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APSAAR
Asia-Pacific Society for Alcohol and Addiction Research

IDARS

4th APSAAR / 5th IDARS Conference

August 18-21, 2015

THE WESTIN Australia
SYDNEY

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*

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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

THE WESTIN SYDNEY

Conference 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.

APSAAR
Asia-Pacific Society for Alcohol and Addiction Research

IDARS

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

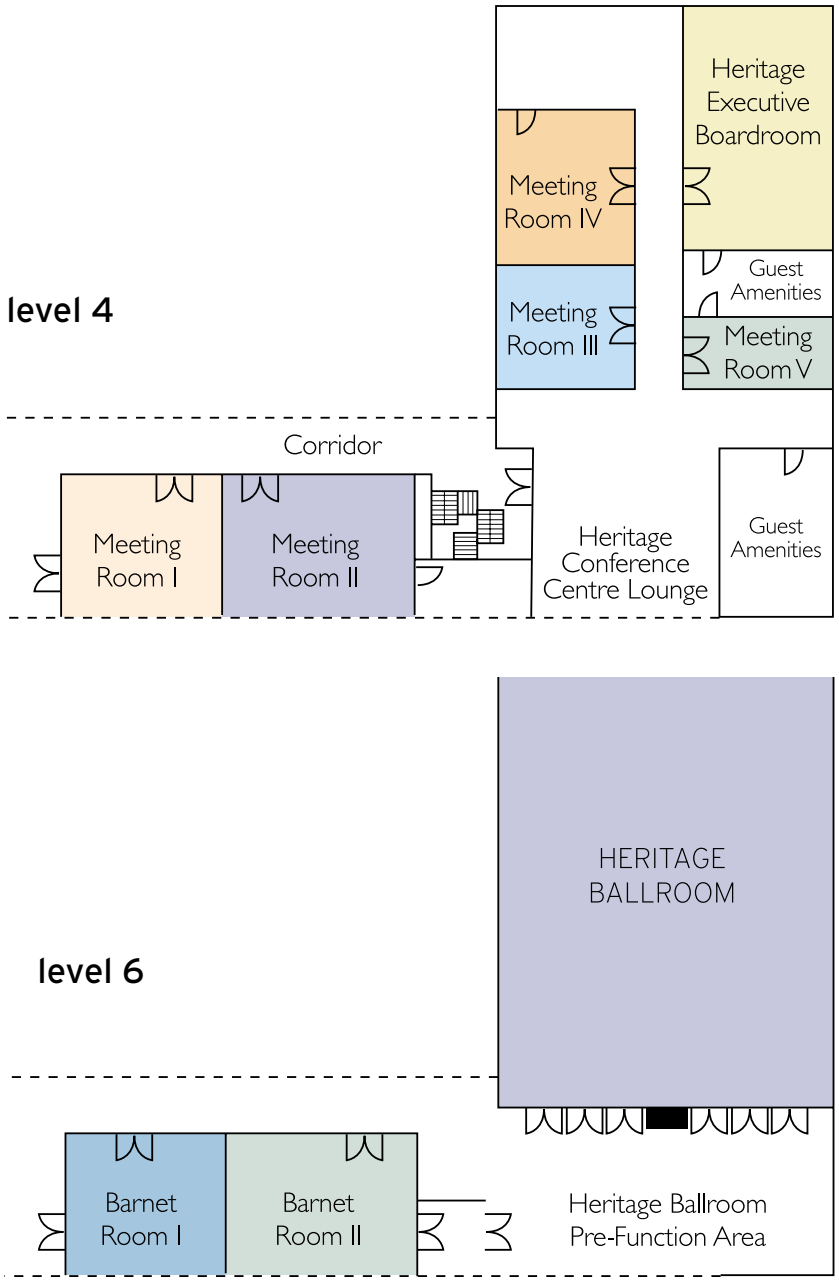
Cost: $0 (included in 'registration package')
or $ 150 per person

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.

FLOORPLAN


level 4
Heritage Executive Boardroom
Meeting Room IV
Guest Amenities
Meeting Room III
Meeting Room V
Corridor
Meeting Room I
Meeting Room II
Heritage Conference Centre Lounge
Guest Amenities
HERITAGE BALLROOM
level 6
Barnet Room I
Barnet Room II
Heritage Ballroom Pre-Function Area

CONFERENCE PROGRAM OVERVIEW

Time	**Tuesday 18 August Stream 1** Heritage Ballroom	**Tuesday 18 August Stream 2** Barnet Rooms	**Wednesday 19 August Stream 1** Heritage Ballroom	**Wednesday 19 August Stream 2** Meeting Room 1
07:30				
08:00				Breakfast and registration
08:15	**Conference opening, welcome**			
08:30	1: Fetal Alcohol Spectrum Disorder - Overview	6: Psycho-stimulants	10: Preventing Drug-Seeking and Relapse: 1	14: Genetics
09:00				
09:30				
10:00				
10:30	Morning tea and coffee			
11:00	2: FASD in the Asia-Pacific Region	7: Infection and Addiction	11: Preventing Drug-Seeking and Relapse: 2	15: Behavioral Sensitization
11:30				
12:00				
12:30				
13:30	APSAAR Board of Directors		Lunch and poster viewing	
14:00	3: FASD – Basic and Clinical Science	8: The Vulnerable Brain	12: The Victims of Alcohol Misuse: Impacts on Indigenous Children	16: Free Oral Communications
14:30				
15:00				
15:30				
16:00	Afternoon tea and coffee with posters			
16:30	4: FASD – Selected Oral Presentations	9: Current Controversies in Internet Use Disorders	13: Comorbidity and Complications in Addiction	17: Free Oral Communications
17:00	5: FASD – Policy & Legal Perspectives			
17:30				
18:00				
18:30			Poster viewing	
19:00	**Conference Reception**			
19:30			**Conference Dinner** (until 22:00)	

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)

Wednesday 19 August Stream 3 Meeting Room 2	Thursday 20 August Stream 1 Meeting Room 1	Thursday 20 August Stream 2 Meeting Room 2	Friday 21 August Stream 1 Heritage Ballroom	Friday 21 August Stream 2 Barnet Rooms
Breakfast and registration				
18: Substance Use and Relaxation (JSND Symposium)	22: The Impact of Addictive Disorders in Asia. 1. Alcohol	24: Free Oral Communications	26: Nature and Diagnosis of Addictive Disorders	29: Anaesthetics, Psychostimulants and Opiates
Morning tea and coffee				
19: Early Career Psychiatrists Symposium	23: The Impact of Addictive Disorders in Asia. 2. Illicit Drugs	25: Free Oral Communications	27: Translational Research: Treatment of Alcohol Misuse	30: Pharmacology and Toxicology
Lunch and poster viewing				
20: Free Oral Communications	Free Afternoon		28: Cannabis and Medicinal Cannabinoids	IDARS Panel Discussion
			Afternoon tea/coffee with posters	
21: Fetal Alcohol Spectrum Disorder Oral Communications			Public Lecture in Heritage Ballroom Prof Marc Potenza: Gambling and On-line Addictions	

