Methamphetamine (METH) and 3,4-methylenedioxymethamphetamine (MDMA) are known to induce a number of neurological effects. Most users are known to smoke cigarettes and, therefore, are exposed to nicotine. Using an in vitro neurotoxicity culture model, PC-12 cells, we examined DNA damage induced by these drugs alone or in combination with nicotine using the Comet assay. METH induced DNA damage at all concentrations used (0.1-2 mM), while MDMA induced its maximum damage at 0.5 mM. Nicotine induced its maximum damage at 10 μM. METH at 1 mM and all concentrations of nicotine significantly increased DNA damage when compared to nicotine alone. MDMA induced less DNA damage than METH. To determine the possible mechanism, studies were conducted to determine the effects of these drugs on the multi-drug resistance gene, ABCB1; expression. METH induced ABCB1 in a dose-dependent manner; however, MDMA induced ABCB1 20-fold. Nicotine and METH revealed a novel finding, METH at 0.1 mM and nicotine at 2 μM completely inhibited ABCB1 expression. This could explain the reduced damage observed in the nicotine/MDMA combination study and the increased damage in the METH/nicotine combination study. Further studies are being conducted to determine other pathways in which these drugs are exerting their effects.
Periconceptional alcohol exposure in the rat results in impaired cardiac and renal function in female offspring but not male offspring

Ms Emily S Doyle1, Ms Emelie M Gardebejer2, Professor Mary E Wlodek1, Dr Kristy A Weir3, Associate Professor Karen M Moritz

1School of Biomedical Sciences, The University of Queensland, St Lucia, Australia, 2Department of Physiology, The University of Melbourne, Melbourne, Australia

Background: Maternal alcohol during pregnancy can induce behavioural and developmental delays in childhood. We have used rat models to determine if prenatal alcohol contributes to adult-onset diseases including hypertension and renal disease. Here, we investigated the effect of alcohol exposure during the periconceptional period (PCEtOH) on the development of cardiac and renal dysfunction.

Methods: Rats received a liquid diet of 12.5% EtOH from four days before to four days after mating. Kidney function (24hr metabolic cage) along with heart function and blood pressure (echocardiography/radio telemetry) were examined in adulthood (12-18 months). Kidneys were collected at 19 months for gene/protein analysis.

Results: Male offspring were relatively unaffected by PCEtOH. In females, PCEtOH increased urine flow during basal and dehydration conditions (P<0.05). PCEtOH increased female AQP2 mRNA and AVPR2 expression (P<0.05). PCEtOH appeared to alter AQP2 membrane trafficking, indicated by more diffuse expression. PCEtOH female offspring had reduced cardiac output (P<0.05), a tendency for reduced fractional shortening (P=0.08), and no hypertrophy.

Conclusions: PCEtOH alters urine flow and expression of AQP2, a key mediator of urine concentration in female offspring. These changes indicate a diabetes phenotype, and combined with the changes in heart function, highlight the importance of avoiding alcohol when planning a pregnancy.

Behaviour problems in children living in an FASD in remote, predominantly Aboriginal Australian communities

Dr Tracey W Tsang1, Prof Heather Carmichael Olson1, Prof Jane Latimer2, Dr James Fitzpatrick3, Ms Marmeingee Hand4, Ms June Oscar5, Ms Maureen Carter5, Prof Elizabeth J Elliott1,2,4,5

1Discipline of Paediatrics & Child Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 2Department of Psychiatry & Behavioural Sciences, University of Washington School of Medicine, Seattle Children’s Research Institute, Seattle, USA, 3The George Institute for Global Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 4Department of Psychiatry & Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington, USA, 5School of Biomedical Sciences, The University of Queensland, St Lucia, Australia

Background: Pregnant women who use alcohol are at risk of harm to their health and pregnancy. Alcohol use in pregnancy can cause Fetal Alcohol Spectrum Disorder (FASD). Parent/carer and teacher ratings of behaviour were obtained using the Child Behavior Checklist (CBCL, n=97), and Teacher Report Form (TRF, n=106) respectively. Total scores, proportions scoring within “Normal/Borderline/Clinical” ranges, and Critical Items (highly concerning specific behaviours) were documented and compared between FASD and Non-FASD groups using Mann-Whitney U and Chi-square tests. Academic performance was the most prevalent problem with 77% scoring in “Borderline/Clinical” ranges. TRF scores were poorer in the FASD group on scales encompassing Attention, Academic performance, Adaptive functioning, Social, Thought, Post-traumatic stress, Internalizing and Total problems, and Sluggish cognitive tempo. More children with an FASD had scores in the “Clinical” range (8/26 TRF scales, p=0.012). Of the TRF Critical Items, “Attacks” was the most prevalent (FASD: 38.1%; Non-FASD: 17.6%; p=0.07), and speaking about suicide was more frequent in the FASD group (14.3% versus 1.2%; p=0.03). CBCL ratings were not significantly different between groups. Access to adequate mental health services is urgently needed as is support for teachers managing the challenging behaviours of affected children.

Trends in alcohol related hospital admissions during pregnancy 2001-2010: results from a population based cohort study in NSW, Australia

Dr Courtney Breen1, Dr Fenglian Xu2, Ms Elizabeth Whittaker1, A/Prof Lucinda Burns1

1National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia

Aim: To examine hospital admissions for alcohol use disorders (AUD) during pregnancy over a decade in NSW, Australia.

Methods: Population based cohort study using linked routinely collected population data from the NSW Perinatal Data Collection (PDC) and the NSW Admitted Patients Data Collection (APDC). All women who gave birth in NSW between 1 January 2001 and 31 December 2010 were included. All hospital admissions for AUD in pregnancy were identified. Descriptive statistics and logistic regression were used to calculate the hospital admission rate, difference over time and to analyse risk factors associated with hospital admissions for AUDs.

Results: In the ten year study period, there were 509 women with a total of 759 hospital admissions for any AUD diagnosis in pregnancy. The majority of the women and admissions did not have a principal diagnosis of AUD. Admission rates for AUD remain low with no significant change over time for principal diagnosis of AUD. There was a decreasing but variable trend for all diagnosis of AUD in pregnancy. Readmission for AUD during pregnancy is high for a minority of women: approximately 10% of women with an AUD in pregnancy had three or more admissions, accounting for 42% and 30% of admissions for principal and all diagnoses respectively. Factors associated with AUD in pregnancy include previous psychiatric disorders (including substance use), smoking, being unmarried, being over 30 and living in remote or regional locations.

Conclusion: Despite a reported increase in the proportions of women abstaining from alcohol consumption during pregnancy in the past decade, this data suggests little change among those most at risk. The rate of admission to hospital for a principal diagnosis of AUD during pregnancy has remained stable and the readmission rate is high. Improvements in the detection and treatment of women with AUD are required to reduce the impacts of alcohol exposed pregnancies.

Supported by: The National Drug and Alcohol Research Centre at the University of NSW is supported by funding from the Australian Government.

Assisting primary care health professionals to reduce the harm associated with alcohol and other drug use in pregnancy: development of a framework and educational resources

Dr Courtney Breen1, A/Prof Lucinda Burns1

1National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia

Assembling primary care health professionals to reduce the harm associated with alcohol and other drug use in pregnancy: development of a framework and educational resources

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1National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia

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Background: Pregnant women who use alcohol are at risk of harm to their health and pregnancy. Alcohol use in pregnancy can cause Fetal Alcohol Spectrum Disorders (FASD) with lifelong impacts. This national project investigated the evidence for the treatment of pregnant women who use substances with a focus on alcohol. It formed the basis of an educational resource to improve primary care practice in the identification and management of alcohol and other drug use in pregnancy.

Methodology: The project collated information through i) a review of literature on the effective assessment and treatment for pregnant women who use alcohol and other drugs, ii) an audit of available specialist services for pregnant women and iii) stakeholder consultation.

Results: Screening, brief intervention and motivational interviewing have been found to have good outcomes. Variable screening practices in primary care mean not all at-risk women are identified. Referral pathways to treatment may be unclear and there are limited specialist antenatal services. Psychosocial correlates of substance use during pregnancy include mental disorders, domestic violence and poor antenatal care and these factors need to be comprehensively addressed. Many pregnancies are unintended and women tend to become aware of unintended pregnancies later, increasing the risk of inadvertent exposure to substances.
Conclusion: An educational resource to assist primary health care professionals to identify, manage and appropriately refer substance using pregnancy women has been developed. It provides a best practice model addressing the risks across a continuum from preconception, pregnancy and after birth. A structure for supportive comprehensive care to address issues associated with use is provided to improve outcomes for both women and their babies. Further workforce development including accessible training is required. Clinicians with specialist skills need to support primary care professionals as specialist antenatal care is limited. The implementation and dissemination of the resource will be discussed.

THURSDAY 21 AUGUST

Attitude of Thai Nurses toward Alcohol-dependent Patients

Mrs Soontaree Srikosai1, Mrs Laddawan Piboonsri2

Rajanagarindra Institute of Child Development Chiang Mai, Chiang Mai, Thailand,1Rajanagarindra Institute of Child Development Chiang Mai, Chiang Mai, Thailand

Nurses’ attitudes can impact quality of care. This study aimed to investigate the attitudes of Thai nurses toward alcohol-dependent patients. Data was collected using the Nurses’ Attitudes Toward Alcohol-dependent Patients Scale (NAADS), and semi-structured interview questions. The sample was nurses who have at least two years’ experience caring for alcohol-dependent patients. Twenty-five nurses were key informants in the focus group interviews, and 1,391 nurses from the government hospitals in four regions of Thailand answered questionnaires. Results revealed that 448 nurses working in psychiatric hospitals have relatively positive attitudes toward alcohol-dependent patients, but 537 nurses working in general hospitals and 406 nurses working in community hospitals have relatively negative attitudes toward alcohol-dependent patients. Content analysis revealed five themes of nurses’ attitudes toward alcohol-dependent patients: ‘burden of care’, ‘disappointed family members’, ‘irresponsible patients’, ‘pitiful patients’, and ‘bad behavior’. The results indicate that general and community hospital nurses need more training to improve their understanding of alcohol-dependent patients. Better understanding of alcoholics can improve both nurses’ attitudes and quality of care.

Alcohol misuse in Cambodia

Sathirany Yong, MCH Ministry of Health, Cambodia

Abstract not supplied

Culture & Alcoholism

Prof Sung-Gon Kim1

1Pusan National University, Yang-San, South Korea

When people get stress, many of them try to relief the stress by taking a spicy food, which is very popular in Korea, even though spicy one causes pain. Based on these assumptions, we found that subcutaneous administration of capsaicin significantly increased POMC mRNA expression in rat brain, and concluded that a spicy food could increase an activity of the central opioid system. On the other hand, many previous studies ascertained that alcohol drinking increases opioid neuronal activity in the brain, too. Therefore, we investigated whether drinking behavior is associated with preference of a spicy food. It was found that subcutaneous administration of capsaicin in C57BL/6 mice significantly decreased alcohol intake and that those who have alcohol dependence prefer a spicy food more than normal control subjects. In addition, in social driner, we found that using BAES naltrexone significantly decreased stimulative effect from acute alcohol drinking in a preference group of a spicy food, but not in non-preference group. Therefore, it is assumed that a food culture of preference of a spicy one can affect not only alcohol drinking behavior but also treatment response when treating alcoholism. It is suggested that central opioid neuronal systems are involved with these relationships.
The prevention of methamphetamine addiction by health workers in rural Thailand

Dr Civilaiz Wanaratwichit1
1 Naesuan University, Phisanulok Province, Thailand

Background and objective: The methamphetamine problem solving was focused on policy of Thailand. Health Centre was emphasized on proactive approach in the prevention for methamphetamine. The aims of this study were to investigate the roles of health workers and problems on the prevention of methamphetamine in rural Thailand.

Methods: This study designed to utilize a case study to investigate, analyze and synthesize role of health workers. There were eleven participants, including eight health workers in Health Centre and three members of the district health management committee in Sawakhonak District, Thailand. Data were collected through in-depth interviews, direct observation and document analysis. Thematic analysis was used data analysis.

Results: Health workers on the prevention of methamphetamine for people in rural Thailand were the participatory working with all sectors. It was found in five domains. They consisted of: 1) Finding the new cases of methamphetamine addiction; screening and identify, 2) Counseling and their parents, 3) Training the cases, 4) Monitoring the behavior of the trained cases, 5) Enhancing awareness in children. The most problem was the budget.

Conclusion: Health workers involving in proactive approach. Therefore, they should be considered the advanced training in skills in case.

Drug abuse behavior and factors related to drug-addiction among the hill tribe youths of Lower Northern Thailand

A/Prof Narongkach Naosorn1
1 Faculty of Public Health, Muang District Phitsanulok Province, Thailand

The objective of this study was to explore the drug abuse behavior and factors related to the drug-addiction among the hill tribe youths of Lower Northern Thailand. The sample size was 900 hill tribe youths. Questionnaires were used as the research instruments. Percentage, odds ratio, and conditional logistic regression were used for statistical analysis.

The results showed that 25.9 percent of youths take alcohol, 13.9 percent smoke and 9.0 percent of youths use addictive substances. The youths who prefer nightlife were likely to use addictive substance 1.27 times more than those who did not go out in the night. Youths from poor family relationship seems to use addictive substances 1.89 times more than those from good family relationship. Those who were made to buy cigarette and alcohol by their relatives are likely to use addictive substances 1.57 and 1.20 times more than the other youths respectively. Those who had sex before are likely to use addictive substance 2.54 times more than those who never had sex before.