OUTLINE OF SCIENTIFIC PROGRAM

STREAM #1: HERITAGE BALLROOM			
Time	**Speaker**	**Topic**	**Affiliation**
07:30	Breakfast and registration		
08:15	Conference opening, Welcome		
08:30	**SESSION 1:** Fetal Alcohol Spectrum Disorder – Overview **CHAIR:** Dr Ken Warren (Deputy Director, NIAAA, USA)		
	Ken Warren	A brief history of Fetal Alcohol Spectrum Disorder	National Institute on Alcohol Abuse and Alcoholism, MD, USA
	Edward Riley	Fetal Alcohol Spectrum Disorder: brain and behavior	San Diego State University, CA, USA
	Elizabeth Elliott	Clinical and public health challenges in Fetal Alcohol Spectrum Disorder	University of Sydney, Australia
	Sharman Stone	The role of governments in addressing Fetal Alcohol Spectrum Disorder	Federal Member of Parliament for Murray, Australia
10:30	Morning tea and coffee		
11:00	**SESSION 2:** Fetal Alcohol Spectrum Disorder (FASD) in the Asia-Pacific Region **CHAIR:** Prof Elizabeth Elliott (Australia)		
	Olga Tulabut	FASD in the Philippines	Angeles University, Philippines
	Carol Bower	Addressing FASD in Western Australia	Telethon Kid's Institute, University of Western Australia
	Denis Lamblin	FASD in Reunion and Tahiti	FASD Program, Reunion
	Heather d'Antoine	Alcohol in pregnancy and FASD in Indigenous Australians	Menzies School of Health Research, Darwin, NT, Australia
	Ira Chasnoff	Prevention and intervention for FASD in Hawaii: developing a system of care	National Training Institute Upstream, Portland, OR, USA
	Christine Rogan	FASD in New Zealand	Alcohol Healthwatch, New Zealand
13:00	APSAAR Board of Directors	Lunch and poster viewing	
14:00	**SESSION 3:** Fetal Alcohol Spectrum Disorder – Basic and Clinical Science **CHAIR:** Prof Jane Latimer (George Institute for Global Health, Australia)		
	Karen Moritz	Long term outcomes of prenatal alcohol exposure – more than just effects on the brain	University of Queensland, Australia
	Dipak Sakar	Endocrine, metabolic and immune disorders in fetal-alcohol-exposed adult animals	Rutgers University, NJ, USA
	Ruth Napper	Studies in animal models identify short and long term risks of prenatal binge alcohol exposure	Brain Health Research Centre, University of Otago, New Zealand
	Vicki Russell	FASD in regional Australia	NoFASD Australia
	Diana Zanfranche	The effects of maternal periconceptional ethanol exposure on long term cognitive outcomes in rat offspring	University of Queensland, Australia
	James Fitzpatrick	The Lililwan Project: neurodevelopmental outcomes and FASD in remote Aboriginal Australian children	University of Sydney and Telethon Kid's Institute, Perth, W Australia
	Claire McCormack	Prenatal alcohol consumption prior to awareness of pregnancy	NDARC, University of NSW, Sydney, Australia
16:00	Morning coffee and tea		
16:30	**SESSION 4:** Fetal Alcohol Spectrum Disorder - Selected Oral Presentations **CHAIR:** Prof Ed Riley (San Diego State University, USA)		
	Barbara Lucas	Paediatric soft neurological signs in FASD: population-based study in remote Australia	University of Sydney, Australia
	Heather Jones	Fetal Alcohol Spectrum Disorder educational resources for justice professionals	Telethon Kid's Institute, Perth, Western Australia
17:00	**SESSION 5:** Fetal Alcohol Spectrum Disorder - Policy and Legal Perspectives **CHAIR:** Dr Margaret Murray (NIAAA, USA)		
	Michael Thorn	Developing national approaches to address alcohol consumption in pregnancy and Fetal Alcohol Spectrum Disorder	Foundation for Alcohol Research and Education, Australia
	Margaret Murray	International initiatives in Fetal Alcohol Spectrum Disorder	National Institute on Alcohol Abuse and Alcoholism, MD, USA
	Judge Linda Chezem	Legal perspectives on Fetal Alcohol Spectrum Disorder	USA
	PANEL DISCUSSION – PANELLISTS: Denis Lamblin (Reunion, France); Sharman Stone (Australia)		
18:25	Presentation of Prizes - best oral and best poster presentations		
18:30 19:00	Conference Reception – Heritage Ballroom Pre-Function Area		

STREAM #2: BARNET COMBINED			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:15	Conference opening, Welcome		
08:30	**SESSION 6:** Psychostimulants **CHAIR:** Dr Jean Zwiller (France) and Prof Eliot Gardner (USA)		
	Ming Xu	DRD1, DRD3 and reconsolidation of cocaine memories in mouse self-administration model	University of Chicago, IL, USA
	Jean Zwiller	Cocaine self-administration and DNA methylation: a genome-wide study	Laboratoire de Neurosciences Cognitives, University of Strasbourg, France
	Eliot Gardner	Agonist replacement therapy for cocaine addiction – On the horizon?	National Institute on Drug Abuse, MD, USA
10:30	Morning tea and coffee		
11:00	**SESSION 7:** Infection and Addiction **CHAIR:** Dr Sulie Chang (USA) and Prof Dipak Sarkar (USA)		
	Mark Hutchinson	The "other brain": how knowing you are sick has implications for drug abuse liability	University of Adelaide, Australia
	Dipak Sarkar	Immune cells in the brain control alcohol programming effect on stress and addictive behaviors	Program of Endocrinology, Rutgers University, NJ USA
	Sulie Chang	NeuroHIV leading to the use of addictive substances	Seton Hall University, NJ, USA
13:00	Lunch and poster viewing		
14:00	**SESSION 8:** The Vulnerable Brain **CHAIR:** Prof Dan Lubman (Australia)		
	Nadia Solowij	Cannabinoid effects on human brain structure and function: injury, protection, recovery	University of Wollongong, Australia
	Kelly Clemens	Nicotine and the brain	University of NSW, Australia
	Raimondo Bruno	Acute and residual effects of stimulant substances among young adults	University of Tasmania, Australia
	Subhash Pandey	Adolescent alcohol exposure: persistent epigenetic & behavioral changes in adulthood	University of Illinois, IL, USA
	Dan Lubman	Substance use and brain development	Monash University, Australia
16:00	Morning coffee and tea		
16:30	**SESSION 9:** Current Controversies in Internet Use Disorders **CHAIR:** Prof Susumu Higuchi (Japan)		
	Wei Hao and Vladimir Poznyak	Position of behavioural addictions in ICD 11	Mental Health Institute, Central South University, China, and WHO, Geneva, Switzerland
	Marc Potenza	Neurodevelopmental features of Internet use and gaming problems	Yale University, CT, USA
	Chang Woo Han	Substance use disorder and internet addiction	Korea University, Ansan Hospital, Korea
	Susumu Higuchi	Clinical description and diagnostic guidelines	Kurihama Hospital, Japan
18:30 19:00	Conference Reception – Heritage Ballroom Pre-Function Area		

OUTLINE OF SCIENTIFIC PROGRAM

STREAM #1: HERITAGE BALLROOM			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 10:** Preventing Drug-Seeking and Relapse: 1 **CHAIR:** Prof Andrew Lawrence (Australia) and Dr Antonio Noronha (USA)		
	Antonio Noronha (Introduction)	Alcohol dependence: a chronic relapsing behavioral disorder	National Institute on Alcohol Abuse and Alcoholism, MD, USA
	George Koob	"Dark side" medications for treating addiction	National Institute on Alcohol Abuse and Alcoholism, MD, USA
	Andrew Holmes	Neural circuits in punished alcohol-seeking	National Institute on Alcohol Abuse and Alcoholism, MD, USA
10:30	Morning tea and coffee		
11:00	**SESSION 11:** Preventing Drug-Seeking and Relapse: 2 **CHAIR:** Prof Andrew Lawrence (Australia) and Dr Antonio Noronha (USA)		
	Gavan McNally	From lapse to relapse: environment and neural circuits for drug seeking reacquisition	University of NSW, Sydney, Australia
	Nick Gilpin	Traumatic stress, nociception and drinking: CRF signaling in the amygdala	LA State University Health Science Center New Orleans, USA
	Bernard Balleine	Neural bases of drug-induced changes in behavioural control	BMRI, University of Sydney, Australia
	Paul Klenowski	Circuits modulating alcohol drinking	Queensland University of Technology, Australia
13:00	Lunch and poster viewing		
14:00	**SESSION 12:** The Victims of Alcohol Misuse: Impacts on Indigenous Children **CHAIR:** Dr Richard Chenhall (Australia)		
	Marcia Langton	The victims of alcohol misuse	Australian Indigenous Studies, University of Melbourne, Australia
	Elizabeth Elliott	FASD research in remote Aboriginal Australia	University of Sydney, Sydney, Australia
	Robyn Doney	Visual-motor integration impairment and FASD: a population-based study of children in the Fitzroy Valley	School of Public Health, Curtin University, Western Australia
	Emily Fitzpatrick	Starting the conversation: seeking consent for research with indigenous populations	University of Sydney, Sydney, Australia
16:00	Afternoon tea and coffee with posters		
	SESSION 13: Comorbidity and Complications in Addiction **CHAIR:** Prof Toshikazu Saito (Japan) and Dr Dai-Jin Kim (Korea)		
	Hisatsugu Miyata	Alcoholism comorbidity with other substance dependence and behavioural addiction	Jikei University, Japan
	Dai-Jin Kim	Comorbidity of alcoholism with diabetes	Catholic University, Korea
	Toshikazu Saito	Comorbidity of alcoholism with depression	Sapporo Medical University, Hokujinkai, Japan
	Mitsuru Itoh	Neuroticism as a risk factor for alcohol use disorders in alcoholics with inactive ALDH2	Kurihama National Addiction Center, Japan
18:30	Poster viewing		
19:30	Conference Dinner Heritage Ballroom Pre-Function Area		

Time	Speaker
07:30	
08:30	**SESSION 14:** Genetics **CHAIR:** Dr Alfreda Stadlin
	Mostofa Jamal
	Asheeta Prasad
	Ihn-Geun Choi
10:30	
11:00	**SESSION 15:** Behavioural **CHAIR:** Prof Kazutaka Ikeda
	James Kasper
	Kazutaka Ikeda
	Susan Schenk
13:00	
14:00	**SESSION 16:** Free Oral Co **CHAIR:** Dr Snehasikta Swa
	Huixi Dong
	Ru-Band Lu
	In-Won Chung
	Snehasikta Swarnakar
	Satoko Mihara
16:00	
	SESSION 17: Free Oral Co **CHAIR:** Dr Jyotshna Kanun
	Ajeet Kaushik
	Frederico Pereira
	Jorge Campusano
	Peter Serrano
	Jyotshna Kanungo
18:30	
19:30	