Hypocretin neurotransmission mediates compulsive-like cocaine taking and seeking: a potential role for the central amygdala

Dr Brooke Schmeichel1, Dr George Koob1
1 NIDA/IRP, Baltimore, United States

Cocaine abuse is characterized by patterns of excessive drug seeking and taking, including a preoccupation with obtaining the drug, and a loss of control over drug intake. The lateral hypothalamic hypocretin/orexin (HCRT) system has been implicated in drug taking and the reinstatement of drug seeking. Limited evidence suggests HCRT may drive drug-seeking through activation of specific brain regions implicated in stress system dysfunction, including the extended amygdala. The role of HCRT in the persistence of compulsive behaviors associated with cocaine addiction has yet to be fully elucidated. Thus, we examined the role of HCRT in the mediation of escalated cocaine intake and reinstatement of drug-seeking following extinction. We found that systemic administration of the HCRT-receptor 1 antagonist, SB-33467, dose-dependently decreased cocaine intake specifically in animals allowed extended access (6h) to cocaine compared to short access (1h) animals. Site-specific injections of SB-33467 into the central amygdala (CeA) had no effect on cocaine intake in extended access animals. Additionally, we observed a significant attenuation of yohimbine-induced reinstatement of cocaine-seeking following SB-33467 administration into the CeA. These findings suggest that HCRT signaling is implicated in compulsive-like cocaine intake and HCRT neurotransmission within the CeA plays a role in stress-induced cocaine seeking.

Cannabinoid type (CB2) receptor agonists diminish neuroinflammation and blood brain barrier (BBB) injury in the setting of HIV infection and alcohol misuse

Dr Yuri Persidsky1, Dr Slava Rom1, Ms. Nancy Reinchenbach1, Ms Holly Dykstra2, Dr Viviana Zuluaga-ramirez3, Dr Servio Ramirez2
1 Dept. of Pathology, Temple University School of Medicine, Philadelphia, United States

Background and objective: Antiretroviral therapy (ART) substantially slowed progression of HIV-1 infection, but ART was unable to prevent HIV-1 associated neurocognitive disorders (HAND). Pathogenesis of HAND is driven by low levels of virus replication in brain macrophages, inefficient immune responses against virus and chronic injury of BBB. Alcohol misuse accelerates HIV progression/HAND. Data obtained in humans, in vitro systems and animal models suggest that alcohol promotes neuroinflammation and BBB injury. Interventions protecting BBB, diminishing inflammation and HIV-1 replication (like CB2 agonists) are beneficial in treatment of the neurodegenerating underlying HAND. Anti-inflammatory and anti-retroviral CB2 effects in the setting of HIV CNS infection have not been studied systematically, and the number of such compounds is very limited. Our recently published studies demonstrated effective suppression of HIV replication in human macrophages in CB2 specific manner, beneficial anti-inflammatory, barrier-tightening effects of CB2 activation in brain endothelium and selective CB2 activation in human macrocytocytes suppresses their ability to engage the brain endothelium/migrate across the BBB preventing its injury. We recently performed rigorous functional testing of novel highly selective, orally available CB2 agonists in a systematic stepwise manner targeting CB2 signaling in macrocytocytes and brain endothelial cells. These compounds demonstrated substantial anti-inflammatory effects in vitro and in vivo.

Airway epithelial cells in cigarette smoke- and HIV-induced lung diseases

Dr Mohan Sopyri1, Sraovani Gundavarapu1, Dr Hiten Chand1, Dr Neerad Mishra1, Dr Shashi Singh1, Dr Christopher Royer1, Dr Edward Barrett1, Dr Shilpa Buch1, Dr Shannon Callen2
1 Lovelace Respiratory Research Institute, Albuquerque, United States, 2 University of Nebraska Medical Center, Omaha, USA

Cigarette smoke (CS) and/or HIV are linked to increased susceptibility to a number of respiratory diseases including chronic bronchitis (CB) and chronic obstructive pulmonary disease (COPD) even after antiretroviral therapy (ART). The mechanism by which CS and HIV promote obstructive lung diseases is not clear. Airway mucus hypersecretion is a key pathophysiologic feature of CB and COPD, and our studies suggest that CS/nicotine induce mucus formation in mouse airways and normal human bronchial epithelial (NHBE) cells via α7-nicotinic acetylcholine receptors (α7-nAChRs). Moreover, NHBE cells express CCR4, CDA, and α7-nAChRs, and HIV-1 gp120 induces mucus formation in these cells that is blocked by CCR4 and α7-nAChR-specific antagonists. Interestingly, HIV- and SIV-infected lungs exhibit high levels of mucus content and gp120-immunoreactivity, and the increased mucus formation is seen even after ART. Furthermore, in SIV- and HIV-infected lungs, HIV-gp120 is also seen on epithelial present in the lung parenchyma. These results highlight the potential importance of lung epithelial cells and α7-nAChRs in cigarette smoke- and HIV-related obstructive lung diseases.

Effect of different doses of nicotine on the metabolism and locomotor activity of rats

Prof Valentina Bashkatova1, PhD Galina Nazarova1, Elena Alexeeva1, Prof Sergey Sudakov1
1PK, Anokhin Research Institute of Normal Physiology, Moscow, Russian Federation

The aim of our work is to study the effects of hourly monitoring of different doses of nicotine on locomotor activity and metabolism of rats during 24 hours. Male Wistar rats were injected subcutaneously with doses of nicotine solution: 0.3 mg/kg (group 1), 1 mg/kg (group 2), and 2 mg/kg (group 3). Rats of control group received an equivalent amount of saline subcutaneously. Immediately thereafter the animals were placed into the standard cages of «Phenomaster system». The metabolic rate, locomotor activity, water and food consumption were registered at every cage every 60 minutes for 24 hours. Our results demonstrate that eating and drinking behavior of rats treated with nicotine at dose 0.3 mg/kg was suppressed significantly. The administration of nicotine at doses of 1.0 mg/kg and 2 mg/kg produced short increase of locomotion in rats. The metabolic rate was suppressed significantly at doses of 1.0 mg/kg and 2 mg/kg but increased significantly at dose 0.3 mg/kg.
Interplay among HIV, HCV and alcohol: Role of HIV-1 Nef protein

Dr Johnny He*

1University of North Texas Health Science Center, Fort Worth, United States, 2 Federal University of Sao Paulo, Brazil, 3 Harvard Medical School, Boston, USA, 4 University of Kline Institute, Orangeburg, USA, 7 New Mexico Healthcare System, Albuquerque, USA,

Infection with HIV, HCV or both HIV and HCV will continue to be a significant public health issue. Alcohol consumption is an important comorbidity factor. HIV-1 accelerates liver diseases among those with HIV/HCV co-infection. But the underlying mechanisms are not fully understood. Studies have so far mostly been focused on immune suppression and altered polarization of type 1 and 2 T helper cell responses induced by HIV-1 and alcohol consumption. We have recently found that intercellular HIV-1 Nef transfer occurs between Nef-expressing or HIV-infected cells and HIV-refractory hepatocytes both in vitro and in vivo. In addition, we have demonstrated that cell-cell contact is the primary route for the intercellular Nef transfer. Furthermore, we have shown that alcohol exposure promotes the intercellular Nef transfer. More importantly, we have demonstrated that intercellular HIV-1 Nef transfer leads to enhanced HCV replication and increased reactive oxygen species production in hepatocytes, which is also potentiated by alcohol exposure. Our findings support the hypothesis that intercellular HIV-1 Nef transfer contributes to accelerated liver diseases in HIV-1/HCV co-infected individuals through enhancement of HCV replication and adverse changes in hepatocyte biology, particularly in the context of alcohol exposure.

Endocannabinoid system (ECS) alterations in an animal model of autism spectrum disorders (ASDS)

Prof Emmanuel Onaivi1, Dr Joao Escosteguy-Neto2, Professor Jair Guilherme Santos-Junior3, Ms Susan Gro4, Mr Norman Schanz5, Mr Eugene Dennis6, Ms Larissa Pamen6, Professor Claire Leonard6, Mr Kevin Penkoski7, Ms Monika Chung7, Ms Ndeah Terry7, Ms Jasmine Wood7, Ms Sneha Tammareddy7, Dr Zhicheng Lin1, Dr Joseph Morgan1, Dr Frank Hall8, Dr Georgianna Gould5, Dr Balapal Basavarajappa3, Dr George Uhl4, Dr Syd Ali9, Dr Hiroki Ishiguro10, Dr Qing-Rong Liu11

1William Paterson University, Wayne, United States, 2 Federal University of Sao Paulo, Sao Paulo, Brazil, 3Harvard Medical School, Boston, USA, 4University of Toledo, Toledo, USA, 5University of Texas Health Sci. Ctr., San Antonio, USA, 6 Nathan Kline Institute, Orangeburg, USA, 7 New Mexico Health Care System, Albuquerque, USA, 8 Natl. Ctr. Toxicology Research/FDA, Jefferson, USA, 9University of Yamanashi, Chuo-Yamanashi, Japan

Endocannabinoid system is involved in neuropsychiatric disorders including ASDS. ECS are involved in embryo neurodevelopment and a regulator of immune system via CB2Rs. BTBR T+tf/j mice exhibit autism-like behavioral phenotypes were used to determine brain expression of CB2Rs throughout neurodevelopment in BTBR T+tf/j and C57BL/6 mice and to measure levels of anandamide and 2-arachidonyl glycerol in brain regions by LC-MS using isotopic dilution method and to evaluate the neurochemical and molecular basis and the impact of SERT, DAT, MOR, and DAT-CI gene knock out on CBR-induced behaviors. CB2Rs are present during neurodevelopment and its enhanced brain expression in the adult BTBR mice might be associated with the differential cannabinoid-induced behavioral effects. [3H] CP55, 940 binding to CB2R did not differ between BTBR and C57BL/6 mice. CB2R-JWH133 and ACEA- CB1R agonist reduced motor activity in both mice. ACEA induced aversive behavior while CB1R antagonist-AM251 reduced aversive behavior in both mice.

In ko mice, the effects of JWH133 was genotype and gender dependent in the motor function and emotionality tests. AEA but not 2-AG levels in the brain regions were reduced in the brain areas analyzed. Dysfunction in the ECS may in part contribute to ASDs.

The insular neural system controls decision-making in healthy and methamphetamine-treated rats

Prof Kiyofumi Yamada1, Dr Hiroiuki Mizoguchi2

1Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan, 2Research Center for Next-Generation Drug Development, Research Institute of Environmental Medicine, Nagoya University, Nagoya, Japan

Decision-making is a key activity of everyday life. Consequently, disturbances in the ability to make appropriate decisions or anticipate their possible consequences can result in massive social, medical, and financial problems. Patients suffering from neuropsychiatric disorders such as substance-related and addictive disorders exhibit altered decision-making patterns, which may be associated with their behavioral abnormalities. However, the neuronal mechanisms underlying such impairments are largely unknown. Using a newly developed gambling test for rodents, we demonstrated that METH-treated rats chose a high-risk/high-reward option more frequently, and assigned higher value to high returns, than control rats, suggestive of changes in decision-making choice strategy. Immunohistochemical analysis following the gambling test revealed aberrant activation of the insular cortex (INS) and nucleus accumbens in METH-treated animals. Pharmacological studies, together with in vivo microdialysis, showed that the insular neural system played a crucial role in decision-making. Moreover, manipulation of INS activity using DREADD technology resulted in alterations to decision-making. Our findings suggest that the INS is a critical region involved in decision-making, and that insular neural dysfunction results in risk-taking behaviors associated with altered decision-making in METH addicts.
Gambling as an addiction

Prof Marc Potenza

Pathological gambling was introduced as a diagnostic entity into the Diagnostic and Statistical Manual (DSM) in 1980 and was classified as an impulse-control disorder. During the 1990s and 2000s, competing conceptualizations of pathological gambling as an obsessive-compulsive-spectrum disorder or as a non-substance or behavioral addiction were proposed and considered. Based on existing data from multiple domains (e.g., epidemiological, phenomenological, clinical, genetic, neurobiological, therapeutic), the DSM-5 Workgroups reclassified pathological gambling (now gambling disorder) together with substance-use disorders in a “Substance-related and Addictive Disorders” category. In this presentation, data relating to this reclassification will be presented and implications for ICD-11 will be considered.

How do we describe and define substance use and other addictive disorders?

Prof John B Saunders

Disciplines of Psychiatry and Addiction Medicine, Sydney Medical School, University of Sydney, and Faculty of Medicine and Biomedical Sciences, University of Queensland, Australia

Approaches to understanding, defining and classifying substance use disorders have drawn on many disciplines, and we have a good understanding of the epidemiological and socio-cultural influences, the aetiology and mechanisms of disorders of substance use, the pathogenesis of dependence and the multiple physical and psychiatric complications of psychoactive substance use. This wealth of information has caused difficulties in formulating coherent diagnostic entities to which health professionals, scientists and epidemiologists can agree upon. Because of the parallel developments in knowledge and the diverse disciplines which have contributed to this synthesis of unifying concepts and diagnostic entities has been challenging. This presentation will summarise the current status of work on the development of substance use disorders diagnosis and classification within the draft version of the latest revision of the International Classification of Diseases, namely ICD 11. The substance use diagnoses which are being subjected to field testing for coherence, reliability and utility, comprise the core syndromes of (i) substance dependence and (ii) harmful substance use, and a range of substance-induced disorders including (i) substance intoxication, (ii) substance withdrawal, and (iii) several substance-induced mental disorders. A new entity of single-episode harmful use is being tested. In addition, hazardous substance use which is a pattern of substance use that confers a risk of future harm is being evaluated. The current clinical descriptions and diagnostic guidelines for each of these conditions in the draft ICD 11 will be presented.

ICD 11: how are substance disorders understood in different cultures?

A/Prof Sawitri Assanangkornchai

The attitudes and understanding of the causes and definitions of substance use and its disorders of both clinicians and lay people in different societies can affect the criteria used for clinical diagnosis of substance use disorders. Cultural and linguistic background, socio-demographic contexts and type of drug use may also determine the way people manifest their symptoms and signs of substance use disorders. In translating international diagnostic criteria for substance use disorders or a psychiatric research instrument to be used in a non-English using country to achieve both cultural and linguistic equivalency of certain concepts, interactive procedures are needed. In this presentation, methods used in translation and adaptation of the Composite International Diagnostic Interview (CIDI) V3.0 to be used in the National Mental Health Survey in Thailand in 2013 will be described, including, translations with back translation of some items, expert review, key informant review and cognitive interviews. Results of the Survey on the alcohol module will be presented as an example of how Thai people perceived their symptoms and signs of alcohol use disorders. It was found that 62% of the sample drank alcohol in their lifetime. The prevalence of lifetime ICD-10 harmful alcohol use and dependence was 13.9% and 4.1%. Among harmful use criteria, drinking in a situation where one could get hurt had the highest endorsement rates in both harmful (60.5%) and dependent (66%) drinkers whereas drinking resulted in a problem with police was reported by only 8-10% of those drinkers. Regarding alcohol dependence criteria, not able to stop or cut down and drinking when planned not to or more than intended were most frequently accepted by dependent drinkers (66-68%).

Despite being diagnosed as alcohol dependent by the CIDI, the scores of severity of interference of alcohol on daily activities were very low (mean 2.7 – 3.2 of the 0-10 scale). Lessons learned from the translation process and interviews in this Survey may inform clinicians and researchers when translating and adapting the ICD-11 substance use disorders module into different cultures and languages.

What do clinicians need from a diagnostic system?

Dr Ben Teoh

Current diagnostic systems in mental health are based on operational criteria, with most conditions lacking solid pathological evidence or clear biological markers. Although this may improve reliability, the validity of such diagnosis remains unclear. Clinicians would welcome a diagnostic system that is objective and determined by physiological evidence. This would lead to specific and effective treatment.

Mental conditions, including addiction, are complex – it may not be possible to fully adopt a medical model in the evaluation and diagnosis of these conditions. There are limitation and problems with the current diagnostic system in clinical practice.

In some conditions, it may be more useful to treat symptoms related to brain circuits than the broad and heterogeneous diagnoses that are currently used. Research may offer us a better diagnostic system based on neurobiology. The Research Diagnostic Criteria (NIMHCR) looks promising.

Dysregulation of glucocorticoid systems in alcohol dependence

Leandro F Vendruscolo,
National Institute on Drug Abuse, USA

Repeated episodes of alcohol intoxication and withdrawal activate the hypothalamic-pituitary-adrenal (HPA) axis to release glucocorticoids, leading to excessive activation of glucocorticoid receptors (GRs) in the brain. Here, we tested the hypothesis that excessive activation of GR in extrahypothalamic brain regions is functionally linked to compulsive alcohol drinking. We made rats dependent on alcohol via chronic, intermittent alcohol vapor exposure, a model that generates reliable signs of alcohol dependence that resemble the human condition. Molecular and pharmacological studies were performed during acute withdrawal (6-8 h after removal from alcohol vapor), when somatic and motivational signs of withdrawal are evident. We found that GR signaling, as indexed by GR phosphorylation, was increased in the central amygdala (CeA), a stress-related brain region implicated in drug taking and seeking in alcohol-dependent rats. Blockade of GR signaling with mifepristone, injected systemically, intracerebroventricularly, or intra-CeA, specifically reduced compulsive-like alcohol drinking in dependent rats. Together, these studies support a key role for GR signaling in driving excessive alcohol drinking in alcohol dependence. GR antagonism via mifepristone may represent a novel therapeutic strategy for alcoholism.

Translational research on mifepristone: prospects for the treatment of alcohol dependence

Dr Barbara Mason

1 The Scripps Research Institute, The Jolla, United States

Chronic heavy alcohol use and withdrawal is associated with abnormal HPA axis activity and glucocorticoid receptor (GR) feedback and sensitization of CRF in the amygdala. We hypothesized that administering mifepristone (a GR antagonist) to recently-abstinent alcoholics may normalize HPA axis dysregulation and thereby protect against relapse during protracted withdrawal. Fifty-six non-treatment-seeking volunteers (43 males, 13 females, 21-65 years of age) with current alcohol dependence were randomized to 1-week of treatment with mifepristone 600mg/day or matched placebo. Alcohol abstinence was verified during the last 3 days of the 7-day dosing period, and alcohol cue reactivity manipulations, followed by craving ratings, were conducted at the conclusion of the dosing interval. Mifepristone was associated with significantly greater reductions than placebo in alcohol-cued craving, alcohol consumption and liver enzyme activity. There was no evidence of abuse potential, and no serious or unexpected adverse events were observed. These results suggest that mifepristone may have therapeutic potential in alcohol dependence and a clinical trial is underway to replicate and extend these findings.
Susceptibility to relapse is linked to multiple factors including craving, stress, anxiety, and impaired impulse control. Approaches to treatment drug discovery toward concurrent protection from these relapse “triggers” are likely to offer significant therapeutic benefits as well as improved compliance. Agents with such a profile of actions are emerging in preclinical research. One among these is cannabidiol (CBD), the main non-psychoactive, non-addictive component of the cannabis sativa plant. CBD significantly reduced both stress and cue-induced ethanol seeking in animal models of relapse during a 7-day treatment period, without producing tolerance, sedative effects, or interfering with normal motivated behavior. Remarkably, ethanol seeking remained attenuated as late as 5 months after treatment termination. CBD also reduced experimental anxiety both during and after and CBD treatment. Finally CBD reversed high impulsivity associated with an ethanol intoxication history. The findings reveal two unique “dimensions” of CBD effects: (1) beneficial actions relevant for multiple vulnerability states associated with relapse risk, and (2) long-lasting effects with only brief treatment. Although CBD’s mechanisms of actions remain unclear at present, the findings suggest that CBD exerts neuroregulatory actions that restore normal function to brain regulating reward, incentive motivation, impulsivity, stress and anxiety.

Increased human dopamine transporter gene activity spurs alcohol consumption

Dr Z. Carl Lin1, Assistant Professor Scott Hall1, Professor Xiaowu Chen1, Associate Professor Yanhong Zhou1, Associate Professor Nian Xiong2, Associate Professor Richard Bell2, Professor Tao Wang3, Professor Jürgen Rehm3

1McLean Hospital, Belmont, United States, 2Department of Pharmacology, College of Pharmacy and Pharmaceutical Sciences, The University of Toledo, Toledo, USA, 3Department of Neurology, Affiliated Hospital of Hainan Medical College, Haikou, China. *Molecular Genetics Laboratory, Cancer Research Institute, Xiangya School of Medicine, Central South University, Changsha, China, 2Department of Neurology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, 3Department of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, USA, 4Social and Epidemiological Research Department, Centre for Addiction and Mental Health, Toronto, Canada

We aim to identify dopaminergic genetic factors for alcohol abuse. Re-analysis of the Collaborative Studies on Genetics of Alcoholism (COGA) GWAS dataset after re-sequencing the human dopamine transporter gene (hDAT or SLC6A3) promoter region for COGA subjects and imputation with the sequences suggested that two promoter polymorphisms interact with each other in alcoholism. One of the polymorphisms, termed DNP, is a common variant and has two alleles, A and B, which differentially regulate promoter activity. A study of the association between B frequency and alcohol-related behaviors reveals that B appears to inhibit alcohol consumption and promote abstinence among populations of ten different countries. Gene expression analysis of postmortem human dopamine neurons isolated from healthy subjects suggests that B is associated with reduced hDAT activity. Preclinically, in the P (ethanol-prefering) vs NP (nonpreferring) rat model, DAT expression is significantly higher in P than in NP, in DAT knockout mice, the heterozygote displays attenuated escalation of ethanol consumption. Together, these clinical and preclinical findings consistently suggest that high hDAT activity confers risk for alcohol abuse.


Prof Emmanuel Onavi1, Dr George Koob2

1William Paterson University, Wayne, United States, 2Committee on the Neurobiology of Addictive Disorders, La Jolla, USA

Drug addiction is not a moral failure but a complex neuroadaptive process and chronic relapsing brain disease characterized by compulsive drug use despite adverse consequences to the individual and society. Addiction is characterized by entry at multiple stages: binge-intoxication, withdrawal-negative affect and preoccupation-anticipation (“craving”) that overlap and provides a heuristic basis for vulnerability and resilience. Developmental, genetic, epigenetic and environmental risk factors have been linked to molecular neurobiological mechanisms responsible for the three stages of the addiction cycle. Understanding the triggers for compulsive drug seeking and taking and relapse after abstinence may provide the targets for resistance in substance use disorders and new therapeutic targets. In this presentation we update and highlight new development and strategies including optogenetic, epigenetic, neuroimaging and pharmacotherapeutic strategies in substance abuse therapy. Some of these concepts like immunotherapeutics, nanotherapeutics, or gene-editing technologies (CRISPR or RNAi) still require more development and studies for efficacy and safety to treat drug addiction. This may open new therapeutic approaches in the era of pharmacogenomics to individualize drug addiction treatment.

Development of medicinal cannabinoids

Dr Iain McGregor

University of Sydney, Australia

Abstract not supplied

Research on medicinal cannabis: practical steps and political influences

Dr Alex Wodak AM

Medical use of cannabis and related scientific research has been obstructed for decades. The global prohibition of cannabis was first agreed at an international meeting in 1925. The later international drug treaties prohibited the use of specified psychoactive drugs, including cannabis, while specifying that medical or scientific use of prohibited drugs would not be interfered with. Neither aim was met. After many decades of unsuccessfully attempting to enforce global drug prohibition, an estimated 147 million people around the world now use cannabis recreationally and drug prohibition is generally in retreat. The medical and scientific use of cannabis is now advancing. The identification of THC as the major psychoactive component of cannabis in 1964 required research that was then illegal. Cannabis is still classified in the USA under the most stringent schedule, ahead of cocaine, in a category reserved for drugs with no medical use and the greatest risk of abuse. Cannabis research has been obstructed in the US and elsewhere with funding, approval and access to suitable agents made as difficult as possible. But it is clear from research that cannabis is a very useful drug. Damage to science and medicine has been one of the costs of drug prohibition.

Sevoflurane-induced neuronal injury in neonatal nonhuman primates: protection by acetyl-L-carnitine

Dr Merle Paule1, GD Newport1, R Callcott1, JM Thompson1, W Silsker Jr1, C Wang2, MS Bertridge2, X Zhang2, SM Apana2, S Liu2

1National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, United States, 23D Imaging, LLC, Little Rock, AR 72113 and University of Arkansas for Medical Sciences, Little Rock, United States

Sevoflurane is one of the most widely used general anesthetics in the pediatric setting and, in animals, it has been shown that exposure during the brain growth spurt can cause neuronal cell death in the brain. In this study, in vivo microPET/ICT imaging using 18F-labeled fluoroethoxybenzyl-N-(4-phenoxypyridin-3-y1) acetamide (FEPBA), a biomarker of activated microglia/neuroinflammation in brain, was utilized as a surrogate marker of neuronal injury to monitor the location and time course of sevoflurane-
induced neurotoxicity in a neonatal nonhuman primate model. On postnatal day (PND) 5 or 6, rhesus monkeys (4-6/group) were exposed to 2.5% sevoflurane mixed with oxygen or acetyl-L-carnitine (ALC) (100mg/kg given i.p.) plus this mixture for 8 hours; control monkeys with and without ALC were exposed to room air only. One day later, [18F]-FEPPA (56 MBq) was injected into the lateral saphenous vein and microPET/CT images were obtained over the next 2 hours. MicroPET/CT scans were repeated for each monkey 1 and 3 weeks and 6 months after the anesthetic exposure.

On the day after anesthetic exposure, the uptake of [18F]-FEPPA was significantly increased in the frontal and temporal lobes and one week after exposure the uptake of [18F]-FEPPA in the frontal lobe of treated animals was also greater than that in controls. No significant differences were detected in radioactivity uptake in the brains of treated monkeys three weeks or six months after sevoflurane exposure, although at 3 weeks, levels remained elevated in some brain areas. Co-administration of ALC effectively blocked the increase in FEPPA uptake in both the temporal and frontal lobes. These findings suggest that early exposure to sevoflurane triggers neurotoxicity in the nonhuman primate brain and that anesthetic-induced brain damage in different brain regions can be monitored using microPET imaging. In addition, ALC appears to be a potential protective agent against at least some of the adverse effects associated with such exposures. Supported by NCTR/FDA (E-7285) and CDER/FDA.