STREAM #2: MEETING ROOM1

Topic	Affiliation
Breakfast and registration	
(Korea)	
Ethanol and acetaldehyde alter extracellular DA and 5HT in ALDH2-/- mouse striatum	Kagawa University, Japan
Chemogenetics of Nacc in alcohol seeking	University of NSW, Australia
Association of BRAP polymorphisms with alcohol dependence risk	Hallym University, Korea
Morning tea and coffee	
Sensitization (Japan) and Dr James Kasper (USA)	
A novel neuropeptide regulator of behavioural sensitization to cocaine	University of Texas, USA
GIRK in drug and alcohol dependence	Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
MDMA-induced behavioural sensitisation	Victoria University, Wellington, New Zealand
Lunch and poster viewing	
mmunications rnakar and Dr Syed Ali (USA)	
Co-morbid DSM-IV Axis I mental disorders in heroin and methamphetamine users in China	Mental Health Inst., 2nd Xiangya Hosp, Central South University, China
Opioid patients on methadone maintenance	National Cheng Kung University, Taiwan
EEG characteristics of alcohol dependent patients: 3-dimensional source localization	Dongguk University, Seoul, Korea
Tobacco & MMP 7 PMs in gastric cancer risk	IICB Kolkata, India
Internet use disorder in Japanese adolescents	Kurihama National Addiction Center, Japan
Afternoon tea and coffee with posters	
mmunications go (USA) and Dr Frederico Pereira (Portugal)	
Delivery of methanandamide across the blood-brain barrier	NanoMed, FL International University
Methamphetamine anhedonia & cortical energetics in mice	University of Coimbra, Portugal
5HT release & 4-MTA on olfactory responses	Pontificia Universidad Católica de Chile, Chile
Methamphetamine and long-term deficits in spatial learning	Hunter College, USA
Reversal of ketamine toxicity in zebrafish	National Center for Toxicological Research, USA
Poster viewing	
Conference Dinner Heritage Ballroom Pre-Function Area	

STREAM #3: MEETING ROOM 2

Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 18:** Substance Use and Relaxation (JSND Symposium) **CHAIR:** Profs Hisatsugu Miyata and Kohji Takada (Japan)		
	Hisatsugu Miyata	Can proper use of alcohol promote relaxation?	Jikei University School of Medicine, Japan
	Keun Ho Joe	Nicotine: beneficial for stress relief?	Dasarang Central Hospital, Korea
	Kohji Takada	Caffeine: addictive substance or lubricant?	Teikyo University, Japan
	Moritoshi Kido	Casino in Japan, to do or not to do?	Osaka University of Commerce, Japan
10:30	Morning tea and coffee		
11:00	**SESSION 19:** Early Career Psychiatrists Symposium **CHAIR:** Profs Ihn-Geun Choi (Korea) and Toshikazu Saito (Japan)		
	Tomohiro Shirasaka	Internet overuse: comorbidity of high school students in Japan	Sapporo Medical University, Sapporo, Japan
	Chia Chun Hung	Brain activity in ketamine abusers	Yang Ming University, Taiwan
	Woraphat Ratta-apha	Research in substance use disorders in a general hospital setting	Mahidol University, Thailand
	Masuo Tanaka	Prevention of alcohol use disorder in working persons with habitual drinking	Koryo Hospital Japan
	Tetsuji Cho	Earthquake reconstruction support in Japan	Mie Mental Care Centre
13:00	Lunch and poster viewing		
14:00	**SESSION 20:** Free Oral Communications **CHAIR:** Prof Ratna Sircar (USA) and Dr Hwei-Hsien Chen (Taiwan)		
	Hwei-Hsien Chen	Toluene enhancement of brain stimulation	National Health Research Institutes, Taiwan
	Santanu Banerjee	Morphine and HIV induced bile acid imbalance in NSG-BLT humanized mice	University of Minnesota, MN, USA
	Lauren Orio	Oleoylethanolamide prevents neuroimmune signaling after ethanol binge administration	Universidad Complutense de Madrid, Spain
	Ratna Sircar	GHB antagonists & amnesia in adolescent rats	City College, NY, USA
	Beverly Lyn-Cook	ABCB1 transporter in psychostimulant and nicotine-induced neurotoxicity	National Center for Toxicological Research, USA
16:00	Afternoon tea and coffee with posters		
16:30	**SESSION 21:** Fetal Alcohol Spectrum Disorder Oral Communications **CHAIR:** To be advised		
	Emily Dorey	Periconceptional alcohol exposure in the rat results in impaired cardiac and renal function in female offspring but not male offspring	University of Queensland, Brisbane, Australia
	Tracey Tsang	Behaviour problems in children with FASD in remote, predominantly Aboriginal communities	University of Sydney, Sydney, Australia
	Courtney Breen	Hospitalisations for alcohol use disorders in pregnancy	NDARC, University of NSW, Sydney, Australia
	Courtney Breen	Educational resources for primary care health professionals on alcohol and drug use in pregnancy	NDARC, University of NSW, Sydney, Australia
18:30	Poster viewing		
19:30	Conference Dinner Heritage Ballroom Pre-Function Area		

OUTLINE OF SCIENTIFIC PROGRAM

STREAM #1: MEETING ROOM 1			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 22:** The Impact of Addictive Disorders in Asia. 1. Alcohol **CHAIR:** To Be Advised		
	Soontaree Srikosai	Attitudes of Thai nurses toward alcohol-dependent patients	Rajanagarindra Institute, Thailand
	Sathiarany Vong	Alcohol misuse in Cambodia	MCH Ministry of Health, Cambodia
	Sung-Gon Kim	Culture and alcoholism	Pusan National University, Korea
10:30	Morning tea and coffee		
11:00	**SESSION 23:** The Impact of Addictive Disorders in Asia. 2. Illicit Drugs **CHAIR:** Prof John Saunders (Australia)		
	Roongnapa Kamplang and Sawitri Assanangkornchai	Estimating the size of IDU population and developing responses in Thailand	Prince of Songkla University and Health Innovation and Technology Assessment Programme, Thailand
	Sawitri Assanangkornchai and Li Lei	Methamphetamine use among IDUs and current harm reduction responses in a border area of Yunnan, China	Prince of Songkla University, Thailand and Yunnan Institute of Drug Abuse, China
	Civilaiz Wanaratwichit	Prevention of methamphetamine addiction by rural health workers	Naresuan University, Thailand
	Narongsak Noosorn	Drug addiction among hill tribe youth of lower Northern Thailand	Naresuan University, Phitsanulok, Thailand
13:00	Lunch and poster viewing		
14:00	FREE AFTERNOON		

STREAM #2: MEETING ROOM2			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 24:** Free Oral Communications **CHAIR:** Prof Glen Hanson		
	Brooke Schmeichel	Hypocretin neurotransmission mediates compulsive-like cocaine taking and seeking	National Institute on Drug Abuse, MD, USA
	Yuri Persidsky	CB2R agonists diminish inflammation and BBB injury in HIV infection and alcohol use	Temple University School of Medicine, USA
	Mohan Sopori	Airway epithelial cells in lung diseases	Lovelace Research Institute, USA
10:30	Morning tea and coffee		
11:00	**SESSION 25:** Free Oral Communications **CHAIR:** To Be Advised		
	Valentina Bashkatova	Effect of nicotine on the metabolism and locomotor activity of rats	PK Anokhin Research Institute, Russia
	Johnny He	HIV, HCV and alcohol: Role of HIV-1 Nef	University of Texas Health Science Center, TX, USA
	Emmanuel Onaivi	Endocannabinoid system alterations in an animal model of autism spectrum disorders	William Paterson University, NJ, USA
	Kiyofumi Yamada	The insula controls decision-making in healthy and methamphetamine-treated rats	Nagoya University, Japan
13:00	Lunch and poster viewing		
14:00	FREE AFTERNOON		

OUTLINE OF SCIENTIFIC PROGRAM

STREAM #1: HERITAGE BALLROOM			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 26:** The Nature and Diagnosis of Addictive Disorders **CHAIR:** Prof John Saunders		
	Vladimir Poznyak	ICD 11: overall approach and current status	World Health Organization, Geneva, Switzerland
	Marc Potenza	Gambling as an addiction	Yale University, CT, USA
	John Saunders	ICD 11: How do we describe and define substance & other addictive disorders?	University of Sydney and University of Queensland, Australia
	Sawitri Assanangkornchai	ICD 11: how are substance disorders understood in different cultures?	Prince of Songkla University, Thailand
	Ben Teoh	What do clinicians need from a diagnostic system?	South Pacific Private Hospital, Sydney, Australia
10:30	Morning tea and coffee		
11:00	**SESSION 27:** Translational Research: Treatment of Alcohol Misuse **CHAIR:** Prof Barbara Mason (USA)		
	Leandro Vendruscolo	Dysregulation of glucocorticoid systems in alcohol dependence	National Institute on Drug Abuse, MD, USA
	Barbara Mason	Translational research on mifepristone: prospects for the treatment of alcohol dependence	The Scripps Institute, CA, USA
	Paul Haber	Update on alcohol pharmacotherapy	University of Sydney, Sydney, Australia
	Friedbert Weiss	Pharmacotherapies for relapse prevention	The Scripps Institute, CA, USA
	Carl Lin	Increased human DAT gene activity spurs alcohol	McLean Hospital, MA, USA
10:30	Lunch with posters		
14:00	**SESSION 28:** Cannabis and Medicinal Cannabinoids **CHAIR:** Prof Eliot Gardner and Prof Emmanuel Onaivi (USA)		
	Emmanuel Onaivi	THC pharmacotherapy & potential treatments	WM Paterson University, NJ, USA
	Iain McGregor	Development of medicinal cannabinoids	University of Sydney, Sydney, Australia
	Alex Wodak	Research on medicinal cannabis: practical steps and political influences	St. Vincent's Hospital, Sydney, Australia
16:00	Afternoon tea and coffee		
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		

STREAM #2: BARNET COMBINED			
Time	Speaker	Topic	Affiliation
07:30	Breakfast and registration		
08:30	**SESSION 29:** Anæsthetics, Psychostimulants, and Opiates **CHAIR:** Prof Merle Paule and Dr Shilpa Buch (USA)		
	Merle Paule	Anæsthetics in pædiatric populations	National Center for Toxicological Research, AR, USA
	Glen Hanson	Broadening the dimensions methamphetamine preclinical studies: links with Parkinson's disease	University of Utah, UT, USA
	Cheng Wang	Sevoflurane-induced neuronal damage and its potential biomarkers	National Center for Toxicological Research, AR, USA
	Shilpa Buch	Cocaine mediates microglial activation via down-regulation of microRNA 124	University of Nebraska, USA
	Sabita Roy	Morphine induces distinct gut microbiome signatures via the TLR2 pathway	University of Minnesota, USA
10:30	Morning tea and coffee		
11:00	**SESSION 30:** Pharmacology and Toxicology **CHAIR:** TBA		
	Jason White	Wastewater analysis as a tool in monitoring drug use	University of South Australia, Adelaide, SA, Australia
	Nadine Ezard	The case for incorporating drug checking into Australia's drug trend monitoring systems	St. Vincent's Hospital, Sydney, Australia
	Nadine Ezard and Robin Butterfield	Casualties of an unknown substance in an inner Sydney hospital	St. Vincent's Hospital, Sydney, Australia
	Monica Barratt	Improving the monitoring on new psychoactive substances in Australia	St. Vincent's Hospital, Sydney, Australia
10:30	Lunch with posters		
14:00	IDARS Panel Discussion: 14.00–16:00 [Panel members TBA]		
16:00	Afternoon tea and coffee		
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		

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ORAL ABSTRACTS

(IN ORDER OF PROGRAM)

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[1]

[1]*National 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[1]

[1]*San 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 place 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[1,2]

[1]*University of Sydney, Camperdown, Australia,* [2]*Sydney 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 Teopaco[2], Elvira Balinas[1]

[1]*Angeles University Foundation, Philippines,* [2]*Colegio 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 behaving appropriately. These difficulties are a reflection of limitations in memory, problem solving, attention, comprehension, perceptual ability, and adaptive, behavioural and emotional functioning. On the other hand, respondents of the study showed abilities in solving non-verbal as compared to verbal problems. In 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 Bower[1]

[1]*Telethon 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.

Design and Methods: 1. epidemiology and surveillance of FASD using routinely collected data from the WA Register of Developmental Anomalies and data linkage; 2. Prevention and diagnosis – mass media, health promotion strategies and workforce development, and consensus process; 3. Indigenous communities – population surveys; 4. Juvenile justice – screening and diagnosis and workforce development.

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[1]

[1]*NTI 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 infants and children noted to be affected by the prenatal exposure to alcohol. 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 undertaken 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 effected 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.

ORAL ABSTRACTS

Endocrine, metabolic and immune disorders in fetal-alcohol-exposed adult animals

Prof Dipak Sarkar[1]

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

A number of studies have shown that alcohol exposure during pregnancy results in a set of birth defects called fetal alcohol spectrum disorders (FASDs), which 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 show 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[1]

[1]*University 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, 6g/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[1]

[1]*NOFASD Australia, Wynyard, 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 Zanfirache[1], Dr Carlie Cullen[1], Associate Professor Karen Moritz[1]

[1]*University 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 epigenome 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 of epigenetic modifiers 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[1], Prof Jane Latimer[4], Prof Elizabeth Elliott[2,3,4]

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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, 85% 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 McCormack[1,2], Dr Delyse Hutchinson[1,2,3,4,5], Dr Lucy Burns[1], Dr Judy Wilson[1], Prof Elizabeth Elliott[6], Prof Steve Allsop[7], Prof Jake Najman[8], Dr Craig Olsson[4], Dr Sue Jacobs[9], Prof Richard Mattick[1]

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Australia, [7]National Drug Research Institute, Curtin University, Perth, Australia, [8]Queensland Alcohol & Drug Research Education Centre, University of Queensland, Brisbane, Australia, [9]Department of Obstetrics, RPA Hospital, Sydney, Australia

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 Lucas[1,2,3,4], Ms Jane Latimer[2], Mr James Fitzpatrick[1,2,5], Ms Robyn Doney[6], Ms Rochelle Watkins[5], Ms Tracey Tsang[1,2], Ms Tracy Jirikowic[7], Ms Heather Carmichael Olson[8], Ms June Oscar[9,10], Ms Maureen Carter[11], Prof Elizabeth Elliott[1,2,12]

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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=0.045). 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 Jones[1], Associate Professor Raewyn Mutch[1]

[1]Telethon 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 uninformed 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.

ORAL ABSTRACTS continued

Dopamine D1 and D3 receptors mediate reconsolidation of cocaine memories in mouse models of drug self-administration

Prof Ming Xu[1], Dr Yijin Yan[2], Dr Amy Newman[3]

[1]The University of Chicago, Chicago, United States, [2]The University of Chicago, Chicago, United States, [3]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 Zwiller[1], Dr Mathieu Fonteneau[1], Dominique Filliol[1], Dr Katia Befort[1], Dr Patrick Anglard[1], Dr Pascal Romieu[1]

[1]CNRS 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 methyl-transferase 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 9% 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 methylome 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 Gardner[1], Dr Rui Song[2], Dr Xia Li[1], Dr Guan-Yi Lu[2], Dr Xiao-Qing Peng[1], Dr Guo-Ha Bi[1], Dr Hong-Ju Yang[1], Dr Yi He[1], Dr Hai-Ying Zhang[1], Dr Jin Li[2], Dr Mark Froimowitz[3], Dr Zheng-Xiong Xi[1]

[1]National Institute on Drug Abuse, Baltimore, United States, [2]Beijing Institute of Pharmacology and Toxicology, Beijing, China, [3]Massachusetts 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-naive 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 Hutchinson[1]

[1]University 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 neurokine 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 Sarkar[1]

[1]The 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 (BEP) neurons. We found that alcohol exposures stimulate microglia to produce inflammatory cytokines including TNF-α that activates the NF-κB 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).

States HIV-1 infection, neuroHIV, and the use of addictive substances

Dr Sulie Chang[1,2]

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Addiction is a brain disease involving changes in the reward circuitry following chronic or repeated use of substances which activate the reward circuitry. Despite the ability of current combination anti-retroviral therapy (cART) to limit the progression of HIV-1 to AIDS, HIV-positive individuals continue to experience various forms of HIV-associated neurological disorders resulting from neuroHIV. According to the United Nations Program on HIV/AIDS, approximately 16 million people inject drugs and, among them, about 3 million are living with HIV worldwide. Epidemiological studies show that the percentage of HIV-infected patients who use addictive substances including morphine, methamphetamine and alcohol, is greater than that in the general population in the US. Our working hypothesis is that NeuroHIV may lead to use/abuse of, as well as dependence on, addictive substances in HIV-positive individuals. Among several rodent models that have been generated to study HIV infection, the HIV-1 transgenic (HIV-1Tg) rat stands out as a reliable model of neuroHIV because it mimics the conditions of HIV-infected patients on cART. Research using this model supports our hypothesis that the presence of HIV-1 viral proteins in the central nervous system increases the sensitivity and susceptibility of HIV-positive individuals to substance abuse (partially supported by DA036175, AA023172).

Cannabinoid effects on human brain structure, function and neurochemistry: injury, protection and recovery

A/Prof Nadia Solowij[1], Dr Samantha Broyd[1], Dr Hendrika van Hell[1], Dr Valentina Lorenzetti[2], Dr Chao Suo[2], Prof Dan Lubman[2,3], Prof Murat Yücel[2]

[1]University of Wollongong, Wollongong, Australia, [2]Monash University, Melbourne, Australia, [3]Turning 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 (eg. 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 Clemens[1], Ms Belinda Lay[1], Dr Nathan Holmes[1]

[1]University of New South Wales, Sydney, 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 Bruno[1], Dr Amy Peacock[1]

[1]University 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 high-caffeine 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 (V1) but not those involving prestriate cortex (V2); and impairing motion processing on tasks tapping both V1 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 Pandey[1]

[1]Center 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 post-natal 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. Neuropeptide 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 NPY and BDNF exon IV gene promoters in the amygdala of AIE adult rats most likely due to an increase in DNMT and HDAC function, and a decrease in LSD1 and LSD1+8a expression. Treatment with DNMT or HDAC inhibitors attenuated AIE-induced anxiety-like and alcohol-drinking behaviors in adulthood, and also relaxed the chromatin of NPY and BDNF genes in the amygdala. These results suggest that AIE produces an enduring dysregulation in epigenetic processes in the amygdala which may contribute to anxiety and alcoholism in adulthood.