Broadening the dimensions of the methamphetamine preclinical studies; Links with Parkinson's disease

Dr Glen Hansen1, Lisa McFadden1, Paula Vieira-Brock, Annette Fleckenstein1, Karen Curtin2
1School of Dentistry, University of Utah; School of Dentistry, University of Utah, UT, United States, 2School of Medicine, University of Utah, UT, United States, 3College of Pharmacy, University of Utah, UT, United States

Preclinical and clinical studies suggest that abuse/dependence of methamphetamine (METH) causes damage to the same ngoristrial dopamine (DA) neurons lost in Parkinson’s disease (PD); suggesting that METH dependence increases the risk of PD later on in life. This was confirmed in 2012 by Callaghan et al. (Drug Alcohol Depend. 120 (2012) 35-40) showing a ~2-fold increase in the risk of PD in patients with a history of METH/AMPH dependence. We extended these findings using databases of records from the Utah Population Data Base (UPDB) and Intermountain Healthcare (IHC) (1995-2012) years to determine linkage between METH/AMPH dependence and PD. Our METH/AMPH cohorts had no other significant drug use except tobacco and were separated into male and female groups. We observed that persons with a history of METH/AMPH dependence were 3.7 times more likely to develop PD, with females having a hazard ratio of ~6 and males a hazard ratio of ~2.

Because individuals with a history of Attention Deficit Hyperactivity Disorder (ADHD) often self-administer amphetamines to help relieve ADHD symptoms, we also used our UPDB and IHC databases to assess linkage between ADHD and PD expression. We observed that persons diagnosed with ADHD were 2.8 times more likely to develop PD later in their lives and had a 10.0-fold greater expression of PD if they were also prescribed methylphenidate. Neither of these effects were gender-selective; however, the linkage was particularly profound in persons <60 years of age.

Sevoflurane-induced neuronal damage and its potential biomarkers

Dr Cheng Wang1
1National Center for Toxicological Research, Jefferson, United States

Sevoflurane is a volatile anesthetic that has been widely used in general anesthesia, yet its safety in pediatric use is of public concern. The present study sought to evaluate whether prolonged exposure of infant monkeys to a clinically-relevant concentration of sevoflurane is associated with any adverse effects on the developing brain. Infant monkeys were exposed to 2.5% sevoflurane for 9 hours, and frontal cortical tissues were collected for DNA microarray, lipidomics, Luminox protein and histological assays. DNA microarray analysis showed that sevoflurane exposure resulted in 576 differentially expressed genes (DEGs) in the monkey brain. Notably, a number of DEGs were closely related to lipid metabolism. Lipidomic analysis demonstrated that critical lipid components, e.g., phosphatidylethanolamine (PE), phosphatidylserine (PS) and phosphatidylycerol (PG) were significantly down-regulated. Luminox analysis indicated abnormal levels of cytokines in sevoflurane-exposed brains. Consistently, Fluoro-Jade C staining revealed more degenerating neurons after sevoflurane exposure. These data demonstrate that a clinically-relevant exposure to sevoflurane is capable of inducing profound changes in gene expression, cytokine levels, lipid metabolism, and subsequently, neuronal damage. And specific lipid changes could be sensitive biomarkers for the early detection of anesthetic-induced neuronal damage.

Cocaine mediates microglial activation via downregulation of microRNA 124

Prof Shilpa Buch1, Dr Minglei Guo2, Dr Palsamy Periyasamy3, Mr Ke Liao4, Ms Fang Niu5
1University of Nebraska Medical Center; Omaha, United States

Cocaine, a widely abused psychoactive drug, is known to increase synaptic dopamine levels leading to elevated neural activities in the CNS. Recently, emerging evidence indicates that cocaine can also activate microglia leading to increased neuroinflammation. Detailed mechanisms by which cocaine mediates microglial activation however, remain elusive. Recently, miRNA-mediated regulation of disease pathogenesis is emerging as an evolving area of research. MicroRNA-124 is a brain-enriched miRNAs that is critical for maintaining microglial quiescence. The goal of the current study was to examine how cocaine regulates miR-124, leading to microglial activation. Our findings demonstrated that cocaine downregulated miR-124 levels in microglial cells. In parallel, cocaine increased the levels of DNA methyltransferases (DNMTs), enzymes critical for enhancing the methylation status of miR-124 promoter Kruppel-like factor 4 (KLF4), a transcriptional factor downstream of toll-like receptor 4- (TLR4-) mediated pathway, was identified as a novel direct target for miR-124. Overexpression of miR-124 in microglia ameliorated cocaine-mediated microglial activation evidenced by increased M2 and a concomitant decreased M1 phenotype. Our findings were validated in brain homogenates and isolated microglia from cocaine-treated mice, that demonstrated decreased levels of miR-124 levels compared to saline treated controls. MIR-124 can thus be harnessed as a potential target to dampen neuroinflammation.

Morphine disrupts gut homeostasis and induces distinct gut microbiome and metabolome signatures partially through the TLR2 pathway

Prof Sabita Roy1, Santanu Banerjee1, Jingjing Meng1, Li Zhang2, Timothy Johnson1, Chi Chen1
1Department of Surgery, University of Minnesota, Twin Cities, United States, 2College of Veterinary Medicine, University of Minnesota, Twin Cities, United States, 3Department of Food Science and Nutrition, University of Minnesota, Twin Cities, United States, 4Department of Pharmacology, University of Minnesota, Twin Cities, United States

Opioids are the gold standard for pain management but we recently show that chronic use results in significant disruption in gut barrier function and increased systemic translocation of gut commensal bacteria. The primary objective of this study, using a murine model of morphine treatment, was to investigate the effects of morphine treatment on gut microbiome, metabolome, and their consequences on gut barrier function. On characterization of the phylogenetic profiles of gut microbes, we show that morphine treatment resulted in a significant and distinct change in the gut microbial profile when compared to placebo animals with an increase in pathogenic bacteria. LC-MS based metabolomics profiling analysis, show a distinct shift in the metabolomics profile in the morphine treated animals when compared to placebo animals particularly in fatty acid and bile acid metabolism, implicating that changes in the microbial community has functional consequences. In a longitudinal study, we found naltrexone, an opioid receptor antagonist, reversed the effect of morphine on bile acid metabolism, indicating morphine induced changes are opioid receptor dependent. Furthermore, we confirmed that morphine induced changes were attenuated in TLR2KO day 3 post morphine treatment compared to wild type mouse, indicating opioid-receptor dependent changes may be dependent TLR2 activation.

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Wastewater analysis as a tool in monitoring drug use
Jacobs P Gerber1, Prof Jason White, Ben J Tschkarke*
1School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia

Wastewater analysis is an objective method for estimating community consumption of drugs. Depending on the metabolic and urinary excretion profile of the substance of interest, the concentration of the parent drug or a metabolite is determined (typically using LC/MS/MS) in samples of municipal sewer water. With additional data on flow rates, urinary excretion profiles and population levels, estimates can then be made of rates of community drug use. Our group has had an ongoing monitoring program for stimulants (including novel psychoactive drugs), opioids, cannabis and tobacco over 4 years. A range of long and short-term trends in drug use have emerged from the data generated by this monitoring program. These include a pronounced increase in methamphetamine use, fluctuating levels of use of both MDMA and the novel psychoactive stimulants, increases in use of prescription opioids and seasonal variation in cannabis use. A number of these trends have not been evident in the data collected from surveys, indicating the value of wastewater analysis as a complement to current epidemiological approaches. This information is currently being utilised by health and police, influencing policy and allocation of resources, and as a method to evaluate interventions.

The case for incorporating drug checking into Australia’s drug trend monitoring systems
A/Prof Nadine Ezard1,2, Dr Monica Barrett1-4, Dr Robin Butterfield1
1St Vincent’s Hospital, Darlinghurst, Australia, 2UNSW, Sydney, Australia, 3Centre for Population Health/Burnet Institute, Melbourne, Australia, 4Drug Policy Monitoring Program, National Alcohol and Drug Research Centre, UNSW, Kensington, Australia

New psychoactive substances are emerging rapidly into the illicit drug space and now outnumber those under international controls. Some of these substances are hazardous to human health; increasing numbers of clusters of presentations to emergency departments reported in the literature. In an illicit and uncontrolled market place with limited pharmacological data it is difficult to protect the health of the population. An additional data source, used in several European countries, is drug checking. This involves the anonymous donation of drugs to health workers for laboratory testing. Drug checking can be conducted on-site where substances are being consumed (such as at dance parties and festivals) or off-site (such as at health facilities or drug treatment clinics, or of anonymous samples left in specially marked bins). In addition, face-to-face checking can be a moment to deliver brief interventions for behaviour change. Using examples from Vienna, the Netherlands, and the UK, this paper argues that drug checking is a health initiative which can be useful to reduce harm from psychoactive substance use by:
1. monitoring trends, detecting new substances, identifying emerging hazards
2. changing behaviour and promoting help seeking, and
3. improving the knowledge base for clinical management of acute and chronic presentations.

“Don’t run with the blue scissors” - case series of 11 casualties of an unknown substance in an inner Sydney hospital
A/Prof Nadine Ezard1-4, Dr Monica Barrett1-4,5
1St Vincent’s Hospital, Darlinghurst, Australia, 2UNSW, Sydney, Australia, 3Centre for Population Health/Burnet Institute, Melbourne, Australia, 4Drug Policy Monitoring Program, National Alcohol and Drug Research Centre, UNSW, Kensington, Australia, 5National Drug Research Institute/Curtin, Perth, Australia

11 patients presented to St Vincent’s Hospital in Sydney from the same dance party being held over a long weekend in 2015, and all claimed to have used blue tablets with scissors embossed on them. The clinical toxidrome was confusing and had hallmarks of sympathomimetic poisoning. All required admission and four required invasive monitoring and management in the ICU. Most had uncomplicated recoveries but two had prolonged admissions developing acute renal failure secondary to rhabdomyolysis. All patients recovered. All patients posed serious risk to themselves, one had assaulted police and another was found naked in a park and required immediate stabilisation in hospital. Resources were stretched by the simultaneous presentation to hospital by all 11 patients, requiring high level nursing care alongside IV sedation. No psychoactive substance was identified in blood and no substances were tested: a new (previously unidentified) psychoactive substance was suspected. As new psychoactive substances are rapidly emerging, healthcare settings need to be able to detect emerging health threats in a timely fashion. As yet no formal surveillance programme has been established in Australia, where even forensic reports from police authorities who have made drug seizures are difficult to access.

Improving the monitoring of New Psychoactive Substances (NPS) in Australia
Dr Monica Barratt1,2, Dr Robin Butterfield, A/Prof Nadine Ezard1-4
1Drug Policy Modelling Program, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia, 2National Drug Research Institute, Curtin University, Perth, Australia, 3Centre for Population Health, Burnet Institute, Melbourne, Australia, 4St Vincent’s Hospital, Sydney, Australia, 5Faculty of Medicine, University of New South Wales, Sydney, Australia

The past decade has seen the emergence of an increasing number of new psychoactive substances (NPS) that have similar effects to established illicit drugs such as cannabis, amphetamines, cocaine, MDMA (‘ecstasy’) and LSD. The monitoring of NPS use in Australia relies on the following data sources: the most recent national household survey, annual surveying of regular ecstasy users, regular monitoring of website NPS sales, police and customs seizures, waste water analysis, sales figures from adult store industry representatives, and one-off surveys and case series. This paper will outline what we currently know from each source and their limitations, and how they apply to three different NPS use patterns: deliberate use of specific NPS, deliberate use of NPS blends, and unintentional NPS use. Currently, we lack an understanding of the level of congruency between what people think they are taking and what they are actually taking. This key information can be ascertained through implementing drug checking or testing services, where people who use drugs submit samples for testing to determine pharmacological content. The information from such services would ideally be integrating into existing monitoring systems and acted upon swiftly where clusters of adverse events are detected.
Behavioral and neurochemical effects of adolescent treatment with nicotine, harmine, or norharmane in male Sprague-Dawley rats

Dr Syed Ali1, Dr Amy Goowin1, Dr Susan Lantz-McPeak1, Ms Bonnie Robinson1, Mr C Delbert Law1, Dr Sherry Ferguson1

1Division of Neurotoxicology, NCTR, Jefferson, United States

The present study determined the long-term effects of adolescent exposure to nicotine (NIC), harmine (HAR), or norharmane (NOR) on locomotor activity, learning and memory, anxiety-like behavior and monoamine concentrations in the striatum and nucleus accumbens of male Sprague-Dawley rats. On postnatal day (PND) 27 and continuing through PND 55, subjects received twice daily IP injections of 1 mg/kg saline (CON), 0.5 mg NIC/kg, 0.5 mg HAR/kg, or 0.5 mg NOR/kg. BW, food, and water were measured daily. Locomotor activity was assessed on PND 40/41. PND 55, and PND 8/82. Anxiety-like behavior, motor coordination, and spatial learning and memory were assessed after drug exposure (PND 80-91). On PND 97, subjects were euthanized and the striatum and nucleus accumbens were dissected and frozen for analysis. NIC treatment significantly decreased food intake. HAR and NOR treatment caused significant open field hypoactivity. Other behaviors and concentrations of monoamines/metabolites in the striatum and nucleus accumbens were unaltered by any drug treatment. These results indicate a long-lasting effect on activity levels from adolescent HAR or NOR treatment; however, there were few long-lasting NIC effects. Given the paucity of data describing effects of HAR or NOR exposure, these data should encourage additional studies of these tobacco constituents.