Intervening early to reduce developmentally harmful substance use among youth populations

Prof Dan Lubman[1,2]

[1]Turning Point, Melbourne, Australia, [2]Monash 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 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 11th revision 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 "behavioural 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 "behavioural 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[1]

[1]*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 or 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[2]

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

** This abstract is one of 4 themes symposium titled "Comorbidity or Complication in Addiction". **

Now there has been many studies about shared common vulnerable factors between internet addiction (IA) and substance use disorder (SUD) in temperament, psychopathology, psychosocial aspect and brain region. Recently in many countries, large cross-sectional online self-report surveys by adolescent students were conducted to analyze comorbidity and causal relation between IA and SUD, containing two 1-year follow up studies(Sun, 2012; Chang 2014). Major finding from these studies showed that severity of IA was correlated with the severity of substance use, and IA was preceded by substance abuse, especially smoking may predict a high risk for IA(Lee, 2013; Chang 2014; Rucker, 2015). Reversely IA may be early predictor of adolescent SUD. One year follow-up study (Sun,2012) showed that the relationship between IA and substance use was not consistently positive. The prevalence of alcohol use was not linearly correlated with the severity of IA (Choi, 2009). The different correlation IA risk may due to different pharmacological action. Alcohol is sedative, but nicotine is stimulant. Furthermore Internet use and substance use may substitute effect for each other. Actually in Korea, adolescent's inhalant abuse was social hot issue in 1990s, but from 2000s instead of inhalation abuser, rapidly increasing Internet addictor became social hot issue.

Clinical description and diagnostic guidelines for Internet use disorders

Susumu Higuchi, Hideki Nakayama, Hiroshi Sakuma, Satoko Mihara

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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, SNSs, 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[1]

[1]*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 binge-intoxication stage includes enhanced habit (stimulus- response) activity in involving the neurocircuitry 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-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 punished suppression of reward-seeking. Collectively, the current findings add to growing body of evidence demonstrating that chronic exposure to EtOH fosters resistance to punished EtOH-seeking in association with adaptations in cortical glutamatergic transmission.

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

Prof Gavan McNally[1]

[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.

Traumatic Stress Increases Nociception & Alcohol Drinking: A Role for Corticotropin-Releasing Factor (CRF) Signaling in the Central Amygdala (CeA)

Assistant Professor Nick Gilpin[1]

[1]*Louisiana State University Health Science Center, Department of Physiology, United States*

Some (but not all) humans exposed to traumatic stress develop post-traumatic stress disorder (PTSD), which is defined by high avoidance of trauma-related stimuli, hyperarousal, and negative affect, and which is highly co-morbid with Alcohol Use Disorder (AUD). Our lab utilizes a stress model in which rats are indexed for avoidance of a predator odor-paired context, and divided into "Avoiders" (i.e., high stress reactivity) and "Non-Avoiders" (i.e., low stress reactivity). Avoiders exhibit persistent increases in alcohol drinking, and systemic antagonism of corticotropin-releasing factor (CRF)-1 receptors (CRFR1s) reduces alcohol drinking in stressed rats. Because CRF signaling in central amygdala (CeA) has been implicated in escalated alcohol drinking and negative affect in alcohol-dependent animals, we measured predator odor stress effects on CRF transcript, CRF peptide content, CRF cell counts, and steroid co-activator-1 (SRC-1), a regulator of CRF transcription, in the CeA of Avoiders, Non-Avoiders, and unstressed Controls. We also used pharmacological and optogenetics approaches to test the role of CeA CRFR1 signaling in stress-induced hyperalgesia, and we are conducting similar experiments to probe the role of CeA CRFR1 signaling in stress-induced alcohol drinking. Relative to Non-Avoiders and unstressed controls, Avoider rats have more total CRF peptide content in CeA, and intra-CeA CRF infusion produces conditioned avoidance in naïve rats. Avoiders do not exhibit higher CRF transcript or cell counts or SRC-1 in CeA, suggesting that the higher CRF peptide content may not be locally produced. Avoiders exhibit thermal hyperalgesia that is reversed by systemic and intra-CeA antagonism of CRFR1s. The systemic CRFR1 antagonist rescue of stress-induced thermal hyperalgesia is blocked by intra-CeA tetrodotoxin (TTX) infusion. Furthermore, intra-CeA TTX and CeA neuronal inactivation with AAV5/Syn1-eNpHR3.0-eYFP each produce thermal hyperalgesia in naïve rats. Finally, intra-CeA CRF produces thermal hyperalgesia in unstressed rats, and this effect is blocked by antagonism of CRFR1s and GABA-A receptors in CeA. These results suggest that CRFR1 signaling in CeA may be a promising therapeutic target for treatment of co-morbid traumatic stress and alcohol use disorders. This work was supported by NIH grants AA018400 and AA023305.

The neural bases of drug-induced changes in behavioral control

Prof Bernard Balleine[1]

[1]*Brain & Mind Research Institute, University of Sydney, Sydney, Australia*

The smooth integration of cognitive and emotional processes is necessary for everyday decisions. Dysfunction of this integrative capacity accompanies many major psychiatric conditions and neurodegenerative disorders. It is also powerfully affected by exposure to various drugs in a manner that precipitates the poor decision-making surrounding the drug seeking actions associated with addiction. Here I will discuss recent evidence on the neural bases of cognitive-emotional integration in reward-related actions associated with normal decision-making. I will then outline how we think this neural system is affected by drug exposure, particularly with regard to the changes in behavioural control made manifest in maladaptive decisions and consider what implications these views have for treatment. Although it has recently been suggested that drug seeking reflects a form of habit and depends on enhancements in the circuitry that controls habitual actions, our current evidence suggests that it is better characterized as a deficit in countervailing processes associated with goal-directed action through which habitual actions are regulated.

Circuits modulating alcohol drinking

Dr Paul Klenowski

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.

ORAL ABSTRACTS continued

The victims of alcohol misuse

Marcia Langton

University of Melbourne

Abstract not supplied

FASD research in remote Aboriginal Australia

Prof Elizabeth Elliott[1,2]

[1]University of Sydney, Camperdown, Australia, [2]Sydney 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. Woman 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 Doney[1], Ms Barbara R Lucas[2,3,4,5], Dr Rochelle E Watkins[6], Dr Tracey W Tsang[2,3], Dr Kay Sauer[1,7], Professor Peter Howat[1,7], Professor Jane Latimer[3], Dr James P Fitzpatrick[2,3,6], Ms June Oscar[8,9], Ms Maureen Carter10, Professor Elizabeth J Elliott[2,3,11]

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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 (1.9%), but the prevalence of moderate VMI impairment was very high (47.2%). 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 Fitzpatrick[1,2], Associate Professor Alexandra Martiniuk[3,4], Ms Heather D'Antoine[5], AO June Oscar[6], Ms Maureen Carter[7], Professor Elizabeth Elliott[1,2,3,4]

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Introduction: Methods of obtaining consent for research from Indigenous communities are rarely documented. A literature search revealed only one study evaluating consent for Indigenous research. Other research projects use interpreters, voice-recording, videos, flipcharts and "plain-language" forms to seek consent but do not evaluate the process.

Methods: 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 Miyata[1]

[1]Department 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 systems 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 Kim[1]

[1]Catholic 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 evaluated. The serum IGF-I and BDNF levels were significantly lower and the serum GH levels were significantly higher in the O-E group than in L-C group. Diabetic model show lower IGF-1 level and higher anxiety-like behavior in chronic alcohol group.

In human study, we conducted in alcohol dependence subjects. All the subjects were divided into two groups according to Oral Glucose Tolerance Test (OGTT); diabetic and non-diabetic. The cognitive function was then

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 Toshikazu Saito[1]

[1]*Miki 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 group 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 Alcoholics with Inactive ALDH2 Study (AIA Study)

Dr Mitsuru Itoh[1], Ms Tomoko Yonemoto[1], Ms Satoko Mihara[1], Dr Tomomi Toyama[1], Dr Yosuke Yumoto[1], Dr Chie Iwahara[1], Dr Tsuyoshi Takimura[1], Dr Atsushi Yoshimura[1], Dr Hiroshi Sakuma[1], Dr Hideki Nakayama[1], Dr Yasunobu Komoto[1], Dr Hitoshi Maesato[1], Dr Mitsuru Kimura[1], Dr Sachio Matsushita[1], Dr Susumu Higuchi[1]

[1]*Natinal Hospital Organization Kurihama 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 (AIAs) 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 AIAs (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 AIAs, 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 Jamal[1], Dr Kiyoshi Ameno[1], Ms Naoko Tanaka[1], Dr Asuka Ito[1], Ms Ayaka Takakura[1], Dr Hiroshi Kinoshita[1]

[1]*Kagawa 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 Prasad[1], Professor Gavan McNally

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The nucleus accumbens shell (AcbSh), located in the ventral striatum, and is a key brain region for drug seeking behaviour. We transduced 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 Gq-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 Choi[1], Prof Jee Wook Kim[1]

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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 ($p = 1.29 \times 10\text{-}16$, OR = 0.19). Further association analysis in normal controls showed that BRAP rs3782886 was strongly associated with overall AUDIT score ($p = 1.40 \times 10\text{-}24$, $pcorr = 6.30 \times 10\text{-}24$ 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

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ORAL ABSTRACTS continued

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 (0.3 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

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G-protein activated inwardly rectifying potassium (GIRK, Kir3) channel is one of the effectors in signal pathways from Gi/o 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 5HT 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 criterion 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 dopamine 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

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Aim: This study compared current prevelence (CP) and lifetime prevelence (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 epidemiological survey 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. Compared with MA users, heroin 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.46.9%, 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

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Memantine and dextromethorphan might possess anti-inflammatory and neuroprotection effect. In a randomized, double-blind, controlled 12-week study, we investigated whether using low dose of memantine or dextromethorphan to reduced cytokine levels and treat opioid dependent patients with methadone maintenance treatment (MMT).Patients were randomly assigned to a group 1: DM60 (dextromethorphan [60 mg/day]) (n = 65), DM120 (dextromethorphan [120 mg/day]) (n = 65), or Placebo (n = 66). 2: 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)-a, C-reactive protein (CRP), interleukin (IL)-6, IL-8, transforming growth factor (TGF)-b1, and brain-derived neurotrophic factor (BDNF) levels were examined during weeks 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-a 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-a and significantly higher TGF-b1 levels. We provide evidence of the benefit of dextromethorphan and memantine in opioid dependent patients undergoing MMT.

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

Prof In-Won Chung[1], Dr Sandchul Seo[2], Dr Sungjin Im[3], Dr Sang-Gu Lee[3], Professor Chul-Jin Shin[2]

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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 alcohol 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, beta1, beta2, and beta3 bands in alcohol dependent patients compared to normal controls. The voxels showing the maximum significance were in the left transverse temporal, left superior temporal, left anterior cingulate, and left fusiform gyrus in alpha, beta1, beta2, and beta3 bands respectively.

These results suggest that chronic alcohol intake may cause neurophysiological changes in cerebral activity. Therefore, the measuring of EEG can be helpful in understanding the pathophysiology of cognitive impairments in alcohol dependence.

Additive effect of tobacco over promoter polymorphism of matrix metalloprotease7 in gastric cancer risk

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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 MMP7–181 A/G polymorphism and gastric cancer risk, and dependence on age, sex as well as tobacco addiction. Our results suggest that MMP7–181GG 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 (17.3%) 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 GG 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

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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 Methannadamide across blood brain barrier to block cannabinoid induced effects in HIV patients

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Abstract not supplied

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

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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.

Herein, 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 Campusano[1], Mr Sergio Hidalgo[1], Ms Daniela Molina[1], Dr Angelica Fierro[1], Dr Patricio Iturriaga-Vasquez[2], Dr Rodrigo Varas[3], Mr Nicolás Fuenzalida-Uribe[1]

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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 aminergic 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.

ORAL ABSTRACTS continued

Acute methamphetamine produces long-term deficits in spatial learning and memory retention involving decreased PKMζ and increased COX-2 and ubiquinated protein levels in the hippocampus

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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 D1 receptor, and inflammatory markers, cycloxygenase-2 (COX-2), microglia (IBA-1), including ubiquinated 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 (30 mg/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 D1 receptor while increasing COX-2, IBA-1 (a marker for microglia) and levels of ubiquinated 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

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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 channels and also generate ATP. We tested whether in 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[1]

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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[1], Dr Jeong Seok Seo[2]

[1]*Dasarang Central Hospital, Euiwang, South Korea,* [2]*Kunkuk 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. These mentions look like plausible excuses for continuing of 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 percept 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[1]

[1]*Teikyo 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 caffeine-containing materials are clearly reinforcing, by definition of the term. Caffeine itself exhibits physiologic effects (e.g. increasing 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[1]

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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

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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 as 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

problematic Internet use was estimated at 2.6% in 2008 but within five years the incidence had increased by a factor of 1.5. A variety of psychiatric disorders associate with problematic Internet use. ADHD, depression, social anxiety, and hostility were all reported associating with Problematic Internet use.

Social withdrawal (hikikomori) has increasingly become a problem in Japan. The Japanese Ministry of Health, Labour and Welfare defines hikikomori as people who refuse to leave their house and, thus, isolate themselves from society in their homes for a period exceeding six months and it has been hypothesized to be related to problematic internet use. Particularly amongst students, problematic Internet use may be a major factor of social withdrawal. We conducted a survey of Internet addiction and social withdrawal among students to examine this hypothesis.

Brain imaging study on ketamine abusers

Dr ChiaChun Hung[1], Prof Tony Szu-Hsien Lee[3], Prof Jeng-Ren Duuan[2], Prof Ching-Po Lin[1]

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The number of Ketamine use among young adults increases rapidly in many parts of the world including Taiwan. Limited attention has been paid to drug use pattern, risk behavior, depression, psychosis, cognitive execution and behavioral control resulted from ketamine use. Despite the prevalent abuse problem of ketamine currently, however, there are only few neuroimaging studies on possible damages induced by ketamine on the brain. A recent study reported brain damages on chronic ketamine abusers by MRI study and showed atrophy over several regions. Also white matter changes were found in bilateral frontal and left temporo-parietal cortices. Another study was conducted on healthy subjects received ketamine challenge and revealed ketamine decreases functional connectivity of default mode network.

Although some progress in identifying changes in behavior and brain function following heavy ketamine use, our current understanding of the effects of long term ketamine on the brain is poor. Specifically, we plan to conduct a two-year study with 30 ketamine users being recruited. We will characterize behavioral performance, changes of brain structural and activities in ketamine users, as compared the healthy controls. The potential findings will extend the literature in addiction neuroscience and provide critical information facilitating research and treatment of ketamine misuse.

From the clinical approach to biological research; Development of research in substance use disorders in general hospital setting

Dr Woraphat Ratta-Apha[1], Dr Nantawat Sitdhiraksa[1], Sontuss Bussaratid[1], Thienchai Ngamthipwatthana[1]

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Substance-related problems are common in general medical settings. They are implicated in various physical diseases, injuries and trauma. Patients with substance-related problems also exhibited co-morbidity with other mental disorders. Patients cannot avoid visiting medical units due to their physical sufferings but can deny consulting psychiatrists regarding their substance use problems. Many of them believe that these issues are not their primary problems. Therefore, set up an intra-hospital consultation-liaison system between psychiatric and other departments will care this group of patients comprehensively. This emphasizes the need for the development of services and research focusing on substance use disorders.

The psychiatric and special clinics for substance use problems of the psychiatric department has set up research teams and performed various studies, including analysis of services provided, prevalence survey studies, and validation of instruments.

In my presentation, I would like to highlight the progress of research projects related to substance use disorders that have been carried out in our hospital. We also aim to develop biological research in addiction, including genetic studies with various inter-departmental collaboration. Furthermore, we hope that we can apply the knowledge obtained from these studies to continuously improve our services.

The prevention of alcohol use disorder among working persons with habitual drinking "Young Psychiatrist Symposium".

Dr Masuo Tanaka[1,2], Prof Junichiro Ota[3], Ms Etsuko Doki[3], Ms Norie Kishi[3], Dr Nozomu Hashimoto[4], Dr Takashi Sunami[4], Prof Shigeo Horii[2]

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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-administrated 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 Cho[1,2], Dr Masuo Tanaka[3], Dr Kazuki Kuno[1], Dr Seiichiro Obata[1], Dr Takashi Egami[1], Dr Takahiro Fukuda[4], Dr Keizo Hara[5], Dr Sachio Matsushita[6], Dr Masayuki Morikawa[1,2], Prof Toshifumi Kishimoto[2]

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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 distressed 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 scare 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

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ORAL ABSTRACTS continued

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Toluene, a widely used and commonly abused organic solvent, has been reported to negatively modulate N-methyl-D-aspartate receptors (NMDARs) and causes a variety of behavioral disturbances in both humans and animals similar to the behavioral signs of noncompetitive NMDA receptor antagonists, such as phencyclidine (PCP) and ketamine. The glutamatergic modulating agents shown to reverse the behavioral disturbances induced by PCP or ketamine were evaluated in toluene-induced facilitate brain reward function and behavioral effects. Male NMRI mice were pretreated with various doses of glutamatergic modulating agents including sarcosine (glycine transporter inhibitor), sodium benzoate (D-amino acid oxidase inhibitor), LY379268 (mGluR2 agonist), or N-acetylcysteine (glutamate-cystine antiporter activator), prior to toluene treatment and assessed for intracranial self-stimulation (ICSS) thresholds, rotarod test, novel object recognition task, and social interaction test. Sodium benzoate, LY379268, and N-acetylcysteine, but not sarcosine, dose dependently reversed the toluene-induced lowering of ICSS thresholds. All these agents blocked the toluene-induced impairment in novel object recognition task and social withdrawal, but only attenuated the toluene-induced motor incoordination in the rotarod test. These findings suggest that modulation of synaptic NMDARs and glutamate release might be effective treatment approaches for toluene addiction and prevention of toluene intoxication caused by occupational or intentional exposure.