Ketamine and acetyl L-carnitine alter dopamine system in zebrafish larvae

Dr Syed Ali1, Mrs Bonnie Robinson1, Dr Merle Paule1, Ms Melanie Dumas1, Dr Yotjohna Kanungo1

1Division of Neurotoxicology, National Center for Toxicological Research, Jefferson, AR, USA, Jefferson, United States

Ketamine, a noncompetitive N-methyl-D-aspartic acid (NMDA) receptor antagonist is commonly used as a pediatric anesthetic. Studies show that ketamine is neurotoxic in developing mammals and zebrafish. Acetyl L-carnitine (ALCAR) prevents ketamine toxicity in mammals and zebrafish embryos. In mammals, ketamine is known to modulate the dopaminergic system. Here, we measured the levels of dopamine (DA) and its metabolites, 3, 4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA), in the larvae exposed to ketamine in the presence and absence of ALCAR using HPLC/EC. Ketamine, at 0.1–0.3 mM, did not alter the DA, DOPAC and HVA levels and hydroxylation (TH) mRNA expression in 3-day-old larvae. However, 2 mM ketamine significantly reduced DA and HVA levels indicating that DA synthesis was adversely affected. In presence or absence of ketamine, ALCAR significantly reduced DA, but increased the DOPAC level compared to the control and increased HVA levels compared to both control and ketamine-treated larvae. ALCAR significantly reduced TH mRNA expression in the presence or absence of ketamine. These results indicate that ketamine dose-dependently alters DA synthesis but not DA metabolism, whereas ALCAR accelerates DA metabolism. These distinct effects of ketamine and ALCAR on DA metabolism may correlate with ALCAR’s protective effects on ketamine-induced neurotoxicity.

Methamphetamine induces neurotoxicity in blood-brain-barrier endothelial cells: protective role of prolactin

Dr C Gonzalez1, Dr R Rosas-Hernandez1, Dr E Cuevas1, Ms S Lantz-McPeak1, Dr M Paule1, Dr Q Gu1, Dr S Imam1, Dr Syed Ali1

1Division of Neurotoxicology, NCTR, Jefferson, AR, USA, Jefferson, United States

Methamphetamine (METH) is a highly addictive drug of abuse which exerts its toxic effects by affecting the dopaminergic system. Recent reports suggest that METH disrupts the blood-brain barrier (BBB). There are reports suggest that hormone prolactin (PRL) exerts protective vascular effects associated with the stimulation of endothelial cell proliferation. Therefore, the aim of this study was to evaluate the protective effect of PRL on METH-induced neurotoxicity in primary bovine brain microvessel endothelial cells (bBMVEC), as in vitro model of BBB. Confluent bBMVEC monolayers were treated with METH (0.1–2.5 mM). METH increased permeability associated with a transendothelial electrical resistance (TEER) decrease in a dose-dependent manner. These changes in permeability were related with a reduction in the expression of the tight junction proteins claudin-5 and occludin. The effects of METH on TEER were prevented by co-administration of 100 nM PRL. Co-treatment of METH (1 mM) with PRL (10 and 100 nM) also protected against METH-induced decrease in cellular proliferation and apoptosis, however, at higher concentration of METH (2.5 mM), PRL failed to protect against the METH-induced decrease in proliferation and apoptosis. These data suggest that PRL protects against METH-induced neurotoxicity in bBMVEC, through restoring the permeability of the BBB.

Methamphetamine, MDMA and the “bath salts” constituent MDPV induce cytotoxic effects in bovine brain microvessel endothelial cells

Dr Syed Ali1, Mr H Rosas-Hernandez1, Dr E Cuevas1, Ms S Lantz-McPeak1, Ms BL Robinson1, Dr SZ Imam1, Dr MG Paule1, Dr C Gonzalez1, Dr KC Rice1, Ms BG Gonzalez1, Dr WE Fantegrossi1

1Division of Neurotoxicology, NCTR, Jefferson, AR, USA, Jefferson, United States, Facultad de Ciencias Quimicas, UA de San Luis Potosi, SLP, Mexico, San Luis Potosi, Mexico, 1Drug Design and Synthesis Section, Chemical Biological Research Branch, NIDA/NIAAA, Bethesda, MD, USA, Bethesda, USA, “Department of Pharmacol & Toxicol, UAMS, Little Rock; AR, USA, Little Rock, US

The aim of this study was to compare the effects of METH, MDMA and MDPV on bovine brain microvessel endothelial cells (bBMVEC) as an in vitro model of the BBB. Confluent bBMVEC monolayers cultured 10–14 days were treated with METH, MDMA and MDPV (0.5–2.5 mM) for 24 hours. METH and MDMA increased LDH release at the highest concentration (2.5 mM), whereas MDPV was cytotoxic at all concentrations. MDMA decreased cellular proliferation at 2.5 mM, while similar effects of METH and MDPV observed at 1 mM. MDPV and MDMA produced cytotoxicity as measured by increases in nitric oxide and reactive oxygen species. Morphological analysis revealed METH induced vacuole formation at 1 mM in conjunction with disruption of the monolayer at 2.5 mM. MDMA induced disruption of the endothelial monolayer from 1 mM without vacuolization, whereas MDPV induced disruption of monolayer at doses > 500 mM. These data suggest that even though these synthetic psychostimulants have similar effects on monoaminergic systems, they each induce BBB toxicity by different mechanisms. With the emergence of ‘bath salts’ on the drug scene, it is important to understand the physiological implications of its abuse to aid clinical treatment.

The effect of MDMA or cocaine self-administration on behavioural responses to 5-HT1A and 5-HT1B agonists

Mr Dane Arosen1, Dr Susan Skench1

1Victoria University of Wellington, Wellington, New Zealand

MDMA initially has less efficacy as a reinforcer in the self-administration paradigm than other drugs of abuse. However, over time, some animals develop reliable self-administration behaviour. MDMA exposure has been shown to produce changes in serotonin receptor populations, and we think that some of these changes might underlie the development of reliable MDMA self-administration. This study assessed the effect of MDMA or cocaine self-administration on behavioural responses to the 5-HT1B/1A agonist, RU 24969, and the 5-HT1A agonist, 8-OH-DPAT. Male rats self-administered MDMA or cocaine in 2 hr daily sessions until total drug intake reached 350mg/kg. Either the adipsic response to RU 24969, or the hypervigilant response to 8-OH-DPAT was assessed 48 hours after the last self-administration session. We show no effect of self-administration on the 5-HT1B-mediated adipsic response to RU 24969, or on the 5-HT1A-mediated hyperactive response to 8-OH-DPAT. These findings suggest that 5-HT1A and 5-HT1B receptors are not critically altered by MDMA or cocaine self-administration.
Propentofylline hampers methamphetamine-induced striatal dopamine release: a microdialysis approach  
Mr Bobby Gough1, Dr Frederico Pereira1, Dr Carmen González2, Dr Syed Ali3, Dr Zbigniew Binienda1  
1National Center for Toxicological Research/FDA, Jefferson, United States,  
2Laboratório de Farmacologia e Terapêutica Experimental/BILIB, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal,  
3Autonomous University of San Luis Potosi, Faculty of Chemistry Sciences, San Luis Potosi, Mexico

Propentofylline (PPF), an atypical methylxanthine, modulates glial activity under pathological conditions. It has been shown that PPF can suppress the rewarding effects of METH and diminish METH-evoked astrogliotic activation. Here, the impact of intrastriatally perfused PPF (10-40 mM, 80 min) on the effect of METH (5 mg/kg, i.p.) on striatal dopamine (DA) release was investigated in rats using brain microdialysis. METH was injected after PPF was perfused for 60 min. The effect of PPF (10 mg/kg, i.p.) on METH (30 mg/kg, i.p.) induced dopaminergic striatal neurotoxicity was also evaluated in C57BL/6J adult mice. Concentrations of DA and its metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) were determined using high performance liquid chromatography with electrochemical detection (HPLC-ED). PPF alone induced a concentration-dependent increase in DA, DOPAC and HVA release starting 30 min after the onset of PPF perfusion. DA levels evoked by 40 mM PPF were similar to those induced by 5 mg/kg METH i.p. However, in PPF perfused rats they were decreased by 70% within 30 min after METH injections. Data suggest that PPF has dopaminergic modulator capacity. The increase in HVA caused by PPF that was further enhanced by METH may reflect the glial modulating properties of PPF.

Is Khat use disorder a valid diagnostic entity?  
A/Prof Raimondo Bruno1, Mr Samson Duresso1  
1University of Tasmania, Hobart, Australia

Background: Khat (Catha edulis) is a cathinone-based stimulant which is legal in several African countries. Little is known about the potential for khat to induce a substance use disorder syndrome. We aimed to validate a khat use disorder syndrome using DSM-5 criteria.

Method: 400 current khat consumers completed a survey comprising clinical symptoms (AUDADIS-IV and CIDI), and validated measures of psychological distress, and quality of life.

Results: Using DSM-5, 10.5% were categorised as experiencing mild, 8.8% moderate and 54.5% severe khat use disorder. Confirmatory factor analysis demonstrated good fit of symptom items to a single underlying construct, consistent with other use disorders. Dependent individuals demonstrated significantly greater frequency, quantity and duration of use, with younger consumption onset. They also demonstrated increased financial problems associated with use, greater problems with academic functioning, higher psychological distress and poorer quality of life. Treatment access was poor, with only 31% of dependent individuals reporting lifetime treatment access.

Conclusion: The construct of a khat use disorder syndrome appears valid and performs in a consistent manner to other substances. Despite its legality and cultural acceptability, it is clear that some experience substantial problems from khat use, and improving awareness and treatment access and uptake is crucial.

Repeated exposure to a serotonin1B/1A agonist facilitates acquisition of MDMA self-administration  
Miss Natasha Bukholt, Mr Dane Arosen, Professor Susan Schenk  
1Victoria University of Wellington, Wellington, New Zealand

There is remarkable variability in the latency to acquisition of MDMA self-administration. Some rats acquire self-administration relatively slowly, whereas others acquire self-administration more rapidly. The present study was designed to determine whether the latency to acquisition of MDMA self-administration could be altered by a manipulation that modified 5-HTVA and 5-HT1B receptor mechanisms. Rats were pretreated with the 5-HT1B/1A receptor agonist, RU 24969 (3.0 mg/kg, bid for 3 days), or the saline vehicle, and the latency to acquisition of MDMA self-administration was subsequently determined. As we have previously reported, about 50% of control rats met a criterion for acquisition of self-administration within 25 daily test sessions. The RU 24969 pretreatment decreased the latency to acquisition of MDMA self-administration and increased the percentage of rats that acquired self-administration. Pre-exposure to RU 24969 also decreased the behavioural response to 8-OH-DPAT and RU 24969, suggesting a potential mechanism for the facilitated reinforcing effect.

Does periconceptional ethanol exposure in the rat alter offspring adrenal steroidogenesis?  
Miss Danielle Burgess1, Dr James Cuffe1, Associate Professor Karen Mortiz2  
1University of Queensland, St. Lucia, Australia,  
2Ethanol (EtOH) consumption stimulates the hypothalamus-pituitary-adrenal (HPA) axis. When consumed throughout pregnancy, offspring develop impaired responses to stress, emotional regulation and altered HPA activity. While -50% of women consume alcohol during the periconceptional period (PC), most women cease alcohol consumption upon pregnancy recognition. It is therefore important to determine the impact of PCEtOH exposure on the offspring HPA.

Female Sprague-Dawley were exposed to PCEtOH (liquid diet ± 12.5% v/v ethanol, n=12 per group) from 4 days prior to cohabitation (E-4) until to embryonic day 4 (E4). Offspring adrenal glands were weighed and collected at 12 months for qRT-PCR analysis of steroidogenic gene expression. Body and adrenal weight was not affected by PCEtOH in male or female offspring. Preliminary analysis suggests that PCEtOH does not alter mRNA levels of enzymes that regulate production of corticosterone (Cyp11a1, Cyp21a1, Nr3c1 or Mc2r).

Results of this study suggest that the enzymes controlling steroid biosynthesis in the adrenal are not altered in response to periconceptional ethanol exposure under basal conditions however future studies examining hormone concentrations and stress responses are required.

Transcriptional and epigenetic factors underlying the extinction of nicotine-seeking behaviour in the rat  
Mr Matthew Castino1, Dr Neil Youngson1, Ms Danay Baker-Andresen1, Dr Vikram Ratnu1, A/Prof Timothy Bredy2,4, Dr Kelly Clemons1  
1School of Psychology, The University of New South Wales, Kensington, Australia,  
2Department of Pharmacology, School of Medical Sciences, The University of New South Wales, Kensington, Australia,  
3Psychiatric Epigenomics Laboratory, Queensland Brain Institute, The University of Queensland, Brisbane, Australia,  
4Department of Neurobiology and Behaviour, School of Biological Sciences, University of California Irvine, Irvine, USA

Recent research in the field of epigenetics suggests that both the formation and extinction of drug-associated memories are regulated by dynamic modifications to chromatin. In support of this, previous work in our laboratory has found that administration of the histone deacetylase (HDAC) inhibitor, sodium butyrate (NaB), facilitates the extinction of nicotine-seeking in a manner that provides resistance to reinstatement. The present study aimed to investigate the molecular mechanisms involved in this potentiated extinction learning, examining the effect of both nicotine exposure and NaB treatment on mRNA expression and histone acetylation in the rat medial prefrontal cortex. Sodium butyrate induced a significant increase in gene expression of the neuronal protein kinase, Cdk5, and in both saline and nicotine treated rats. In contrast, NaB increased BDNF mRNA only in saline control rats. Furthermore, nicotine, but not saline, exposure induced a decrease in histone H3K4 acetylation at the BDNF Exon IV promoter that was normalised by NaB treatment. These findings indicate that NaB and nicotine may act individually and in concert to regulate the genetic profile of the brain, though the behavioural consequences of their interactions are yet to be fully elucidated.
Reversal effects of betaine and dimethylglycine on behavioral impairment after a binge regimen of methamphetamine in mice

Prof Ming-Huan Chan¹, Mr Ying-An Chen¹, Mr Mei-Yi Lee⁶, Prof Hwei-Hsien Chen²-⁶

¹Institute of Neuroscience, Research Center for Mind, Brain, and Learning, National Chengchi University, Taipei, Taiwan, ²Master/PhD Program in Pharmacology and Toxicology, Tsu Chi University, Hualien, Taiwan, ³Center for Neuropsychiatric Research, National Health Research Institutes, Miaoli, Taiwan

A neurotoxic regimen of methamphetamine (METH) is known to cause cognitive dysfunction, social interaction deficits, and hypersensitivity to hallucinogens. Methyl derivatives of glycine N,N,N-trimethylglycine (TMG) and N,N-dimethylglycine (DMG) are potential to treat neurological disorders. This study aimed to examine the therapeutic effects of TMG/DMG on persistent behavioral aberrations in mice with a binge regimen of METH (4×5mg/kg, i.p.) for one day treatment via four injections at 2h interval. TMG and DMG were administered once daily for seven consecutive days after the behavioral impairment confirmed in METH-treated mice. Seven days after final injection of TMG/DMG, the novel recognition tests, social interaction, and head twitch response induced by hallucinogenic 2,5-dimethoxy-4-iodoamphetamine (DOI) were monitored. Results showed that TMG/DMG dose-dependently improved METH-induced cognition deficits, social withdrawal, and hypersensitivity to hallucinogens. The NMDA receptor glycine binding site antagonist 7-CK administered prior to TMG/DMG was found to reverse the improving effects of TMG and DMG on behavioral deficits after METH exposure, yet had minor effect on hypersensitivity to DOI. It suggests that TMG/DMG might activate the glycine binding site of NMDA receptor to improve METH-induced cognition deficits and social withdrawal. TMG/DMG may be the novel therapeutic agents for psychiatric disorders related to METH abuse.