Morphine and HIV induced bile acid imbalance leads to gut barrier compromise and systemic inflammation in NSG-BLT humanized mice.

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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.

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

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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/neuroprotectant properties of the satiety factor oleoylethanolamide (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-1beta (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. Elevations 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

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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

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Methamphetamine (METH) and 3,4-methylene dioxymethamphetamine (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 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

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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 +/-12.5%v/v ethanol from four days before to four days after mating. Kidney function (24hr metabolic cage) along with heart function and blood pressure (echocardiography/radiotelemetry) were examined in adulthood (12-18months). 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 hypertension.

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

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

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Behaviour was investigated in 108 predominantly Aboriginal children (aged 7.4-9.6 years) living in remote Australia, and comparisons made between those with (n=21) and without (n=87) a diagnosis of 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 73% 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

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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 disorder (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.

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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

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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

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.

ORAL ABSTRACTS continued

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

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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 towards alcohol-dependent patients, but 537 nurses working in general hospitals and 406 nurses working in community hospitals have relatively negative attitudes towards 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

Sathiarany Vong, MCH Ministry of Health, Cambodia

Abstract not supplied

Culture & Alcoholism

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When people got 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 drinker, 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.

Estimating the size of the IDU population, and developing responses

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Injection drug use remains a health concern worldwide as well as in Thailand. The number of IDUS based on the network scale-up method was approximately 40,300 in Thailand. To encounter HIVAIDS related problems among these IDUs, harm reduction approaches have been initiated as a research project in 1990 in Bangkok; findings supported the benefits of the harm reduction strategies reported internationally. After that, under the support of the Global Fund Round 8, harm reduction work has been actively implemented in some areas, mainly by civil society organisations, including needle and syringe exchange program (NSP), condom programme and targeted information and education. In 2008-2009, the Office of the Narcotics Control Board appointed a workgroup, composed of all stakeholders, including public health workers, police, solicitors, IDU representatives and academics to develop a harm reduction policy. In 2014, the Government ordered a harm reduction guideline for IDUs and set 19 pilot testing sites across the country, involving IDUs, their family and relatives and community. A set of 10 interventions, including methadone maintenance therapy (MMT), needle and syringe exchange program (NSP), counselling and testing for HIV, HBV, HCV, treatment and prevention for tuberculosis (TB) and sexually transmitted infections (STIs), condom program and targeted information and education were mandated in the pilot areas. An evaluation study in Songkhla, one of the pilot provinces in southern Thailand found that 68% of IDUs in the area received sterile needles and syringe from the NGO outreach workers in the past 6 months. Over one quarter (26.1%) reported not having any test of HIV, HBV or HCV in the past 12 month while 35.7% reported having been tested for all three viruses. Major difficulties in accessing to MMT included travelling problems, opening hours of the clinic and cost of the travel to the clinic. In conclusion, despite tremendous efforts in promoting harm reduction strategies for IDUs in Thailand, there is still room to improve the services and utilisation of the services.

METH use by IDUs and current harm reduction responses in a border area of China

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Amphetamine-type stimulants (ATS) have become one of the most widely used illicit substances in the world and continues to pose significant health and social challenges. ATS users are at extremely high risk for transmission of HIV and STDs, both due to potential needles and syringes sharing if it gets injected, and high risky sexual behaviours associated with drug use because of its pharmacological action.

The East and South-East Asia regions have emerged as a global hub for methamphetamine production and trafficking, along with rising ATS use problem over the past decade, thereafter are home to 50-80% of the estimated total number of ATS users in the whole Asia. This study aimed to identify the prevalence, patterns and context of ATS use among current IDUs in Ruilli, a city located in the border region between China and Myanmar. A total of 370 IDUs who were Chinese, had injected drugs within the past six months and aged at least 18 years were recruited in a cross-sectional survey using respondent-driven sampling (RDS) in 2012.

Results reveal that methamphetamine pill was the most commonly used ATS and smoking/snorting were the only routes of administration reported by our participants. IDUs who had cross-border activities, including purchasing drugs and visiting family/friends, doing business or odd jobs in Myanmar, were more likely to use methamphetamine in the past six months. Not only the IDUs but also the public community perceived that methamphetamine use was less harmful and more acceptable than using heroin. There were no significant associations found between current methamphetamine use with sexual risk behaviours and with HIV infection status, however methamphetamine was used to increase libido and facilitate sexual encounters and having sexual intercourse while being high on drugs was common practice. This highlights the role of methamphetamine in sexual contexts which increases the risk of sexually transmitted diseases among this primary heroin injecting population. Current prevention and harm reduction approaches will be described.

The prevention of methamphetamine addiction by health workers in rural Thailand

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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 Sawakhalok District, Thailand. Data were collected through in-depth interviews, direct observation and document analysis. Thematic analysis was used data analysis.

Results: Roles of 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 the cases 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: Roles of 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

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The objective of this study were 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 smokes and10.9 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 substance 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. The youths 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

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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-334867, 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-334867 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-334867 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

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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 neurodegeneration 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 monocytes 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 monocytes 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

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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 CXCR4, CD4, and α7-nAChRs, and HIV-1 gp120 induces mucus formation in these cells that is blocked by CXCR4 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-gp20 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

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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

of rats treated with nicotine at dose of 1 mg/kg was substantially increased during all 24 hours. It should be noted that parameters of metabolism and locomotor activity might altered in opposite directions, depending on the dose of nicotine and the time after its administration. Obtained results need to be considered in the development of new approaches to treatment of tobacco smoking.

Interplay among HIV, HCV and alcohol: Role of HIV-1 Nef protein

Dr Johnny He[1]

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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-1/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 Onaivi[1], Dr Joao Escosteguy-Neto[2], Professor Jair Guilherme Santos-Junior[2], Ms Susan Sgro[1], Mr Norman Schanz[1], Mr Eugene Dennis[1], Ms Larissa Pamen[1], Professor Claire Leonard[1], Mr Kevin Penkoski[1], Ms Monika Chung[1], Ms Ndeah Terry[1], Ms Jasmine Wood[1], Ms Sneha Tammareddy[1], Dr Zhicheng Lin[3], Dr Joseph Morgan[1], Dr Frank Hall[4], Dr Georgianna Gould[5], Dr Balapal Basavarajappa[6], Dr George Uhl[7], Dr Syed Ali[8], Dr Hiroki Ishiguro[9], Dr Qing-Rong Liu[1]

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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/6J mice and to measure levels of anandamide and 2-arachidonlyl 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 CB1Rs did not differ between BTBR and C57BL/6J 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 BTBR mice 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

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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 activation 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.

FRIDAY 22 AUGUST

ICD 11: overall approach and current status

Dr Vladimir Poznyak[1]

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The World Health Organization (WHO) is currently working on the development of the eleventh revision of International Classification of Diseases (ICD) that is planned to be released in 2017 after its approval at the World Health Assembly. The classification of disorders due to psychoactive substance use are largely presented in the chapter of mental and behavioural disorders, though some related conditions such as hazardous use of psychoactive substances are included in other chapters of the draft ICD-11. The overall focus of ICD-11 development is on improving clinical and public health utility of the classification and its diagnostic categories in a broad range of health system settings. Public health utility of the classification is reflected, for example, in its utility for monitoring the situation with substance use and substance-induced disorders and related health conditions, such as overdoses, in any defined population as well as at the international level to inform adequate policy and program responses. Also, from public health perspective, international classification is expected to facilitate implementation of preventive interventions at levels and patterns of substance use outside the boundaries of substance use disorders. Reducing the hazardous use of psychoactive substances at population level would bring significant public health benefits, but this objective can be achieved only with sufficiently high coverage of interventions focused on substance use at different levels and sectors of health care.

The current draft of ICD-11 maintains diagnostic categories of substance dependence and harmful substance use as separate diagnostic entities. The diagnostic guidelines for dependence are revised and represent three major diagnostic features which are consistent with ICD-10 criteria for dependence. The concept of "harmful substance use" is revised with inclusion of harm to health of others into the diagnostic guidelines. The changes are suggested in the grouping of psychoactive substances with increased number of categories for different types of substances to be included in ICD-11.

There is an unprecedented plan of field testing of all chapters of ICD-11. The current draft of the protocol for clinic-based field testing of classification of substance use disorders and related health conditions will be presented, and existing opportunities for participation in field testing of a draft CD-11 for disorders due to substance use described.

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 (65%) 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 2.1-. 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 (NHMRC) 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]

[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.