Exploring the profiles of different drug users in Singapore

Xinyu Chin, P.K Koh

Introduction: In the field of drug rehabilitation, policy makers and service providers are as keen in identifying risk factors and prevention of drug use. Hence it is paramount to understand the profiles of various drug users. Given that drugs are used for varied reasons, a simple view that they are homogeneous will not suffice. The aim of this study is to compare profiles of heroin, benzodiazepines, amphetamines and codeine users among the treatment seeking population.

Method: A total of 279 heroin, 79 benzodiazepines, 38 amphetamines and 22 codeine cases were diagnosed with drug abuse or dependence at National Addiction Management Services during April 2013 to October 2014. Demographic and forensic were obtained from the standard intake assessment and case notes.

Results: Univariate ANOVA and chi-square analyses found that age, gender, educational level, marital status, living arrangement, trouble with the law and age of first use of drug of concern to be significantly different among the drug types. Body mass index, suicidal ideation and employment were not significant.

Discussion: Differences in certain demographic background of drug users further supports that policies targeting prevention need to consider tailoring campaigns to address the range of drug users. Further studies may explore specific risk factors for each of the drug use.

Rats Selectively Choose High Doses of Nicotine in Compensation for and Anticipation of Restricted Access to Nicotine

Dr Kelly Clemens, Jiajing Pan¹, Nathan M. Holmes⁵, Marios Panayi⁵

¹School of Psychology, University of New South Wales, Sydney, Australia

People adapt to restrictions on when and where they can smoke by adjust their smoking patterns: they increase their rate of nicotine intake both before and after a period when they cannot smoke. The present study used an animal model, nicotine intravenous self-administration in rats, to investigate the factors that underpin the shift towards greater nicotine intake under restricted access conditions. In Experiment 1, rats were trained to choose between three doses of nicotine (15, 30 or 60 µg/kg/infusion). Restricted access was modelled by progressively increasing the post-infusion time-out interval from 20 s (free access) to 300 s (restricted access). Rats equally sampled all doses of nicotine under free access conditions, but exhibited a preference for the highest dose (60 µg) as access was restricted across sessions. This preference was immune to treatment with a partial nicotine receptor agonist, Varenicline, but decreased when the response requirement for the highest dose increased and when rats were returned to conditions of free access. Experiment 2 replicated the main finding from Experiment 1 using a procedure in which the time-out interval varied within each self-administration session. It additionally showed that rats can use a signal of future access conditions to regulate their current dose selection. Together these results indicate that rats, like people, seek higher doses of nicotine under restricted access conditions. Critically, the preference for a higher dose is not simply a consequence of extended nicotine exposure, but instead, reflects both compensation for and anticipation of a restricted access period.

Does low to moderate prenatal alcohol consumption influence placental epigenetics?

A/Prof Jeffrey Craig¹, Ms Evie Muggli², Professor Jane Halliday³, Dr Juk Jing Loke³

¹MCRI, Parkville, Australia

The AQUA is a cohort of 1600 Victorian women, recruited in pregnancy and is currently following offspring until two years of age. The aims of AQUA are to develop a multifactorial risk model for the effects of prenatal alcohol consumption on the health and development of offspring, to provide evidence-based advice to the public and health professionals on the consequences of low, moderate and heavy levels of prenatal alcohol consumption and to complement similar studies of higher levels of prenatal alcohol exposure that lead to FASD. Here we report on a pilot study of the epigenetic mark of DNA methylation in placental DNA from 200 AQUA pregnancies representing six patterns of prenatal alcohol consumption. 200 placental DNA samples were analysed for DNA methylation at a global level and in two imprinted gene loci. A subset of samples from abstinent and moderate to heavy alcohol exposures were examined across the whole genome using the Infinium HM450 arrays. Multiple regression techniques adjusted for factors, such as maternal smoking and supplementary folate intake, known to alter epigenetic profile in utero. No strong correlation with alcohol exposure was observed.

Looking at Alzheimer’s disease through Einstein’s brain:

Some exciting cues

Prof Kaneez Fatima Shad¹, Dr Yashar Aghazadah¹, Prof Bodo Kress²

¹School of Life Sciences UTS, Sydney, Australia, ²Chefarzt des Instituts für Neuroradiologie, Frankfurt, Germany

We always looked at the diseases through the dark holes of anomalies. The purpose of this study was to compare the brains of Alzheimer’s disease (AD) patients with the profile of Einstein’s brain who was also known as the ‘Absent Minded Genius’. In this retrospective study, our main objective was to identify the hallmark areas in the brains of AD patients and compare them with that of Einstein’s brain. Twenty-seven patients diagnosed by neuropathological tests were observed using magnetic resonance imaging. MR examinations were done on 1.5T Scanner before and after intravenous administration of contrast agent. Bi temporal atrophy with consecutive dilatation of temporal horn, and marked enlargement of the Sylvian fissure were observed in patients with AD. Both temporal lobes and Sylvian fissure were also hall mark regions of Einstein brain. It is possible that these atypical aspects of Einstein’s brain were related to the difficulty with which he acquired language; his preference for thinking was in sensory parodies including visual images rather than words, and his early training on the violin. These results suggest that we need to find stimulants such as the violin Einstein played so one day AD patients may also say “I got it.”
POSTER PRESENTATIONS continued

Alcohol problem investigation when renewing driver's licenses on Ishigaki island
Dr Takahiro Fukuda1, Fumiko Ooya1, Kyouko Hanashiro2
1NHRI Ryukyu Hospital, Kin, Japan, 2Yayama Public Health Care Center, Ishigaki, Japan

Objectives and Methods: We examined a total of 840 participants (mean age 45.1 years, SD=16.5, all men) who renewed their driver's licenses at the driver's license testing and issuing center in Ishigaki island from June 2014 to September 2014. We administered the Alcohol Use Disorders Identification Test (AUDIT), and classified participants to 96 traffic offenders (mean age 47.7 years, SD=13.2) and 723 other drivers (mean age 45.8 years, SD=13.0) including safe drivers, general drivers and first-time renewal drivers.

Results: The ratio of the high risk drinker (8-14 points) in Ishigaki island is higher than that of the national average (9% vs 19%). The ratio of the high risk drinker (15 points or over) in Ishigaki island is higher than that of the national average (3% vs 5%). Also, the ratio of the problematic drinking in traffic offenders is higher than that of other drivers in Ishigaki island. (19% vs 12%) p<2 test

Conclusions: There are many problematic drivers in Ishigaki island, especially among traffic offenders.

Therefore, we need to intervene not only drunk drivers but also traffic offenders to prevent serious traffic accidents and alcoholisms.

Epigenetics in Tobacco Smoke Addiction
Dr George Hammons1, Lascelles Lyn-Cook Jr.1, Beverly Word1, Dr Nysia George1, Marta Pogribny1, Dr Beverly Lyn-Cook1
1FDA/NCTR, Jefferson, United States

The role of epigenetic mechanisms in drug addiction has been increasingly demonstrated. Changes in the epigenome can regulate transcription of specific genes that contribute to drug-induced behavioral responses. DNA methylation, a major epigenetic mechanism, generally exerts a repressive effect on gene transcription. While nicotine is the primary addictive drug that promotes tobacco use, recent studies suggest that tobacco smoke contains additional chemical constituents with addictive potential. However, underlying mechanisms have not been determined. In the present study, we examined the degree of promoter methylation across a defined panel of genes was evaluated in control and cigarette smoke condensate (CSC) exposed human cells using Methyl-Profiler DNA Methylation PCR System Array technology. Cells were exposed to 0.3 µg/ml, 1.0 µg/ml, or 10 µg/ml CSC for 72 hrs and chronically for 14 and 30 days. Promoters of several addiction-associated genes, CDH13, CXCL12, and CDKN1C, were identified as being methylated (50% to 90%) after CSC exposure. Level of methylation tended to increase with dose and duration of exposure. Additional studies are needed to confirm these findings, to screen other genes, and to further characterize the role and their impact of epigenetic changes in genes contributing to tobacco smoke-induced addiction.

Antiretroviral Therapy Reverses HIV-Mediated Suppression of Antiviral Cellular Factors
Dr Manqing Liu1, Dr Min Zhao1, Dr Wang Zhou1, Dr Jinsong Peng1, Dr Xu Wang2, Dr Fang Wang2, Dr Dunjin Zhou1, Dr Wenzhe Ho1
1Division of Virology, Wuhan Centers for Disease Prevention & Control, Wuhan, China, 2Wuhan AIDS Care Center, Wuhan Municipal Institute of Dermatosis, Wuhan, China, 3Temple University, Philadelphia, United States

Recent studies have identified a number of HIV cellular restriction factors. Thus, we examined the expression of several key antiviral cellular factors (OAS-1, MxA, A3G, PKR and Tetherin) in PBMCs from HIV-infected patients before and during the course of antiretroviral therapy (cART). Compared with uninfected control subjects, age-matched HIV-infected individuals had lower levels of the antiviral factors in PBMCs prior to the cART. The treatment of these subjects with antiretroviral drugs significantly suppressed viral load and increased CD4 counts, which was associated with a remarkable increase in the expression of the antiviral cellular factors, particularly OAS-1, A3G, and MxA, 3 months after cART. The expression of these antiviral cellular factors remained significant higher 6 months post the therapy. These findings indicate that antiretroviral therapy can reverse virus-mediated suppression of host innate immunity, providing additional benefit for HIV-infected individuals.

HIV infection and/or Heroin use dysregulate the plasma exosome miRNA expression
Ms Li Sun1, Dr Yu Zhou1, Dr Xu Wang1, Dr Jieliang Li2, Dr Li Zhou2, Dr Min Sang2, Dr Ke Zhuang2, Mr Qianghao Xiao1, Dr Wenzhe Ho2
1Department of Pathology and Laboratory Medicine, Temple University, PHILADELPHIA, United States, 2Center for Animal Experiment/ABSL-III Laboratory, Wuhan University School of Medicine, Wuhan, China

Exosomes are small membrane vesicles abundant in plasma. Exosomes are important in cell-to-cell communication, as they contain microRNAs (miRNAs) that can be delivered into recipient cells, exerting biological functions. As miRNAs are known now to participate in host innate immunity and HIV infection, we investigated the impact of HIV infection and/or heroin use on the expression of miRNAs in plasma exosomes. We found that the miRNAs (16, let-7a, 146a, 29b, 29c, 21, 126) related to HIV and immune system were dramatically increased in heroin users with HIV infection. The long-term (>5 years) methadone treatment of heroin users restored the levels of these miRNAs. We also observed an increase of plasma exosome miRNAs (150, 146a, 29b) in the subjects with advanced HIV disease (CD4 T cell count<350 cells). In addition, individuals with cART reduced the expression of HIV-induced miRNA-150 and miRNA-29b. These data provide evidence that HIV infection and/or heroin use dysregulate plasma exosomal miRNA expression, which may contribute to immunopathogenesis of HIV disease.

Effects of amphetamine on sign-tracking behaviour in the rat
Dr Martine Hofmann1, Prof Dr Simon Killcross2
1University of New South Wales, Sydney, Australia

When a lever extension serves as a Pavlovian cue to signal food delivery upon retraction, such lever can gain strong incentive salience. Rats will learn to approach the lever and engage with it, a behaviour called sign-tracking (ST). ST has been proposed as a measure of incentive salience attribution to cues and drugs of abuse are proposed to enhance incentive salience. Therefore, we explored the effects of systemic administration of amphetamine (AMPH) on ST in two sets of experiments. Rats were presented with one lever followed by reward. We found that vehicle-treated rats all acquired a ST response and that administration of AMPH did not affect ST.

Further, rats were presented with a sequence of two levers followed by reward (L1→L2→US). All vehicle-treated rats developed a ST response to both levers. The effect of AMPH on responding to L2 was similar to that in the previous experiment, whereas AMPH abolished ST to L1. We further show that both levers are equally rewarding in both vehicle- and AMPH-treated rats and that, in both treatment groups, ST to L1 is not mediated by a direct representation of the outcome, whereas ST to L2 is. The implications of the data will be discussed.

NRCAM related neural system in an animal model of addiction
Dr Hiroki Ishiguro1, Prof Emmanual Onaivi1, Mr Kouichi Tabata2, Ms Sakura Nakayama2, Mr Hirohumi Sogabe2, Prof Takeshi Sakurai3, Prof Takeo Kubota2, Prof Nobutaka Motohashi1
1University of Yamanashi, Chuo, Japan, 2Department of Biology, William Paterson University, Wayne, USA, 3Department of Epigenetic Medicine, Graduate Faculty of Interdisciplinary Research, University of Yamanashi, Chuo, Japan, 4Medical Innovation Center, University of Kyoto, Sakyo, Japan
Low NrCAM expression in brain had a protective effect against addiction vulnerability in humans. Nrcam knockout mice do not develop conditioned place preferences for illegal drugs, possibly through some behavioral traits, including novelty seeking, obsessive compulsions and responses to aversive or anxiety-provoking stimuli. NrCAM works in neural plasticity in development of addicted brain. We previously revealed that glutaminase was reduced in low NrCAM expression tissue, and that an inhibitor of the enzyme seemed to reduce preferences to addicts and anxiety-like behavior. In order to prove glutamatergic and GABAergic homeostasis in addicted brain, we further analyzed expression patterns of brain molecules regulated by methamphetamine (MAP) treatment in Nrcam knockout mice using micro-array gene expression analysis in comparison between wild and heterozygote genotypes, and between treatment with saline and MAP. The results demonstrate that metabotropic glutamate receptor 2 appears to be reduced in MAP treated Nrcam heterozygote mice. GABAergic molecules are also detected differences in their expression. The data indicate that NrCAM could affect addiction-related behaviors via modulation of some glutamatergic and GABAergic neural networks in brain. The results from cocaine-treated Nrcam knockout mice were compared to evaluate common molecules involved in the etiology of addiction.

The prevalence of Alcohol Use Disorders in Japan

Comparisons with the United States and Korea

Doctor CHIE IWAHARA1, Doctor Tsuyoshi Takimura1, Doctor Hiroshi Sakuma1, Doctor Mitsuhiro Kimura1, Doctor Matsuhiro Fujita1, Doctor Sachio Matsushita1, Prof Younetu Osaki1, Doctor Susumu Higuchi1

1National Hospital Organization, Kurihama Medical and Addiction Center, Yokosuka, Japan. 1Division of Environmental and Preventive Medicine, Tottori University, Yonago, Japan

Introduction: For the first time in Japan, we investigated the prevalence of alcohol use disorders (AUD) using criteria from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Comparing our results with those from Korea and the U.S., we attempted to clarify AUD characteristics in Japan.

Method: Using the two-stage stratified random sampling method, we surveyed 2,000 adults nationwide. Using the DSM-IV and face-to-face interviews, we obtained valid answers from 1,085 people (54.3%). We used the National Epidemiologic Survey on Alcohol and Related Conditions and Korean Epidemiologic Catchment Area samples for comparison.

Results: Alcohol abuse was more prevalent in the U.S. (5.7%) than in Japan (1.7%). Conversely, Japan’s alcohol independence rate (9.3%) was comparable to that in the U.S. (8.8%). In both countries, AUDs were more prevalent among men than women. In Japan, AUDs were more common among middle-aged than young people; however, in the U.S., they were more common among young people.

Conclusion: Previously, the Japanese perceived excessive drinking as symbolizing masculinity. Thus, middle-aged men—who had adequate money and enjoyed social drinking—excessively consumed alcohol and were likely to become alcoholics. Conversely, women—who experienced societal constraints on drinking—rarely had such opportunities.

Spicy Food Preference and the HPA Axis Reactivity to Stress

in Korean Social Drinkers

Prof Sung-Gon Kim1, Prof Woo-Young Jung1, Dr Ji-Hun Park1

1Department of Psychiatry, School of Medicine, Pusan National University, Yangsan, South Korea, Yangsan, South Korea

Some reports suggest that if individuals prefer spicy foods, they may be more vulnerable to stress; thus, their HPA axis reactivity to stress may be abnormal. We investigated the relationship between HPA axis reactivity to stress and spicy food preference in Korean social drinkers.

The subjects were 40 healthy. They were exposed to stress as cold pressor test and mathematical calculations. Salivary cortisol level was measured before and after the stress. The subjects were divided into two groups of those who preferred spicy foods (SP n=20) and less preferred spicy foods (LP n=20) by using a food preference scale.

Repeated measures ANOVA on salivary cortisol concentration revealed a significant group by block interaction (p=0.036). Basal and salivary cortisol immediately after stress were significantly higher in SP than LP (respectively p=0.009, p=0.011). The salivary cortisol at 80 min after the stress decreased significantly compared to the basal salivary cortisol in SP (p=0.004).

Salivary cortisol 20 min after the stress increased significantly compared to the basal salivary cortisol in LP (p=0.031).

HPA axis reactivity to stress in SP was more sensitive than that in LP. These results suggest that HPA axis reactivity in those who prefer spicy foods may be vulnerable to stress.

Access to needle and syringe programme in a rural area of southern Thailand

Ms Roongnapa Khampaeng1, Dr Sawitri Assanangkornchai2

1Health Intervention and Technology Assessment Program, Muang, Noo Thaburi, Thailand. 2Epidemiology unit, Prince of Songkla University, Hatyai, Songkhla, Thailand

Background: Providing access to sterile needles and syringes for injection drug users (IDUs) is an important component to prevent and control for HIV transmission. Needle and syringe program (NSP) was initiated in Songkhla since 2009 by an NGO-run facility. This study aimed to explore access to NSP and determine factors associated with the access.

Methods: A cross-sectional study among 157 male IDUs in Songkhla province of southern Thailand was conducted. Participants were recruited through a snowball technique. Face-to-face interviews using structured questionnaire were carried out.

Results: The most common drug injected by these IDUs was heroin (98%), followed by methamphetamine (19%) and crystal methamphetamine (5%). Around two third (68%) of participants reported accessing NSP in the previous 6 months and almost half of them (47%) received sterile needles and syringes weekly. IDUs who used heroin and stimulants concurrently, who had knowledge of HCV risk, or lived in a city where the drop-in center was located were more likely to access NSP than their counterpart.

Discussion and Conclusions: Not accessing NSP among current IDUs may lead to needle sharing and reusing. Providing knowledge of risks together with increasing outreach activities should improve the access to NSP among these IDUs.

Factors affecting re-admission amongst substance abusers in a detoxification treatment unit in Singapore

PK Koh, Xin Yu Chin

Re-admissions during drug and alcohol treatment are a common occurrence. We examine patient attributes and clinical data that influence re-admission at the National Addictions Management Service in Singapore. Data was taken from 254 patients who received inpatient care between April 2013 to May 2014. Within 1 year of their first visit, 36.3% were re-admitted. Chi-square and ANOVA was used to analyse the data. Initial analyses found differences between the drug and alcohol group. There were significant associations between re-admission and education level (X2 = 7.98, p = 0.018), trouble with the law (X2 = 4.36, p = 0.037) and substance type (X2 = 4.01, p = 0.045). In the alcohol group, significant associations were found between re-admission and marital status (X2 = 6.21, p = 0.013) and completion of the intensive 1st week of medication regime (X2 = 5.43, p = 0.02). In the drug group, there were significant associations between re-admission and education level (X2 = 7.30, p = 0.026) and age at admission (FI, 197) = 6.33, p = 0.013. The results support the idea that different factors are associated with re-admission between the drug and alcohol patients. Hence, such differences have to be taken into account when preventing relapse and improving retention during the patients’ first inpatient treatment stay.

Different behavioral motivation system in juvenile internet addiction between the types

Dr So Hee Lee1

1National Medical Center, Seoul, South Korea

Purposes: This study aimed to know the clinical characteristics between the types of internet addiction in children & adolescents.

Methods: The subjects of this study were 62 children & adolescents who had been referred for the treatment of internet addiction by a adolescent media center. We performed Korean educational development institute Wechsler intelligence scale(KEDI-WISC), Child Behavior Checklist(CBCL), Inventory of parent and peer attachment(IPPA) and Behavioral Inhibition System/Behavioral Activation System(BIS/BAS) to the subjects. The subjects were divided into two groups as SNS(social network service) use and Game only(not using SNS), and their clinical characteristics were analysed.
POSTER PRESENTATIONS continued

Results: Subjects (mean age = 13.9±6.2) were consisted with 40(66%) Boys and 21(34%) Girls. Boys proportion were higher than the girls in the Game only group (p=0.01). Game only group started internet use earlier than the SNS use group (p=0.05). We could not find any significant differences between two groups in CBCL and IPPA scores. Game only group were significantly higher in BIS/BAS total (p=0.05), BAS total (p=0.02) and BAS fun seeking subscale (p=0.01).

Conclusion: This study suggested the internet addicted children & adolescents might have different behavioral motivational systems whether they use SNS or not.

Economic crisis and hospitalization from alcohol attributed diseases in Taiwan
Dr Chih Ming Lin, Dr Chen Mao Liao
1MING-CHUAN UNIVERSITY, Taoyuan City, Taiwan, 2MING-CHUAN UNIVERSITY, Taoyuan City, Taiwan

In the third quarter of 2008, a major economic crisis hit many developed industrial countries. Taiwan suffered a plunge in exports and a severe decline in GDP. Using a registry-based cohort design, we estimated the impacts of the 2008 economic recession on acute and chronic alcohol attributable cause (AAC) admissions to Taiwanese hospitals. The admissions data for subjects aged 20-75 years in 2003 between 2003 and 2012 was retrieved from the National Health Insurance Research Database. A cohort of 6,009,999 men and 6,347,826 women was followed-up and examined over this 10-year period. In total, 708,194 men and 378,512 women were admitted for AACs. The quarterly incidence rate of hospitalization for AACs was calculated and stratified by sex. The interrupted time series method was used to evaluate the effects of crisis intervention. This study found that both sexes showed significant (p=0.05) changes in the rate of AAC admissions in the first quarter of 2009. Men had an abrupt increase in the AAC admission rate (7.5%). A 12.6% increase in the AAC admission rate was also found in women after the 2008 economic crisis. This study provides evidence that the economic recession resulted in an increase of AAC admissions in Taiwan.

Gross motor performance in primary school aged children living in high-risk drinking communities in remote Australia – a population based study
Ms Barbara Lucas
The Discipline of Paediatrics and Child Health, Sydney Medical School, the University of Sydney, Sydney, Australia.

Gross motor (GM) performance was characterised in 108 children (Aboriginal: 98.1%; males: 52.7%; mean age 8.7 years) residing in remote Aboriginal communities in the Fitzroy Valley, Western Australia as part of a population based study using case ascertainment called the Lililwan Project. GM performance was assessed using the Q-GlobalTM GM Composite of the Bruninks-Oseretsky Test of Motor Proficiency and compared between children with and without (I) Fetal Alcohol Spectrum Disorders (FASD), (ii) prenatal alcohol exposure (PAE) and (iii) Chronic Suppurative Otitis Media (CSOM). Composite scores at the 2nd and 16th centiles defined ‘diagnostic’ and ‘clinical’ impairment respectively. FASD diagnoses were assigned using Modified Canadian Guidelines. CSOM was detected using clinical examination and tympanometry. The mean GM Composite score for all participants was similar to population norms (50±10) for all participants (47.0±8.4), but was significantly lower in children with than without a FASD diagnosis (p=0.006) or CSOM (p=0.031), and comparable between children with and without PAE (p=0.27). Higher prevalence of GM impairment at 2nd and 16th centile was found in children with FASD (9.5%: 23.8%) and CSOM (4.4%: 24.4%). Assessment of GM performance should be included in children with FASD and CSOM to optimise child development through targeted therapy.

Effects of methamphetamine on habits, cognitive control and structural plasticity.
Ms Helena Pacitti, Professor Bernard Balleine, Professor Simon Killcross
1UNSW, Sydney, Australia; 2BMRI, Sydney, Australia

In humans, chronic use of methamphetamine has long been associated with deficits in executive function and response inhibition. However, the mechanism underlying these deficits is not yet fully understood and causality remains to be determined. In rodents, chronic exposure to methamphetamine causes structural changes to the brain. Specifically, increases in spine density are found in the dorsolateral striatum, an area involved in habits, whereas decreases are observed in the dorsomedial striatum, an area involved in goal-directed behaviour. There is also evidence that psychostimulant use causes structural plasticity in the medial prefrontal cortex, an area that is involved in cognitive control. The experiments conducted here used instrumental learning, outcome devaluation and response-Conflict paradigms in rodents to characterize the effects of methamphetamine administration on habits and cognitive control, and their relationship to structural changes in the striatum and prefrontal cortex.

NOFASD Australia: Fetal Alcohol Spectrum Disorder and three years of work in Australia 2012-2015
Mrs Ardelle Rist, Vicki Russell
1NOFASD Australia, Wynyard, Australia

For the first twelve years, NOFASD Australia support services, education and advocacy were delivered by volunteers who struggled to raise public awareness to the issue of Fetal Alcohol Spectrum Disorder in Australia. This small but uniquely placed national organisation has evolved from a small “kitchen table” organisation to be recognised as the non-government peak body representing individuals and families living with FASD. Our Mission is to be a strong and effective voice for individuals and families living with FASD and NOFASD Australia has a strong commitment to FASD prevention. At a primary prevention level, we continue to raise public awareness through community education and building a national network of supporters. At a secondary level, training delivered to service providers builds their capacity to better respond to target groups who may be at increased risk for alcohol use in pregnancy or FASD. At an early intervention level, consultation, advocacy and support for individuals and families whose lives are directly affected by FASD is a key activity. NOFASD Australia promotes an understanding that children and adults who live with FASD can experience success with appropriate support and access to interventions. This poster is a snapshot of NOFASD Australia’s significant achievements.