ORAL ABSTRACTS continued

Update on alcohol pharmacotherapy

Prof Paul Haber

University of Sydney, Australia

Abstract not supplied

Pharmacotherapies for relapse prevention: Targeting of multiple vulnerability states linked to relapse risk by agents with broad spectrum of actions

Prof Friedbert Weiss[1]

[1]The Scripps Research Institute, La Jolla, USA

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 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 Lin[1], Assistant Professor Scott Hall[2], Professor Xiaowu Chen[1,3], Associate Professor Yanhong Zhou[1,4], Associate Professor Nian Xiong[1,5], Associate Professor Richard Bell[6], Professor Tao Wang[5], Professor Jürgen Rehm[7]

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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-preferring) 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.

Neurobiology of Drug Addiction-New Tools for a Pharmacogenomic Approach

Prof Emmanuel Onaivi[1], Dr George Koob[2]

[1]William Paterson University, Wayne, United States, [2]Committee 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 resilience 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

Medicinal 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 Paule[1], GD Newport[1], R Callicott[1], J Thompson[1], W Slikker Jr[1], C Wang[1], MS Berridge[2], X Zhang[1], SM Apana[2], S Liu[1]

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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/CT imaging using 18F-labeled fluoroethoxybenzyl-N-(4-phenoxypyridin-3-yl) acetamide (FEPPA), 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 radiotracer 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 methamphetamine preclinical studies; Links with Parkinson's disease

Dr Glen Hanson[1], Lisa McFadden[3], Paula Vieira-Brock, Annette Fleckenstein[1], Karen Curtin[2]

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Preclinical and clinical studies suggest that abuse/dependence of methamphetamine (METH) causes damage to the same nigrostriatal 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/AMP dependence and PD. Our METH/AMP 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/AMP dependence were 3.1 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 Wang[1]

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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, Luminex 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 phosphatidylglycerol (PG)] were significantly down-regulated. Luminex 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 Buch[1], Dr Minglei Guo[1], Dr Palsamy Periyasamy[1], Mr Ke Liao[1], Ms Fang Niu[1]

[1]University 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 Roy[1], Santanu Banerjee[1], Jingjing Meng[1], Li Zhang[4], Timothy Johnson[2], Chi Chen[3]

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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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ORAL ABSTRACTS continued

Wastewater analysis as a tool in monitoring drug use

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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 Ezard[1,2], Dr Monica Barrett[3,4,5], Dr Robin Butterfield[1]

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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 Ezard[1,2], Dr Monica Barrett[3,4,5]

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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

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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.

POSTER PRESENTATIONS

Behavioral and neurochemical effects of adolescent treatment with nicotine, harmane, or norharmane in male Sprague-Dawley rats

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The present study determined the long-term effects of adolescent exposure to nicotine (NIC), harmane (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 ml/kg saline (CON), 0.5 mg NIC/kg, 0.5 mg HAR/kg, or 0.5 mg NOR/kg. BW, food, and WI were measured daily. Locomotor activity was assessed on PND 40/41, PND 55, and PND 81/82. 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

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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 hydroxylase (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

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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

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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 µM. 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

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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 hyperactive 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-mediatated 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.

POSTER PRESENTATIONS continued

Propentophylline hampers methamphetamine-induced striatal dopamine release: a microdialysis approach

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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 astrocytic 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/6N adult mice. Concentrations of DA and its metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanilic 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?

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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 32% 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

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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-HT1A and 5-HT1B receptor mechanisms. Rats were pre-treated 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?

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Ethanol (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 conception (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

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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, 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 H3K14 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

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A neurotoxic regimen of methamphetamine (METH) is known to cause cognitive dysfunction, social interaction deficits, and hypersensitivity to hallucinogen. 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 hallucinogen. 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

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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 homogenous 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

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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?

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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

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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 neuropsychological 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

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Objectives and Methods: We examined a total of 840 participants (mean age 45.1years, 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 41.7years, SD=13.2) and 723 other drivers (mean age 45.8years, 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 (36% vs 19%).The ratio of propable alcoholics(15 points or over) in Ishigaki island is higher than that of the national average (13% 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%) $\chi 2$test

Conclusions: There are many problematic drinkers 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

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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, 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. Promotors of several potential 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

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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

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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, 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

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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

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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 compulsion 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 glutamatargic 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 IWAHARA[1], Doctor Tsuyoshi Takimura[1], Doctor Hiroshi Sakuma[1], Doctor Mitsuru Kimura[1], LPSW Sakae Fujita[1], Doctor Sachio Matsushita[1], Prof Yoneatsu Osaki[2], Doctor Susumu Higuchi[1]

[1]National Hospital Organization, Kurihama Medical and Addiction Center, Yokosuka, Japan, [2]Division of Environmental and Preventive Medicine, Tottori University, Yonago, Japan

Introduction: For the first time in Japan, we investigated the prevalence of alcohol use disorders (AUDs) 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. (4.7%) than in Japan (1.7%). Conversely, Japan's alcohol dependence rate (3.9%) was comparable to that in the U.S. (3.8%). 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

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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 those in 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

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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 (43%) 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, Xinyu 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 ($X2 = 7.98$, $p = .018$), trouble with the law ($X2 = 4.36$, $p = .037$) and substance type ($X2 = 4.01$, $p = .045$). In the alcohol group, significant associations were found between re-admission and marital status ($X2 = 6.21$, $p = .013$) and completion of the intensive 1st week of medication regime ($X2 = 5.43$, $p = .020$). In the drug group, there were significant associations between re-admission and education level ($X2 = 7.30$, $p = .026$) and age at admission $F(1, 197) = 6.33$, $p = .013$. 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 Lee[1]

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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.

Results: Subjects(mean age = 13±2.6) 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($p<0.05$) 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

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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 20-55 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

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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 Liliwan Project. GM performance was assessed using the Q-GlobalTM GM Composite of the Bruininks-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 (50.0±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 (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[1], Professor Bernard Balleine[2], Professor Simon Killcross[1]

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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[1]

[1]NOFASD Australia, Wynyard, Australia

For the first twelve years, NOFASD Australia support services, education and advocacy were delivered by volunteers who struggled to raise public attention 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[1], Ms Satoko Mihara[1], Prof Hideki Nakayama[1], Takashi Kitayuguchi[1], Kumiko Miura[1], Masaki Maezono[1], Takuma Hashimoto[1], Prof Susumu Higuchi[1]

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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 nn DSM-IV Alcohol Abuse and Alcohol Dependence

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[1]*The University of Sydney, Sydney, Australia*

The NSW 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 (D87: A71%), have used benzodiazepines (D26%: A7%), obese (D32%: A20%), 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. Vermal atrophy was present in 40% 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-IV dependence cases.

The effects of chronic smoking on Alcohol-related Brain Damage

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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 11 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

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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

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Behavioural ratings obtained with the internationally-utilised 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 scales. 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 (12.5 [95%CI: 7.9-17.0]) in FASD than No FASD; with greater odds of scoring in the "Clinical" range. Pooled PAE 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 Tsang[1,2], Ms Zoe Laing-Aiken[1], Prof Jane Latimer[2], Dr James Fitzpatrick[1,2,3], Ms June Oscar[4], Ms Maureen Carter[5], Prof Elizabeth J Elliott[1,2,6,7]

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Digital photographs from the Lililwan Project (a study of FASD prevalence in remote Australia) were analysed for facial features of Fetal Alcohol Syndrome (FAS) using the FAS Facial Photographic Analysis Software (FPA) 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

charts were applied; and iii) agreement with clinician measures. Thirteen children had FAS/PFAS and 58% were prenatally exposed to alcohol. Categorical PFL, lip and philtrum ratings, and 4-Digit Diagnostic Code Rank for the face (Severity) were recorded. Intra- and inter-rater reliability of digital ratings was examined in two assessors; and agreement between African-American and Caucasian charts, and digital and clinician ratings was assessed using weighted kappa. Reliability was substantial within and between assessors (kappa range: 0.7–1.0). Application of different ethnic charts yielded large differences in numbers having "Absent/Mild" and "Moderate/Severe" ratings of Severity (kappa: 0.15 [95%CI: 0.07–0.23]). Clinician and digital ratings showed moderate agreement. The FAS FPA Software demonstrated good reliability in an Australian Aboriginal child cohort. Australian Aboriginal facial charts need to be developed to ensure accurate diagnosis in this high-risk population.

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

Mr Ross Van De Wetering[1]

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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. Priddy[1], Mrs Janaina Vendruscolo[1], Dr Stephanie A. Carmack[1], Dr George F. Koob[2], Dr Leandro F. Vendruscolo[1]

[1]*National Institute on Drug Abuse, Baltimore, United States,* [2]*National Institute on Alcohol Abuse and Alcoholism, Bethesda, United States*

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[1], Professor David Harper[1], Professor Susan Schenk[1]

[1]*Victoria University of Wellington, Wellington, New Zealand*

Most drug discrimination studies involving ±3,4-methylene dioxymethamphetamine (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 × vehicle] or three-choice [MDMA × AMPH × 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.

NOTES

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