Treatment with the Self-Discovery Camp (SDiC) Improves Internet Use Disorder
Prof Hiroshi Sakuma, Ms Satoko Mihara, Prof Hideki Nakayama, Takashi Kitayuguchi, Kumiko Miura, Masaki Maezono, Takuma Hashimoto, Prof Susumu Higuchi
1NHO Kurihama Medical and Addiction Center, Yokosuka, Japan

Background: Internet use disorder (IUD) is a novel behavioral addiction that may affect a large percentage of the population due to the spread of Internet technology. A therapeutic residential camp (TRC) has been developed in Korea and administered to many patients with IUD. However, the efficacy of this treatment in other countries is still unknown. We investigated the efficacy of the Self-Discovery Camp (SDiC), a Japanese version of the TRC and the correlation between individual characteristics and outcome measures.

Methods: We recruited 10 IUD patients to spend 8 nights and 9 days at the SDiC, which included CBT, psychoeducation, recreational activities, and group therapy. We measured Internet use/gaming time as well as scores on the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES, an indicator of therapeutic motivation and problem recognition).
Results: Internet use/gaming time had significantly decreased 3 months after camp attendance. Problem recognition and self-efficacy towards positive change also improved. Furthermore, age of onset correlated with problem recognition.

Conclusions: Our results demonstrate the effectiveness of the SDIC for IUD, especially in terms of problem recognition and self-efficacy. We also demonstrate that age of onset may be a useful predictor for IUD prognosis.

Clinical, Pathological and Demographic Correlations on DSM-IV Alcohol Abuse and Alcohol Dependence

Mrs Donna Sheedy1, Ms Toni McCrossin1, Professor Jillian Kril1

1The University of Sydney, Sydney, Australia

The NZS Brain Tissue Resource Centre (NSW BTRC) is an established post-mortem brain bank with a focus on alcohol related brain damage. This study correlated pathology findings, clinical histories and demographics of ninety brain donors with DSMIV Substance Dependence (alcohol) and Substance Abuse (alcohol). Data analysed related to alcohol consumption, smoking, BMI, medical conditions, toxicology and post-mortem findings. The majority of cases were male (81%) and had a mean age m55y and f56y. Dependence cases were more likely to smoke (D: 57%; A: 51%), have used benzodiazepines (D:26%; A: 27%), obese (D:2%; A:0%), and an abnormal liver pathology (D 87%; A 66%). Significant differences between the dependence and abuse classification was found for age began drinking alcohol p=0.045; mean daily alcohol intake p=0.012; age of death p=0.03. Females had more liver cirrhosis compared with males (f56%; m38%). Increasing body mass index (BMI) correlated with a decrease in the mean alcohol intake p=0.04. Verbal atrophy was present in 42% of dependence cases compared with 25% of abuse cases. Findings including age at which drinking commenced, use of benzodiazepine, liver pathology and BMI are shown to correlate with the degree of alcohol intake in DSM-V dependence cases.

The effects of chronic smoking on Alcohol-related Brain Damage

Dr Greg Sutherland1, Mr Andrew McCorkindale1, Mrs Donna Sheedy2, Prof Jillian Kril

1Charles Perkins Centre, University of Sydney, Sydney, Australia

Pathological and neuroimaging studies both demonstrate that chronic alcohol abuse causes brain atrophy and neuronal loss. Recent neuroimaging studies suggest that smoking also causes brain atrophy. This novel pathological study investigated potential additive or synergistic effects of concomitant alcohol and tobacco consumption on the human brain. A total of 44 cases and controls were split into four groups: 16 non-smoking controls, 9 smoking controls, 8 non-smoking alcoholics and 9 smoking alcoholics. The volume of 26 grey matter and white matter regions was measured using a point-counting technique. There were no interactions between smoking and alcohol in any brain region and no region affected of smoking, but there was a significant loss of both regional and total white matter in alcoholics (p < 0.004). Similarly there was no smoking or smoking x alcohol interaction effects on neuronal density but a significant reduction in neurons (23%) was seen in the prefrontal cortex of alcoholics (p < 0.002). These results do not support the hypothesis that smoking exacerbates alcohol-related brain damage. Furthermore the alcoholic brain is characterized by localized neuronal loss but generalized white matter atrophy suggesting that two different pathogenic mechanisms may be operating.

Online Monitoring of movements in Drug Supply and Demand

Miss Kanittha Thaikla1

1Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand

The internet is a medium used by buyers and sellers of drugs. The objectives of this study are (a) to develop an online drug-monitoring program and (b) to review knowledge and information on drug network trafficking movements, including demand, supply and spread of drugs. A total of 2,353 pages were queried, including 52 pages that provided new knowledge on drugs. Among these pages, 46 had content related to prescription drug abuse and included 41 pages in the form of websites containing news and information, and 5 Facebook pages that were online social media with introductions on the ingredients of sedatives and antipyretics available for sale and use for intoxication instead of normal treatment, e.g., mixing analgesics (Tramadol) with cough syrup and soft drinks. Six webpages concerned marijuana, including 5 Facebook pages with content on the benefits of marijuana and attempts to mobilize the legal sale of marijuana, following overseas precedents. The webpages also sold marijuana and paraphernalia. Prescription drugs and marijuana can be sold online, with payment made to a bank account and delivery by mail. Health professionals and narcotics control officers may need to increase awareness in monitoring the World Wide Web as a new drug resource for information.

Behaviour in children with FASD assessed using the Achenbach System of Empirically Based Assessment for school-aged children: A systematic review with meta-analysis

Dr Tracey W Tsang1, Ms Barbara R Lucas2,3, Prof Heather Carmichael Olson1, Dr Rafael Z Pinto1, Prof Elizabeth J Elliott1,2,4,5,6

1Discipline of Paediatrics & Child Health, Sydney Medical School, The University of Sydney, Westmead, Australia, 2The George Institute for Global Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 3Pancha Centre for Indigenous Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 4Physiotherapy Department, Royal North Shore Hospital, St Leonards, Australia, 5Department of Psychiatry & Behavioural Sciences, University of Washington School of Medicine, Seattle Children’s Research Institute, Seattle, USA, 6Departamento de Fisioterapia, Faculdade de Ciências e Tecnologia, UNESP – Univ Estadual Paulista, Presidente Prudente, Brazil, 7The Sydney Children’s Hospital Networks (Westmead), Westmead, Australia, 8The Australian Paediatric Surveillance Unit, Kids’ Research Institute, Westmead, Australia

Behavioural ratings obtained with the internationally-validated Achenbach System of Empirically Based Assessment School-Age Forms in children with FASD and/or prenatal alcohol exposure (PAE) were summarised. The parent-rated Child Behavior Checklist, Teacher’s Report Form, and Youth Self-Report were included. A comprehensive search of electronic databases and reference lists was conducted in March 2014. Eligibility screening and data extraction were undertaken by two independent reviewers. Meta-analyses were performed for parent-rated Internalizing, Externalizing, and Total problems scores. All other scales were summarised qualitatively. After screening 491 articles, 23 papers were included with 16 utilised in meta-analyses. Pooled results showed higher Total (mean difference: 12.1 [95%CI: 7.7-16.5]), Internalizing (6.3 [95%CI: 3.1-9.5]), and Externalizing problems scores (12.9 [95%CI: 7.9-17.9]) in FASD than No FASD; with greater odds of scoring in the “Clinical” range. Pooled FAE results demonstrated higher problem scores in exposed children (p<0.05). Qualitative summaries of other scales from parents, teachers, and self-report suggest poorer behaviour ratings in those with FASD and PAE on Problem and Competence composite scores, and many Syndrome subscales. FASD and PAE are associated with poorer behaviour in many, but not all domains, and should be a consideration for all service providers who interact with children who have these exposures.

Digital assessment of the facial phenotype for fetal alcohol syndrome in Australian Aboriginal children: Reliability and Agreement

Dr Tracey W Tsang1, Ms Zoe Laing-Aiken1, Prof Jane Latimer2, Dr James Fitzpatrick1,2, Mr June Oscar3, Ms Maureen Carter4, Prof Elizabeth J Elliott1,2,5,6

1Discipline of Paediatrics & Child Health, Sydney Medical School, The University of Sydney, Westmead, Australia, 2The George Institute for Global Health, Sydney Medical School, The University of Sydney, Sydney, Australia, 3The Telethon Institute of Child Health Research, West Perth, Australia, 4Marninwarntikura Women’s Resource Centre, Fitzroy Crossing, Australia, 5Nindjavigi Cultural Health Services, Fitzroy Crossing, Australia, 6The Sydney Children’s Hospital Networks (Westmead), Westmead, Australia, 7The Australian Paediatric Surveillance Unit, Kids’ Research Institute, Westmead, Australia

Digital photographs from the Lilliwack Project (a study of FAS prevalence in remote Australia) were analysed for facial features of Fetal Alcohol Syndrome (FAS) using the FAS Facial Photographic Analysis Software (FPAS) in an Aboriginal child cohort (n=106; age: 7.4–9.6 years). The current study was conducted to determine: i) intra- and inter-rater reliability; ii) agreement when different ethnic
POSTER PRESENTATIONS continued

The selective D2 dopamine receptor antagonist eticlopride prevents the development of MDMA-induced behavioural sensitisation in rats.

Mr Ross Van De Wetering
Victoria University of Wellington, Wellington, New Zealand

Rationale: Repeated, intermittent exposure to MDMA results in behavioural sensitisation and cross sensitisation to both amphetamine and the D2 agonist, quinpirole. These findings suggest a dopaminergic mechanism underlying the sensitised response. Objectives: The present study investigated the effect of the selective dopamine receptor D2 antagonist, eticlopride on the development of MDMA-induced behavioural sensitisation in rats. Methods: Eticlopride (0.0 or 0.3 mg/kg, IP), was administered 30 min prior to MDMA (0.0 or 10.0 mg/kg, IP) on each of five pre-treatment days. Following two days of withdrawal, the locomotor activating effect of MDMA (5.0 mg/kg, IP) was measured. Results: MDMA pre-treatment produced a sensitised response that was blocked by eticlopride. Conclusions: These data suggest that activation of the D2 receptor is critical to the development of sensitisation to the behavioural effects of MDMA. Studies are in progress to determine the role of sensitisation in MDMA self-administration.

Sex Differences in Alcohol Drinking in Rats

Ms Brittany M. Pridy, Mrs Janaina Vendruscolo, Dr Stephanie A. Carmack, Dr George F. Koob, Dr Leandro F. Vendruscolo

Although women appear to be more vulnerable to alcohol-induced behavioral and physical detrimental consequences than men, the majority of studies are conducted in male subjects. We examined sex differences in alcohol consumption in two rat strains: Long Evans and Wistar. The rats were given 10% alcohol vs. water over a 21-day period in their home cages using a two-bottle choice paradigm followed by twenty-one 30-min daily alcohol vs. water operant self-administration sessions. Another group of rats was given intermittent access to 20% alcohol in their home-cages for 2 months. Vaginal smear samples were collected to investigate the influence of the estrous cycle on alcohol consumption. We found that females consumed more alcohol than males in both protocols (continuous 10% and intermittent 20%) of home-cage two-bottle choice drinking, but not operant self-administration. The phases of the estrous cycle (proestrous, estrous, and diestrous) had no effect on alcohol intake in any experimental conditions. In conclusion, females (especially Long Evans) drank more alcohol than male rats in a low workload and low stress environment, but no sex differences were found for operant alcohol self-administration. The estrous cycle does not appear to be a confounding factor in alcohol drinking studies.

Analysis of the Acquisition of Drug Discrimination Reveals Differences in the Discriminative Stimulus Properties of a High vs. Low Dose of ±3,4-methylenedioxymethamphetamine (MDMA)

Mr Jeremy Webster, Professor David Harper, Professor Susan Schenk
Victoria University of Wellington, Wellington, New Zealand

Most drug discrimination studies involving ±3,4-methylenedioxymethamphetamine (MDMA) employ training- doses which are lower than those used in many other behavioural paradigms. Such doses produce selective increases in serotonin with minimal impact on other neurotransmitters and therefore these studies may be biased toward attributing findings to serotonergic mechanisms. Higher doses of MDMA also produce significant increases in dopamine and this may be reflected in the drug’s discriminative stimulus profile. Our laboratory has previously suggested that higher doses of MDMA may share stimulus properties with the stimulant amphetamine (AMPH). The present study investigates whether the discriminative stimulus effects of a high dose of MDMA (3.0mg/kg) are qualitatively distinct from those produced by a typical low dose (1.5mg/kg). Two experiments were carried out examining the acquisition profile of a high vs. low dose of MDMA in either a two-choice (MDMA vs. vehicle) or three-choice (MDMA vs. AMPH vs. vehicle) discrimination. Acquisition was assessed using a series of increasingly stringent criteria. Our results suggest that a high dose of MDMA produces a more robust discriminative stimulus than the low dose typically used in drug discrimination studies. Poor consistency in the three-choice paradigm may be due to high dose MDMA sharing discriminative stimulus properties with AMPH.
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